Review article

The effect of complementary medicines and therapies on maternal anxiety and depression in pregnancy: A systematic review and meta-analysis

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A B S T R A C T

Background: Depression and anxiety are common during the antenatal and postnatal period, and are known to have a significant impact on the woman and her unborn infant. Pregnant women state a preference for non-pharmacological treatment options, and use complementary medicines and therapies to manage these symptoms. We examined the effectiveness and safety of these modalities on depression and anxiety during pregnancy.

Methods: CENTRAL, EMBASE and PubMed databases were searched for randomised controlled trials comparing complementary therapies and medicines to a control, for pregnant women with depression or anxiety. The primary outcome measure was antenatal depression or anxiety.

Results: Twenty randomised controlled trials containing 1092 women were included in the review. We found some evidence of reduced antenatal depression from three modalities. Acupuncture reduced the number of women diagnosed with antenatal depression (RR 1.68, 95% CI 1.06–2.66, 1 trial). Massage reduced the severity of antenatal depression in one trial of 149 women (SMD −0.73, 95%CI −1.07–−0.39). One small trial of bright light therapy found reduced antenatal depression (RR 4.80, 95% CI −8.39–−1.21, 27 women). There was no evidence of a reduction in depression and anxiety from relaxation, yoga, mindfulness and fish oils. Overall the risk of bias was high or unclear for the majority of studies.

Limitations: There are few high quality randomised controlled trials of complementary medicines and therapies examining the effect on anxiety and depression.

Conclusion: Acupuncture, bright light therapy, and massage may reduce antenatal depression. There is a need for high quality and larger studies that include postnatal follow up and maternal and neonatal outcomes.

1. Background

Depression and anxiety in pregnancy frequently co-exist (Lee et al., 2007), and are common conditions experienced by pregnant women across countries. Up to 13% of women will experience major depression during pregnancy, with increasing prevalence up to around 22% in the first twelve months postpartum (Wisner et al., 2013). Postnatal depression (PND) is one of the most common forms of maternal morbidity following childbirth, and can lead to a chronic or recurring depression throughout the woman's life (Goodman, 2004). The incidence of PND peaks at around four to 12 weeks postpartum, and for 50% of women it may last for six months.

The prevalence of self-reported anxiety symptoms fluctuates across pregnancy from approximately 18% in the first trimester to 25% in the third trimester (Dennis et al., 2017). The prevalence of anxiety disorders in the year following birth is estimated to be 20% (Fairbrother et al., 2015) with high rates of comorbid depression and anxiety at this time.

Whether antenatal symptoms are mild, moderate or severe, depression and anxiety are known to have a significant impact on all aspects of the woman's life including her unborn baby and her family (Eastwood et al., 2012). Depression and anxiety is associated with poor maternal self-care behaviours and may also influence the baby's health due to impaired maternal-infant interactions (Murray et al., 1996), negative perceptions of infant behaviour which may be linked to insecure maternal attachment, and this may cause delays in emotional development (Mayberry and Affonso, 1993), and social and interaction difficulties (Murray et al., 1990). If not treated, or poorly treated, depression and anxiety in pregnancy has been associated with prematurity and low birth weight (Eastwood et al., 2017), deficits in neurological development with impairments in physical and psychological development, language development and emotional and behavioural problems and decreased immune function with concomitant allergic reactions and an increased risk of depression in adulthood (Biaggi et al.,

2016). Older children in the family may also be affected due to a lack of parental involvement in play, and physical care (Murray et al., 1996). Furthermore, depression may impact on the women's relationship with her significant others during the time of adjusting to parenthood, resulting in an increased burden of care.

While medication is prescribed for severe depression (Austin et al., 2011) and indicated for moderate depression, the potential for harm to the fetus, and a reluctance to prescribe and to take medication results in low use throughout pregnancy (Sanz et al., 2001). Therefore, for first line treatment the use of psychosocial or psychological options is usually recommended (Austin et al., 2011). Women may experience difficulties with accessing these modalities in rural and remote areas, and if used, the benefits from counselling and psychotherapy may take 12 weeks to take effect (Yonkers et al., 2009). Personal preferences have a significant influence on treatment decision making, and pregnant women and mothers state a preference for non-pharmacological treatment options (Battle et al., 2013). Australian survey data indicate 48% of women (*n* = 623) have used a complementary medicine and therapies during pregnancy (Frawley et al., 2013).

Complementary alternative medicines and therapies known as complementary health approaches include a diverse range of modalities to promote, treat and maintain wellbeing and health (National Institute of Health, 2015). The term *complementary* refers to non-mainstream practices that are used with conventional medicine, whilst *alternative* refers to those approaches which are used in place of conventional medicine. The most common complementary health approaches. Firstly mind and body practices which include; yoga, chiropractic and osteopathic manipulation, meditation, and massage therapy, meditation, acupuncture, relaxation techniques (such as breathing exercises, guided imagery, and progressive muscle relaxation), tai chi, qi gong, healing touch, hypnotherapy, and movement therapies; and secondly, natural products that include herbs, probiotics, vitamins and minerals (National Institute of Health, 2015). Given the use of complementary health approaches by pregnant women to assist with depression and anxiety (Frawley et al., 2013), the prevalence of anxiety and depression in pregnancy and the risks of existing treatment, there is a need to undertake a review of evidence of these modalities to inform clinical research and practice. The aim of this review was to undertake a comprehensive and current assessment of the effectiveness and safety of complementary health modalities to treat depression and anxiety during pregnancy. Prior systematic reviews of complementary health interventions have included bright light therapy, yoga, acupuncture, nutraceuticals, massage and herbal remedies (Dennis and Dowswell, 2013a; van Ravesteyn et al., 2017). These reviews omitted evidence from other complementary health approaches including mindfulness and relaxation techniques. Our review includes a search up until 2018, and presents data from 20 trials including new publications and the inclusion of additional complementary health modalities used by women during pregnancy.

2. Methods

2.1. Study selection and eligibility

A priori we included parallel randomised, cross over or quasi randomised controlled trials comparing complementary health approaches for women diagnosed or screening positive for clinical anxiety and depression during the antenatal period with placebo/no treatment, medication, or any psychological intervention. We included studies of women with antenatal anxiety and or depression (variously defined), and aged 16 years or above. The primary outcome was antenatal depression or anxiety. Secondary outcomes included; perinatal stress, postpartum anxiety or depression, maternal infant attachment, maternal satisfaction, maternal and neonatal outcomes, and adverse events and side effects. The following characteristics of the studies were collected: country, year, inclusion criteria, description of the intervention

and control and outcome measures. Due to limited resources we excluded studies not published in English.

2.2. Literature review

We searched the following databases (CENTRAL, EMBASE, and PubMed) from inception to March 2018, conference proceedings, Goggle Scholar and reference lists of primary and reviewed articles. MESH terms and keywords are available (Supplementary file 1). We also searched the WHO clinical trials registry platform.

2.3. Quality assessment

Two independent researchers (CS, ZS) performed the study selection and two authors (CS, ZS, HD, VS, MG, ZS) undertook quality appraisal and data extraction for each study. The authors independently assessed the risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2011). Any disagreement was resolved through discussion by involving a third assessor. The quality of the evidence was assessed using the GRADE approach to assess the quality of the body of evidence (Schünemann et al., 2013). The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to asses**s t**he quality of the body of evidence for each outcome. The quality of evidence was assessed relating to the following outcomes for the main comparisons: omega-3 fatty acids mind body practice antenatal compared with controls for antenatal depression and anxiety.

2.4. Data synthesis

Dichotomous data were presented using relative risk ratios (RR). We used the mean difference (MD) if outcomes were measured in the same way between trials. We used the standardised mean difference (SMD) to combine trials that measured the same outcome, but used different methods. Statistical analyses for pooling intervention effects were performed using Review Manager 5.3, effects sizes with 95% confidence intervals (95% CI) are reported. We assessed statistical heterogeneity in each meta-analysis using I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if I^2 was greater than 30%, or there was a low *P* value (less than 0.10) in the Chi^2 test for heterogeneity. If we identified substantial heterogeneity (above 30%), provided sufficient data were available, a random effects model was used. If data could not be pooled we reported individual studies narratively. Trials with multiple arms were included. For example, two types of fish oils might be compared with another and with a placebo, we planned that data from both treatment arms would be combined into one group. For cross over trials we planned to analyse group data in the first phase only prior to groups crossing over into the second study phase.

3. Results

A total of 156 potential references were identified from database searches and other sources. After duplicates were removed, the studies were sequentially examined by title, abstract, and full text for eligibility (Fig. 1). Twenty trials containing 1092 women met the inclusion criteria for our review. Twenty studies were excluded. Thirteen studies were excluded due to women not meeting a clinical diagnosis of anxiety or depression (Field et al., 1999; Haakstad et al., 2016; Karol and von Baeyer, 1992; Makrides et al., 2010; Matvienko-Sikar and Dockray, 2017; Muthukrishnan et al., 2016; Newham et al., 2014; Nwebube et al., 2017; Satyapriya et al., 2013; Teixeira et al., 2005; Ventura et al., 2012; Vieten and Astin, 2008; Woolhouse et al., 2014), two studies examined anxiety associated with labour (Chang et al., 2002; Moghimi-Hanjani et al., 2015). Two studies did not meet the criteria of a RCT (Corral et al., 2000; Oren et al., 2002). Furthermore, one study was a
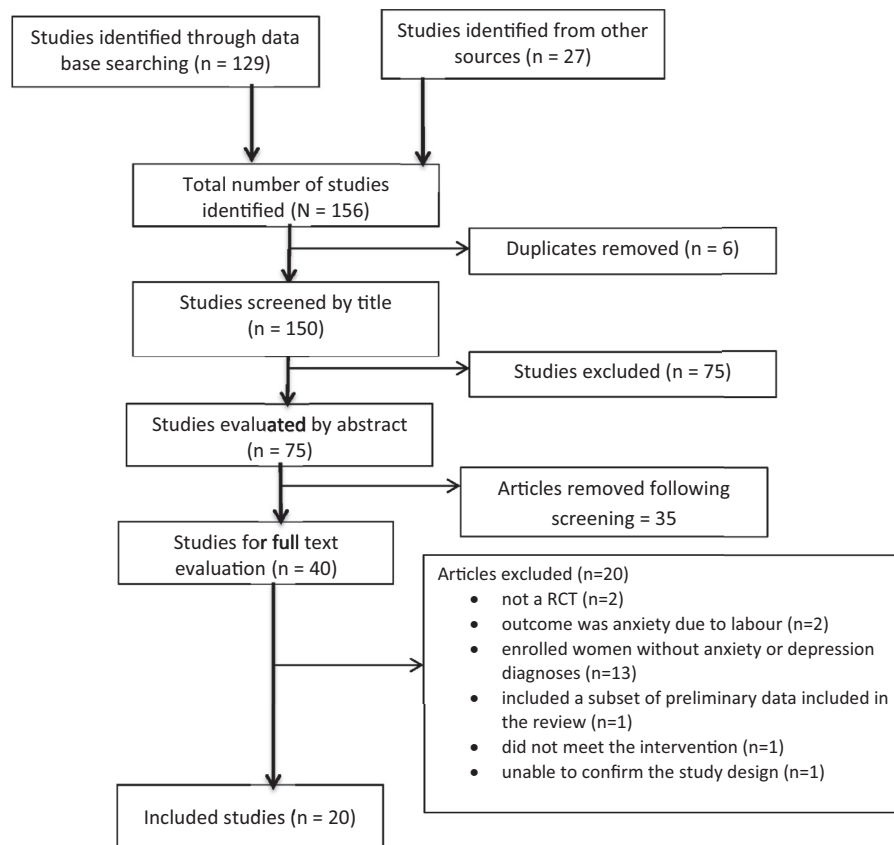
Fig. 1. PRISMA flow chart of included studies.

subset of preliminary data included in the review (Dimidjian and Goodman, 2011), one study did not meet the described intervention (Van Ravesteyn et al., 2018), and for one study we were unable to confirm the study design (Rahimi et al., 2015).

3.1. Description of studies

Characteristics of the studies are shown in Table 1. Fourteen studies were undertaken in the USA. Within Iran there were three studies, and single studies were undertaken in Australia, Taiwan and Switzerland. Sample sizes ranged from 10 to 200 women, and studies were reported between 2004 to 2016. The duration of the treatment interventions ranged from 4 weeks and from treatments onset to six weeks postnatal. Massage and yoga practices were administered for the longest periods ranging from 12 to 16 weeks, acupuncture trials were administered over eight weeks. Shorter interventions up to five weeks were administered for bright light therapy, and between five to eight weeks for relaxation and mindfulness interventions.

3.2. Intervention and control groups

Interventions were grouped into mind and body practices (relaxation training, yoga, mindfulness, bright light therapy, massage, acupuncture) and natural products. Details of the interventions are described in more detail in Table 1. Four trials used a natural product comprising of omega-3 fatty acids (Freeman et al., 2008; Mozurkewich et al., 2013; Rees et al., 2008; Su et al., 2008). Mind body practices comprised of; five yoga trials (Davis et al., 2015; Field et al., 2013a, b; Field et al., 2012; Uebelacker et al., 2016). One of these studies combined both yoga and tai chi (Field et al., 2013a). Mindfulness was reported in three trials (Dimidjian et al., 2016; Guardino et al., 2014; Shahtaheri et al., 2016). Shahtaheri included additional yoga postures

in the mindfulness intervention (Shahtaheri et al., 2016). Two trials evaluated massage (Field et al., 2008, 2009), two trials assessed acupuncture (Manber et al., 2004, 2010), and two trials examined relaxation techniques (Akbarzadeh et al., 2016; Bastani et al., 2005). Both relaxation interventions delivered a progressive muscle relaxation technique together with a breathing exercises, and Akbarzadeh provided instruction on anxiety and stress control (Akbarzadeh et al., 2016). Two trials used bright light therapy (Epperson et al., 2004; Wirz-Justice et al., 2011).

Control groups varied. Eight trials evaluating acupuncture, bright light or omega fatty acids used a placebo or sham control (Epperson et al., 2004; Freeman et al., 2008; Manber et al., 2004, 2010; Mozurkewich et al., 2013; Rees et al., 2008; Su et al., 2008; Wirz-Justice et al., 2011). Seven studies used treatment as usual (Akbarzadeh et al., 2016; Bastani et al., 2005; Davis et al., 2015; Dimidjian et al., 2016; Field et al., 2008, 2009; Shahtaheri et al., 2016). Two trials presented women with information (Guardino et al., 2014; Uebelacker et al., 2016), two trials used a time and attention control (Field et al., 2012, 2013b) and one trial used a wait list control (Field et al., 2013a).

3.3. Outcome measures

Fifteen trials reported on antenatal depression and eight trials reported on anxiety. Three trials reported on stress. Side effects or adverse events were reported in six (30%) trials. Satisfaction, an assessment of relationships and quality of life measures were reported in four trials.

3.4. Risk of bias assessment

Overall the study quality was low (Fig. 2). One study evaluating fish oils was at a low risk of bias on six of the seven domains. Five trials were assessed as low risk of bias with the randomisation sequence

Table 1
Characteristics of included studies.

First author/ year of publication	Country	Setting	Participants	Intervention	Control	Outcome measures
Akbarzadeh et al. (2016)	Iran	Single centre	126 primigravida pregnant women 18–35 years, meeting score for anxiety on the STAI.	Relaxation or maternal-fetal attachment training. Weekly intervention of 60–90 min over four weeks, with a focus on managing anxiety, stress, and muscle relaxation techniques and breathing exercises.	Treatment as usual	STAI
Bastani et al. (2005)	Iran	Multi-centre	110 primigravida pregnant women aged 18–30 years, meeting score for anxiety on the STAI.	Relaxation training, seven weekly sessions 90 min each. Use of progressive muscle relaxation and breathing techniques.	Treatment as usual	STAI Perceived stress scale
Davis et al. (2015)	USA	Single center	46 pregnant women meeting anxiety and depression thresholds on scales.	Yoga; 8 weekly sessions, each class lasting 75 min. Instruction based on Ashtanga Vinyasa system modified for pregnancy. Class included 15 min of breathing practice, gaze and movement, 20 min of standing postures, 20 min of seated postures, and 20 min of cool down and sitting. Participants received a video for home practice.	Treatment as usual	STAI EPDS
Dimidjian et al. (2016)	USA	Multi-centre	86 pregnant women meeting criteria for prior major depressive disorder using the SCID.	Mindfulness-based cognitive therapy 8 sessions held weekly for 2 h, designed for use in pregnancy and postpartum. Protocol emphasised informal mindfulness practices, and loving kindness meditation. DVD provided for home practice.	Treatment as usual	EPDS, SCID, Longitudinal interval Client satisfaction
Epperson et al. (2004)	USA	Single centre	10 pregnant women screened for depression using the SCID and meeting a score of ≥20 on SIGH-AD.	Bright light therapy: daily treatment for 5 weeks using 2.7 kg light box providing 7000 lx ultraviolet screened diffuse broad banned fluorescent illumination at a distance of 33 cm. Began treatment within 10 min of rising and continued for 60 min.	Same procedure using 500 lx	SIGH-AD
Field et al. (2008)	USA	Single centre	47 pregnant women meeting depression criteria using the SCID.	Massage, twice weekly from 20 weeks gestation until the end of their pregnancy.	Treatment as usual	CES-D, STAI, relationship questionnaire,
Field et al. (2012)	USA	Single centre	84 pregnant women meeting depression criteria using the SCID.	Yoga, 20-min sessions once per week for 12 weeks.	Massage and a second control of treatment as usual	CES-D, STAI, relationship questionnaire, birthweight, gestational age at delivery
Field et al. (2013a)	USA	Single centre	92 pregnant women meeting depression criteria using the SCID.	Tai chi + yoga stretches, 20-min sessions once per week for 12 weeks.	Waitlist control	STAI CES-D
Field et al. (2013b)	USA	Single centre	92 women at 22 weeks gestation meeting depression criteria using the SCID.	Yoga, 20-min sessions once per week for 12 weeks.	Social support	POMS, EPDS, CES-D, STAI
Field et al. (2009)	USA	Single centre	200 pregnant women between 16 and 20 weeks gestation meeting depression criteria using the SCID.	Massage, 12 weeks of twice per week massage therapy by their significant other	Treatment as usual	STAI CES-D
Freeman et al. (2008)	USA	Single centre	59 pregnant (12–32 weeks) and postpartum women (within 6 months) with major depressive disorder major depressive verified by a SCID, (and a score >8 on EPDS.	Omega-3 fatty acids, EPA and DHA, 4 capsules per day for a total daily dose of 1.9 g of omega-3 that included 1.1 g of eicosapentaenoic acid (EPA) and 0.8 g of docosahexaenoic administered over 8 weeks, plus supportive psychotherapy, 6 30 min sessions.	4 placebo capsules per day containing corn oil with 1% fish oil + supportive psychotherapy	EPDS, HAMD; maternal self-reported side effects
Guardino et al. (2014)	USA	Single centre	47 pregnant women (10–25 weeks) with scores above 34 on the PSS or 11 on the PSA.	Mindfulness weekly training over 6 weeks, trained in the practice of mindfulness meditation (5–17 min practice), lectures about mindfulness practices and discussions, discussion. DVD for home practice (daily meditations ranging from 5 to 17 min).	Presented with a copy of the book "You and Your Baby"	STAI PSS PAS
Manber et al. (2004)	USA	Single centre	61 pregnant women (11–24 weeks) with major depressive disorder diagnosed using SCID, and >14 score on HAMD.	Acupuncture specifically targeted depression symptoms, over 8 weeks and 12 sessions (25–30 min).	Control acupuncture or massage	HAMD, BDI

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Table 1 (*continued*)

First author/ year of publication	Country	Setting	Participants	Intervention	Control	Outcome measures
Manber et al. (2010)	USA	Single centre	150 pregnant women 12–30 weeks, with major depressive disorder diagnosed using SCID, and >14 score on HAMD.	Acupuncture for depressive symptoms according to TCM pattern differentiation, 12 sessions for 25 min each, two times per week for the first 4 weeks and weekly for 4 more weeks.	Control acupuncture or massage	HAMD BDI Side effects
Mozurkewich et al. (2013)	USA	Single centre	126 pregnant women, 12–20 weeks, meeting EPDS score 9–19.	Omega-3 fatty acids, (1) EPA-rich fish oil supplementation (1060 mg EPA plus 274 mg DHA); (2) DHA-rich fish oil supplement (900 mg DHA plus 180 mg EPA) contained DHA and EPA in an approximate 4:1 ratio (900 mg DHA plus 180 mg EPA). EPA group received 2 large EPA-rich fish oil capsules and 4 small placebo capsules identical to DHA-rich fish oil capsules. DHA group received 2 large placebo capsules identical to EPA-rich fish oil capsules, administered until 6 weeks postpartum.	Soy oil placebo	MINI BDI Medication use Maternal and neonatal outcomes
Rees et al. (2008)	Australia	Single centre	26 women in the third trimester or up to 6 months post partum, depression diagnosed using SCID.	Omega-3 fatty acids, fish oil divided doses every 2 weeks for 6 weeks, (27.3% DHA, 6.9% EPA (total omega-3 fatty acids_ 35.6%) and 3.3% omega-6 fatty acids).	Matched placebo using Sunola oil	EPDS, HAMD, MADRS Side effects
SShahtaheri et al. (2016)	Iran	Single centre	30 pregnant women with depression and stress screened using HAMD.	Mindfulness and conscious yoga training in 8 weekly sessions.	Treatment as usual	PSS HAMD SF36
Su et al. (2008)	Taiwan	Single centre	36 pregnant women 16–32 weeks gestation with major depression, screened using the EPDS and HAMD.	Omega-3 fatty acid, daily dose of 2.2 g of EPA and 1.2 g of DHA for 8 weeks.	Placebo treatment (olive oil ethyl esters)	HRSD, EPDS, BDI
Uebelacker et al. (2016)	USA	Single centre	20 pregnant women, 12–26 weeks gestation with depression screened using the SCID and QIDS score >7 and <20.	Yoga: 9 weekly sessions for 75 min. Each class included breathwork, meditation, standing poses, floor poses, final resting pose, and homework discussion.	Health education workshop on mother baby wellness	EPDS QIDS CSQ-8 Adverse events
Wirz-Justice et al. (2011)	Switzerland	Single centre	27 pregnant women 4–32 weeks gestation, depression diagnosed using the SCID and HAMD score >20.	Bright light therapy: white light 7000 lx (60 min/day for 5 weeks).	Red light with 70 lx for 60 min/day	HAMD SIGH-AD MADRS BDI Side effects

BDI: Beck Depression Inventory, CES-D: Centre for Epidemiological Studies Depression Scale, CSQ-8: Client Satisfaction Questionnare-8, EPDS: Edinburgh perinatal depression scale, HAMD: Hamilton Depression Rating Scale, MADRS: Montgomery Asberg Depression Rating Scale, MINI: Mini-International Neuropsychiatric Interview, PSA: pregnancy specific anxiety scale, PSS: perceived stress scale, POMS: Profile of Mood States, QIDS: Quick Inventory of Depressive Symptomatology, SCID: Structured Clinical Inventory, SIGH-AD: Structural Interview Guide for the Hamilton Depression and Anxiety Scales, STAI: State Trait Anxiety Inventory.

Fig. 2. Risk of bias summary.

adequately concealed. Seventeen trials were assessed as an unclear risk of bias due to insufficient reporting.

Three trials were assessed at a low risk of bias for both performance and detection bias. Performance bias was assessed at low risk in eight trials with participants and clinicians were blind to study group. Seven trials were at a high risk of bias due to a lack of blinding of women and/ or their clinicians. The risk of bias was unclear in five trials. Detection bias was low risk in eight trials, high risk in two trials, and unclear in 11 trials.

Attrition bias was at a low risk of bias in 12 trials. Loss of participants to follow-up was at a high risk of bias (at least 20%) in four trials. The risk of bias was unclear in four trials. One trial was assessed at a low risk of selective reporting. All other studies were assessed as unclear. Other sources of bias were assessed at low risk in 11 trials. One trial was assessed at high risk. All other trials were assessed as unclear risk of bias.

3.5. Effects of the interventions

3.5.1. Natural products: omega-3 fatty acids

Three trials and 172 women are included in the meta-analysis (Freeman et al., 2008; Mozurkewich et al., 2013; Su et al., 2008). There was no evidence of a difference between fish oils and placebo with reducing the severity of antenatal depression (SMD −0.12, 95% CI −0.76 to 0.52, 172 women, 3 trials, Fig. 3), and the risk of women with an antenatal major depressive disorder (RR 0.88, 95% CI 0.30–2.54, 23 women, 1 trial) (Uebelacker et al., 2016). There was no evidence of a difference between groups in the severity of postnatal depression (MD 0.25, 95% CI −1.93–2.43, 118 women, 1 trial), the risk of women with a postnatal major depressive disorder (RR 0.83, 95% CI 0.23–3.03, 20 women, 1 trial) (Mozurkewich et al., 2013), the risk of remission (RR 2.12, 95% CI 0.51–8.84, 24 women 1 trial) (Su et al., 2008), and use of medication (RR 0.98, 95% CI 0.41–2.35, 43 women, 1 trial (Mozurkewich et al., 2013). Side effects were reported by 27 women and included nausea, diarrhoea, insomnia, burping, heartburn/reflux and unpleasant breath, these did not differ between groups (RR 0.94, 95% CI 0.55–1.59, 57 women, 2 trials). Maternal and neonatal outcomes were reported in one trial (Mozurkewich et al., 2013), and an increase in gestational age at delivery was found for the fish oil group (40.4 weeks) compared with control (39.1 weeks). There was no evidence of a difference between groups for the outcomes, mode of delivery, hypertension, pre-eclampsia and induction of labour. The trial by Rees recruited women from both the antenatal and postnatal period, and data were not reported in a form to be included in the meta-analysis (Rees et al., 2008). This trial found no significant difference in depression scores between those receiving fish oil or placebo.

3.6. Mind and body practices

3.6.1. Yoga

Yoga involves a focus on the mind and its functions, and includes physical postures and movement; breathing exercises; relaxation; and mindfulness and meditation (de Manincor et al., 2015). There was no evidence of a difference between yoga and control for a reduction in antenatal depression (SMD −0.21, 95% CI −0.48–0.06, 211 women, 4 trials, Fig. 4), and postnatal depression (MD −0.60, 95% CI −4.28–3.08, 79 women, 1 trial), and antenatal anxiety (MD −1.60, 95% CI −5.67–2.46, 193 women, 3 trials, Fig. 3). One small trial found an increase in client satisfaction for women receiving yoga (MD 7.23, 95% CI 1.12–13.34, 20 women, *p* = 0.02) (Uebelacker et al., 2016). This trial also reported no adverse events for women receiving yoga. Data was not in a form that could be included in the analysis for one other study (Field et al., 2012). This study found reduced depression and anxiety, and increased birthweight and gestational age at delivery for babies born to women practicing yoga.

computer generated, and two studies were at a low risk of bias on both randomisation domains relating to selection bias. In 14 trials there was an unclear risk of bias due to insufficient reporting. One study was assessed at a high risk of bias due to selecting participants by convenience. Two trials were assessed at low risk with randomisation
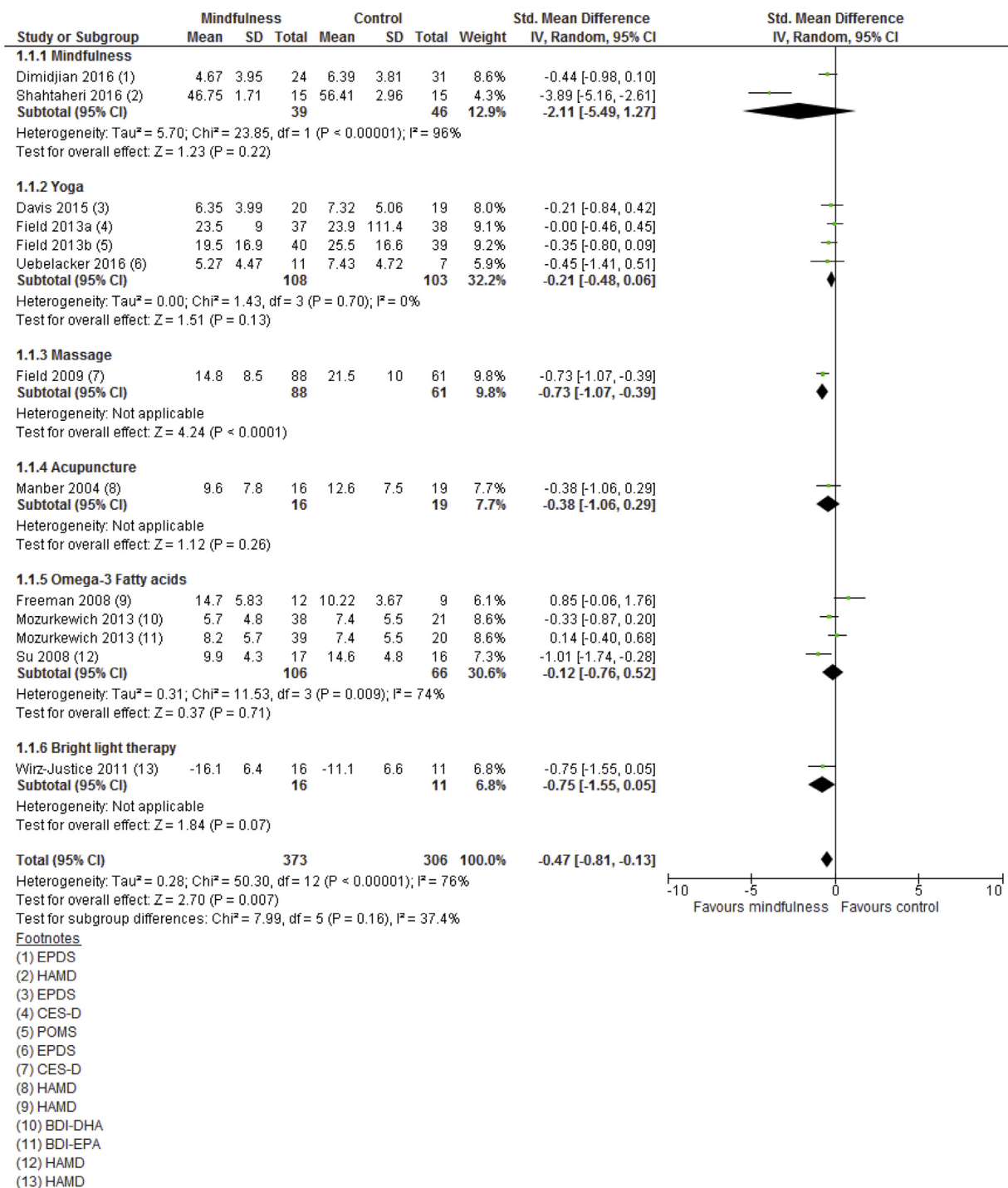
Fig. 3. Complementary health approaches vs control: antenatal depression.

3.7. Mindfulness

Mindfulness involves a practice of developing awareness and acceptance of thoughts, emotions and body sensations. Three trials, and 156 women were included in the meta-analysis. There was no evidence of a reduction in the severity of antenatal depression (SMD -2.11, 95% CI -5.49–1.27, 85 women, 2 trials) between groups. There was significant heterogeneity $I^2 = 96\%$ and a random effects model was applied. This heterogeneity may have been explained by the use of different instruments to assess depression and the lower levels of clinical depression in one trial (Dimidjian et al., 2016). One trial reported on postnatal depression (Dimidjian et al., 2016) and found no evidence of

a reduction in the severity of depression (MD -1.65, 95% CI 4.57–1.27, 52 women). This study found a reduced rate of relapse in the mindfulness group (RR 0.13, 95% CI 0.02–0.96, 48 women). One trial reported on antenatal anxiety and found no evidence of a difference between groups (MD 2.12, 95% CI -3.05–7.27, 47 women) (Guardino et al., 2014). Two trials found no evidence of reduced antenatal stress between groups (MD -1.20, 95% CI -5.90–3.50, 77 women, $I^2 = 78\%$, a random effects model was applied). There was no evidence of a reduction in medication use (RR 0.57, 95% CI 0.24–1.40, 78 women, one trial). Women in the mindfulness group reported greater satisfaction from the intervention (MD 7.41, 95% CI 5.45–9.37, 79 women). No adverse events were reported.

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.2.1 Mindfulness								
Guardino 2014 (1)	39.47	6.27	24	37.35	11	23	13.6%	2.12 [-3.03, 7.27]
Subtotal (95% CI)			24			23	13.6%	2.12 [-3.03, 7.27]
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
1.2.2 Yoga								
Davis 2015 (2)	38.35	9.87	20	40.37	10.91	19	12.5%	-2.02 [-8.56, 4.52]
Field 2013a (3)	46.1	7.9	37	44.3	11.4	38	14.1%	1.80 [-2.63, 6.23]
Field 2013b (4)	46.6	8.7	40	51	8.7	39	14.4%	-4.40 [-8.24, -0.56]
Subtotal (95% CI)			97			96	41.0%	-1.60 [-5.67, 2.46]
Heterogeneity: Tau² = 6.84; Chi² = 4.31, df = 2 (P = 0.12); I² = 54%								
Test for overall effect: Z = 0.77 (P = 0.44)								
1.2.3 Massage								
Field 2009 (5)	39.2	10.6	88	41	9.4	61	14.8%	-1.80 [-5.04, 1.44]
Subtotal (95% CI)			88			61	14.8%	-1.80 [-5.04, 1.44]
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.09 (P = 0.28)								
1.2.4 Relaxation								
Akbarzadeh 2016 (6)	39.95	3.9	42	42.01	3.6	42	15.5%	-2.06 [-3.67, -0.45]
Bastani 2005 (7)	22.71	7.38	52	38.5	5.73	52	15.1%	-15.79 [-18.33, -13.25]
Subtotal (95% CI)			94			94	30.6%	-8.89 [-22.34, 4.57]
Heterogeneity: Tau² = 93.08; Chi² = 80.24, df = 1 (P < 0.00001); I² = 99%								
Test for overall effect: Z = 1.29 (P = 0.20)								
Total (95% CI)			303			274	100.0%	-3.32 [-8.42, 1.77]
Heterogeneity: Tau² = 42.92; Chi² = 102.12, df = 6 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 1.28 (P = 0.20)								
Test for subgroup differences: Chi² = 3.02, df = 3 (P = 0.39), I² = 0.7%								

Footnotes
(1) STAI
(2) STAI
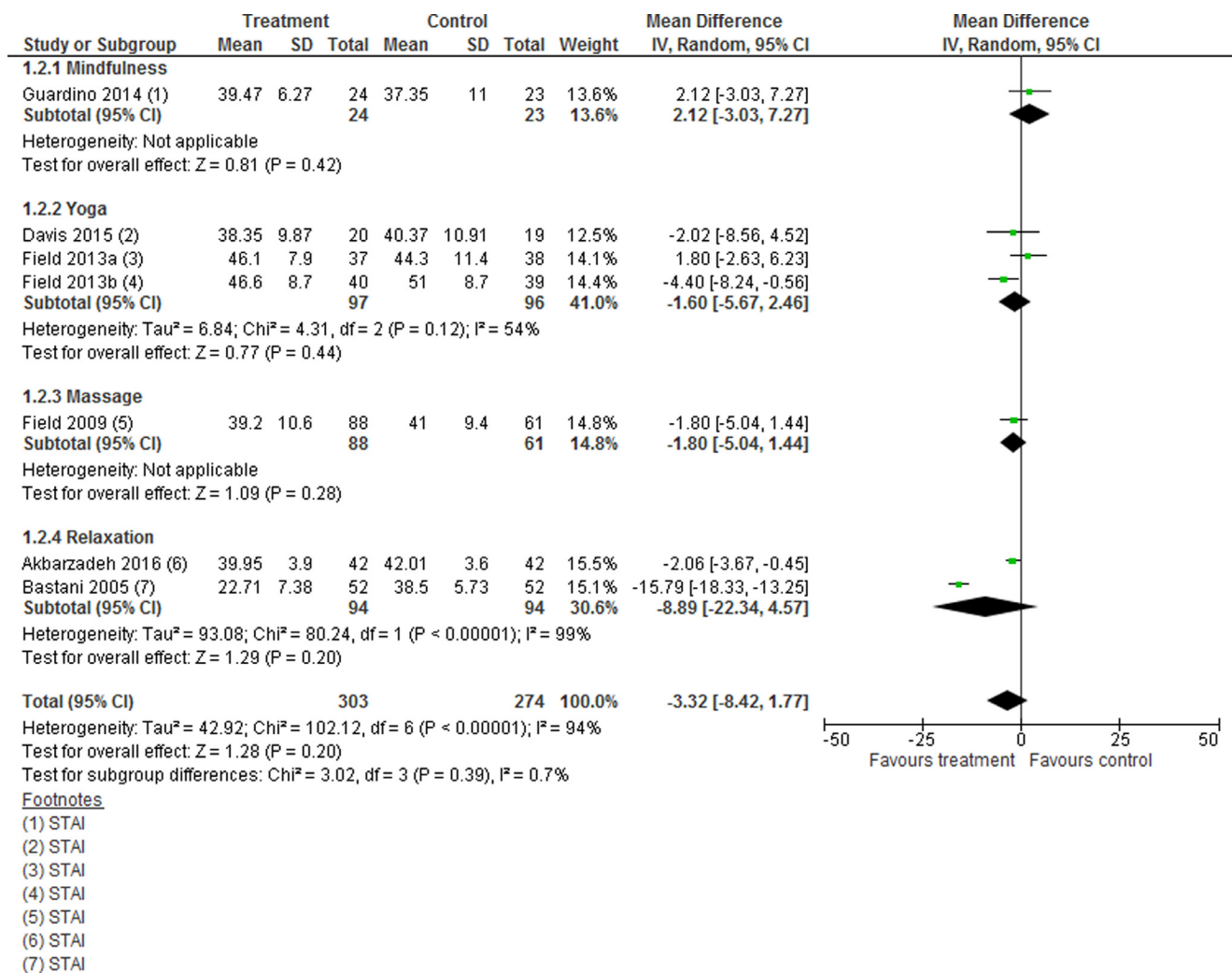(3) STAI
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(7) STAI

Fig. 4. Complementary health approaches antenatal anxiety.

3.8. Massage

Massage involves manipulation of the body's soft tissues and is commonly used to help relax tense muscles and to soothe and calm the individual (Vickers and Zollman, 1999). Antenatal depression was reduced following massage compared to the control in one trial of 149 women (SMD −0.73, 95% CI −1.07−−0.39, p > 0.001), there was no evidence of a difference in antenatal anxiety between groups (MD −1.80, 95%CI −5.04–1.44) (Field et al., 2009). Data from one study did not report the denominators and we were unable to include this study in the meta-analysis (Field et al., 2008). The authors reported that women receiving massage compared to the control experienced decreased depression (t = 5.06, p > 0.001), and anxiety (t = 5.81, p > 0.001).

3.9. Acupuncture

Acupuncture involves the stimulation of acupuncture points through the insertion of needles and applying stimulation of the needles manually or through a small current (electro-acupuncture). Two trials and 189 women are included in the analysis. A pilot RCT compared manual acupuncture with two control groups (Manber et al., 2004). There was no evidence of a difference between acupuncture and control for the number of women diagnosed with depression post treatment (RR 0.48, 95% CI 0.11–2.13, 35 women, 1 trial), postnatal depression (RR 0.64, 95% CI 0.06–6.39), or the severity of depression (MD −3.00,

95% CI −8.10–2.10).

A subsequent larger RCT of 150 women (Manber et al., 2010) found a significant response from manual acupuncture compared with the control in reducing the number of women with depression (RR 1.68, 95% CI 1.06–2.66). Acupuncture-related side effects were reported by 43 participants including some transient pain, and minor bleeding from the site of needle insertion, (four in the group receiving massage, 19 in the group receiving acupuncture control, and 20 in the acupuncture group). Significantly fewer participants reported any side effects in the group receiving massage than in the two acupuncture groups (p = 0.01).

3.10. Relaxation

Relaxation techniques aim to produce the body's natural relaxation response, characterised by slower breathing, lower blood pressure, and a feeling of increased well-being. Two trials including 188 women were included in the meta-analysis (Akbarzadeh et al., 2016; Bastani et al., 2005). There was significant heterogeneity and a random effects model was applied. There was no evidence of reduced anxiety between groups (MD −8.89, 95% CI −22.34–4.57, 188 women, 2 trials). One trial reported reduced stress in the relaxation group (MD −13.08, 95% CI −15.29−−10.87, 104 women, p = >0.001) (Bastani et al., 2005). No side effects were reported.

Table 2
CAM health approaches compared to placebo for anxiety and depression during pregnancy.

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty of the evidence GRADE	CAM health approaches n	Control n	Absolute (95% CI)
Antenatal depression								
2	very serious[a]	very serious[b,c]	serious	serious[d]	VERY LOW	Mindfulness n = 39	46	SMD **2.11 lower** (5.49 lower–1.27 higher)
4	serious[e]	not serious	serious	serious[d]	LOW	Yoga n = 108	103	SMD **0.21 lower** (0.48 lower–0.06 higher)
1	very serious[e]	not serious	serious	not serious	LOW	Massage n = 88	61	SMD **0.73 lower** (1.07 lower–0.39 lower)
1	serious[1,f]	not serious	not serious	serious[d]	MODERATE	Acupuncture n = 16	19	SMD **0.38 lower** (1.06 lower–0.29 higher)
3	serious[g]	very serious	serious	serious[b]	LOW	Omega-3 fatty acids n = 106	66	SMD **0.12 lower** (0.76 lower–0.52 higher)
1	serious[e]	not serious	not serious	serious[d]	MODERATE	Bright light therapy n = 16	11	SMD **0.75 lower** (1.55 lower–0.05 higher)
Antenatal anxiety								
1	very serious	serious[b]	not serious	very serious	VERY LOW	Mindfulness n = 24	23	MD **2.12 higher** (3.03 lower–7.27 higher)
3	serious[h]	serious	not serious	serious[b,d]	LOW	Yoga n = 97	96	MD **1.6 lower** (5.67 lower–2.46 higher)
1	serious[e]	not serious	not serious	serious[b,d]	MODERATE	Massage n = 88	61	MD **1.8 lower** (5.04 lower–1.44 higher)
2	very serious[h]	very serious[c]	not serious	serious[c,d]	VERY LOW	Relaxation n = 94	94	MD **8.89 lower** (22.34 lower–4.57 higher)

GRADE Working Group grades of evidence
    High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
    Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
    Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
    Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

CI: Confidence interval; **SMD:** Standardised mean difference; **MD:** Mean difference
Explanations
  [a] High risk of bias due to attrition and selection bias: downgraded 1 level.
  [b] Confidence intervals cross line of no effect: downgraded 1 level.
  [c] High statistical heterogeneity: downgraded 1 level.
  [d] Small studies: downgraded 1 level.
  [e] Attrition bias: downgraded 1 level.
  [f] Unclear risk of bias on 5 domains: downgraded 1 level.
  [g] Unclear risk of bias and high risk of attrition bias: downgraded 2 levels.
  [h] Unclear risk of bias and lack of blinding: downgraded 2 levels.

3.11. Bright light therapy

This therapy involves exposure to artificial light. One trial of 27 women was included in the meta-analysis. A reduction in depression with a mean change in the depression post-treatment score was found for the bright light therapy group (RR 4.80, 95% CI −8.39–−1.21, 27 women) (Wirz-Justice et al., 2011). There was no difference in a reduction in depression scores from baseline between groups (RR 1.79, 95% CI 0.90–3.56, 27 women). The Wirz-Justice trial reported no clinically meaningful side effects, and all women gave birth with no complications (Wirz-Justice et al., 2011). Data from Epperson trial could not be included in the meta analysis, however no difference in depression was found between groups (Epperson et al., 2004).

Overall the quality of the evidence for the interventions was graded from very low to moderate (Table 2) with trials of massage, bright light therapy and acupuncture rated as moderate, and relaxation and mindfulness rated as very low.

4. Discussion

This review included 20 clinical trials containing 1092 women with anxiety or depression during pregnancy. Seven complementary health modalities were included, studies were conducted in five countries, and varied in their methodological quality. There was some evidence from four CM approaches of a potential benefit. Acupuncture reduced the number of women with depression during the antenatal period, but not in the postnatal period, and did not reduce the severity of symptoms. Although animal and human studies indicate potential biological responses from acupuncture to treat depression including regulation of neural, endocrine, and immunological pathways (Liu et al., 2009; Stewart et al., 2009), the primary mechanisms in relation to perinatal depression remain unclear. Trials evaluating massage found evidence of reduced antenatal depression but not anxiety. Bright light therapy was associated with a change in antenatal depression. This therapy has been shown to synchronize the biological clock and to normalise circadian rhythm (Lam and Levitan, 2000). Among pregnant women who may experience disturbed sleep benefits from light therapy have been shown

to mediate the effects on depression by supporting enhanced sleep patterns and rhythms of melatonin and cortisol (Lieverse et al., 2011). Relaxation therapy was found to reduce antenatal stress but there was no evidence of reduced antenatal anxiety. There was no evidence of a benefit from yoga with reducing antenatal anxiety and depression, although women receiving yoga reported greater satisfaction. Trials evaluating mindfulness found no evidence of reduced depression, anxiety, stress or use of medication, although there was a small benefit of reduced relapse of depression during the postnatal period. Emotional regulation strategies of rumination for example has been proposed as one mechanism by which mindfulness may influence anxiety and depression (McLaughlin and Nolen-Hoeksema, 2011). One study demonstrated an increase in satisfaction from mindfulness intervention. Trials evaluating fish oils found no evidence of a difference of reduced depression or anxiety between groups. Acupuncture treatment related side effects were found but were minor. No side effects were associated with yoga, relaxation or mindfulness. The quality of the evidence was downgraded for a number of reasons, notably, insufficient reporting preventing an assessment of a risk of bias and attrition of women from individual studies.

Anxiety and depression frequently co-exist, (Lee et al., 2007) however the effects from complementary health approaches suggest greater beneficial effects on depression than anxiety. These findings may be influenced by how the underlying mechanism of the treatment modality may directly influence the development of anxiety and depression or buffer the effect of risk factors. Early phase mechanistic studies of complementary health approaches are not common, and it is possible that the doses of the intervention delivered in a clinical trial may be sub-optimal when delivered in a clinical trial setting. In our review there were too few studies of individual modalities to examine dosing characteristics in any sub group analysis. There was significant variation in the duration of the interventions examined. Longer periods of evaluation were noted for yoga practices and massage. Furthermore, as highlighted by Blackmore et al, the course of pregnancy related worry and anxiety over the perinatal period may have a trajectory (Blackmore et al., 2016) that differs to the constructs measured on a generalised anxiety measures such as the State Trait Anxiety Inventory.

A single study was assessed at low risk, suggesting that complementary health approaches overall have not been subjected to rigorous evaluation. Generally, the quality of trial reporting was poor which made an assessment of the risk of bias difficult, particularly in relation to randomisation. The quality of the evidence of these studies is limited by the small sample sizes, and some studies were assessed at high risk of bias in relation to blinding (performance and detection bias). Attrition bias was low in the majority of the trials. There was evidence of some study heterogeneity, this may be explained by clinical and statistical heterogeneity relating to the inclusion of women with differing severity of symptoms, the use of different outcome measures, and design of the interventions used. The small number of studies within each comparison and lack of high-quality trials indicates there is currently insufficient evidence of a consistent treatment effect from the modalities included in the review. The quality of the evidence ranged from very low to moderate and was frequently downgraded due to small sample sizes, heterogeneity and the high risk of bias. Overall few studies included a broad range of relevant secondary endpoints relevant to maternal and neonatal wellbeing, and although these interventions would be described as low risk, few studies included an assessment of side effects and adverse events. There was variation in how these treatment interventions were practised, the external validity of the treatment protocols is unclear and whether the findings are generalisable to clinical practice or self-practice within the community.

We attempted to minimise bias in this review by involving two authors with determining the eligibility of studies, carrying out data extraction and assessing the risk of bias. There are some limitations to our study. It is possible that some literature on complementary medicines and therapies may not be published in peer-reviewed journals that are not indexed to the main databases, or are published in the grey literature and consequently may have been missed in the search. We did not search for publications in non-English databases. For some complementary health approaches language bias has been found to be present when non-English studies are excluded (Pham et al., 2005). We cannot exclude the possibility that some other studies have been missed although we have searched the grey literature extensively. We included women with a clinical diagnosis or positive screening of depression and anxiety however there was some variability in how the diagnosis was made and this may contribute to the clinical heterogeneity found in the meta analysis. We excluded women less than 16 years and the results are not generalizable to this age group.

Our findings are similar to other published systematic reviews that have examined the evidence for complementary health and other non-pharmacological interventions as adjunctive treatments for anxiety and depression during the perinatal period (Dennis and Dowswell, 2013b; Dhillion et al., 2017; Evans et al., 2018; van Ravesteyn et al., 2017). These reviews identified promising interventions that have not been subject to rigorous evaluation. Our finding suggests some evidence that bright light therapy may have a role with treating depression, this differs to the finding from review reported by (van Ravesteyn et al., 2017) and is likely explained by fewer eligible studies included (RCT and crossover designs) and excluding open label designs. In a review of mindfulness (Dhillion et al., 2017), a benefit was found from this intervention on anxiety and depression. This differs to our finding, but is explained by our exclusion of women without a clinical diagnosis of depression or anxiety on joining the trial. Our review focuses solely on complementary health approaches that are used outside of conventional health services, the scope of the review did not include psychological interventions. This review provides updated evidence of additional studies evaluating complementary health modalities used by women in pregnancy and not previously included in these systematic reviews.

There is a need for further well designed randomised controlled trials. Acupuncture, bright light therapy, massage and mindfulness should be subject to future rigorous evaluation. There is a need for larger studies that include follow up into the postnatal period of at least three months. Interventions being tested in clinical trials should be co-designed between researchers and clinicians to ensure interventions are evidence-informed and informed by best clinical practice. In addition, there is a need for studies to be informed by early phase research to determine optimal treatment dosing regimens, and studies to include maternal, neonatal outcomes and safety outcomes, and appropriate pregnancy related anxiety outcome measures. There are methodological and study design challenges for complex complementary health interventions. Many women may have strong treatment preferences and randomisation can be challenging, alternative approaches such as the Zelen design or cluster designs could be explored. Frequently the active components of an intervention are unclear, and use of appropriate sham/placebo controls may be problematic. Use of pragmatic study designs and comparison to comparator groups or active controls could be considered.

5. Conclusion

There is preliminary very low to moderate quality evidence from complementary health approaches to reduce anxiety and depression. However few well designed RCTs have been conducted evaluating complementary health modalities on perinatal mental health during pregnancy and in the postnatal period. These interventions are accessible to women in the community and further studies are needed to assist women and their clinicians to make evidence-based, informed decisions about the management of anxiety and depression during pregnancy and the postnatal period.

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Author statement

Author contributions

CS deigned the study.
ZS undertook the search of the literature.
CS and ZS screened all studies.
All authors contributed to data extraction, read and commented on the draft and approved the final version of the paper.

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