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REVIEW

The Effect of Mindfulness-Based Interventions on Stress, Depression and Anxiety During the Perinatal Period in Women Without Pre-existing Stress, Depressive or Anxiety Disorders: a Systematic Review and Meta-analysis of Controlled Trials

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Abstract

Objectives The objective of this systematic review and meta-analysis was to examine controlled trial evidence for the effectiveness of mindfulness-based interventions on stress, anxiety and depression in the perinatal period in women without pre-existing mental health issues.

Methods Six databases were searched for studies exploring the effects of mindfulness-based interventions on mental health outcomes of women during the perinatal period. Quality of both controlled trial meeting inclusion criteria were assessed using a tool specifically designed for meta-analyses of mindfulness-based interventions. Effect sizes were extracted for measures of mindfulness, depression, stress and anxiety outcomes. Effects were pooled in separate meta-analyses for all outcomes except anxiety which lacked sufficient studies.

Results Twelve studies were analysed. Pooled effects suggest that mindfulness-based interventions cause small but clear increases in mindfulness and reductions in depression in women without pre-existing disorders. Effects of mindfulness-based interventions on other outcomes were unclear and confounded by heterogeneity.

Conclusions Available controlled trial evidence suggests that mindfulness-based interventions improve mindfulness and decrease symptoms of depression during pregnancy in women without pre-existing mental health issues and might be a useful approach to prevent or attenuate the development of depression in the perinatal period.

Keywords Pregnancy · Mental health · Mindfulness · Perinatal · Childbirth · Labour

Pregnancy, childbirth and the postnatal period are times of immense physical and emotional change (Cowan, 1991). The transition to motherhood can be stressful, increasing vulnerability to anxiety and depression (Grote & Bledsoe, 2007). Mental health issues are prevalent at this time, with around 1 in 5 women experiencing depression during pregnancy and in the postnatal period (Dhillon et al., 2017; Fairbrother et al., 2015; NICE, 2014). Stress has been found to affect 58% of pregnant women (Stone et al., 2015). Stress and depression during the perinatal period are predictive of short- and long-term negative consequences for mothers and infants (Staneva et al., 2015). Mental health issues during pregnancy have been associated with an increase in the risk of premature and stillbirths (Dunkel Schetter, 2011; Webb et al., 2005) and congenital malformations (Pereira et al., 2011). Maternal mental health issues are also associated with greater risk of the baby going on to develop behavioural and emotional problems in later life, with increased risk of a negative impact on IQ and educational attainment (Stein et al., 2014). Prompt and effective treatment not only minimises the risks for the mother, but also minimises the risks to her child's emotional, social and cognitive development (National Collaborating Centre for Mental Health, 2018). Perinatal stress is also known to increase the use of analgesia and the risk of surgical/caesarean deliveries and post-partum depression (Saeed et al., 2015; Saunders et al., 2006; Togher et al., 2017). Moreover, suicide continues to be

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a leading cause of maternal death in the UK (Knight et al., 2015). Given this context, preventing or attenuating stress, anxiety and depression during pregnancy is a crucial public health goal (Cooper & Murray, 1998). The need to establish pathways for effective prevention and treatment of maternal mental health issues has driven substantial government funding into maternal mental health care in England. There are plans to provide evidence-based mental health care in the perinatal period for 30,000 women in England (Maruthappu et al., 2014). As the perinatal period (pregnancy and a year postnatally) is considered a time of increased risk for mental health issues in women (National Maternity Review, 2016), NHS resources are being directed to strategies that are effective for detecting and preventing mental health issues during the perinatal period. Given that prevention is a key public health agenda, the optimal target population for interventions aimed at preventing the development of mental health issues is women without pre-existing mental health disorders (Woolhouse et al, 2014). This is the scope of this review.

The management of mental health problems that develop during pregnancy and the postnatal period presents unique challenges. There are risks associated with taking psychotropic medication in pregnancy and during breastfeeding (NICE, 2016). Given the importance of preventing and managing mental health issues in the perinatal period, and the difficulties associated with medication, mindfulness-based interventions are a potential solution for supporting women during this period. Attending a mindfulness-based intervention has also been described as enabling flexibility in choice during childbirth, with this contributing to positive experiences (Fisher et al., 2012). Kabat-Zinn (2013) described mindfulness as 'paying attention in a particular way: on purpose, in the present moment, and non-judgmentally'. He outlined nine attitudes underlying mindfulness as beginner's mind, non-judging, acceptance, letting go, trust, patience, non-striving, gratitude and generosity (Kabat-Zinn, 2019). These attitudes are the foundation of mindfulness-based interventions. Mindfulness teachers are trained to develop an awareness of these attitudes within their mindfulness practice and in delivering mindfulness-based interventions (Crane et al., 2017). Kabat-Zinn (2013) originally developed mindfulness-based stress reduction (MBSR), with mindfulness-based cognitive therapy (MBCT) being developed as a relapse prevention approach for depression (Segal et al., 2013). Mindfulness-based interventions have flourished since their inception in the 1980s, with evidence for their effectiveness with anxiety, depression, stress, managing chronic physical conditions and suicidality (Hofmann & Gómez, 2017; Kuyken et al., 2016; Williams & Swales, 2017; Zhang et al., 2015). Increasing capacity to be aware of and accept situations, thoughts and feelings as they are can lead to greater tolerance of stress and discomfort (Kashdan & Rottenberg, 2010; Warriner et al., 2018). The perinatal period is a time when such skills and attitudes may benefit women through reducing the effects of the stressors involved in this transition.

Previous systematic reviews of mindfulness-based interventions in the perinatal period have included both pre-post and RCT studies, some of which sample from populations of women with pre-existing mental health disorders and others that sample from populations of women without pre-existing disorders. Previous systematic reviews have found some evidence from pre-post studies of reductions in stress, anxiety and depression, but no significant benefit in RCTs (Hall et al., 2016). In agreement with Hall et al. (2016), Lever Taylor et al. (2016) found small to moderate benefits for depression, anxiety, stress and mindfulness from pre-post studies. Larger effect sizes were found for studies on participants with pre-existing, or a history of, depression, anxiety and stress, suggesting, in agreement with Woolhouse et al. (2014), that such participants form a separate study population from participants without pre-existing disorders. Between group comparisons from RCTs again showed no significant benefits for depression, anxiety, stress and mindfulness. The most recent systematic review and meta-analysis found no significant differences between the intervention and control groups for anxiety, depression and perceived stress, with mindfulness being the only outcome variable with a significant between-group difference (Dhillon et al., 2017). Similar to preceding meta-analyses, Dhillon et al. (2017) found significant benefits in pre-post studies for anxiety, depression, perceived stress and mindfulness.

Given contrasting evidence from pre-post versus controlled trials, and acknowledging the inherent bias in, and inability to claim causal effects from, pre-post studies, previous meta-analyses have concluded that additional large-scale, adequately powered, randomised controlled trials are needed to evaluate the effectiveness of mindfulness-based interventions (Dhillon et al., 2017; Hall et al., 2016; Lever Taylor et al., 2016; Matvienko-Sikar et al., 2016; Shi & MacBeth, 2017). This recommendation has also been motivated by high degrees of heterogeneity reported in previous reviews. In response to these recommendations, there have been several studies published since Dhillon et al. (2017).

A source of heterogeneity that does not seem to have been addressed in previous meta-analyses is the pooling together of studies that have sampled from populations with and without pre-existing mental health disorders. Given the large difference in effects from studies on women with and without pre-existing conditions reported by Lever Taylor et al. (2016), it is surprising that subsequent meta-analyses have not sought to examine these populations separately. There is currently no pooled effect size estimate for the benefits of mindfulness interventions in women without pre-existing mental health issues that is not currently clouded by the effects on women that begin mindfulness interventions with

pre-existing mental health disorders. Given the inherent bias of pre-post studies, and the absence of pooled evidence for the causal effects of mindfulness interventions on health in women without pre-existing conditions, a systematic review and meta-analysis of controlled trials conducted only on women without existing mental health issues is required. A review of RCT evidence from women without pre-existing mental health disorders is the only way to examine the possible preventative benefits of mindfulness interventions during pregnancy.

Existing meta-analyses examining the efficacy of mindfulness interventions on mental health outcomes in the perinatal period have combined studies sampling from populations with and without pre-existing disorders. The pooling of sample populations prevents a clear summary of the possible preventative benefits of mindfulness interventions for women without pre-existing stress, anxiety or depression. Moreover, existing summaries of evidence and recommendations are confounded by the inclusion of weak and conflicting evidence from pre-post studies. Therefore, the aim of this systematic review and meta-analysis is to provide an up-to-date evaluation of controlled trial evidence for the efficacy of mindfulness-based interventions to attenuate anxiety, depression and stress in the perinatal period in women without pre-existing depression, stress or anxiety disorders.

Methods

Search Strategy and Study Selection

We conducted the review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Hutton et al., 2015). The content of six databases (Cochrane Library, Web of Science, PsycArticles, MEDLINE and PubMed, CINAHL and Scopus) was searched from inception to 4th April 2020. The databases were chosen due to comprehensive data coverage and their use in previous meta-analyses (Dhillon et al., 2017; Lever Taylor et al., 2016). The following search terms were applied and were based on search strings used in previous systematic reviews in this area: Mindful* OR MBCT OR MBSR AND prenatal OR antenatal OR postnatal OR post-partum OR puerperal OR pregnancy OR pregnant OR trimester OR childbirth.

The search was restricted to peer-reviewed studies written in English and available in full text. Only quantitative controlled trials exploring the effectiveness of a mindfulness-based intervention during the perinatal period (i.e. during pregnancy or the first year following childbirth) were included. A mindfulness-based intervention was defined as mental practice to promote a structured mind set to being aware of the present-moment experience in an accepting, non-judging and non-avoiding way (Kabat-Zinn, 2013). Practices falling under this definition include MBCT, MBSR, ACT, mindfulness-based yoga or other interventions described by the authors. Included studies also needed to include a control group and measures at baseline and after the intervention using validated measures of depression, anxiety, stress and/or mindfulness. No other methodological requirements were set, but study quality was rated.

We included studies if they were available at any time before the date of the search.

Articles from the search were tracked and a further search of potentially relevant articles and review papers in the reference sections was conducted. Duplicates were removed and the remaining studies were further screened by title, abstract and full text. Irrelevant articles were excluded. Inclusion or exclusion decisions were based on the judgment of two independent researchers. Any discrepancies were resolved through discussion.

Inclusion Criteria

In accordance with the PICOS approach (population (P), intervention (I), comparators (C), main outcome (O) and study design (S)), the following inclusion criteria were used:

Participants were pregnant females (P); studies had to include mindfulness-based interventions (as defined above) delivered during the perinatal period (i.e. during pregnancy of the first year after birth) (I); passive-inactive, alternative-active or usual-care control groups not receiving mindfulness interventions were acceptable controls (C); validated quantitative measures of mindfulness, state and/or trait anxiety, stress and depression constituted the outcome measures (O); and only controlled trials (both randomised and non-randomised) were included (S).

After removal of duplicates, 870 papers were screened by abstract. Subsequently, 29 full-text papers were reviewed and 12 met the criteria for inclusion (Fig. 1).

Quality Assessment

Studies were evaluated using a tool developed specifically for a large-scale meta-analysis of mindfulness-based interventions (Khoury et al., 2013). This tool was chosen due to its ability to assess both randomised and non-randomised designs and the inclusion of items specific to the validity of tools used to measure mindfulness, the mindfulness protocol and the training of the therapists to deliver mindfulness interventions (Khoury et al., 2013). The quality scoring tool included items from the Jadad et al. (1996) scale and items not specific to controlled studies. The items assessed by the tool included the following: (1) whether the intervention followed a clearly described protocol based on,

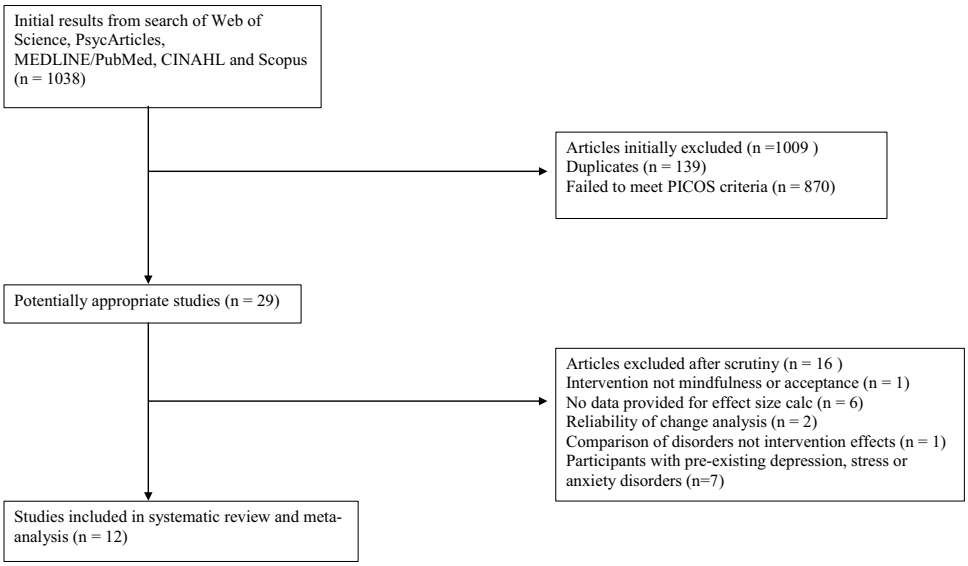

Fig. 1 Flow diagram of study selection process

or adapted from, an established programme (score of 0 or 1); (2) whether measures were administered at follow-up (score of 0 or 1); (3) whether a validated measure of mindfulness was used (score of 0 or 1); (4) whether therapists were trained in delivering mindfulness-based interventions and (for studies with clinical populations only) were clinically trained based on good practice guidelines for teaching mindfulness-based courses (UK mindfulness-based teacher trainer network, 2015). Mindfulness training was required for any study to obtain a score of 1, but clinical training was only required for studies including clinical populations (score of 0 or 1); (5) whether the study was randomised (score of 0 if not randomised, 1 if randomised with a no intervention/waitlist control, 2 if randomised with a usual-care control and 3 if randomised with an active control); and (6) whether investigators and/or participants were blinded to their allocated condition (score of 0 if not blinded, 1 if single-blinded, 2 if double-blinded). The maximum score from the scale was 9, with higher scores reflecting studies of higher quality. Two independent researchers completed the quality assessments. As with study inclusion, discrepancies were resolved through discussion.

Data Extraction and Analysis

Participant characteristics, demographic data, type and characteristics of intervention, type of control/comparison group, outcome measures and effect sizes for post-intervention difference between intervention and control groups were extracted.

Effect size was calculated as Cohen's *d* using the mean difference and pooled SD when reported. Where SD was not reported, it was calculated either from the reported exact *p* values or from *t* or *F* statistics using formulas provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins et al., 2021). Studies not reporting the statistics required to calculate effect size as described were excluded from the analysis.

We extracted only composite scores from mindfulness questionnaires with subscales. Where multiple scales were used to assess depression, the Edinburgh Postnatal Depression Scale (EPDS) (Cox & Holden, 1987) was used in line with other meta-analyses in this area (Lever Taylor et al., 2016; Sockol, 2015;). The EPDS is the most frequently used self-report measure of perinatal depressive symptom severity with strong psychometric properties amongst both pregnant and post-partum samples (Cox & Holden, 1987; Murray & Carothers, 1990). For other outcomes (i.e. anxiety and stress) and in cases where the EPDS was not used to assess depression, but more than one scale was used to measure the construct, the scale with the strongest psychometric properties was used to calculate effect size. Where more than one scale was used to measure the construct, and there was no clear evidence for superiority of one scale over another based on psychometric properties, a weighted mean effect size was calculated to ensure only a single effect size estimate from each study sample (Lipsey & Wilson, 2001, p. 114).

For meta-analysis, random effects models were run in JASP (version 0.14.1). Tables and forest plots were produced for each outcome, and heterogeneity was assessed using the Q statistic and I^2 statistic. The I^2 statistic was interpreted against the following categories from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins et al., 2021): 0–40% not important; 30–60% moderate; 50–90% substantial; and > 75–100% considerable heterogeneity. Influential case analyses and funnel plots were used to identify outliers and examine

publication bias, respectively. Influential cases were identified by a Cook's distance value of > 0.5 (Viechtbauer & Cheung, 2010). If outliers were identified, they were removed and the analysis was repeated.

Results

Study Characteristics

A summary of studies included for analysis is shown in Table 1. There were 704 participants across the 12 included studies with 635 involved in RCTs and the remaining 69 from non-RCTs. Demographic data from study participants are summarised in Table 2. Of these studies, only Chan (2015) used an intervention not based on an established mindfulness programme. Three RCTs did not measure mindfulness as an outcome of the intervention (Chan, 2015; Muthukrishnan et al., 2016; Zhang et al., 2019). One study examined the impact of a mindfulness-based intervention on outcomes after birth (Perez-Blasco et al., 2013). The remaining RCTs focused on reducing general distress or anxiety or improving wellbeing during the pregnancy period in samples not recruited for elevated baseline measures of depression, stress and anxiety.

There were two non-randomised control trials in the included studies. Bowen et al. (2014) did not explain how participants were allocated to the mindfulness-based intervention or the alternative interpersonal therapy active control groups. Gambrel and Piercy (2015) used a waiting-list control for comparison, with a primary aim of examining the effects of a mindfulness-based intervention during the pregnancy period on relationship satisfaction. Nevertheless, quantitative data were reported for outcomes of interest to this review for the pregnant females separately. Bowen et al. (2014) sought to examine the effects of a mindfulness-based intervention versus interpersonal therapy on depression and worry symptoms in pregnant, anxious and depressed participants.

Across the 12 included studies, the duration of interventions ranged from 4 to 8 weeks, with most delivering approximately eight 2–3 h weekly sessions albeit with some variability between studies. No study explicitly followed the MBCT course structure. The remaining studies mostly used variations or adaptations of MBCT, though two studies delivered bespoke programmes that contained mindfulness elements including: Eastern-based meditation (Chan, 2015) and mindful transition to parenthood (Gambrel & Piercy, 2015). Where reported, the duration of instructor-led and home-practice sessions was generally less than recommended in MBSR or MBCT (see Table 1).

Quality Assessment of Included Studies

Scores on the quality assessment ranged from 3 to 7 out of a possible 9, with a mean score of 4.9, a median of 5 and a modal score of 4. Quality scores were generally reduced by a lack of trained mindfulness practitioners delivering interventions, failure/inability to blind participants and researchers to the allocated conditions, failure to specify the random allocation process and not including an assessment of mindfulness. Assessment scores for all included studies are shown in Table 3.

Intervention Effects

Of the 12 studies included, 11 reported group comparison data for at least one measure of depression (total $n = 607$), 7 for stress (total $n = 403$) and 8 for mindfulness (total $n = 396$). Only 3 studies included measures of general anxiety (total $n = 81$).

General Anxiety

The effect sizes for anxiety reduction differences between intervention and control groups at post-test ranged from $d = -0.04$, $d = -0.25$ and $d = -1.23$ from Woolhouse et al. (2014), Bowen et al. (2014) and Perez-Blasco et al. (2013), respectively. Because of the small number of, and a large variation in reported effects on general anxiety, a meta-analysis was not performed on this outcome. Perez-Blasco et al. (2013) delivered the mindfulness intervention in the post-partum period with a sample of breastfeeding women. The difference in intervention period could be a factor in the larger reduction observed in that study.

Depression

There was a small and statistically significant reduction in depression after mindfulness interventions compared with controls. The effect size estimate for the intervention-control post-test difference was $d = -0.20$ (95% CI, −0.40, −0.00, $p = 0.04$). Moreover, estimates of heterogeneity were statistically non-significant and indicated unimportant between-study variation in effect sizes ($Q_{10} = 11.1$, $p = 0.35$, $I^2 = 23.1\%$). There were no influential cases and no indication of publication bias. Figures 2 and 3 display a forest plot and funnel plot respectively for the depression outcome.

Mindfulness

There was a small, statistically significant increase in mindfulness after mindfulness interventions compared with controls. The effect size estimate for the intervention-control post-test difference was $d = 0.24$ (95% CI, 0.04, 0.43,

Table 1 Summary of included studies

Citation	Participant description, *n*, (mean, SD) age	Study type	Intervention description	Comparison	Outcome measures
Beattie et al. (2017)	$n=48$, $n=24$ exp (28.9, SD 5.7 years), $n=24$ control (28.5, SD 6.4 years)	RCT	Mindfulness in pregnancy programme (MIPP). 8 weeks, 2 h/week	Active control-pregnancy support programme	PSS, EPDS, MAAS, birth outcomes
Bowen et al. (2014)	$n=19$ exp (30.67, SD 3.94 years), $n=18$ control (28.94, SD 3.55 years)	Non-RCT	Mindfulness-based therapy. 5 weeks, unspecified frequency and duration of sessions	Interpersonal therapy	EPDS, STAI, CWS, MSSS
Chan (2015)	$n=64$ exp (33.34, SD 4.11 years), $n=52$ control (33.84, SD 3.74 years)	RCT	Eastern-based meditation intervention. 6 sessions, unspecified duration and frequency	Usual care	PDQ, PCI, EPDS, BMSWBI, salivary cortisol
Duncan et al. (2017)	$n=30$, $n=15$ exp and control	RCT	PEARLS based on mindfulness-based childbirth and parenting education (MBCP). 8 weekly sessions, unspecified duration	Active control	FFMQ, CES-D, CBSEI, PCS, W-DEQ
Gambrel and Piercey (2015)	$n=32$ (31.56 years) $n=15$ exp, $n=17$ control	Non-RCT	Mindful transition to parenthood programme. 4 weeks, 2 h/week	Waiting list	CSI, FFMQ, IRI, DASS-21, PANAS
Lonnberg et al. (2020)	$n=75$ exp (32, SD 3.86 years), $n=89$ control (32, SD 4.14 years)	RCT	Child Birth and Parenting (MBCP). 8 weeks, 2 h 15 min/week	Active control	PSS, EPDS, PSOM, FFMQ
Muthukrishnan et al. (2016)	$n=34$ intervention (21, SD 2.56 years), $n=34$ control (23, SD 2.4 years)	RCT	Mindfulness meditation programme; 2 session/week for 5 weeks plus 30 min/day home practice. Modified MBCT	Standard obstetric care	PSS, autonomic function tests: (a) HR response from sit to stand, (b) HR response from stand to lying and (c) HRV d) BP response to hand cold water immersion
Pan et al. (2019)	$n=74$ (32.8, SD 3.9 years), $n=39$ exp, $n=35$ control	RCT	MBCP 8 weeks, 3 h session/week plus 6×30-min home session/week	Standard treatment	PSS, EPDS, FFMQ
Perez-Blasco et al.(2013)	$n=21$ (34.33, SD 4.72 years), $n=13$ exp, $n=8$ control	RCT	Based on MBCT/MBSR and Mindful self-compassion. 8 weeks, 1×2-h session/week	No treatment	Parental Evaluation Scale, FFMQ, SCS, DASS-21, SWLS, SHS
Woolhouse et al. (2014)	$n=23$, $n=13$ exp (30.81, SD 0.75 years), $n=10$ control (34.08, SD 0.09 years)	RCT	Mind baby body, 6 weeks, 2 h/week	Usual care	DASS-21, CES-D, STAI, PSS, FFMQ
Zhang and Emory (2015)	$n=33$ (25.3, SD 4.6 years), $n=16$ exp, $n=17$ control	RCT	Mindful motherhood	Usual care	TMS, PSS, cortisol, PES, BDI-II
Zhang et al. (2019)	$n=58$, $n=28$ exp (25.7, SD 2.79 years), $n=30$ control (25.58, SD 2.33 years)	RCT	MBSR, 8×90 min/week	Usual care	STAI, PSRS, SDS

Key to abbreviations: *STAI*, State Trait Anxiety Inventory; *PSS*, Perceived Stress Scale; *PSRS*, Pregnancy Stress Rating Scale; *SDS*, Self-rating Depression Scale; *BDI-II*, Beck Depression Inventory-II; *PES*, Pregnancy Experience Scale; *DASS-21*, Depression, Anxiety and Stress Scale-21; *CES-D*, Centre for Epidemiological Studies Depression Scale; *TMS*, Toronto Mindfulness Scale; *FFMQ*, Five-Factor Mindfulness Questionnaire; *SCS*, Self-compassion Scale; *SWLS*, Satisfaction with Life Scale; *SHS*, Subjective Happiness Scale; *EPDS*, Edinburgh Postnatal Depression Scale; *PSOM*, Positive States of Mind; *HDS*, Hamilton Depression Scale; *ERDS*, Emotion Regulation Difficulties Scale; *CSI*, Couple Satisfaction Index; *IRI*, Interpersonal Reactivity Index; *PANAS*, Positive and Negative Affect Schedule; *CBSEI*, Child Birth Self-Efficacy Inventory; *PCS*, Pain Catastrophising Scale; *W-DEQ*, Wijima Delivery Expectancy/Experience Questionnaire; *PDQ*, Prenatal Distress Questionnaire; *PCI*, Prenatal Coping Inventory; *BMSWBI*, Body-Mind-Spirit Well-Being Inventory; *CWS*, Cambridge Worry Scale; *MSSS*, Maternity Social Support Scale; *MAAS*, Mindfulness Attention Awareness Scale; *MBCP*, mindfulness-based childbirth and parenting; *MBSR*, mindfulness-based stress reduction; *MBCT*, mindfulness-based cognitive therapy

Table 2 Participant demographics from included studies

Citation	Race/ethnicity	Education/employment	Civil status	Sexual orientation	Other
Beattie et al. (2017)	Intervention: 62.5% Australian and 37.5% other	Intervention: 72.7% employed	I, 100%	–	–
	Control: 71.4% Australian and 25% other	Control: 71.4% employed	C, 100%		
Bowen et al. (2014)	No data	Intervention: grade 12/ > 10%; post-secondary 90%	I, 100%	–	Gestation at intake: I, 21.35 ± 5.59 weeks; C, 23.42 ± 4.22 weeks
		Control: grade 12/ > 16.7%; post-secondary 83.3%	C, 85.7%		
Chan (2015)	All Chinese	Intervention: Middle school or < 7.9% High school 31.7% College or > 60.3% FT employment 87.5% Control: Middle school or < 14.5% High school 34.5% College or > 50.9% FT employment 80%	–	–	Present obstetric issues: I, 3.1%; C, 0%
Duncan et al. (2017)	Hispanic 18% White 59% Asian 14% Multiracial 7% Black 3% American Indian 3%	–	–	–	> 55% of sample below area median household income
Gambrel and Piercey (2015)	White 82% Native American 4.5% Asian American 1.5% Multiracial 3% Other 9%	High school only 3% College 21.2% Bachelor's degree 36.4% Graduate school 39.4%	Married 75.8% Co-habiting 18.2% Engaged 6.1%	1 lesbian couple	Religion: Christian 28.7%; Catholic 12.1%; Agnostic 6.1%; Atheist 9.1%; None 28.8%
Lonnberg et al. (2020)	Intervention: Swedish 89.6%; Swedish + other 3.1%; European 5.2%; non-European 2.1% Control: Swedish 83.6%; Swedish + other 6.2%; European 6.2%; non-European 2.1%	Intervention: Elementary 1% Secondary 12.5% College 86.5% Control: Elementary 0% Secondary 12.6% College 86.6%	Intervention: Single 3.1% Co-habiting 59.4% Married 37.5% Living apart 0% Control: Single 2.1% Co-habiting 61.7% Married 34% Living apart 2.1%	-	-
Muthukrishnan et al. (2016)	Indian	–	–	–	–
Pan et al. (2019)	Taiwanese	Junior college or < 12.2% University or > 87.8% Employed 81% Unemployed 19%	Married 98.6% Single 1.4%	–	No prior births 91.8% 1 + prior births 8.2%
Perez-Blasco et al. (2013)	Spanish	–	–	–	First child 57.1% 2 or > children 42.9%
Woolhouse et al. (2014)	Australian 50% Not born in Australia 50%	Higher Uni degree 43.8% Uni degree 40.6% Below Uni education 15.6%	Married 65.6% Co-habiting 31.3% Single 3.1%	–	Trimester at enrolment: First 25% Second 62.5% Third 12.5%

Table 2 (continued)

Citation	Race/ethnicity	Education/employment	Civil status	Sexual orientation	Other
Zhang and Emory (2015)	African-American	Unemployed 84.6%	Single 29.4% Not living with partner 19.1% Co-habiting 38.2% Married 13.2%	-	Have children 84.6% Gestation 21.5 weeks Complications 32.3%
Zhang et al. (2019)	Chinese	Intervention: Middle school or > 28.1% High school 31.3% College or > 40.6% Control: Middle school or > 22.6% High school 38.7% College or > 38.7% Intervention: Housewife 40.6% Employed 59.4% Control: Housewife 48.4% Employed 51.6%	–	–	Pregnancy period Intervention: 1st trimester 43.8% 2nd trimester 56.2% Control: 1st trimester 48.4% 2nd trimester 51.6% Previous births Intervention: One 84.4% ≥ two 15.5% Control: One 90.3% ≥ two 9.7%

I, intervention group; *C*, control group; '–' no data

Table 3 Quality assessment

Citation	Protocol based on established mindfulness programme	Measures administered at follow-up	Valid measure of mindfulness included	Therapists mindfulness trained	Randomised	Researchers and/or participants blinded	Total
Beattie et al. (2017)	1	1	1	1	3	0	7
Bowen et al. (2014)	1	1	0	1	0	0	3
Chan (2015)	0	1	0	0	2	0	3
Duncan et al. (2017)	1	1	1	1	3	0	7
Gambrel and Piercey (2015)	1	1	1	1	0	0	4
Lonnberg et al. (2020)	1	1	1	1	3	0	7
Muthukrishnan et al. (2016)	1	1	0	0	2	0	4
Pan et al. (2019)	1	1	1	1	2	0	6
Perez-Blasco et al. (2013)	1	1	1	0	1	0	4
Woolhouse et al. (2014)	1	1	1	1	1	0	5
Zhang and Emory (2015)	1	1	1	1	1	0	5
Zhang et al. (2019)	1	1	0	1	1	0	4

The quality score outcome can range from 0 = lowest quality to 9 = highest quality

$p = 0.02$). Heterogeneity estimates were small and statistically non-significant ($Q_7 = 6.52$, $p = 0.48$, $I^2 = 0.01\%$). There were no influential cases and no indication of publication bias. Figures 4 and 5 display a forest plot and funnel plot respectively for improvement in mindfulness.

Stress

Influence analysis suggested that the unusually large effect size for stress reduction reported by Muthukrishnan et al. (2016) was a clear outlier. After removal of this effect from

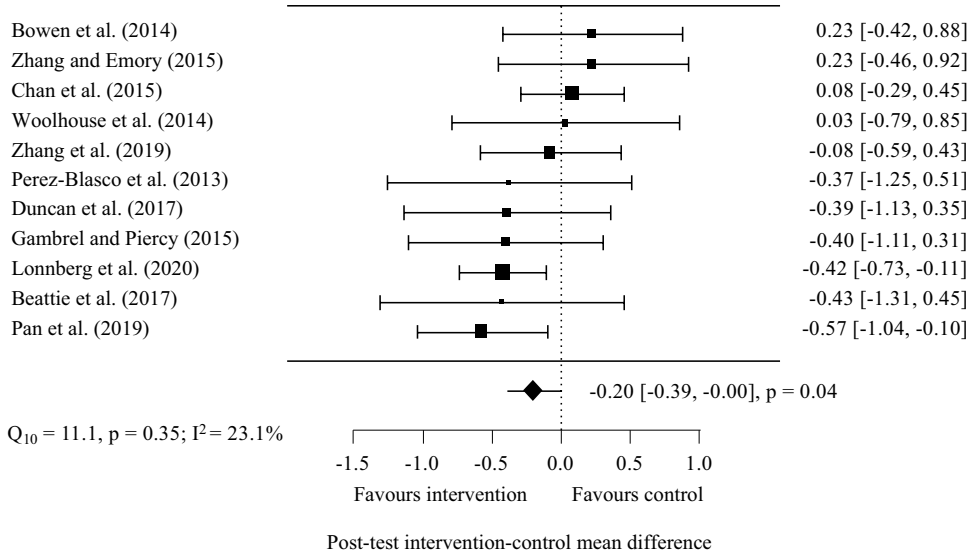

Fig. 2 Forest plot of intervention-control post-test standardised mean differences in depression

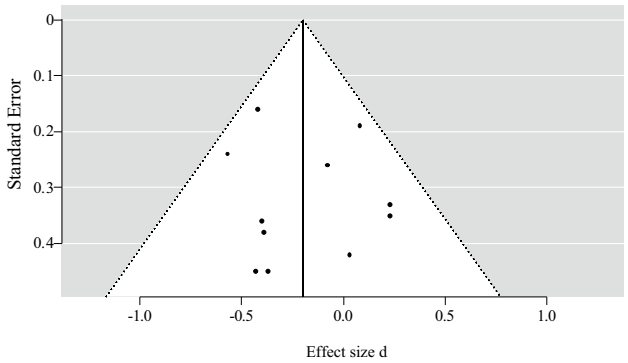

Fig. 3 Funnel plot of effect sizes for intervention-control post-test standardised mean differences in depression

the analysis, the evidence of the remaining 6 studies estimated a small but statistically non-significant reduction in stress after mindfulness interventions compared with controls. The effect size estimate for the intervention-control post-test difference was $d = -0.21$ (95% CI, −0.59, 0.16, $p = 0.27$). Heterogeneity statistics were statistically non-significant but suggestive of moderate heterogeneity in the remaining 6 studies ($Q_5 = 10.5$, $p = 0.06$, $I^2 = 54.2\%$). There was no indication of publication bias. Figures 6 and 7 display a forest plot and funnel plot respectively for the stress outcome. Other than lack of evidence for the training of the mindfulness instructors, there were no obvious aspects of the methods used by Muthukrishnan et al. (2016) that

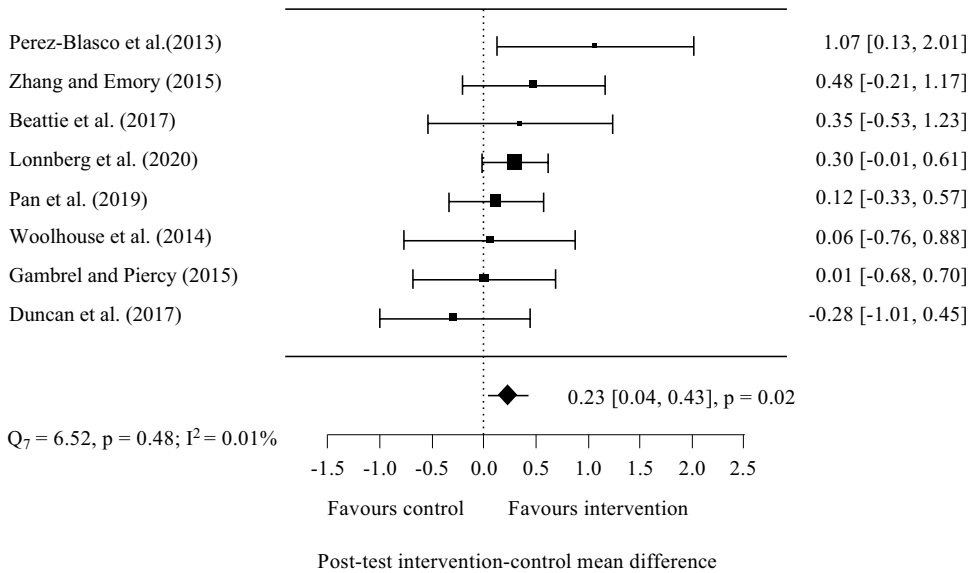

Fig. 4 Forest plot of intervention-control post-test standardised mean differences in mindfulness

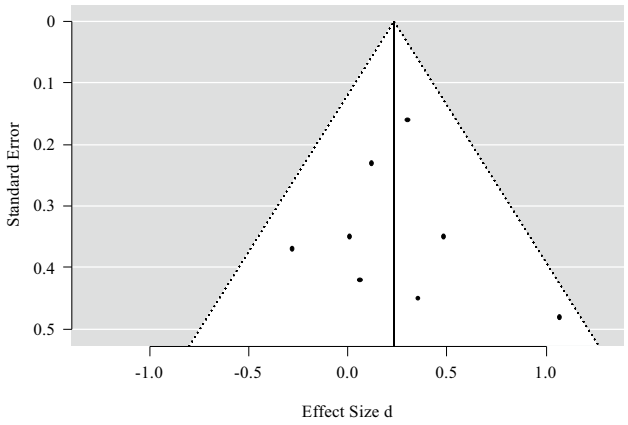

Fig. 5 Funnel plot of effect sizes for intervention-control post-test standardised mean differences in mindfulness

could account for the large reduction in stress reported in that study.

Discussion

This systematic review and meta-analysis has sought to provide an up-to-date summary of controlled trials on the effectiveness of mindfulness-based interventions in the perinatal period for reducing stress, anxiety and depression in women without pre-existing stress, anxiety or depression disorders. The analysis included 12 studies comprising 10 randomised and 2 non-randomised controlled trials on this population of women.

There was evidence to suggest that mindfulness interventions result in small, but clear and statistically significant reductions in depression and increases in mindfulness in participants without pre-existing disorders. The evidence for reductions in anxiety and stress was limited and unclear. There were insufficient and highly variable effects for anxiety reduction, and non-significant effects for stress reduction, with potentially problematic heterogeneity in the findings.

Studies were evaluated using a tool developed specifically for a large-scale meta-analysis of mindfulness-based interventions (Khoury et al., 2013). The maximum possible score of 9 would indicate studies of the highest quality in this field of research. The included studies were, on average, of moderate quality despite all being controlled trials. The failure/inability to blind participants to their allocated condition is understandable given the nature of mindfulness interventions; however, it is possible to blind researchers to the allocation, though this was not generally reported. The lack of trained mindfulness practitioners in the delivery

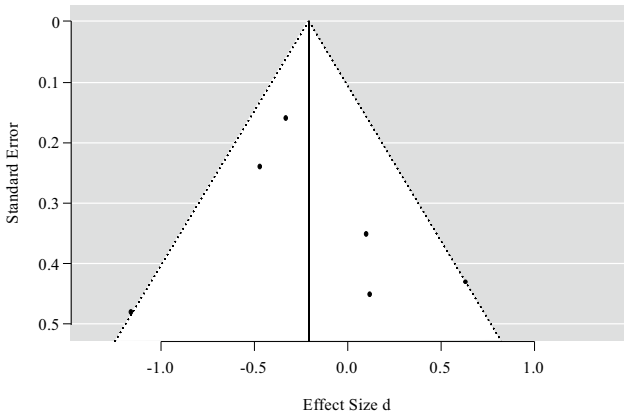

Fig. 7 Funnel plot of effect sizes for intervention-control post-test standardised mean differences in stress

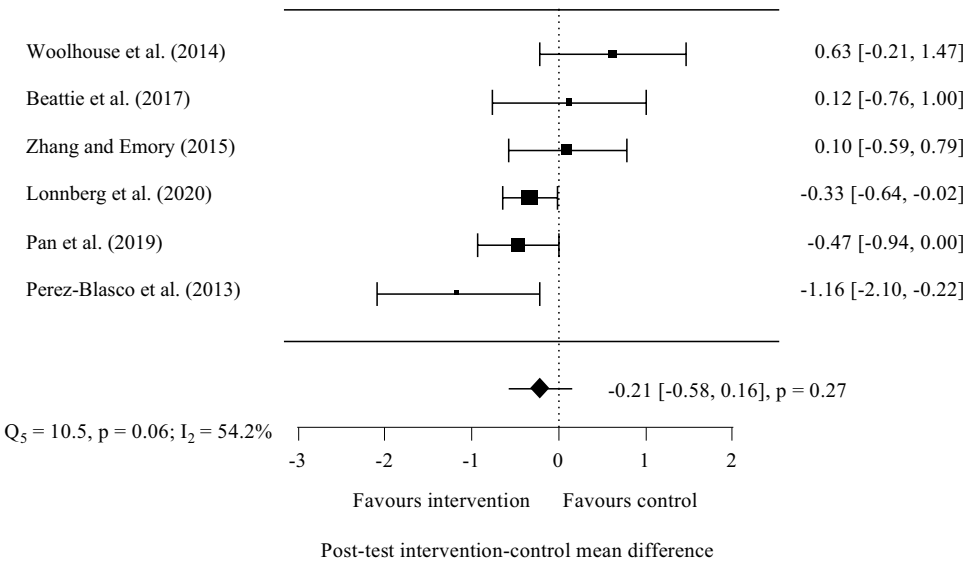

Fig. 6 Forest plot of intervention-control post-test standardised mean differences in stress

of mindfulness interventions is possibly more problematic. Evidence of appropriate training was lacking in 4 of the included studies. There was also considerable variation in the mindfulness-based interventions used, with only one study explicitly following MBCT course structure. The well-established approaches of mindfulness-based cognitive therapy and mindfulness-based stress reduction are adapted in multiple ways, potentially providing different mechanisms for change across studies and accounting for variability and magnitude of effects.

Stress and anxiety effects were confounded by heterogeneity. Even after removal of an outlier, the I^2 statistic suggested moderate to problematic heterogeneity in the remaining studies. Though the Q statistic was not significant for the stress outcome, the small number of remaining studies could result in insufficient power to reject the null hypothesis in this test. Meta-analysis was not performed on the anxiety outcome as there were only three studies. Nevertheless, the variation in effect sizes between these three studies was notable and ranged from very small to very large. Even for depression and mindfulness outcomes, the pooled analyses combine relatively small numbers of studies. As such, caution should possibly be exercised in the interpretation of pooled effects, though the non-significant and very low heterogeneity for mindfulness and non-significant and low heterogeneity for depression might provide some reassurance. Potential sources of heterogeneity include length and number of intervention sessions and different tools for measuring outcomes. Studies have also been carried out in different countries with the potential for cultural influences on intervention delivery and effectiveness, though these effects are speculative and beyond the scope of this review to examine. There were also considerable study design limitations, such as small sample sizes, lack of formal sample size estimation and specification of practical/clinically meaningful effects sizes and subsequently, unspecified type two error rates. Studies also often had many outcome measures/hypotheses being tested. Such issues inflate standard error in individual studies and subsequently in the pooled effect size estimate and challenge meta-analysis outcomes (Mayo-Wilson et al., 2017).

This review examined only controlled trials on women without pre-existing mental health issues. The goal was to obtain estimates of the effects of mindfulness interventions in mentally healthy women, free from the bias introduced by samples of women belonging to a population with existing mental health issues. As such, comparisons with previous meta-analyses that pooled samples from populations both with and without mental health disorders may be of limited value. However, our analysis of controlled trials provided no evidence of benefit of mindfulness-based interventions on anxiety and stress, supporting the findings of previous reviews (Dhillon et al., 2017; Lever Taylor et al., 2016). The heterogeneity of these outcomes was also in agreement with the previous analyses, despite our studies being only from the population of women without pre-existing disorders. In contrast to both previous reviews, however, our estimated effect on depression suggested a clear albeit small reduction in depression compared to controls after mindfulness interventions. The pooled effect on depression was unclear/non-significant in the previous two meta-analyses of this topic. In agreement with Dhillon et al. (2017), we found clear evidence for increased mindfulness after mindfulness-based interventions from controlled trials, though the size of effect was smaller in our analysis than previously reported. Lever Taylor et al. (2016) reported similar effect sizes to ours that were non-significant for controlled trials and with significant heterogeneity. The contrast in finding between our review and previous reviews, and the difference in effect size magnitude where findings agreed, could be explained by the single focus on studies from the population of women without pre-existing mental health disorders in this review. It is likely that removing studies on women with existing conditions reduced heterogeneity and allowed for a clearer estimate of the effect size of interest in this review.

Limitations and Future Research

The specific focus on controlled trials and studies of women without pre-existing conditions meant that the pool of studies in this meta-analysis is smaller than previous meta-analyses. However, this volume-quality trade off was required to address the research question.

We performed this review in accordance with PRISMA guidelines (Hutton et al., 2015). To our knowledge, this is the first up-to-date systematic review and meta-analysis of controlled trials on the effectiveness of mindfulness-based interventions on mental health outcomes during pregnancy performed solely in women without pre-existing stress, anxiety or depression. One aspect of the method that could have been strengthened was the approach to quality assessment. Two independent researchers assessed study quality, but inter-rater reliability of scores was not formally calculated. Such formal calculations are, however not often reported in other reviews in this field. The limitations of this review are primarily due to the volume and quality of the studies included. Some studies failed to report effect sizes or statistics from which effect size could be calculated in the results. Several studies included more than one psychometric measure of an outcome variable. Weighted average effect sizes were calculated where psychometric properties of the multiple tools could not differentiate. However, this does not address the issue of multiple and unnecessary hypothesis tests being conducted in the original studies. Such practices are known to inflate type 1 error rate, a problem that, in combination with underpowered studies,

further confounds meta-analysis in this field of study. Furthermore, and despite the homogeneity of the outcome for mindfulness and depression, the relatively small number of studies analysed should be considered when interpreting the findings.

Future research should define clinically-meaningful effects for intervention studies using mindfulness. Future studies should limit the number of measurement tools and, where possible, choose single tools with good psychometric properties to assess variables of interest. Future studies should also simplify their designs to use the smallest number of samples of sufficient size to detect a clinically meaningful effect in mental health variables of interest. It would also be of value to explore if the benefits of a mindfulness-based intervention are maintained in the postnatal period, building on the few studies available in this area. In general, and in agreement with the recommendation of the previous meta-analyses on the topic, there is a need for more well-designed, controlled trials with trained mindfulness practitioners and established interventions performed on women without pre-existing stress, anxiety or depression. Moreover, a meta-analysis of controlled trials including only studies on women with pre-existing depression, stress and anxiety disorders is warranted given that different and clearer effects sizes appear when analyses separate studies on women with and without pre-existing conditions.

This study suggests that mindfulness-based interventions cause small reductions in depression and small increases in mindfulness in women without pre-existing disorders. If the cost of offering mindfulness-based interventions is not prohibitive, such interventions could be a useful addition to existing support for pregnant women without existing mental health issues and could serve to prevent or attenuate the development of depression symptoms during the perinatal period. There remains a need for robust controlled trials with clear hypotheses and parsimonious designs.

Author Contributions LC had the idea for the review. LC and MW performed the literature search, screening and risk of bias assessment. MW performed the data analysis. LC drafted the introduction and discussion. MW drafted the methods and results. Both authors revised and agreed the final version of the manuscript.

Declarations

Ethical approval Not applicable.

Conflict of interest The authors declare no conflict of interest.

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