Mindfulness Meditation for Chronic Pain
A Systematic Review Protocol

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Preface

The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE) is interested in determining the efficacy and comparative effectiveness of integrative medicine approaches for psychological health conditions. This document is a systematic review protocol for a review to be performed during year two of this two-year project. The review will be of interest to military health policymakers and practitioners, civilian health care providers and policymakers, payers, and patients.

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

This research is conducted within the Forces and Resources Policy Center of the RAND National Defense Research Institute, a federally funded research and development center sponsored by the Office of the Secretary of Defense, the Joint Staff, the Unified Combatant Commands, the Navy, the Marine Corps, the defense agencies, and the defense Intelligence Community. For more information on the RAND Forces and Resources Policy Center, see http://www.rand.org/nsrd/ndri/centers/frp.html or contact the director (contact information is provided on the web page).

Acknowledgments

This research is sponsored by the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE).
Abstract

Chronic pain is a frequent symptom reported by service members and a common cause of work disability in the military. The high prevalence and refractory nature of chronic pain in conjunction with the negative consequences of pain medication dependence drives investigation of innovative treatment modalities. One such modality that has been increasingly utilized is mindfulness meditation. The purpose of this systematic review is to synthesize the evidence from randomized controlled trials (RCTs) of mindfulness meditation to provide estimates of its effectiveness for treatment of chronic pain.

We will search electronic databases (PubMed, CINAHL, PsycINFO, AMED, CENTRAL), as well as bibliographies of existing systematic reviews and included studies, to identify English-language reports of RCT testing the efficacy and safety of mindfulness meditation—used adjunctively or as mono-therapy—to treat adults with chronic pain. Two independent reviewers will screen identified literature using predetermined eligibility criteria, abstract study-level information and outcome data, and assess the methodological quality of included studies. Outcomes of interest include pain, use of analgesics, functional status, quality of life, and adverse events. If we identify sufficient numbers of homogeneous studies, we will synthesize data via meta-analysis, and conduct pre-planned subgroup and sensitivity analyses as data allow. Lastly, the reviewers will assess the quality of evidence for each outcome using the GRADE approach. The review will be registered in PROSPERO.

The methods, literature search results, findings, conclusions, and quality of the evidence will be reported in a comprehensive report, and all studies will be described in evidence tables. The results of this review aim to help Department of Veterans Affairs/Department of Defense (VA/DoD) clinical decision-making regarding mindfulness meditation used adjunctively or as mono-therapy in treating chronic pain.
Introduction

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

The high prevalence and refractory nature of chronic pain in conjunction with the negative consequences of pain medication dependence drives investigation of innovative treatment modalities. Patients who seek a treatment plan for chronic pain that includes more than just medication are increasingly turning to complementary and alternative medicine (Chiesa and Serretti, 2011). One such modality that pain patients are using is mindfulness meditation. The Army Surgeon General’s Pain Management Task Force recommended that mind-body therapies such as mindfulness meditation be a Tier 1 therapy option (along with acupuncture, yoga, chiropractic care, therapeutic medical massage, and biofeedback) in the interest of providing a holistic, integrative approach to pain management (Office of the Army Surgeon General).

Meditation is the intentional self-regulation of attention from moment to moment (Goleman and Schwartz, 1976). Mindfulness meditation is a Western, non-sectarian form of meditation derived from a 2,500 year old Buddhist practice called Vipassana or Insight Meditation. Mindfulness facilitates an attentional stance of detached observation. It is characterized by paying attention to the present moment with openness, curiosity, and acceptance. It can be trained systematically to be used in daily life by people of any background (UCLA Mindfulness Awareness Research Center (MARC), 2015).

Clinical uses of mindfulness include applications in substance abuse, tobacco cessation, stress reduction and treatment of chronic pain (UCLA Mindfulness Awareness Research Center (MARC), 2015). Early studies in pain patients showed promising outcomes on pain symptoms, mood disturbance, anxiety and depression, as well as pain-related drug utilization (Kabat-Zinn,
A 2011 systematic review of ten mindfulness based interventions for chronic pain patients showed improvements in depressive symptoms and coping, with limited evidence for specific pain effects (Chiesa and Serretti, 2011). This review concluded that further research, using larger, adequately powered studies with robust designs, was warranted. A later review (Lee, Crawford and Hickey, 2014) funded by the US Army also concluded that additional high quality research was needed before a recommendation for the use of mindfulness meditation for chronic pain symptoms could be made. Eleven RCTs included in the review investigated the use of mindfulness meditation for chronic pain symptoms, including chronic back pain, fibromyalgia, and musculoskeletal pain. More than half of the studies were poor quality, i.e. high dropout rates, lack of safety reporting, and weak randomization procedures. However, the majority of studies showed promising effects for mindfulness meditation. After reviewing the high quality studies, Subject Matter Experts agreed that supplementary research would have a significant impact on the confidence in the estimate of the effect.

Our proposed review aims to synthesize data from existing randomized controlled trials (RCTs) in order to provide reliable estimates of the effectiveness and safety of mindfulness-based meditation interventions for chronic pain, henceforth referred to as “chronic pain” in this protocol. The review will focus on chronic headache, back pain, migraine, osteoarthritis and neuralgic pain, due to the high prevalence in the military population (Cameron et al., 2011; Theeler, Mercer and Erickson, 2008; Knox et al., 2011).

Key Questions

The following questions and sub-questions will guide this systematic review:

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

Methods
We will perform a systematic review to identify RCTs testing the efficacy and safety of mindfulness meditation for chronic pain. The literature flow will be documented in a flow diagram (see Figure 1), and identified literature will be mapped onto the Key Questions as per previous evidence synthesis reports for VA/DoD clinical practice guidelines (The Lewin Group and ECRI Institute, 2014) (see Table 1). The systematic review will be registered in PROSPERO, an international registry for systematic reviews.

Sources

We will search PubMed, CINAHL, PsycINFO, AMED, and Cochrane CENTRAL for English-language randomized controlled trials. In addition to this search and the reference mining of all included studies identified through it, we will also screen included studies of prior systematic reviews related to this topic.

Search strategy

The search strategy is being developed by the Chief Reference Librarian for RAND’s Knowledge Services, informed by search results of the prior environmental scan (Sorbero, Grant and Hempel, October 2014) and existing reviews. The draft PubMed search string is described in the Appendix.

Eligibility criteria

The inclusion and exclusion criteria we will apply to the retrieved publications can be summarized in the following “PICOTSS” framework of participants, interventions, comparators, outcomes, timing, settings, and study design.

PICOTSS

- Participants: Studies will be limited to male and female participants who are 18 years of age or older who report chronic pain. We will accept the author’s definition of chronic pain or studies in patients reporting pain for a minimum of three months will be included. Studies not specifying the duration of pain and not referring to chronic pain will be excluded.
- Interventions: Studies involving mindfulness meditation, either as an adjunctive or mono-therapy, will be included—e.g., mindfulness cognitive therapy (MBCT), mindfulness stress reduction (MBSR), Vipassana, Zazen, Zen, and Shambhala interventions. Studies testing other meditation interventions such as yoga, tai chi, qigong, and transcendental meditation techniques without reference to mindfulness meditation will be excluded.
- Comparators: Studies that include wait-list control, no-treatment, or standard care (e.g. physical activity, pain medications) or compare mindfulness meditation offered adjunctive versus mono-therapy, and comparison of two or more mindfulness meditation interventions will be included.
Outcomes: Studies that report patient pain measures including pain assessed with a Visual Analog Scale, the SF-36 pain subscale, McGill Pain Questionnaire, etc. and studies reporting on change in analgesia use will be included.

Timing: Studies can involve any treatment duration and any follow-up time period.

Setting: Studies will not be limited by setting.

Study Design: Included studies will be limited to parallel group, individually- or cluster-RCTs.

Inclusion Screening

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

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

Data extraction

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

Study-level data will be abstracted for the following information:

- Participants: gender, age, medical condition(s) and type of pain, baseline pain data, comorbid psychological / behavioral health conditions
- Interventions: content of mindfulness meditation sessions, dosage (intensity, frequency, duration), and co-intervention(s)
- Comparators: type of comparator
- Outcomes: primary endpoint; longest follow-up; measures of pain, use of analgesics, functional status, health-related quality of life, adverse events, for each time point of measurement: domain, method of measurement, metric of data expression (e.g., means, proportions) and corresponding results (e.g., effect estimate, precision)
- Timing: time-points of outcome assessment, timing of intervention
- Setting: geographic region, clinical setting, interventionist training
- Study design: aim of study, definition of chronic pain, inclusion and exclusion criteria,
sample size, reported power calculations, items relevant to risk of bias and quality ratings

If different reports appear to be from the same study, descriptions of participants will be compared to ensure that data from the same study populations enter the analysis only once. For each included study, findings will be reported in an Evidence Table that will include details about the intervention, specific comparison(s), and outcome(s) measured (see Table 2).

Risk of bias and study quality

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

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

- **Good:** Comparable groups are initially assembled and maintained throughout the study with at least 80 percent follow-up; reliable, valid measurement is used and applied equally to all groups; interventions are clearly described; all important outcomes are considered; appropriate attention is given to confounders in analysis; intention-to-treat analysis is used.

- **Fair:** One or more of the following issues is found in the study: some though not major differences between groups exist at follow-up; measurement instruments are acceptable but not ideal, though are generally applied equally; some but not all important outcomes are considered; some but not all potential confounders are account for in analyses. Intention-to-treat analysis must be done.

- **Poor:** One or more of the following “fatal flaws” is found in the study: initially assembled groups are not comparable or maintained throughout the study; unreliable or invalid measurements are used or applied unequally across groups; key confounders are given little to no attention in analyses; intention-to-treat analysis is not used.

Planned synthesis
The primary aim of this systematic review is to identify whether mindfulness meditation for chronic pain in adults is effective and safe. As such, when sufficient data are available and statistical heterogeneity is below agreed thresholds (Higgins and Green, 2011), we will perform meta-analysis to pool effectiveness results across included studies for the outcomes of interest and present forest plots for these meta-analyses. For efficacy outcomes we will use the Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis (Hartung, 1999; Hartung and Knapp, 2001; Sidik and Jonkman, 2006). This approach may be preferred when the number of studies pooled is small and when there is evidence of heterogeneity (IntHout, Ioannidis and Borm, 2014) and it has been shown that the error rates are more robust than the previously used DerSimonian and Laird method (Sánchez-Meca and Marín-Martínez, 2008). Adverse events will be classified and grouped according to the Common Terminology Criteria for Adverse Events (CTCAE) system. For specific adverse events, many of which may be very rare, we will use exact conditional methods to estimate odds ratios (OR) and 95 percent confidence intervals (CI) if a sufficient number of studies report specific adverse events.

In addition, when sufficient data are available, we will describe results of head-to-head comparisons and conduct subgroup analyses and meta-regressions to address secondary questions of this systematic review. Specifically, we will examine whether there are differences in effect sizes between different mindfulness meditation interventions; studies conducted in different population groups (e.g., patients with headache, migraine, back pain, or pain due to osteoarthritis); and by mindfulness meditation intervention as mono-therapy versus an adjunctive therapy. Given the complexity of the topic, subgroup and sensitivity analyses will only be performed for those outcomes with sufficient data. However, due to the small number of expected studies, differences between studies will at least be narratively described. For meta-analysis of data with clear outliers, sensitivity analysis may be conducted (excluding the outliers), if appropriate (Hamling et al., 2008). If sufficient data are available, we will conduct sensitivity analyses omitting the lower quality studies for major comparisons.

Quality of evidence

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

The quality of evidence is graded on a 4-item scale:

- **High** indicates that the review authors are very confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has few or no deficiencies. As such, the reviewers believe the findings are stable: i.e., further research is very unlikely to change confidence in the effect estimate.

- **Moderate** indicates that the review authors are moderately confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has
some deficiencies. As such, the reviewers believe that the findings are likely to be stable, but further research may change confidence in the effect estimate and may even change the estimate.

- **Low** indicates that the review authors have limited confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has major or numerous (or both) deficiencies. As such, the reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the effect estimate lies close to the true effect.

- **Very low** indicates that the review authors have very little confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has very major deficiencies. As such, the true effect is likely to be substantially different from the estimated effect; thus, any estimate of effect is very uncertain.

The data sources, basic study characteristics, and each quality-of-evidence domain rating will be summarized in a Quality of Evidence table detailing our reasoning for arriving at the overall rating (see Table 4).

### Summary of findings

Review findings will be summarized in a table and organized by outcomes that reflect the key questions for this systematic review. This table will list the intervention and comparators evaluated and the outcomes assessed for each type of comparison; the number of studies and number of participants included for each outcome assessment, the direction and magnitude of the effect for each outcome, and the quality of the evidence for each outcome. (see Table 4). For each outcome, results of pooled analyses will be described first, followed by narrative descriptions of individual studies not included in the pooled analyses (if any). Findings will first be reported for the broad comparison of mindfulness meditation compared with any comparison group. Findings will then be reported separately by: intervention (e.g. MBSR), population (patients with headache, migraine, back pain, or pain due osteoarthritis), by therapy characteristic (i.e. monotherapy, adjunctive therapy), and type of comparator. All study level and synthesis information will be shown in concise tables to allow a transparent overview and results will be described in more detail in the text.
References


UCLA Mindfulness Awareness Research Center (MARC), 2015. As of May 29, 2015: http://marc.ucla.edu/default.cfm
Figures

Figure 1: Draft Flow Diagram

1. Identification
   - Records identified through database searching (n = )
   - Additional records identified through other sources (n = )

2. Screening
   - Records after duplicates removed (n = )

3. Eligibility
   - Records screened (n = )
   - Records excluded (n = )
   - Full-text articles assessed for eligibility (n = )
   - Full-text articles excluded, with reasons (n = )

4. Included
   - Studies included in qualitative synthesis (n = )
   - Studies included in quantitative synthesis (meta-analysis) (n = )
# Tables

**Table 1: Draft Table—Evidence Base for Key Questions**

<table>
<thead>
<tr>
<th>Number of Question</th>
<th>Question</th>
<th>Number of RCTs</th>
</tr>
</thead>
</table>
| 1                  | What is the efficacy and safety of mindfulness meditation interventions, as an adjunctive or mono-therapy, for adults with chronic pain compared to treatment as usual, wait-lists, no-treatment, or other active treatments? | # RCTs with efficacy data:  
# RCTs with safety data: |
| 1a                 | Does the effect vary by the type of mindfulness meditation intervention? | # MBSR RCTs:  
# MBCT RCTs: |
| 1b                 | Does the effect vary by medical condition targeted?                       | # migraine RCTs:  
# other headache RCTs:  
# back pain RCTs:  
# osteoarthritis RCTs:  
# neuralgic pain RCTS: |
| 1c                 | Does the effect differ when the interventions is offered as an adjunctive therapy rather than as a mono-therapy? | # adjunctive therapy:  
# mono-therapy: |
| 1d                 | Does the effect vary depending on the duration and frequency of mindfulness meditation (i.e., dose effect)? | # head-to-head RCTs: |
Table 2: Draft Evidence Table

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Participants</th>
<th>Intervention/Treatment</th>
<th>Outcomes/Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference:</td>
<td>Number of patients:</td>
<td>Content of intervention:</td>
<td>Pain:</td>
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<tr>
<td>Country:</td>
<td>Medical condition / type of pain:</td>
<td>Setting:</td>
<td>Analgesic use:</td>
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<td>Purpose:</td>
<td>Definition of chronic pain:</td>
<td>Dosage, duration:</td>
<td>Functional status:</td>
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<td>Quality rating:</td>
<td>Baseline pain score:</td>
<td>Co-interventions:</td>
<td>Health-related QoL:</td>
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<td></td>
<td>Comorbid conditions:</td>
<td>Comparator:</td>
<td>Adverse events:</td>
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<td></td>
<td>Age (years):</td>
<td>Primary endpoint:</td>
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<td>Gender:</td>
<td>Power calculation:</td>
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<td>Inclusion criteria:</td>
<td>Follow-up:</td>
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<td>Exclusion criteria:</td>
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Note: For each outcome reported, we will collect the following information when available: domain, method of measurement (e.g., questionnaire, observation), data metric (e.g., mean score, proportion with outcome), time(s) of follow-up (e.g., 3 and 6 months after baseline), and corresponding results (effect estimate, precision); QoL = Quality of Life
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and providers (performance bias)</th>
<th>Blinding of outcome assessors (detection bias)</th>
<th>Completeness of reporting outcome data (attrition bias)</th>
<th>Selective outcome reporting (reporting bias)</th>
<th>Involvement of intervention developer in trial (independent replication)</th>
<th>Other biases (balance of confounders, crossovers/contamination, measurement, intervention definition, ITT)</th>
<th>USPSTF Quality rating (Good, Fair, Poor)</th>
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Note: See Methods section of this document for USPSTF Quality rating criteria.
### Table 4: Draft Quality of Evidence and Summary of Findings Table

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of RCTs and Participants</th>
<th>Findings: Direction/Magnitude of Effect</th>
<th>Study Limitations (Study Quality; RoB)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>GRADE of Evidence for Outcome</th>
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<tbody>
<tr>
<td>KQ 1 Comparison: any mindfulness meditation intervention vs treatment as usual (TA)</td>
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<td>Pain measure</td>
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<td>Use of analgesics</td>
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<td>KQ 1 Comparison: any mindfulness meditation intervention vs physical therapy</td>
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<td>Analyzed outcomes depend on available evidence</td>
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<td>KQ1 Comparison: mindfulness meditation interventions vs standard care: opioids</td>
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<td>KQ1 Comparison: mindfulness meditation interventions vs standard care: TAU (combination of conventional pain management techniques)</td>
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<td>KQ1 Comparison: mindfulness meditation interventions vs passive comparator (e.g., waitlist, no treatment)</td>
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<td>KQ1a: If meta-regression indicates a difference in intervention subgroups: MBCT vs any comparator</td>
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<td>KQ1b: If meta-regression indicates a difference in patient subgroups: Mindfulness meditation in patients with tension headaches</td>
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<td>KQ1b. If meta-regression indicates a difference in patient subgroups: Mindfulness meditation in patients with back pain</td>
<td>Analyzed outcomes depend on available evidence</td>
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</tbody>
</table>
### KQ1b. If meta-regression indicates a difference in patient subgroups:
*Mindfulness meditation in patients with osteoarthritis*

<table>
<thead>
<tr>
<th>Ana</th>
<th>lyzed outcomes depend on available evidence</th>
</tr>
</thead>
</table>

### KQ1b. If meta-regression indicates a difference in patient subgroups:
*Mindfulness meditation in patients with neuropathic pain*

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<thead>
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<th>lyzed outcomes depend on available evidence</th>
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### KQ 1c. If meta-regression indicates a difference:
*Comparison: mindfulness meditation as mono-therapy vs any comparator*

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<th>lyzed outcomes depend on available evidence</th>
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### KQ 1c. If meta-regression indicates a difference:
*Comparison: mindfulness meditation as adjunctive therapy vs any comparator*

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<th>lyzed outcomes depend on available evidence</th>
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### KQ1d. Head-to-head trial results

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<th>lyzed outcomes depend on available evidence</th>
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### KQ1d. Meta-regression result for dose

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<th>Ana</th>
<th>lyzed outcomes depend on available evidence</th>
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</table>

Note: Results of TAU analyses will be considered primary outcomes for this review.
Appendix

Draft Search Strategy

DATABASE
PubMed

TIME PERIOD COVERED:
Since inception to June 2015

PubMed
SEARCH STRATEGY:
"Mindfulness"[Mesh]) OR "Meditation"[Mesh] OR mindfulness* or mindfulness-based or mbsr or mbct or m-bct or meditation or meditat* OR Vipassana or satipaṭṭhāna OR anapanasati OR Zen OR Pranayama OR Sudarshan OR Kriya OR zazen OR shambhala OR buddhis*
AND
Pain[MH] OR pain*[tiab] OR headache disorders[mh] OR headache* or head ache* or head-ache* or migraine* OR cephalalgi* OR neuralgi* OR osteoarthritis OR arthrosis OR backache* OR back ache* OR back-ache* OR Neuralgia OR neuropathic pain OR neuropathy OR radiculopathy OR, complex regional pain syndrome* OR CPRS OR causalgia OR herpetic neuralgia OR sciatic* OR cervicalgi*
AND
systematic[sb] OR systematic review* OR random* OR rct* OR randomized controlled trial*[pt]
OR "Randomized Controlled Trial" [Publication Type] OR "Randomized Controlled Trials as Topic"[Mesh] OR meta-analy* OR metaanaly* OR meta analy*

LANGUAGE:
English

After importing all results into endnote, duplicates and animal-only studies will be deleted.