Systematic Review and Meta-Analysis

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The efficacy of mindfulness-based interventions in acute pain: a systematic review and meta-analysis

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Abstract

Recent meta-analyses have shown mindfulness-based interventions (MBIs) to be effective for chronic pain, but no pooled estimates of the effect of MBIs on acute pain are available. This meta-analysis was conducted to fill that gap. A literature search was conducted in 4 databases. Articles were eligible if they reported on randomized controlled trials of MBIs for people with acute pain and one of the following outcomes: pain severity, pain threshold, pain tolerance, or pain-related distress. Two authors independently extracted the data, assessed risk of bias, and provided GRADE ratings. Twenty-two studies were included. There was no evidence of an effect of MBIs on the primary outcome of pain severity in clinical {Hedges' g = 0.52; (95% confidence interval [CI] −0.241 to 1.280)} or experimental settings (Hedges' g = 0.04; 95% CI [−0.161 to 0.247]). There was a beneficial effect of MBIs on pain tolerance (Hedges' g = 0.68; 95% CI [0.157-1.282]) and pain threshold (Hedges' g = 0.72; 95% CI [0.210-1.154]) in experimental studies. There was no evidence of an effect of MBIs compared to control for pain-related distress in clinical (Hedges' g = 0.16; 95% CI [−0.018 to 0.419]) or experimental settings (Hedges' g = 0.44; 95% CI [−0.164 to 0.419]). GRADE assessment indicated that except for pain tolerance, the data were of low or very low quality. There is moderate evidence that MBIs are efficacious in increasing pain tolerance and weak evidence for pain threshold. However, there is an absence of good-quality evidence for the efficacy of MBIs for reducing the pain severity or pain-related distress in either clinical or experimental settings.

Keywords: Mindfulness, Meditation, Acute pain, Meta-analysis, Systematic review, Experimental pain

1. Introduction

Mindfulness is an effective intervention for a range of indications.[3,23,24] Meta-analyses confirm that mindfulness-based interventions (MBIs) are efficacious for managing stress,[3,24] depression,[16,22] and physical health problems.[19] A systematic review[5] and 2 meta-analyses[13,41] show that MBIs are efficacious for managing chronic pain; however, their efficacy for acute pain has not been robustly demonstrated. Given concerns about the prescription of opioids for acute pain, establishing the efficacy of psychosocial interventions in the management of pain is a priority.[42] However, in acute pain, research on MBIs is mixed with some studies finding evidence for their efficacy[25,35] and others finding either no benefits[34] or benefits to only certain patient subgroups.[31] It is likely that variation in the type of MBI, the dose, duration and intensity of practice, the type of participants, or methodological issues such as the nature of the control group might all contribute to these mixed results.[39] It is imperative to synthesize available research to draw firm conclusions about what is known about the efficacy of MBIs in acute pain and/or to highlight gaps in the literature.

There are 3 review articles relevant to the efficacy of mindfulness in acute pain.[13,28,33] Reiner et al. investigated the effect of MBIs on pain severity in acute or chronic pain. Only half of those trials (n = 16) were randomized controlled trials (RCTs) and only one RCT was in acute pain.[33] McClintock et al.[28] reviewed brief MBIs (<1.5 hours). Of the 20 studies they included, 14 were in acute pain (all experimental) and 4 of those were not RCTs. Furthermore, neither study meta-analysed the data and so quantitative estimates of the effect of MBIs on pain outcomes are absent.[28,33] Similarly, Garland et al.[13] examined the effect of meditation or acceptance-commitment therapy on pain but only one study of mindfulness in acute pain was included. Although all reviews concluded that MBIs showed promise in the treatment of pain, because none were specific to acute pain, this severely limits the confidence that we can have in the conclusions specifically in relation to acute pain.

The goal of the present meta-analysis was to synthesize and quantify the effect of MBIs on acute pain (<3 months duration) in clinical or experimental settings. This meta-analysis examined the efficacy of MBIs on the primary outcome of pain severity, and secondary outcomes of pain tolerance (the duration for which a painful stimulus can be withstood), pain threshold (the point at which a stimulus is reported to become painful), and pain-related distress. We chose pain severity as the primary outcome because (1) clinically in acute pain settings, the aim is typically to reduce the severity of pain; and (2) to be consistent with previous reviews in which pain severity was investigated.[13,28,33] Furthermore, we aimed to investigate the role of a range of relevant moderators, including sample characteristics, type and dose of MBI, and

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nature of the control group. Although our a priori hypotheses were based on combining clinical and experimental samples, we opted to report these separately due to heterogeneity.

2. Methods

The review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analyses Of Observational Studies in Epidemiology guidelines[30,37] (for the PRISMA checklist, see Appendix B).

2.1. Search strategy

This review was registered with International Prospective Register of Systematic Reviews (PROSPERO) on May 30, 2018. The registration number for the review is CRD42018094038, which can be accessed at http://www.crd.york.ac.uk/prospero.

The current review aimed to identify studies evaluating the effect of MBIs on acute pain, both in clinical/procedural pain settings and in experimental acute pain research settings. A comprehensive literature search was conducted on June 25, 2018 and was updated on the 28 of January 2020 using the PsycINFO, Scopus, PubMed, and CINAHL databases. These databases were searched using a multifield format, using search terms combined with Boolean phrases.

The following search terms were included: Pain AND acute OR experiment* OR induced OR procedural OR dental OR examination OR venipuncture OR biopsy AND "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*."

Reference lists of reviews and meta-analyses relevant to this area of research were manually searched for additional studies that would fulfil eligibility criteria.

2.2. Selection of studies

2.2.1. Participants

Participants were adult (18 years or older) individuals experiencing acute pain, defined here as pain of less than 3 months' duration.[39] This included acute musculoskeletal injury pain, postoperative pain, clinically induced or procedural pain (eg, venipuncture), or experimental pain (eg, cold-pressor test; thermode).

Eligible studies included those published in a peer-reviewed journal, in the English language, up until January 28, 2020. To be included, studies needed to be RCTs that compared 20 or more participants receiving MBIs for acute pain against either: (1) a passive control group (eg, wait-list control, standard care, or treatment as usual); or (2) an active control group (eg, another intervention, a placebo, or an attention placebo). Where MBIs were compared to both an active control and passive control, the passive control was included in the analysis. Randomized controlled trials that compared individuals with acute pain receiving MBIs in conjunction with another intervention (eg, physical therapy or opioid medication) were also considered provided the additional intervention component was controlled for in the other arm, allowing the unique contribution of mindfulness to be determined. Studies were included if they involved at least one session of mindfulness or meditation-based approaches, which constituted >50% of the intervention administered. Studies were required to involve mindfulness meditation, either as an adjunctive or monotherapy; studies testing other meditation interventions such as yoga, tai chi, qigong, and transcendental meditation techniques without reference to mindfulness were excluded.

The primary outcome measure was pain severity, as rated on either a numerical rating scale or a visual analogue scale. We prespecified pain severity in our protocol as the primary outcome, because unlike chronic pain, in acute pain, reducing pain severity is conceptually the aim of pain management techniques. Furthermore, the only other meta-analysis to include acute pain trials also used pain severity as the primary outcome.[13]

The secondary outcomes were: pain tolerance, pain threshold, and pain-related distress. Pain tolerance was defined as the maximum time the participant was able to tolerate pain (eg, for cold pressor) or the maximum amount of pain stimulus the participant could tolerate (eg, for thermode tasks). Pain threshold was defined as the point at which pain was first reported during an experimental or painful procedure. We also considered pain-related distress, capturing measures of pain-related anxiety, fearfulness, or distress.

Moderators of effectiveness were determined a priori. However, we only examined dichotomous moderators when sufficient studies were available, such that there were at least 3 studies in each arm. Planned moderators included: type of pain (ie, experimental vs clinical studies); active vs passive control groups; amount or "dose" of mindfulness training (ie, number of sessions), the types of mindfulness (mindfulness of breath vs mindfulness of body), and the methods of delivery of the mindfulness interventions (ie, guided or audiotaped). Although we planned to investigate clinical vs experimental studies as a moderator of the efficacy of MBIs, we report these separately, as explained below.

2.3. Data extraction

The search retrieved 1307 studies, with 222 duplicates identified and excluded. Title and abstract screening of the remaining 1085 studies was initially conducted by one author (A.S.) with a second reviewer (T.R.O.N.-J.) independently assessing a randomly selected 50% of these studies to determine suitability for inclusion. Ambiguities between reviewers were resolved through discussion, after which complete agreement was reached and studies matching the inclusion and exclusion criteria retained for full-text screening. Full-text versions of these shortlisted articles were then assessed for eligibility. Studies were excluded from the analysis if: (1) no pain outcome measures were used; (2) no mindfulness intervention was used; (3) the study design was inappropriate and/or no control was used; (4) the study was a theoretical or protocol paper only; or (5) the population was not acute pain. We then applied the ancestry method by hand searching the references of identified studies and reviews.

All articles where one reviewer decided that the full text should be retrieved were read in detail. In total, 940 studies were excluded by title or abstract, leaving 145 studies where the full text was retrieved. These 145 studies were read in detail and a further 123 studies were excluded, leaving 22 relevant articles to be included in the final review. A third reviewer (J.N.D.) also screened the full text of the chosen studies. There was discrepancy in the suitability for inclusion of only one study. This was resolved by discussion and consensus was reached for the 22 included studies. A detailed overview of the article retrieval process and inclusion/exclusion criteria at each stage of the search as per PRISMA guidelines is displayed in **Figure 1**.

Data were extracted from each study (**Table 1**) according to the recommendations proposed by Glass et al.[15] and included:

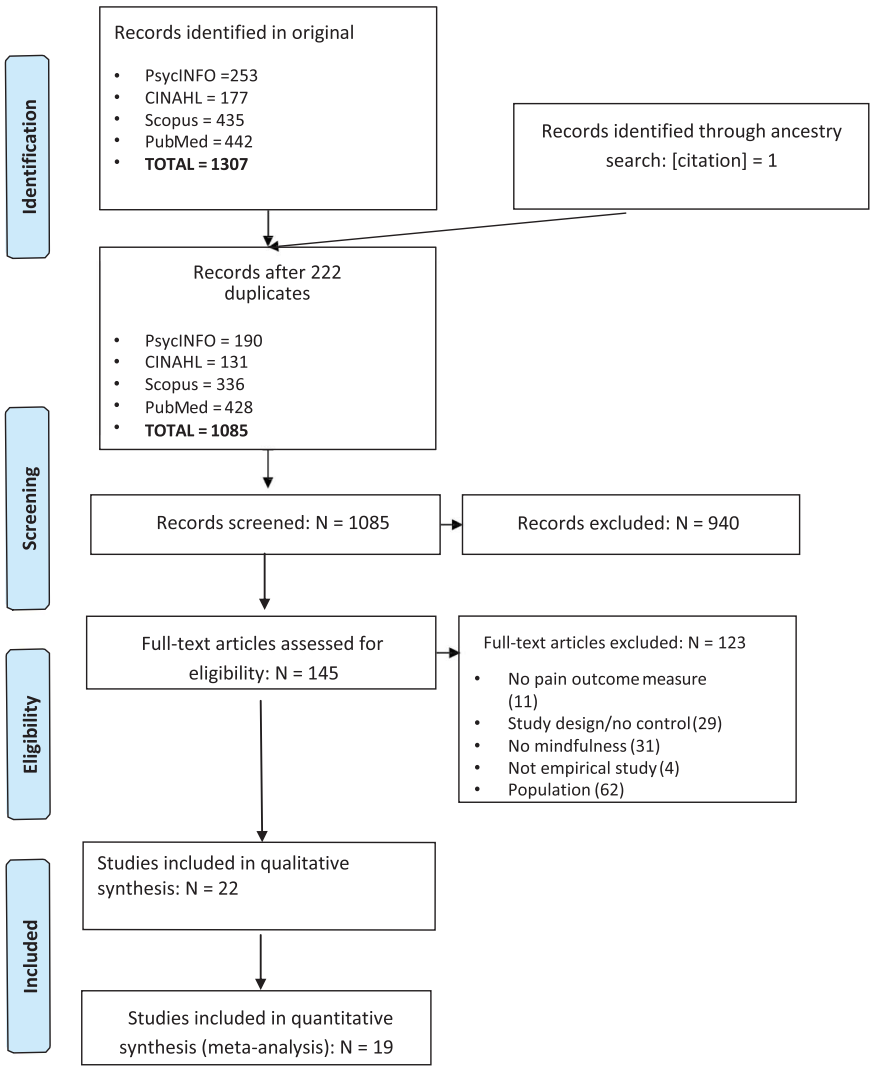

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. N, number.

setting (eg, laboratory, community, and inpatient); sample size, sample demographics (including sex ratio and age); intervention (description of MBI); mean values and SDs of pain measures before and after MBIs (where available); and moderators. The following potential moderators were recorded: experimental vs clinical studies; active vs passive controls; dose of mindfulness; type of mindfulness; and method of MBI delivery (ie, guided or audiotaped). Where mean values and SDs were not available before and after MBIs, we calculated where possible the effect size from other information available in the articles. Where there were insufficient data to calculate an effect size, we emailed the authors requesting them to provide data.

2.4. Assessment of risk of bias

The risk of bias in randomized control studies was assessed using the Cochrane Collaboration's tool for assessing risk of bias.[21] The primary author (A.S.) conducted the initial assessment of methodological quality, and a second reviewer (J.N.D.) independently rated the full complement of studies. A third reviewer (L.S.) also examined the consensus ratings to ensure consistency. Ambiguities between reviewers were resolved through discussion. Through this process, the 22 eligible studies were rated according to the risk of bias in the following domains: random allocation generation; allocation concealment; blinding of participants and outcome assessment; attrition; and selective reporting. Two of the authors (A.S. and L.S.) performed GRADE ratings for each of the outcomes to determine the degree to which confidence in the effect estimate was warranted.[20]

2.5. Data synthesis and analysis

To determine treatment effects on the primary and secondary outcomes, standardized mean differences were extracted from each article. This was achieved by extracting the mean values, SDs, and the number of participants in each group (MBI vs control) from studies at baseline and at the conclusion of treatment, where possible. The authors of 3 included studies were contacted to obtain data that were not reported so that standardized mean differences could be calculated. The list of studies used in the analysis and the specific methods used to extract data from each study are provided in Supplementary Table 1 (available at http://links.lww.com/PAIN/A985). There was no disagreement between authors in the selection of outcome measures during the decision-making process. All meta-analyses were completed using Comprehensive Meta-Analysis software,

Table 1

Summary of included RCT studies.

Study (author, year)	NM	NC	Sample	% Female	Type of intervention	Method and dose	Control	Cohen's d, pain severity	Cohen's d, pain tolerance	Cohen's d, pain threshold	Cohen's d, distress
Coelho et al.,[6] 2018	41	41	Breast biopsy patients	100	Daily MM body scan	Audio/video sent the week before biopsy + MM audio during biopsy	Passive TAU	0.171	n/a	n/a	n/a
Duncan et al.,[8] 2017	15	15	Women in 3rd trimester of first pregnancy,	100	Mind in labor (MIL):	18 h over a weekend (2.5 d)	Passive. Standard care	0.681	n/a	n/a	0.438
Esch et al.,[11] 2017	16	15	Healthy meditation naive adults undergoing tourniquet test	77	Breath awareness, body scan, attention to senses, walking meditation	5 x 1.5 hours over 5 d (7.5 hours)	Passive NTC	n/a	0.311	n/a	n/a
Forsyth and Hayes,[12] 2014	19	21	Healthy adults. undergraduate and community	72	Mindfulness of breath	Audio recorded instructions. Approx. 90 min	Passive NCT	n/a	3.698	3.012	n/a
Garland et al.,[13] 2017	86	85	Adult inpatients reporting intolerable pain or inadequate pain control	57	Attention focussing: Breath and body.	Single scripted MM 15 min.	Passive NTC	0.301	n/a	n/a	0.072
Kingston et al.,[25] 2007	21	21	Asymptomatic university students undertaking cold-pressor procedure	79	Body scan, awareness of breath.	6 × 1 hour mm total over 3 wk audio-guided on cd	Active. Guided visual imagery	0.225	0.317	n/a	n/a
Liu et al.,[26] 2013	20	20	Asymptomatic undergraduate students.	100	Mindfulness of breath and body	Recorded instructions. Approx. 15 min x	Passive. Spontaneous coping	0.619	0.700	n/a	0.839
Miller-Matero[29] 2019	30	30	Acute care surgery patients	50	Mindfulness instruction.	10 min scripted instructor led	Psychoeducation	0.13	n/a	n/a	n/a
Prins et al.,[31] 2014	23	23	Undergraduate students.	84	Open monitoring	Prerecorded audio instructions	Passive spontaneous coping	0.341	n/a	n/a	0.068
Ratcliffe et al.,[32] 2019	30	30	Breast biopsy	100	Open awareness	10 min instruction	Focused breathing	FB: − 0.47	n/a	n/a	FB: 0.71 GM: 0417
Reiner et al.,[33] 2016	20	20	Undergraduate students	50	Mindfulness of breath and body	20 min intro + 14 × 25 min = 370 min, audio guided	Passive NTC	0.229	n/a	0.631	n/a
*Sharpe et al.,[34] 2013	37	35	Undergraduate students	28	Mindfulness of body/ body scan	Prerecorded instructions.1 × 12 min.	Active PMR	0.066 0.436	0.254 0.205	0.091 0.230	n/a
Shires et al.,[35] 2018	40	20	Undergraduate students	65	MIET—mindfulness-based interoceptive exposure task	Prerecorded instructions. 1 × 2 min.	Passive NTC	0.477	1.261	0.515	n/a
Soo et al.,[36] 2016	41	40	Women needing percutaneous imaging-guided breast biopsy randomized	100	Guiding loving kindness meditation	1 × 25 min audio-guided during biopsy	Passive Standard care	2.961	n/a	n/a	n/a
Swain and Trevena,[38] 2014	96	93	Healthy adults	50	Unclear	3 min recorded or therapist led delivery.	Active hypnosis	n/a	n/a	n/a	n/a
Tashani et al.,[39] 2017	12	12	Healthy adults	50	Awareness of breath	1 × 10 min instructor-guided	Passive NTC	0.241	0.548	1.241	1.187

(*continued on next page*)

Table 1 (*continued*)

Study (author, year)	NM	NC	Sample	% Female	Type of intervention	Method and dose	Control	Cohen's d, pain severity	Cohen's d, pain tolerance	Cohen's d, pain threshold	Cohen's d, distress
Wachholtz and Pargament,[44] 2005	21	22	Healthy adults	68	Focused attention	20 min daily over 2 wks	Active. Relaxation	n/a n/a	0.095 0.491	n/a n/a	n/a n/a
Wang et al.,[45] 2019	29	29	Healthy adults	74	Acceptance and awareness of pain	15 min instructor-guided	Neutral reading material	-0.208	0.804	−0.111	-0.172
Wren et al.,[47] 2019	23	16	Breast biopsy patients	100	Loving kindness meditation	Minutes 20 min CD	Music condition	0.068	n/a	n/a	n/a
Westenberg et al.,[46] 2018)	63	62	Adults with musculoskeletal pain	50	Not reported	60 seconds individualised mindfulness-based video exercise	Passive. (educational pamphlet)	0.023	n/a	n/a	n/a
Zeidan et al.,[48] 2015	80		Healthy adults	49	Mindfulness of breath	60 s video based	Passive NTC	n/a	n/a	n/a	n/a
Zeidan et al.,[49] 2016	95		Healthy meditation naïve adults	50	Focussed attention on breath with naloxone or saline	4 × 20 min audio-guided MM over 4 d	Passive. Audio book listening	n/a	n/a	n/a	n/a

Effect sizes are reported separately: HT, high threat; LT, low threat; n/a, not available; NM, number in mindfulness group; NC, number in the control group.
N.B. Some studies had more than one control group, the control group listed above is the one used in the meta-analysis.
* Sharpe et al. conducted their intervention under high- or low-threat conditions.
RCT, randomized controlled trial; MM, mindfulness meditation; VAS, visual analogue scale.

Version 3.[2] Separate effect size estimates were calculated for continuous measures of pain severity, threshold, or tolerance and for pain-related distress. Effect sizes were calculated using Hedges' g with 95% confidence intervals [CI]. Hedges' g, a variation of Cohen's d, was used to correct for biases associated with small sample sizes. The magnitude of Hedges' g can be interpreted as follows: small = 0.2, medium = 0.5, and large = 0.8. We considered P values < 0.05 to indicate that an effect was statistically significant and therefore reliably observed.

3. Results

3.1. Nature of the studies

Twenty-two studies, involving a combined total of 1964 participants, were included in the systematic review. Our analysis included studies with different types of acute pain, including 7 studies (n = 517) with acute pain in a clinical setting, and the remainder (k = 15; n = 1429) with experimental pain in healthy participants. The 7 studies examining the effects of mindfulness on acute pain in clinical settings included 4 studies involving breast biopsy,[6,32,36,47] one examining pain during childbirth,[8] one acute care surgery patients,[29] and one acute upper-limb injury.[46]

Seven of the 22 studies had an active control group: one hypnosis treatment, one attention placebo; one music listening/relaxation intervention; one guided visual imagery intervention; and one progressive muscle relaxation intervention. In the remaining 15 studies, mindfulness was compared to a passive control such as treatment as usual, wait list, or standard care.

The types of MBIs examined in these studies included mindfulness of breath, mindfulness of breath and body, body scanning, open awareness meditations, and loving kindness meditations. We categorized these into MBIs that focused predominantly on mindfulness of breath (k = 5) vs those that focused predominantly on mindfulness of body (k = 11). There were an insufficient number of other types of MBIs (a full description of mindfulness approaches and other key features of the included studies can be seen in **Table 1**). Across the 22 studies, the dose of MBIs varied substantially, from 5 full days of training to a brief two-minute instruction administered once. Most studies used delivery to individuals in a prerecorded form, either an audio recording (n = 10) or video (n = 2) or a script that was read to participants (n = 6). Four studies did not stipulate how mindfulness was instructed within a group training session.

Three studies had insufficient data to include them in the meta-analysis and we emailed authors to gain additional data but further data were not forthcoming. As a result, 19 studies were included in the meta-analysis.

3.2. Main analyses

3.2.1. Primary outcomes: pain severity

We had initially planned to analyse all studies (clinical and experimental) together to determine the impact on pain severity. However, our initial analyses indicated a high level of heterogeneity ($Q = 100.354$, $P < 0.0005$, $I^2 = 83.060$) and so we opted to analyse pain severity separately for clinical and experimental studies. For clinical studies for pain severity, there was no impact of mindfulness compared to control. (k = 5, Hedges' g = 0.52; 95% CI [−0.241 to 1.280], $P = 0.180$) (**Fig. 2**). There was significant heterogeneity ($Q = 75.063$, $P < 0.0005$); however, there were insufficient studies to investigate moderators of this effect. There was asymmetry evident in the funnel plot upon visual inspection, with one study falling far to the right of the distribution, indicating that this study was an outlier. However, Egger regression was not significant (t = 0.539, $P = 0.618$), nor was Begg and Mazumdar[1] rank correlation (tau = 0.066, $P = 0.85$), both indicating that there was no evidence of publication bias for this outcome. To ensure that the outlying study did not interfere with the results, we conducted sensitivity analyses without this study and the pattern of results was unchanged ($P = 0.102$).

The results for the experimental studies also failed to find an effect of MBIs on pain severity (k = 12, Hedges g = 0.043; 95% CI [−0.161 to 0.247], $P = 0.680$) (**Fig. 2**). Unlike the clinical studies, there was no significant heterogeneity ($Q = 17.551$, $P = 0.093$),

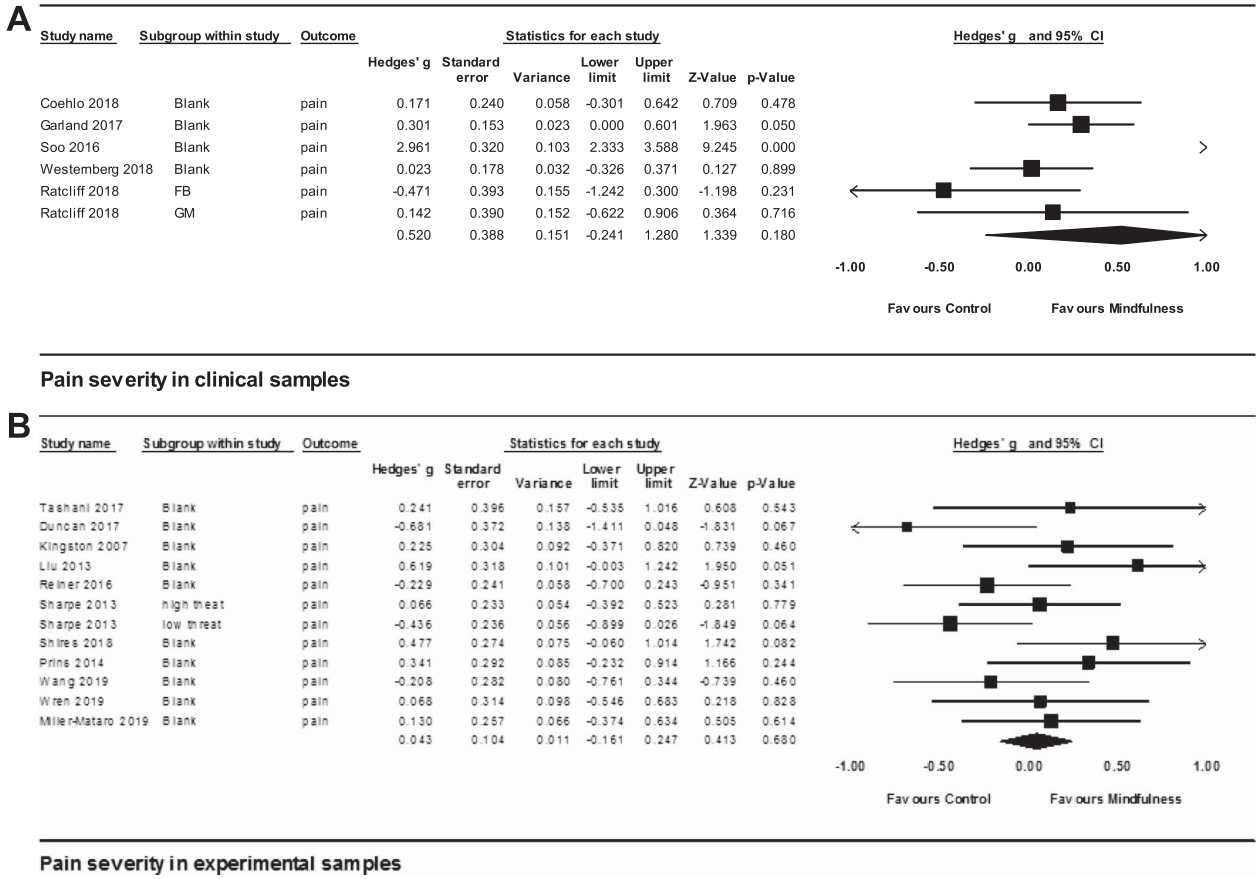

Figure 2. (A) Forest plot for pain severity in clinical studies; (B) Forest plot for pain severity in laboratory studies. CI, confidence interval; Diff, difference; Std, standard.

indicating that there was insufficient variability in the data to support moderator analyses. Egger regression was not significant (t = 0.639, $P = 0.537$). Begg and Mazumdar's rank correlation was also not significant (tau = 0.20, $P = 0.37$). Therefore, there was no indication of publication bias for this effect.

3.2.2. Secondary outcomes: pain threshold, tolerance, and pain-related distress

For pain threshold and pain tolerance, due to the nature of those measurements, only experimental studies reported these outcomes. In contrast to the results for pain severity, there was an impact of mindfulness on pain threshold, with a moderate to large effect size (k = 5, Hedges g = 0.72; 95% CI [0.157-1.282], $P = 0.012$). Although there was significant heterogeneity (Q = 42.400, $P < 0.0005$), there were insufficient studies to be able to conduct moderator analyses. There was asymmetry evident in the funnel plot upon visual inspection, with one study falling far to the right of the distribution. Similarly, Egger regression was significant (t = 2.820, $P = 0.037$), but Begg and Mazumdar rank correlation (tau = 0.33, $P = 0.29$). Overall, there was little evidence of publication bias for this outcome. Duval and Tweedie's trim and fill indicated that there were 2 studies trimmed, and although this analysis affected the effect estimate, it remained in the moderate to large range.

For pain tolerance, there was also an impact of MBIs compared to control (k = 9, Hedges' g = 0.68; 95% CI [0.210-1.154], $P = 0.005$), which indicated a moderate to large effect size. There was evidence of heterogeneity (Q = 58.89, $P < 0.0005$). Although there were more (k = 9) studies of pain tolerance than pain threshold, moderators were not available for all studies. As such, there were insufficient studies (k = 3) in each group for the dichotomous variables. As with pain threshold, the funnel plot appeared asymmetrical, with 2 studies appearing to the right and one to the left of the distribution. However, for pain tolerance, Begg and Mazumdar's rank correlation was not significant (tau = 0.236, $P = 0.311$) and nor was Egger regression (t = 1.364, $P = 0.113$). Furthermore, no studies were trimmed using Duval and Tweedie's trim and fill,[9] and the result remained identical. Although these suggest that publication bias is unlikely to account for the findings, it should be noted that the failsafe n was unacceptably low (failsafe n = 11) but this is likely indicative of the relatively small number of studies.

For pain-related distress, there were 3 studies that used clinical samples and 7 that used mindfulness in experimental pain. Although there was no overall heterogeneity for pain-related distress (Q = 12.466, $P = 0.052$), it did approach significance. We therefore analysed the clinical and experimental studies separately. There was no effect of MBIs compared to control for pain-related distress in clinical samples (k = 3, Hedges' g = 0.159; 95% CI [−0.018 to 0.419], $P = 0.229$). Similar results were obtained in the experimental studies, with no statistical effect of MBIs vs control on pain-related distress (k = 7, Hedges' g = 0.439; 95% CI [−0.164 to 0.419], $P = 0.156$) There was significant heterogeneity for experimental studies (Q = 10.433, $P = 0.015$), but not clinical studies (Q = 1.340, $P = 0.512$). There were again insufficient studies to warrant moderator analyses. Upon visual inspection of the funnel plots, it seemed that they were largely symmetrical for both clinical and experimental studies. For clinical studies, Egger regression intercept was not

significant ($P = 0.065$) and Begg and Mazumdar's rank correlation was also not significant (tau = 0.33, $P = 0.602$). However, there was some indication of publication bias for experimental studies because Egger regression was significant (tau = 1.00, $P = 0.04$).

3.3. Moderator analyses

Due to the smaller number of studies than anticipated, many of the a priori moderation analyses could not be completed. This is particularly the case when we separated the clinical and experimental studies for the analyses of pain severity and pain-related distress. There were insufficient studies to analyse moderators for pain tolerance, except for the type of control group (active vs passive), proportion of females, and dose of mindfulness. There were no effects of sex (t = 0.79, $P = 0.457$) or dose of mindfulness (t = −1.17, $P = 0.293$) on the relative efficacy of MBIs on pain tolerance. The effect of the type of control group on pain tolerance was significant (t = 6.986, $P = 0.008$), which indicates that the effect size of MBIs is greater when compared to a passive control rather than an active control.

3.3.1. Risk of bias and GRADE analyses

All studies had at least one criterion on which risk of bias was either high or unclear (**Table 2**). Most studies had a low risk of bias for random sequence generation (n = 12), concealed allocation (n = 13), attrition (n = 18), and selective reporting (n = 16). As is common in RCTs of psychosocial interventions, most studies failed to blind participants or did not state whether they were blinded (n = 19) or whether assessors were blinded (n = 3).

For our primary outcome of pain severity in clinical studies, we downgraded the outcome 3 times for limitations in study design, sparseness of the data (imprecision), and inconsistency of results. We consider the quality of evidence for the null finding to be very low, and therefore our confidence in this estimate is limited, meaning that the results are consistent with an absence of good evidence for an effect of MBIs on pain severity, rather than strong evidence for no effect. For experimental studies, we only downgraded the outcomes once, for limitations in study design largely due to lack of blinding. Therefore, we can be moderately confident that there is no impact of mindfulness on acute experimental pain. For pain threshold, we downgraded the evidence 3 times for limitations in study design, inconsistency of results, and sparseness of the data (imprecision); however, we upgraded the evidence in light of the large effect size observed. Therefore, our confidence in the estimate is also limited and we consider the quality of evidence to be low. For pain tolerance, we downgraded the evidence for study limitations and inconsistency of results but upgraded the evidence due to the moderate to large effect size. As such, we are moderately confident in the effect estimate. For pain-related distress in clinical samples, we downgraded the outcome for sparseness of data (imprecision) and limitations in study design. Therefore, we have low confidence in the estimated effect of MBIs on distress in clinical samples. Similarly, we downgraded the outcomes 3 times for sparseness of the data (imprecision), inconsistency, and publication bias. As such, we consider the quality of the evidence as very low and have very little confidence in the effect size estimate.

4. Discussion

The primary aim of this meta-analysis was to determine whether MBIs are efficacious for improving pain severity in acute pain. This meta-analysis found an absence of evidence for an effect of MBIs on pain severity in either clinical or experimental pain. In terms of secondary outcomes, there was evidence for an effect of MBIs compared to control for pain tolerance (Hedges' g = 0.68) and pain threshold (Hedges' g = 0.72), both of which favoured MBIs. For pain-related distress, there was an absence of evidence in clinical (k = 3, Hedges' g = 0.159) or experimental settings, (k = 4, Hedges' g = 0.439). It should be noted that the evidence for pain severity in clinical samples, pain threshold, and pain-related distress was low to very low and it is possible that subsequent research might change the estimates of the effect of MBIs on these outcomes. However, we can be moderately confident that MBIs do not produce improvements in experimental pain. By contrast, evidence for the beneficial effect of MBIs on pain tolerance was moderate and thus the true effect is likely to be close to that observed in this meta-analysis.

These findings need to be interpreted within the context of the limitations of this meta-analysis. The main limitation is that there were a small number of heterogenous studies. Although there were 22 studies in total, for some outcomes (eg, pain-related distress in clinical samples), there were as few as 3 studies included. Moreover, in many analyses, there was considerable evidence of heterogeneity. This likely arises from the varied approaches that were used across different studies. For example, there were different types of mindfulness, different doses, different modes of delivery, and different control groups used across studies. Unfortunately, although we had planned to investigate these as moderators, for most variables, we were unable to do so due to the small number of studies.

We did find that for pain tolerance, active vs passive control group affected the beneficial impact of MBIs. These active controls included relaxation, breathing control, and hypnosis, which one might potentially expect to have an impact on pain tolerance themselves. Hence, this result is unsurprising. Interestingly, none of the active control groups included a true sham condition, which means that it is impossible to determine whether it was simply the nonspecific effects of the active controls that accounted for the reduced efficacy of MBIs on pain tolerance or active treatment effects of the comparator treatment. It should be noted, nevertheless, that MBIs still produced a positive impact (albeit smaller) on pain tolerance even when active controls were used. This result underscores the importance of using appropriate control groups to determine the efficacy of the central mindfulness components. The combination of heterogeneity, publication bias, and study limitations meant that evidence for some outcomes was rated as low to very low quality, and indeed the effect sizes for pain severity in clinical settings and pain-related distress in experimental settings were moderate, although estimates of the effect size included zero. Thus, these results are consistent with an absence of good evidence, not evidence of the absence of an effect.

For pain threshold and pain tolerance, the effect sizes were moderate to large. In particular, the evidence for pain tolerance was rated as moderate, according to the GRADE criteria and as such we have some confidence that MBIs are likely to be efficacious for tolerance with an effect size in the moderate to large range. Importantly, our results are consistent with studies comparing experienced meditators to novices which find that mindfulness does not improve pain severity,[14,17,18] and that benefits in other outcomes are observed only amongst those who are experienced meditators.[27] The convergence of findings using different methodologies gives more confidence in the findings.

These limitations notwithstanding, this is the first meta-analysis to assess the efficacy of MBIs for acute pain. Our meta-analysis

Table 2

Summary of methodological quality RCT studies.

Study (author, date)	Random sequence allocation	Allocation concealment	Blinding of participants	Blinding of outcome of assessment	Attrition	Selective reporting
Coelho et al.,[6] 2018	High risk	High risk	High risk	Unclear	Unclear	Low risk
Duncan et al.,[8] 2017	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Esch et al.,[11] 2017	Unclear	Low risk	High risk	Low risk	Low risk	Low risk
Forsyth et al.,[12] 2014	Low risk	Low risk	High risk	Unclear	Low risk	Unclear
Garland et al.,[13] 2017	Unclear	Low risk	High	Low risk	Low risk	Low risk
Kingston et al.,[25] 2007	Unclear	Low risk	High risk	Unclear	Low risk	Low risk
Liu et al.,[26] 2013	Low risk	Low risk	Unclear	Low risk	High risk	Low risk
Miller-Matero,[29] 2019	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk
Prins et al.,[31] 2014	Low risk	Low risk	Unclear	Unclear	Low risk	Low risk
Ratcliffe et al.,[32] 2019	Low risk	Low risk	Unclear	Unclear	Low risk	Low risk
Reiner et al.,[33] 2016	Low risk	Unclear	Unclear	Unclear	Low risk	Unclear
Sharpe et al.,[34] 2013	Low risk	Low risk	High risk	High risk	Low risk	Low risk
Shires et al.,[35] 2018	Low risk	Low risk	High risk	High risk	Low risk	Low risk
Soo et al.,[36] 2016	Unclear	Unclear	High risk	Unclear	Low risk	Low risk
Swain and Trevena,[38] 2014	Unclear	High risk	Unclear	Unclear	Unclear	Low risk
Tashani et al.[39] 2017	Unclear	Unclear	High risk	Unclear	Low risk	Low risk
Wachholtz Pargament,[44] 2008	Unclear	Unclear	High risk	Unclear	Low risk	Low risk
Wang et al.,[45] 2019	Low risk	Unclear	High risk	Unclear	Low risk	Low risk
Wren et al.,[47] 2019	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Westenberg et al.,[46] 2018	Low risk	Unclear	Low risk	Unclear	Low risk	Unclear
Zeidan et al.,[48] 2015	Low risk	Low risk	High risk	Unclear	Low risk	Unclear
Zeidan et al.,[49] 2016	Low risk	Low risk	Low bias	Unclear	Unclear	Unclear

Ratings for RCTs were conducted using the Cochrane Collaboration's tool for assessing risk of bias in RCTs (Higgens & Green, 2011). (1) low risk of bias (satisfies criteria); (2) high risk of bias (does not satisfy criteria); 3) unclear risk of bias (information not provided).
RCT, randomized controlled trial.

benefited from the protocol being preregistered in the PROSPERO database, close adherence to the PRISMA and Meta-analyses of Observational Studies in Epidemiology criteria,[30,37] and the application of the Cochrane Collaborations' risk of bias rating[21] and GRADE criteria.[20] This review adds to prior reviews by suggesting a role for MBIs in managing acute pain but highlights the need for better-quality studies of MBIs in acute pain. Specifically, we need well-matched attention placebo control groups that allow participants to be blind to the hypotheses, so that expectations are matched between the MBI and other interventions, and we need better methods to blind assessors. Laboratory studies need to ensure that they follow standard procedures for randomization and allocation concealment. Studies need to be preregistered and accurately reported, whereas clinical studies need to use intention-to-treat analyses and use strategies to minimize attrition.

Given these limitations in the literature, many of our conclusions can best be described as preliminary. However, this meta-analysis offers moderate-level evidence that MBIs have the potential to increase pain tolerance but do not reduce pain severity at least in laboratory settings. We found an absence of evidence for an effect on pain severity in clinical samples. The absence of an effect on pain severity may not be surprising in a chronic pain setting because most psychosocial interventions for chronic pain do not focus on changing pain severity but rather on accepting the pain and changing behaviours, which lead to improvements in functional outcomes.[10,40,41] However, this is a problem in acute pain, where pain severity is typically the target. That is, if you are about to undergo a lumbar puncture, you want it to hurt less. Therefore, the fact that MBIs in this meta-analysis did not find clear evidence that MBIs reduce pain severity in acute pain is problematic for the use of MBIs for acute pain for some indications.

The lack of efficacy supporting the impact of MBIs on acute pain severity means that MBIs might have less of a role in procedural pain where the aim would be to reduce the pain during the procedure. However, there are other indications in acute pain whereby reductions in pain tolerance might be important. For example, future research should examine the efficacy of MBIs in postsurgical pain or acute musculoskeletal pain. In these conditions, the ability to complete physical rehabilitation is important, and therefore pain tolerance may be important to facilitating appropriate physical therapy and facilitating outcome. In both postoperative pain and acute musculoskeletal injury, the problem of the transition of acute to chronic pain has been difficult to prevent.[4] Furthermore, reductions in pain tolerance could be

important in these settings if it leads to reductions in the use of opiates. A recent study showed that a brief pain app was effective in reducing opioid consumption postoperatively.[7] The present results would support more clinical trials of MBIs in these contexts.

The absence of observed effects on the primary outcome suggests caution should be used in applying MBIs in clinical practice for acute pain. However, it is not necessarily at odds with the aim of MBIs. The original rationale for mindfulness-based stress reduction stated that attending mindfully to pain enabled the person to detach the emotional and cognitive aspects of pain from the sensory aspects of pain (see Ref. 23). Thus, pain would become more acceptable and pain viewed as less distressing. This would allow people to be able to withstand the same level of pain for longer, because they were not distressed by it. Our meta-analysis, however, also finds an absence of evidence in either clinical or experimental settings that MBIs reduce pain-related distress. However, the evidence for this finding is of low to very low quality and therefore we cannot be confident of the effect demonstrated in this study. Importantly, this review highlights that there is a need for further research into the specific effect of different types of MBIs and their optimal dosage to maximise their effectiveness in the management of acute pain. It is possible that instead of a change in pain severity being the key to better outcomes, it may be that changes in functioning should be the target of interventions.

This meta-analysis confirms recent calls for the mindfulness literature to consider carefully methodological issues that render the current evidence base of MBIs as low quality.[40] For 3 of the outcomes (pain severity in clinical samples, pain threshold, and pain-related distress in both clinical and experimental settings), GRADE ratings indicated that we are not very confident of the estimates. Therefore, future research is needed to clarify the efficacy of MBIs on acute pain and related outcomes. However, we did find moderate-level evidence that MBIs do not improve pain severity in laboratory settings and arguably, most importantly we also found that there was moderate-level evidence for a beneficial effect of MBIs on pain tolerance. This is a potentially important finding, because although there are clinical settings in which a reduction of pain tolerance may not be meaningful, there are also settings in which reducing pain tolerance could prove clinically important. However, this meta-analysis has first and foremost confirmed that future research investigating MBIs is needed in the field of acute pain.

Conflict of interest statement

A. Shires has been paid for developing and delivering educational presentations and workshops for the MiCBT Institute Australia. The manuscript from this study has not been submitted or published elsewhere. The remaining authors have no conflicts of interest to declare.

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Author contributions: A. Shires, L. Sharpe, and T.R.O. Newton-John developed the concept and protocol for this meta-analysis.
A. Shires conducted the search, and A. Shires, T.R.O. Newton-John, and J.N. Davies reviewed abstracts and full-text documents.
A. Shires and L. Sharpe conducted the analyses, and all authors contributed to the interpretation of the findings. A. Shires wrote the first draft of the manuscript, and all authors reviewed and approved the final version of the manuscript.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/A985.

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