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Systematic review and meta-analysis of non-pharmacological interventions to reduce the symptoms of mild to moderate anxiety in pregnant women

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Conflict of interest
No conflict of interest has been declared by the authors.

Abstract

Aim: To assess the effectiveness of non-pharmacological interventions for pregnant women with symptoms of mild to moderate anxiety.

Background: Many pregnant women experience mild to moderate symptoms of anxiety and could benefit from additional support. Non-pharmacological interventions have been suggested for use during pregnancy.

Design: A systematic review of randomised controlled trials.

Data sources: Randomised controlled trials published since 1990, identified from electronic databases: Medline; CINAHL; Maternity and Infant Care; PsycINFO; Cochrane Database of Systematic Reviews; CENTRAL; EMBASE; Centre for Reviews and Dissemination; Social Sciences Citation Index; ASSIA; HTA Library; Joanna Briggs Institute Evidence-Based Practice database; Allied and Complementary Medicine.

Review methods: Conducted according to the Centre for Reviews and Dissemination procedure. Papers were screened (N=5,222), assessed for eligibility (N=57) and selected for inclusion (N=25). The Cochrane Collaboration's tool for assessing risk of bias was used. Papers were assessed for clinical and statistical heterogeneity and considered for meta-analysis. Descriptive analysis of the data was conducted.

Results: Psychological, mind-body, educational and supportive interventions were delivered individually and to groups of pregnant women over single or multiple sessions. The State-Trait Anxiety Inventory was the most commonly used anxiety measure. In 60% of studies there were fewer than 40 participants. Meta-analysis of three studies indicated no observed beneficial effect in the reduction of anxiety.

Conclusion: There was insufficient evidence from which to draw overall conclusions regarding the benefit of interventions. Results were predominantly based on small samples.

Many papers provided an inadequate description of methods which prevented a full assessment of methodological quality.

Keywords

anxiety, pregnancy, antepartum, systematic reviews and meta-analyses, nurses, nursing, midwifery

Summary	
Why is this review needed?	• The prevalence of anxiety disorders in pregnancy is reported between 10-15%. Severe symptoms of anxiety are associated with negative health outcomes for women and infants. • Interventions to reduce symptoms of anxiety in pregnancy have the potential to improve health outcomes by developing coping strategies and preventing an escalation of symptoms. • Research is required to confirm the effectiveness of interventions to improve symptoms of mild to moderate anxiety in pregnancy.
What are the key findings?	• A variety of interventions were evaluated which included: psychological, educational, supportive interventions and mind-body interventions. • Most studies had small sample sizes and inadequate procedural reporting.

	• The review provides a discussion of the intervention components in the included studies: duration, recruitment, eligibility criteria and attrition.
How should the findings be used to influence policy / practice / research / education?	• The findings identify where improvements can be made in further research in anxiety in pregnancy. • The findings have relevance for healthcare professionals and researchers for service delivery and research design.

INTRODUCTION

Anxiety disorders are the sixth leading cause of disability globally, in terms of Years Lived with Disability (YLD) and accounted for 390 Disability Adjusted Life Years (DALYs) per 100,000 persons in 2010 (Baxter *et al.* 2014). Symptoms of generalised anxiety disorder (GAD) are associated with significant distress or impairment in social and occupational functioning and include: feeling restless or on edge; having difficulty concentrating; irritability; fatigue; muscle tension and sleep disturbance (American Psychiatric Association 2013). A high proportion of DALYs caused by anxiety disorders were experienced by females (65%) and DALY rates peaked for men and women in the 15–34 year age groups (Baxter *et al.* 2014). Symptoms of GAD below the diagnostic threshold (Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD) criteria) were found to increase the risk of developing co-morbid mental health problems and somatic disorders. They were associated with high levels of distress; poor perceived physical health; impairment in psychosocial functioning and more primary health care use than in non-anxious individuals (Haller *et al.* 2014). Haller *et al.* (2014) reported the median point prevalence rate of sub-threshold GAD symptoms was 4.4% in two general

population studies (Angst et al. 2006, Kessler et al. 2005). In these studies anxiety symptoms were assessed via structured clinical interviews (SPIKE: Angst & Dobler-Mikola 1985, WMH-CIDI: Kessler & Ustün 2004). The prevalence of sub-threshold anxiety symptoms were double the rate of the full disorder and prevalence rates were higher for women than men. In postpartum women, the prevalence of one or more anxiety disorders (assessed via structured diagnostic interview) has been reported as 8.5% (Goodman *et al.* 2016). The prevalence of anxiety disorders in pregnancy varies widely in different reports, from 10 to 15% (National Institute for Health and Care Excellence (NICE) 2014, Rubertsson *et al.* 2014, Goodman *et al.* 2014). In a UK community sample of pregnant women at 18 weeks gestation, the prevalence was reported as 14.6% (Heron *et al.* 2004). Symptoms of self-report anxiety in pregnancy have been reported to be higher in the first and third trimesters with a notable decrease in the second trimester (Öhman *et al.* 2003, Statham *et al.* 1997).

Elevated and prolonged anxiety in pregnancy has been associated with pre-term birth, fetal growth restriction (Ding *et al.* 2014, Littleton *et al.* 2007, Rich-Edwards & Grizzard 2005) and severe behavioural problems in developing children (Blair *et al.* 2011, Cardwell 2013, Davis & Sandman 2010, Glover 2014, Stein *et al.* 2014). Mild to moderate psychological distress can be extremely debilitating for pregnant women and can affect a woman's general functioning (Furber *et al.* 2009). Anxiety during pregnancy has been reported to predict post-traumatic stress disorder (Czarnocka & Slade 2000, Iles *et al.* 2011) and depression in the postnatal period (Heron *et al.* 2004, Coelho *et al.* 2011).

Background

The Healthy Child Programme (Department of Health (DOH) 2009) highlights possible interventions to support women with anxiety in pregnancy, including social support, assisted self-help and Cognitive Behavioural Therapy (CBT). For pregnant women with a diagnosed

anxiety disorder, CBT has been suggested as the first line treatment option (Marchesi *et al.* 2016). The maternal mental health guidance (DOH 2012) stated that all women identified with mild to moderate mental health issues should be offered a range of support tailored to the needs of those women. The NICE guideline for perinatal mental health (NICE 2014) suggested that low intensity psychological interventions may benefit women with symptoms of mild to moderate anxiety which significantly interfere with personal or social functioning. However, services to support the emotional wellbeing of women are not always readily available and need to be strengthened (Maternal Mental Health Alliance (MMHA) 2013). The aim of interventions for pregnant women with symptoms of mild to moderate anxiety is to provide suitable and timely support and treatment to prevent an escalation of symptoms and improve a woman's ability to cope (NICE 2007, MMHA 2013). However, the evidence of the effectiveness of interventions for mild to moderate symptoms of anxiety in pregnancy has not yet been determined (Ryan 2013, Glover 2014) and further research is required.

THE REVIEW

Aim

The aim was to conduct a systematic review to establish the effectiveness of non-pharmacological interventions for pregnant women with symptoms of mild to moderate anxiety. It addressed the following research questions:

1. What non-pharmacological interventions to reduce the symptoms of anxiety in pregnant women have been tested?

2. How effective are non-pharmacological interventions in reducing the symptoms of mild to moderate anxiety in pregnant women?

Design

A scoping review was undertaken to identify appropriate parameters for the development of the PICOS (Population, Intervention, Comparators, Outcomes, Study designs) process for the systematic review (Centre for Reviews and Dissemination (CRD) 2009). The review protocol was registered on the PROSPERO database at the CRD (Evans *et al.* 2015: CRD42015017841). A systematic review was conducted according to the Centre for Reviews and Dissemination guidelines for a quantitative systematic review (CRD 2009). The report follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement guidelines (Moher *et al.* 2009).

Search methods

A systematic search of the following 13 electronic databases was undertaken in January 2015 and updated in August 2016: Medline (Medical Literature Analysis and Retrieval System Online), CINAHL (Cumulative Index to Nursing and Allied Health Literature), Maternity and Infant Care database from MIDIRS (Midwives Information and Resource Service), PsycINFO, The Cochrane Database of Systematic Reviews (CDSR) and The Cochrane Register of Controlled Trials (CENTRAL), EMBASE (Excerpta Medica Database), CRD (Centre for Reviews and Dissemination), SSCI (Social Sciences Citation Index), ASSIA (Applied Social Sciences Index and Abstracts), HTA (Health Technology Assessment) Library, JBI (Joanna Briggs Institute) Evidence-Based Practice Database and AMED (The Allied and Complementary Medicine Database). Visually scanning reference lists from relevant primary studies and reviews identified three additional studies for inclusion.

Inclusion and exclusion criteria

The studies had to meet the following criteria to be included in the review:

Papers written in English and published since 1990. This period reflects the time since non-pharmacological interventions were recommended to support women's mental health during pregnancy (DOH 1999).

Population

Studies with pregnant women of all parities across the three trimesters of pregnancy were included (including pregnant women from general populations and women with symptoms of mild to moderate anxiety). Studies with pregnant women with severe symptoms of anxiety and/or depression; under the care of specialist mental health services; less than 18 years of age; who lack capacity to provide informed consent and pregnant women with complex social factors (NICE 2010) were excluded.

Intervention

Studies of non-pharmacological interventions were included. Non-pharmacological interventions include: physical; cognitive; behavioural and other complementary methods. Studies were included if the evaluation focused on the effects on symptoms of anxiety alone or anxiety and other psychosocial outcomes.

Comparators

Studies with comparison groups which comprised any form of usual maternity care or other pharmacological or non-pharmacological interventions were included.

Outcomes

Studies were included where the primary or secondary outcome measure included symptoms of anxiety identified by various self-report measures or clinical interview measured at any time in the antenatal period prior to the onset of labour. Studies that did not include

symptoms of anxiety as an outcome measure or where symptoms of anxiety were only

measured in the intrapartum or postnatal period were excluded.

Study design

Randomised Controlled Trials (RCTs) and pilot RCTs of non-pharmacological interventions,

systematic reviews and meta-analyses were included. Non-randomised studies were

excluded. Key search terms were: pregnancy; antenatal; prenatal; perinatal; antepartum;

childbearing; intervention; anxiety; randomised controlled trial; clinical trial, review. A full

search strategy is included in Appendix 1.

Search outcome

After 45 duplicates were deleted, the search identified 5,222 potentially eligible papers which

were individually assessed on the information provided in the study title and abstract. From

these 5,168 records were excluded using the inclusion and exclusion criteria. Following

inclusion of 3 additional papers identified through scanning reference lists of relevant studies,

57 papers were retrieved and the full text assessed. From these, 32 papers were excluded and

the remaining 25 papers were selected for inclusion. A research supervisor independently

read the potentially relevant papers and the papers identified for inclusion were agreed with

any disagreements resolved through discussion with a second research supervisor. The

literature search and inclusion process are detailed in the PRISMA Flow Diagram in Figure 1

(Moher *et al.* 2009).

The twenty-five included randomised controlled trials were reported between 1992 and 2016

(Table 1) and were conducted in Australia, Belgium, Canada, Germany, Greece, India, Iran,

New Zealand, Portugal, Switzerland, Taiwan, the UK and the US. Six studies were pilot

RCTs. The components of the interventions are detailed in Table 1. The total number of participants included in the 25 studies was 5,156.

Quality appraisal

Twenty-five included RCTs were independently assessed by two reviewers (KE, JM). The studies were quality assessed using the Cochrane Collaboration's tool for assessing risk of bias (CRD 2009, Higgins *et al*. 2011) to evaluate six quality domains: sequence generation; allocation concealment; blinding; incomplete data; selective outcome reporting; and other sources of bias.

Many domains included in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach are assessed in the review (Guyatt *et al.* 2008), however an overall rating using the GRADE approach was not undertaken as: 1. anxiety symptoms was not the sole outcome measure in many included studies; 2. anxiety symptoms were assessed using different measurement tools; 3. many studies were small studies or pilot studies; 4. most studies were assessed as having 'unclear risk of bias'; 5. there was considerable clinical heterogeneity between the included studies. Therefore, it was not possible to draw overall conclusions for making recommendations based on confidence of the current evidence.

Data extraction and synthesis

Data were extracted using a predesigned and piloted template which included the following headings: study design; intervention design; recruitment rate; number of participants; setting; outcome measures; control/comparators; results and comments. Data extraction tables were produced to present the study characteristics, results and risk of bias. A narrative description of the data was conducted.

Where outcome data were available, the studies were assessed for methodological, clinical and statistical heterogeneity and considered for meta-analysis. Assessment of clinical heterogeneity was informed by the findings from the scoping review (CRD 2009) and considered the types of participants (women with obstetric complications, general antenatal population, women with symptoms of or risk factors for mild to moderate anxiety), duration of interventions (single or multiple sessions), delivery of interventions (delivered to individuals or groups) and types of intervention (psychological, mind/body, educational, supportive interventions) in the included studies.

To evaluate statistical heterogeneity, the Chi-squared test was performed to generate the Q-statistic and the I^2 statistic was calculated (CRD 2009, Higgins & Green 2011). A random effects model was considered to be the most appropriate method of analysis as it involves an assumption that the effects being estimated in the different studies are not identical, but follow some random distribution (CRD 2009, Higgins & Green 2011). The standardised mean difference was used as the summary statistic for the self-report anxiety scores, with 95% confidence intervals and two-tailed p-tests conducted for each outcome where possible. The criteria for conducting sub-group analysis were pre-specified in the review protocol.

RESULTS

Quality of randomised controlled trials

One study was assessed to have an overall 'low risk of bias' (Faramarzi *et al*. 2015). One study was assessed as having an overall 'high risk of bias' (Korol & Von Baeyer 1992). Twenty-three studies were assessed as having an overall 'unclear risk of bias'. The risk of bias assessment summary for all included randomised controlled trials is presented in Figure 2. The sample sizes ranged from 25 participants (Côté-Arsenault *et al.* 2014) to 2,212 participants (Dodd *et al.* 2016).

Participants

Seven studies recruited women from a general pregnant population and four studies included nulliparous pregnant women. Six studies recruited pregnant women with a history of mood concerns or elevated anxiety / depression scores. Other studies included women who were not selected due to anxiety / depression symptoms but women who: had obstetric complications (high BMI, nausea, gestation diabetes mellitus); had social risk factors (single pregnant women or with unemployed partners); were African American pregnant women; were pregnant women attending for amniocentesis and pregnant women with a history of previous pregnancy loss.

Recruitment

Twelve studies reported a power calculation to determine the correct sample required to detect significant changes in the primary outcome where one exists. This comprised self-report measures of anxiety in seven of the studies (Bastani 2015, Bastani *et al.* 2005, Bittner *et al.* 2014, Chang *et al.* 2008, Milgrom *et al.* 2015, Newham *et al.* 2014, Satyapriya *et al*. 2013).

In the included studies, pregnant women were mainly recruited from hospital antenatal clinics. Five studies recruited women from community locations (Bullock *et al*. 1995, Newham *et al*. 2014, Brugha *et al*. 2015, Côté-Arsenault *et al*. 2014, Davis *et al*. 2015). In most studies, a healthcare professional approached potential participants during a clinic appointment. Pregnant women were also recruited by: posting flyers in clinic locations (Vieten & Astin 2008, Woolhouse *et al*. 2014, Guardino *et al*. 2014); via antenatal classes (Korol & Von Baeyer 1992, Vieten & Astin 2008, Woolhouse *et al*. 2014); support groups (Côté-Arsenault *et al.* 2014), attendance at ultrasound scan (Snaith *et al.* 2014) and physiotherapy appointments (Woolhouse *et al.* 2014).

Psychological screening was used to assess participant eligibility in five studies:

- Bittner *et al.* (2014): STAI, BDI and PDQ followed by a diagnostic interview (Wittchen & Pfister 1997). Following screening procedures, 160 (21%) women were eligible and consented to participate.

- Teixeira *et al.* (2005): STAI

- Davis *et al.* (2015) : STAI and EPDS

- Guardino *et al.* (2014): PSA and PSS

- Milgrom *et al.* (2015): EPDS and a Structured Clinical Interview for DSM-IV (SCID). From an initial sample of 169 women referred to the study with an EPDS score of 12 or more, 54 (32%) women were finally eligible and consented to participate in a SCID.

Interventions

Various types of interventions were tested in the included studies. Interventions have been categorised as 1. mind-body: hypnosis, meditation, yoga, biofeedback, tai chi and visual imagery (Wahbeh *et al.* 2008); 2. psychological: CBT, motivational interviewing, psychotherapy (Australian Psychological Society 2010); 3. supportive: social, emotional or practical support provided by healthcare professionals or peer groups. 4. Educational: health education and advice. Categories were defined with reference to the main interventional approach reported in the included studies. Some studies have included multiple components in the intervention design therefore a description of the intervention is included in Table 1.

Fourteen studies evaluated mind-body interventions including:

- relaxation (Bastani *et al.* 2005, Chang *et al.* 2008, Teixeira *et al.* 2005, Tragea *et al.* 2014, Ventura *et al.* 2012)

- guided imagery (Jallo *et al.* 2014, Korol & Von Baeyer 1992, Urech *et al.* 2010)

- mindfulness (Vieten & Astin 2008, Woolhouse *et al.* 2014, Guardino *et al.* 2014)

- yoga (Newham *et al.* 2014, Satyapriya *et al.* 2013, Davis *et al.* 2015).

Four studies evaluated psychological interventions including:

- CBT (Bittner *et al.* 2014, Milgrom *et al.* 2015); CBA (Brugha *et al.* 2015) and MCBT (Faramarzi *et al.* 2015)

Three studies evaluated supportive interventions, including:

- peer telephone support (Bullock *et al.* 1995)

- midwifery telephone support (Snaith *et al.* 2014)

- Home visits by nurses (Côté-Arsenault *et al.* 2014).

Two studies tested educational interventions focused on health, diet and exercise

- (Bogaerts *et al.* 2012, Dodd *et al.* 2016).

Knight *et al.* (2001) evaluated an acupuncture intervention.

Bastani *et al.* (2015) evaluated an acupressure intervention.

Theoretical basis

Some authors described the theoretical basis for CBT interventions (Bittner *et al*. 2014, Milgrom *et al*. 2015), psychological support / CBA interventions (Brugha *et al*. 2015, Côté-Arsenault *et al*. 2014) and mind-body interventions such as acupressure (Bastani 2015), mindfulness (Guardino *et al.* 2014, Woolhouse *et al.* 2014, Vieten & Astin 2008), guided imagery (Jallo *et al.* 2014), yoga (Newham *et al.* 2014, Satyapriya *et al*. 2013) and relaxation

(Bastani 2005, Chang *et al*. 2008, Teixeira *et al*. 2005, Tragea *et al*. 2014, Urech *et al*. 2010, Ventura *et al*. 2012).

Participation

Studies which reported that 40% or more of the eligible target population declined participation in interventions were:

- Educational intervention for pregnant women with a high BMI (Dodd *et al.* 2016), 60% (N=3262) declined due to lack of interest, too busy to participate or were unable to be contacted.

- Group CBT intervention (Bittner *et al.* 2014), following initial anxiety/depression screening 45% (N=209) declined further participation/screening or could not be contacted.

- CBT intervention (Milgrom *et al.* 2015), 47% (N=79) declined or could not be contacted to complete further SCID screening.

- Yoga intervention (Newham *et al. 2014*), 43% (N=44) declined or did not make further contact with the researchers.

- Telephone support intervention (Bullock *et al.* 1995), 41% (N=90) declined or could not be contacted.

Studies which reported that 80% or more of the eligible target population agreed and consented to participation included:

- Educational intervention for women with a high BMI (Bogaerts *et al.* 2012), 87% (N=205) agreed

- Supportive intervention for pregnant women who had previously experienced pregnancy loss (Côté-Arsenault *et al.* 2014), 89% (N=24) agreed.

- Guided imagery intervention for pregnant African American women (Jallo *et al.* 2014), 97% (N=72) agreed.

- Mindfulness intervention for women with high pregnancy anxiety scores on the PRA and PSA scales (Guardino *et al.* 2014), 94% (N=50) agreed.

Interventions delivered to general populations of pregnant women which reported that 80% or more of the eligible target population agreed participation included:

- Yoga intervention (Satyapriya *et al.* 2013), 86% (N=105) agreed.

- Relaxation intervention (Chang *et al.* 2008), 100% (N=136) agreed.

Outcome measures and outcome time points

The STAI (Spitzer *et al.* 2006) was the most commonly used scale, being used in 21 studies. Two studies included women with symptoms of nausea and conducted outcome assessments in the first trimester of pregnancy (Knight *et al.* 2001, Faramarzi *et al.* 2015). Outcome measures were assessed in the second trimester of pregnancy in five mind-body interventions (Bastani *et al*. 2005, Davis *et al.* 2015, Guardino *et al.* 2014, Tragea *et al.* 2014, Ventura *et al.* 2012), one CBT intervention (Bittner *et al.* 2014) and one acupressure intervention (Bastani 2015). All other studies which reported the timing of outcome assessments (N=15) collected post-intervention outcome data in the third trimester of pregnancy. Mid-point data collection were collected in six studies (Bogaerts *et al.* 2012, Davis *et al.* 2015, Dodd *et al.* 2016, Jallo *et al.* 2014, Knight *et al.* 2001, Snaith *et al.* 2014,). Data collection continued into the postnatal period in seven studies (Bittner *et al.* 2014, Bogaerts *et al.* 2012, Bullock *et al.* 1995, Dodd *et al.* 2016, Milgrom *et al.* 2015, Snaith *et al*. 2014, Vieten & Astin 2008).

Attrition

In four multi-session interventional studies, more than 20% of the IG did not complete the intervention (Bittner *et al.* 2014, Knight *et al.* 2001, Newham *et al.* 2014, Woolhouse *et al.* 2014).

Results of individual studies

Studies which reported significant differences in anxiety scores (p<0.05) between the control group (CG) and intervention group (IG) at post-intervention are presented in Table 1 alongside studies which reported no significant between group differences.

Meta-analysis of STAI post-intervention scores

Studies used different versions of the STAI (Spielberg *et al.* 1970, Spielberger *et al.* 1983) and included other anxiety measures (HAD-A, BAI, MAQ, STAI-short) therefore the Standardised Mean Difference (SMD) was used as the summary statistic (Higgins & Green 2011). Four studies (Newham *et al.* 2014, Teixeira *et al.* 2005, Tragea *et al.* 2014, Knight *et al.* 2001) reported anxiety scores as median and inter-quartile ranges (IQR) due to the non-normal distribution of the data, so were excluded from the meta-analysis. Four studies with insufficient details of post-intervention scores (Côté-Arsenault *et al.* 2014, Ventura *et al.* 2012, Bogaerts *et al.* 2012, Bullock *et al.* 1995) were excluded from the meta-analysis.

The results from 17 studies included 1,928 participants in the IG and 1,914 participants in the CG. Pooling of results indicated considerable statistical heterogeneity among the studies (I^2=92%; p<0.001). There was also clinical heterogeneity between the intervention type, timing and duration of the interventions and the characteristics of participants. Sub-group analyses were conducted on studies of interventions with similar characteristics, such as educational, mind-body, psychological and supportive interventions. Only interventions

which included mindfulness group interventions were assessed as having sufficient clinical and statistical homogeneity to perform a meta-analysis (Figure 3) (Higgins & Green 2011).

There was no observed beneficial effect in relation to the reduction of self-report STAI state anxiety score (median=0.09; 95% CI=-0.32 to 0.49), with low statistical heterogeneity among the studies (I^2=0%; p=0.85). However, the pooled number of participants in these three studies is small (N=95), all were assessed to have an unclear risk of bias and therefore the results of the meta-analysis should be interpreted with caution.

DISCUSSION

The aim of the systematic review was to identify and assess the effectiveness of non-pharmacological interventions for pregnant women with symptoms of mild to moderate anxiety.

Strengths of the review

A comprehensive search strategy maximised the potential to identify relevant studies and the review used a robust, independent and appropriate assessment method. The review assessed a wide range of non-pharmacological interventions to improve mild to moderate symptoms of anxiety in pregnancy and included different populations of pregnant women across the three trimesters of pregnancy. Previous systematic reviews have sought evidence of the effectiveness of interventions to support women with symptoms of distress in pregnancy (depression, anxiety, stress, fear, self-efficacy and self-esteem) (Fontein-Kuipers *et al.* 2014), mind-body interventions for women with symptoms of anxiety in pregnancy (Marc *et al.* 2011) and pharmacological and non-pharmacological treatments for pregnant and postpartum women with a diagnosed anxiety disorder (Marchesi *et al.* 2016). The findings highlight

points for consideration in the practical aspects of delivering non-pharmacological interventions in maternity care contexts including training needs for intervention providers.

Limitations of the review

Studies not published in English were not included in the review. Most of the included RCTs had relatively small sample sizes and thirteen studies did not include a sample size calculation. As a meta-analysis of post-intervention anxiety scores was only achievable for a small sub-group of studies, the aim of the study to assess the effectiveness of interventions was only partially achieved.

Quality of the included RCTs

Most of the included studies were assessed as having an unclear risk of bias. Details of allocation concealment, blinding of study personnel, sampling methods and outcome assessors were not reported in many of the studies.

Participants and eligibility screening

The studies included women from general pregnant populations or pregnant women with obstetric, social or psychological symptoms or risk factors. Attention to recruitment rates and recruitment strategies in the included studies has revealed the possibility of selection bias and highlighted limitations to the reach, generalisability and relevance of the findings. Therefore, addressing the limitations to recruitment processes will assist the design of future studies (Dzewaltowski *et al.* 2004, Toerien *et al.* 2009, Tarquinio *et al.* 2014). Studies which targeted women with obstetric complications or risk factors or where women had an option to self-select into the study reported higher percentages of women recruited from the initial sample. Most studies which reported lower participation rates from the initial sample population used

anxiety and/or depression measures to assess participant eligibility and the majority of potential participants were referred by healthcare professionals. Darwin *et al.* (2013) reported that women have concerns that psychological assessment may lead to unwanted interference from social services or healthcare professionals and such concerns may partly explain the lower consent rates into studies based on healthcare professional referral or psychological assessment. The rationale for applying inclusion criteria and referral should be clearly communicated to potential participants in a supportive context. Six studies reported using convenience sampling methods (Bastani *et al.* 2005, Dodd *et al.* 2016, Guardino *et al.* 2014, Tragea *et al.* 2014, Urech *et al.* 2010, Ventura *et al.* 2012) and six studies provided little information of the sample population and sampling methods (Chang *et al*. 2008, Côté-Arsenault *et al.* 2014, Knight *et al.* 2001, Korol & Von Baeyer 1992, Vieten & Astin 2008, Woolhouse *et al.* 2014). Without transparent reporting of the sampling methods it is difficult to assess whether the characteristics of the sample represent those of the population and whether the results would be subject to change depending on the research context (Sedgwick 2015).

Intervention components

The studies included in the review evaluated psychological, educational and mind-body interventions. Many interventions were complex and combined psychological or mind-body approaches with elements of education, discussion, professional support and peer support. Women who have psychological or obstetric risk factors may feel especially isolated during pregnancy and may benefit from discussing their situation and feelings with healthcare professionals. Women who are socially isolated may benefit from interventions which act as a proxy for enhanced social support. The Boots Family Trust Alliance (2013) reported that women who experienced mental health problems in pregnancy stated the main cause as being

isolation and lack of support. Interventions delivered to pregnant women which combine

education, professional support, peer support and psychological approaches are suggested as

approaches to improve women's postnatal psychological outcomes and health outcomes for

infants (Glover 2014, Marchesi *et al.* 2016, Morrell *et al.* 2016). The Acorn and First steps

trials are currently being conducted to evaluate multi-component interventions delivered to

pregnant women (Barnes et al. 2013, Wilkinson et al. 2016).

Intervention providers

Most mind-body interventions were delivered by trained instructors (mindfulness, yoga,

acupuncture, relaxation), while mindfulness and CBT interventions were delivered by

psychologists or psychotherapists. Four studies recruited healthcare professionals (nurses and

midwives) to deliver interventions and provided additional training in psychological and

motivational interviewing techniques. Only one study recruited and trained peer volunteers to

deliver a telephone support intervention (Bullock *et al.* 1995). Details of intervention

provider skills and additional training provided to deliver interventions were underreported in

the included studies. The Medical Research Council (MRC 2000) advise that variations in

levels of skills across providers may affect delivery of the intervention and / or outcomes.

The training and practitioner skills required to deliver RCTs is valuable information for

researchers, practitioners and service providers reviewing and potentially implementing

interventions.

Attrition and compliance

Five studies reported attrition rates of greater than 20% for the IG and/or CG (Tragea *et al.*

2014, Woolhouse *et al.* 2014, Newham *et al.* 2014, Bittner *et al.* 2014, Knight *et al.* 2001)

and only four studies indicated the numbers of sessions attended by participants (Davis *et al.*

2015, Milgrom *et al.* 2015, Guardino *et al.* 2014, Bittner *et al.* 2014). Bittner *et al.* (2014)
excluded women from final analysis who did not attend more than 74% of the sessions.
Delgadillo *et al.* (2014) suggested that non-pregnant participants in low intensity
psychological interventions for anxiety and/or depression report the highest attrition rates by
session four, implying that sessions 1–3 are key periods to maximise engagement and
retention. They suggest that at least 4 therapy sessions are required to achieve reliable and
clinically significant improvement rates. Three studies which evaluated single-session
relaxation interventions (Teixeira *et al.* 2005, Urech *et al.* 2010, Ventura *et al.* 2012)
measured anxiety symptoms directly following the intervention and recommend that the
psychobiological effects of the interventions are evaluated over a longer follow-up period.

Outcome measures

Two studies were solely focused on evaluating the effects of the intervention on symptoms of
anxiety with other studies including anxiety alongside other psychosocial outcomes. It is
recognised that multidimensional psychosocial aspects of pregnancy are important in
developing models of care to promote the psychological wellbeing of women (Jomeen 2004).
This multidimensional approach was employed in six of the included studies which included
anxiety in a composite of primary outcome measures alongside depression, stress, positive
and negative affect and social support. However, the presence of anxiety may reduce the
effectiveness of the treatment of depression or vice versa. Interventions targeting one
condition may not be effective for the other co-morbid condition (Garber & Weersing 2010).
Interventions that focus on improving symptoms of anxiety and depression need to have a
proposed logic and theory of change before testing the mechanism by which an improvement
in symptoms is likely to occur for each condition. Studies of interventions which aim to

improve symptoms of anxiety to prevent postnatal depression require a sufficient one year follow-up period to determine their effectiveness (Morrell *et al.* 2016).

CONCLUSION

The introduction of interventions to reduce symptoms of mild to moderate anxiety in pregnant women has the potential to improve health outcomes for pregnant women and their infants. The results of the review were inconclusive and need to be interpreted with caution as many of the included studies provided an inadequate description of their methods to allow a full assessment of methodological quality and the results of the review were predominantly based on small samples. Future RCTs should be adequately powered and reported in accordance with the CONSORT guidance (Schulz *et al.* 2010). Including an assessment of the recruitment process, level of engagement with interventions and the criteria for completion will assist researchers to maximise recruitment and identify the optimal duration of interventions, balancing resources and commitment required with potential beneficial effects.

The review found insufficient evidence to draw overall conclusions regarding the benefit of non-pharmacological interventions for pregnant women with anxiety and future studies are required to develop the current evidence base.

Author Contributions:

All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE*):

1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;

2) drafting the article or revising it critically for important intellectual content.

* http://www.icmje.org/recommendations/

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Appendix 1

Search strategy for: **AMED, Medline, EMBASE, Psycinfo and Maternity and Infant care**.

• Anxiety disorders/ OR • anx*.mp OR • Anxiety/	• Intervention studies/ OR • intervention*.mp OR • Randomized Controlled Trials as Topic/ OR • rct.mp OR • randomi*ed controlled trial.mp OR • Clinical trial/ OR • clinical trial.mp OR • trial.mp OR • randomi*.mp OR • systematic review.mp OR • Meta analysis/ or meta analysis.mp	• pregnan*.mp OR • Pregnancy/ OR • Peripartum period/ OR • peripart*.mp OR • childbearing.mp OR • Perinatal care/ OR • perinat*.mp OR • antenatal.mp OR • ante-natal.mp OR • antepartum.mp OR • ante-partum.mp OR • Prenatal care/ OR prenat*.mp

Table 1. Data extraction from the randomised controlled trials and pilot randomised controlled trials included in the review

First author Country Year	Intervention category (duration)	Intervention, control and comparison group. * Description of intervention ** Facilitator / facilitator training	Included women	Primary outcome (secondary outcome)	Gestation at start / post intervention. (weeks of pregnancy)	Analysed n= Post-intervention / baseline (method)	Main anxiety measure mean score: Baseline / post-intervention	Key anxiety results as reported in the included RCTs / pilot RCTs	Risk of bias assessed as:
Bogaerts Belgium 2013	**Educational** (4 group sessions)	IG: Motivational interviewing, CG: Standard care Comp: Brochures * Discussed energy intake and expenditure and women's concerns in pregnancy ** Midwife / Motivational techniques	Pregnant women: BMI 29 or more	1. Maternal weight gain (Depression, anxiety, birthweight, prematurity)	<15 / (30-34)	IG:76 / 78 CG:63 / 63 Comp: 58 / 64 (Direct likelihood model)	STAI-S IG: 36.5 / 34.0 CG: 35.0 / 38.0 Comp: 35.9 / 37.6	RCT: reported STAI-S scores significantly decreased in the IG and increased in the CG post-intervention (p=0.02, n=141) (multivariate linear mixed effects model, time by group interaction)	Unclear
Dodd Australia 2016	**Educational** (5 individual sessions, 20-30 weeks)	IG: Diet / exercise education, CG: Standard care * Healthy eating advice; dietary and exercise goals and support with lifestyle changes. ** Dietician and trained research assistants / NR	Pregnant women: BMI 25 or more	1. Birthweight (Quality of life, depression, anxiety)	(12-17) / 36	IG: 1108 / 1108 CG: 1104 / 1104 (ITT analysis)	STAI short IG: 10.7 (SD 3.8) / 10.6 (SD 3.6) CG: 10.8 (SD 3.9) / 10.4 (SD 3.6)	RCT: reported no significant differences in STAI scores between groups post-intervention (p=0.51, n=2122) (multivariate linear mixed effects model, time by group interaction, 95% CI=0.19-0.38)	Unclear
Bastani Iran 2005	**Mind body** (7 group sessions)	IG: Relaxation, CG: Standard care * Discussion of and information on anxiety, stress and relaxation in pregnancy. Taught relaxation techniques. ** Instructor/ NR	Nulliparous pregnant women	1. Anxiety 2. Stress	18 (mean) / 25 (approx)	IG: 55 / 55 CG: 55 / 55 (ITT analysis)	STAI-S IG: 37.2 (SD 5.4) / 22.7 (SD 7.4) CG: 38.6 (SD 6.5) / 38.5 (SD 5.7)	RCT: reported significant reductions in STAI-S scores for the IG compared with the CG post-intervention (p=0.001, n=110) († independent samples t-test, post-intervention between group scores	Unclear
Chang Taiwan 2008	**Mind body** (daily exercises via audio CD, 2 weeks)	IG: Relaxing music, CG: Standard care * Audio CD (30 mins) with a choice of: classical music; nature sounds or crystal music performing Chinese children's songs. ** Audio CD / NR	General pregnant population	1. Anxiety 2. Depression 3. Stress	(18-34) / NR	IG: 116 / 120 CG: 120 / 121 (Analysis NR)	STAI-S IG: 37.9 (SD 9.8) / 35.8 (SD 10.9) CG: 37.1 (SD 10.0) / 37.8 (SD 12.1)	RCT: reported IG STAI-S scores were significantly different from the CG post-intervention (2.13 p=0.01). There was a significant between group difference in scores (values not reported, n=241) (ANCOVA, baseline scores as co-variates)	Unclear
Tragea 2014 Greece	**Mind body** (6 individual sessions)	IG: Relaxation / stress reduction, Comp: Educational materials * Audio CD (20 mins) with relaxation techniques and a healthy lifestyle brochure. ** Audio CD / NR	Nulliparous pregnant women	1. Anxiety 2. Stress 3. Locus of control	(14-21) / (21-28)	IG: 31 / 44 Comp: 29 / 41 (Per-protocol analysis)	STAI-S (median/IQR) IG: 38.0 (35-42) / MC -3.5 (95% CI: 2.2) Comp: 40.0 (30-52) / MC -2.0 (95% CI: 2.9)	RCT: reported no significant difference for STAI-S scores between groups post-intervention (mean change= -1.5, 95%CI –2.7 to 1.7, n=60) (ANCOVA, baseline STAI-S score as co-variate)	Unclear
Teixeira UK 2005	**Mind body** (1 individual session)	IG: Active relaxation, Comp: Passive relaxation * Stress management: using imagination to induce feelings of comfort. Based on hypnotherapeutic methods. ** Stress management expert / NR	General pregnant population	1. Cortisol 2. Uterine artery resistance (Anxiety)	(28-32) / (28-32)	IG:29 / 29 Comp: 29 / 29 (ITT analysis)	STAI-S (median/95% CI) IG: 38.5 (35-42) / 24.5 (23-27) Comp: 37.0 (32-42) / 27.5 (25-30)	RCT: reported both IG and Comp groups had reduced STAI-S scores, which were significantly greater in the IG (95% CI, p=0.0001, n=58) († independent samples t-test, comparison of deltas p=0.01, pre/post intervention between groups change score)	Unclear
Urech Switzerland 2010	**Mind body** (1 individual session)	IG: Active relaxation, CG: Passive relaxation Comp: Guided imagery * Monitored women's BP, attached to CTG and inserted a brachial vein catheter. Relaxation and guided imagery exercises. ** Audio CD / NR	General pregnant population	1. Relaxation 2. Anxiety 3. Endocrine parameters 4. Cardiovascular responses	32 (mean) / 32 (mean)	IG: 13 / 13 CG: 13 / 13 Comp: 13 / 13 (ITT analysis)	STAI-S IG: 37.7 / 30.9 CG: 31.5 / 29.9 Comp: 30.9 / 28.1	RCT: reported no significant change of STAI-S scores from baseline to post-intervention. Anxiety scores decreased equally in all groups (d=0.38, p=0.030, F1,35=5.14, n=39) (mixed effect ANOVA, time by group interaction)	Unclear
Ventura Portugal 2012	**Mind body** (1 individual session)	IG: Relaxing music, CG: Sitting, Comp: Magazines * Relaxing music with a choice of: light vocals; light instrumental; classical or vocal jazz.	Pregnant women attending for amniocentesis	1. Anxiety (Maternal cortisol levels)	17 / 17	IG: NR / 61 CG: NR / 47 Comp: NR / 46 (ITT analysis)	STAI-S IG: MD -7.6 (SD 8.3) CG: MD -4.5 (SD 5.7) Comp: MD -5.5 (SD 6.4)	RCT: reported STAI-S scores decreased in all groups (p=0.058). IG scores were significantly different from the comp and CG (F2,150=7.3, p=0.001, n=108) (ANCOVA, baseline STAI-S score	Unclear

First author Country Year	Intervention category (duration)	Intervention, control and comparison group. * Description of intervention ** Facilitator / facilitator training	Included women	Primary outcome (secondary outcome)	Gestation at start / post intervention. (weeks of pregnancy)	Analysed n= Post-intervention / baseline (method)	Main anxiety measure mean score: baseline / post-intervention	Key anxiety results as reported in the included RCTs / pilot RCTs	Risk of bias assessed as:
		** Audio CD / NR						as co-variate)	
Korol Canada 1992	**Mind body** (group sessions, number NR)	IG: Guided imagery, Comp: Antenatal classes * Information about the birth process and relaxation techniques with birth visualisation. ** Instructor / NR	General pregnant population	1. Knowledge of childbirth (Anxiety, depression)	NR	IG: 30 / 30 Comp: 30 / 30 (Analysis NR)	STAI-S IG: 31.1 (SD 6.4) / 33.0 (SD 5.3) Comp: 37.0 (SD 9.9) / 36.9 (SD 10.0)	RCT: reported no significant difference between the STAI-S scores between the groups post-intervention (n=60) (values not reported)	High
Jallo US 2014	**Mind body** (daily exercises via audio CD, 12 weeks)	IG: Guided imagery, CG: Standard care * Relaxation; focused breathing and multisensory images to promote reduction of stress and anxiety and restore levels of energy. ** Audio CD / authored by a trained guided imagery instructor	Pregnant African American women	1. Stress (Anxiety, fatigue)	15 (mean) / (26-29)	IG: 36 / 36 CG: 36 / 36 (ITT analysis)	STAI-S IG: 39.6 (SE 2.3) / 36.4 (SE 2.4) CG: 39.4 (SE 2.2) / 34.4 (SE 2.3)	RCT: reported no significant differences in STAI-S scores between the groups post-intervention (p=0.606, n=72) (multivariate linear mixed effects model, time by group interaction)	Unclear
Vieten US 2008	**Mind body** (8 group sessions)	IG: Mindfulness, CG: Wait list (postnatal period) * Mindfulness: meditation; Hatha yoga. Adaptations for pregnancy: awareness of the developing fetus and body; explanations and discussions about coping with anxiety in labour ** Psychologist / Mindfulness and yoga	Pregnant women: history of mood concerns	1. Stress 2. Depression 3. Anxiety 4. Positive / negative affect	25 (mean) / 35 (approx)	IG: 13 / 15 CG: 18 / 19 (Analysis NR)	STAI-S IG: 43.8 (SD 12.4) / 35.4 (SD 9.1) CG: 35.6 (SD 10.9) / 35.6 (SD 8.4)	Pilot RCT: reported significantly reduced STAI-S scores in the IG in comparison to the CG post-intervention (F2,24=4.32, p=0.04, d=0.58, n=31), (ANCOVA, baseline STAI-S score as co-variate)	Unclear
Guardino US 2014	**Mind body** (6 group sessions)	IG: Mindfulness, Comp: Pregnancy book * Mindfulness meditation, lectures, discussions and sharing experiences. Guided meditations to use at home. ** Mindfulness instructor / Curriculum outlined in a standardised instructor's manual.	Pregnant women with elevated anxiety / stress scores	1. Mindfulness 2. Stress 3. Anxiety 4. Adherence	18 (mean) / 23 (mean)	IG: 24 / 24 Comp: 23 / 23 (ITT analysis)	STAI-S IG: 45.7 (SD 7.6) / 39.5 (SD 6.3) Comp: 44.4 (SD 10.9) / 37.4 (SD 11.5)	Pilot RCT: reported significant between group differences for the PSA and moderately significant for the PRA (p=0.01, p=0.07 respectively, n=47), no significant differences for STAI–S scores (multivariate linear mixed effects model, time by group interaction)	Unclear
Woolhouse Australia 2014	**Mind body** (6 group sessions)	IG: Mindfulness, CG: Standard care * 'MindBabyBody': breathing practice; body scan (communicating with babies); mindfulness of pain and thoughts; meditation; self-compassion; mindfulness skills in motherhood. ** Psychologist and Psychiatrist / Facilitation of mindfulness groups	General pregnant population	1. Stress 2. Depression 3. Anxiety	(11-34) / (17-40)	IG: 13 / 17 CG: 10 / 15 (Analysis NR)	STAI-S IG: 35.9 (SD 14.1) / 32.8 (SD 7.1) CG: 34.8 (SD 11.5) / 33.0 (SD 12.8)	Pilot RCT: reported significant changes on the DASS-21 anxiety subscale for the IG (Cohen's d=0.7). No significant between group differences for the IG and CG for the STAI-S or DASS-21 anxiety post-intervention sub-scale scores (values not reported n=23) (independent samples t-test)	Unclear
Satyapriya India 2013	**Mind body** (12 group sessions and daily home exercises, 16-18 weeks)	IG: Yoga, CG: Standard care * Integrated approach of yoga therapy (IAYT): physical postures; exercises; stretches; relaxation; breathing techniques and meditation. Audio cassette for home use. ** Trained yoga instructor/ NR	General pregnant population	1. Anxiety 2. Depression	(18-20) / 36	IG: 51 / 53 CG: 45 / 52 (Analysis NR)	STAI-S IG: 35.7 (SD 7.1) / 30.1 (SD 5.7) CG: 36.4 (SD 6.0) / 39.7 (SD 6.8)	RCT: reported STAI-S and HADS-A scores reduced in the IG and increased in the CG with significant difference between groups post-intervention (p=0.001, n=105) (Mann-Whitney U test, post-intervention between group scores)	Unclear
Newham UK 2014	**Mind body** (8 group sessions)	IG: Yoga, CG: Standard care * Hatha yoga at each class. Sessions themed to aid common pregnancy ailments, optimal positioning of the fetus and stages of labour. ** Yoga instructor / British Wheel of Yoga	Nulliparous pregnant women	1. Pregnancy specific anxiety (Anxiety, depression)	21 (mean) / (29-30)	IG: 29 / 31 CG: 22 / 28 (Per-protocol analysis)	STAI-S (median/IQR) IG: 28.0 (24-42) / 27.0 (22-36) CG: 32.0 (24-37) / 34.0 (25-38)	RCT: reported no significant difference in STAI-S scores between the groups post-intervention (p=0.5, r=-0.09, n=51) (Mann-Whitney U test, post-intervention between group scores)	Unclear
Davis US 2015	**Mind body** (8 group sessions)	IG: Yoga, CG: Standard care * Ashtanga Vinyasa yoga modified for pregnancy. Instructional video for home use.	Pregnant women with elevated anxiety /	1. Depression 2. Anxiety 3. Positive and	21 (mean) / (28-29)	IG: 23 / 23 CG: 23 / 23 (ITT analysis)	STAI-S IG: 36.9 (SD 12.2) / 34.8 (SD 10.7)	RCT: reported no significant effect of group or the interaction between group and time, STAI-S scores decreased over time in both groups (p=0.05, 95%	Unclear

First author Country Year	Intervention category (duration)	Intervention, control and comparison group. *Description of intervention **Facilitator / facilitator training	Included women	Primary outcome (secondary outcome)	Gestation at start / post intervention. (weeks of pregnancy)	Analysed n= Post-intervention / baseline (method)	Main anxiety measure mean score: baseline / post-intervention	Key anxiety results as reported in the included RCTs / pilot RCTs	Risk of bias assessed as:
		** Yoga instructor / Experience in prenatal yoga		depression scores	negative affect (satisfaction, adherence)			CG: 41.7 (SD 10.8) / 38.8 (SD 13.7)	CI=0.96-0.47, n=46) (multivariate linear mixed effects model, time by group interaction)	
Milgrom Australia 2015	**Psychological** (8 individual sessions)	IG: CBT, CG: Standard care * 'Beating the Blues Before Birth' based on 'Coping with Depression' (Lewinsohn *et al.* 1984): relaxation; behavioural activation before cognitive strategies; building support networks; partner sessions; preparation for parenthood; infant and relationship issues and anxiety. ** Psychologists with a background in CBT / Pregnancy-specific CBT	Pregnant women with elevated depression scores	1. Depression 2. Anxiety (Infant outcomes)	20 (mean) / 29 (approx)	IG: 27 / 27 CG: 27 / 27 (ITT analysis)	BAI IG: 22.4 (SD 10.1) / 10.4 (SD 7.6) CG: 20.6 (SD 10.7) / 17.4 (SD 7.9)	Pilot RCT: reported anxiety scores decreased in the IG but not in the CG. Between group differences for anxiety scores represented moderately large effect sizes post-intervention (p=0.006, d=0.67, 95% CI=0.33–1.01, n=54) (ANCOVA, baseline scores as co-variate)	Unclear
Bittner Germany 2014	**Psychological** (8 group sessions)	IG: CBT, CG: Standard care * CBT: coping strategies; self-assurance; problem solving; discussions around anxiety; prevention and treatment; future challenges. ** Psychologist / CBT Training and supervision	Pregnant women with elevated anxiety and depression scores	1. Depression 2. Anxiety (Fear of childbirth, social support)	16 (mean) / 24	IG: 21 / 80 CG: 53 / 80 (Analysis NR)	STAI-S IG: 38.0 (SD 6.1) / 35.0 (SD 7.0) CG: 38.0 (SD 6.2) / 36.9 (SD 7.7)	RCT: reported no significant difference between groups for the STAI-S scores post-intervention (p=0.246, η2= 0.019, n=74) (2-way repeated measures ANOVA)	Unclear
Faramarzi Iran 2015	**Psychological** Group MBCT (8 group sessions)	IG: MBCT, CG: Standard care * Integrated elements of MBSR, CBT and guided eating meditations. Pharmacological treatment for the IG and CG (pyridoxine hydrochloride) ** MBCT psychotherapist / MBCT methods within obstetric departments	Pregnant women with moderate nausea and vomiting	1. Nausea and vomiting (Anxiety, depression, distress)	8 (mean) / 11 (approx)	IG: 43 / 43 CG: 43 / 43 (ITT analysis)	HADS-A IG: 11.3 (SD 4.4) / 6.2 (SD 3.1) CG: 10.1 (SD 3.7) / 10.1 (SD 3.8)	RCT: reported significant effect for group by time on HADS-A scores (p=0.001, d=0.53, n=86) (mixed effect ANOVA, time by group interaction)	Low
Brugha UK 2015	**Psychological** (up to 3 individual sessions, 22 weeks)	IG: Midwife psychological training, CG: Standard care * Midwife training: assessment of depressive symptoms; CBA; therapeutic relationships; Five Areas approach (Williams *et al.* 2008) ** Midwives / Based on training by Morrell *et al.* (2009) and adapted for pregnancy	General pregnant population	1.Depression (Anxiety and satisfaction)	22 / 34 (approx)	IG: 118 / 165 CG: 94 / 133 (Pilot study – descriptive statistics)	STAI-S IG: NR / 38.2 (SE 0.9) CG: NR / 40.3 (SE 1.0)	Pilot RCT: Anxiety results not discussed in the paper	Unclear
Bullock New Zealand 1995	**Supportive Interventions** (individual sessions 10+ weeks)	IG: Telephone support, Comp: Pregnancy leaflets * Discussions of women's feelings and concerns with questions about wellbeing in pregnancy. ** Peer volunteers / Healthy pregnancy, research and communication	Pregnant women who were single or with an un-employed partner	1. Depression 2. Anxiety 3. Stress 4. Social support	<20 / 34	IG: 59 / 65 Comp: 63 / 66 (Analysis NR)	STAI-S IG: 32.8 / 30.1 Comp: 34.3 / 34.1	RCT: reported no significant difference between the STAI-S scores between the groups post-intervention (p=0.05, n=122) (ANCOVA, baseline STAI-S score as co-variate)	Unclear
Snaith UK 2014	**Supportive Interventions** (3 individual sessions, 17 weeks)	IG: Telephone support / Doppler, CG: Standard care, Comp: Telephone support * Addressed the needs of the woman. Discussion guide: physical health; availability support; personal and fetal wellbeing. ** Midwife / Delivering the intervention	Nulliparous pregnant women	1. Number of antenatal visits (Anxiety)	20 / 36	IG: 170 / 275 CG: 159 / 283 Comp: 166 / 282 (ITT analysis)	STAI-S IG: 35.7 (SD 10.0) / 36.2 (SD 9.9) CG: 36.2 (SD 10.5) / 36.7 (SD 10.9) Comp: 36.9 (SD 10.9) / 37.1 (SD 10.3)	RCT: reported no significant difference between the STAI-S scores between the groups post-intervention (p=0.68, n=495) (one-way ANOVA)	Unclear
Côté-Arsenault US 2014	**Supportive Interventions** (approx 5 individual sessions, 20 weeks)	IG: Home visits, Comp: Information booklets * Providing a safe, supportive environment. Encouraging use of pregnancy diary, information and teaching skills to reduce anxiety and	Pregnant women with a history of at least one spontaneous	1. Anxiety 2. Depression (Intervention evaluation)	14 (mean) / NR	IG: 12 / 13 Comp: 11 / 11 (Analysis NR)	NR	RCT: reported no significant difference between the STAI-S scores between the groups post-intervention (p=0.66, n=23) (multivariate linear mixed effects model, time by group interaction)	Unclear

First author Country Year	Intervention category (duration)	Intervention, control and comparison group. * Description of intervention ** Facilitator / facilitator training	Included women	Primary outcome (secondary outcome)	Gestation at start / post intervention. (weeks of pregnancy)	Analysed n= Post-intervention / baseline (method)	Main anxiety measure mean score: baseline / post-intervention	Key anxiety results as reported in the included RCTSs / pilot RCTs	Risk of bias assessed as:
		depression and promote prenatal attachment. Based on the caring process (Swanson, 1993). ** Nurses with additional training / NR	perinatal loss						
Knight UK 2001	Other (4 individual sessions)	IG: Acupuncture, Comp: Sham acupuncture * Standardised acupuncture procedures. ** Midwife, experienced acupuncture practitioner / Integrated Chinese Medicine acupuncture college	Pregnant women with nausea	1. Nausea (Anxiety, depression)	8 (mean) / (9-14)	IG: 28 / 28 Comp: 27 / 27 (ITT analysis)	HADS-A (median/IQR) IG: 8.0 (6-9) / 7.0 (4-9) Comp: 10.0 (7-13) / 8.0 (5-9)	RCT: reported no significant difference for the HADS scores between the groups (p=0.20, n=57 (repeated measures ANOVA)	Unclear
Bastani Iran 2015	Other (3 individual sessions)	IG: Acupressure, Comp: Pressing at a sham point * Acupressure treatments: massage technique using fingers and palms with a certain amount of force to stimulate true acupoints and meridian lines on the surface of the skin. ** Nurse / Acupressure	Hospitalised pregnant women with GDM who expressed anxiety	1. Anxiety	18 (mean) / 25	IG: 28 / 30 Comp: 29 / 30 (Analysis NR)	MAQ IG: 37.3 (SD 5.9) / 33.3 (SD 4.3) Comp: 36.5 (SD 7.9) / 36.5 (SD 7.3)	RCT: reported significant decreases in the mean MAQ scores for the IG, scores remained unchanged in the comparison group (p=0.05, d=55, t=−1.96, n=57) (independent samples t-test, post-intervention between group scores)	Unclear

Anxiety measures:

ASI - Anxiety Sensitivity Index; **BAI** - Beck Anxiety Inventory; **DASS** - Depression Anxiety Stress Scale; **HADS-A** - Hospital Anxiety and Depression Scale; **MAQ** - Maternal Anxiety Questionnaire; **PRA -** Pregnancy Related Anxiety Scale; **PSA -** Pregnancy Specific Anxiety Scale; **STAI -** State Trait Anxiety Inventory; **STAI - short form**; **STAI-S** - state anxiety; **VASA** - Visual Analogue Scale for the Severity of Anxiety.

(For all of the self-report measures a decrease in scores indicated an improvement in anxiety symptoms)

Intervention descriptions:

BMI - body mass index; **BP** - Blood pressure; **CBA** - Cognitive behavioural approach; **CBT** – Cognitive behavioural therapy; **CG -** control group; **Comp -** comparison group; **CTG** - Cardiotocograph; **GDM -** Gestational diabetes mellitus; **, IG -** intervention group**; MBSR** - Mindfulness-based stress reduction; **MCBT -** Mindfulness cognitive based therapy; **NR -** Not reported

Analysis descriptions:

CI - confidence interval; **IQR - i**nter quartile range; **ITT -** Intention to treat analysis; **MD** - mean difference; **MC** - mean change; **NR -** Not reported; **SD -** standard deviation; **SE** - standard error
† - test not clearly stated in the paper and has been inferred from the information provided

Figure 1. PRISMA study flow diagram (Moher *et al.* 2009), Systematic Review of Randomised Controlled Trials

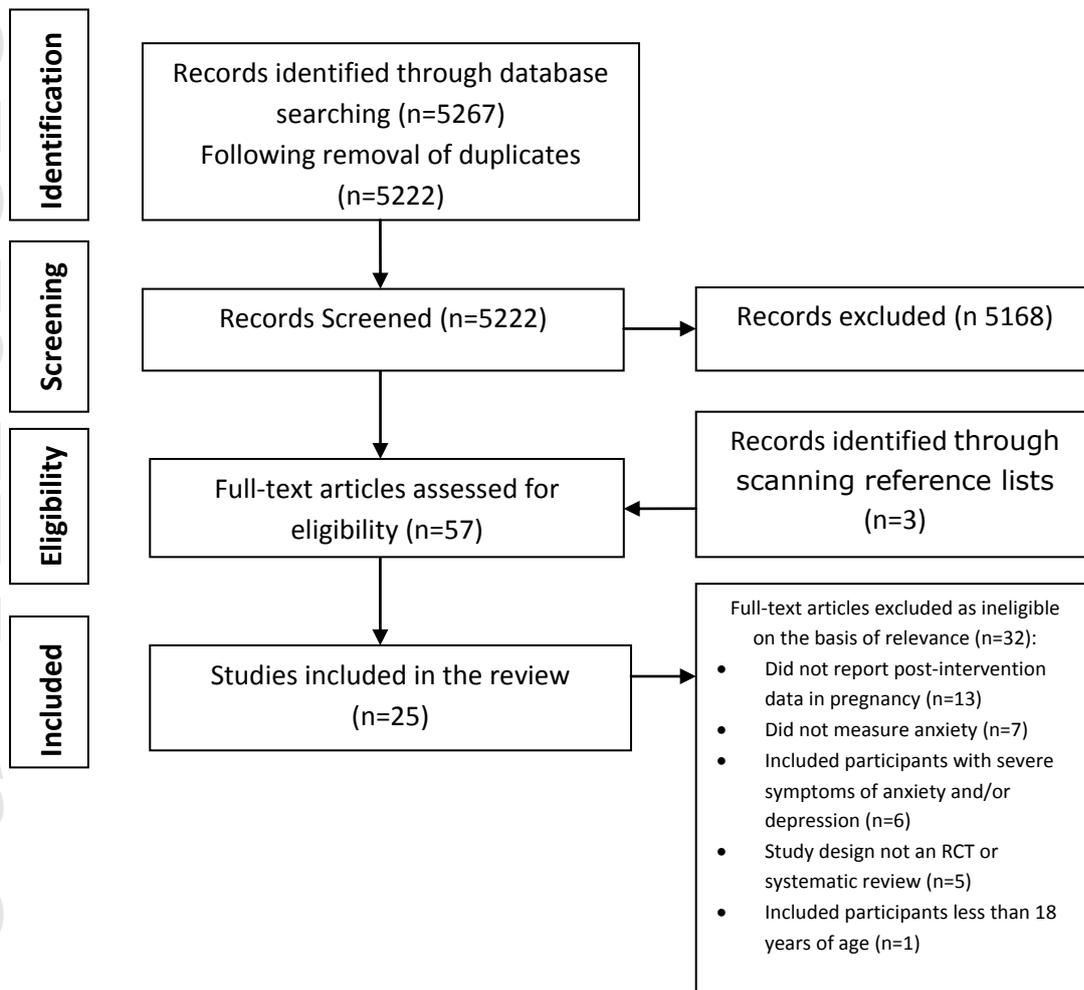|	
Identification	Records identified through database searching (n=5267) Following removal of duplicates (n=5222)
Screening	Records Screened (n=5222) → Records excluded (n 5168)
Eligibility	Full-text articles assessed for eligibility (n=57) ← Records identified through scanning reference lists (n=3)
Included	Studies included in the review (n=25) → Full-text articles excluded as ineligible on the basis of relevance (n=32): • Did not report post-intervention data in pregnancy (n=13) • Did not measure anxiety (n=7) • Included participants with severe symptoms of anxiety and/or depression (n=6) • Study design not an RCT or systematic review (n=5) • Included participants less than 18 years of age (n=1)

Figure 2. Cochrane Risk of Bias summary (Higgins *et al*. 2011): judgements about each risk of bias item for each included study

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bastani 2005	?	?	?	?	+	+	?
Bastani 2015	?	?	?	?	+	+	?
Bittner 2014	+	+	?	?	?	+	?
Bogaerts 2013	?	?	?	?	+	+	+
Brugha 2015	+	+	?	+	?	+	?
Bullock 1995	+	?	?	?	+	+	?
Chang 2008	+	?	?	?	+	+	?
Cote Arsenault 2014	?	?	?	?	+	+	?
Davis 2015	+	?	?	?	+	+	?
Dodd 2016	+	?	?	?	+	+	?
Faramazri 2015	+	+	?	+	+	+	+
Guardino 2014	+	?	?	?	+	+	?
Jallo 2014	+	+	?	?	+	+	?
Knight 2001	+	+	?	+	+	+	?
Korol 1992	?	?	?	+	−	−	?
Milgrom 2015	+	+	?	?	+	+	?
Newham 2014	?	+	+	?	?	+	?
Satyaprigta 2013	+	?	?	+	+	+	?
Snaith 2014	+	?	?	?	+	+	+
Texiera 2005	?	+	?	?	+	+	?
Tragea 2014	+	?	?	?	+	+	?
Urech 2010	+	?	?	+	+	+	?
Ventura 2012	+	?	?	?	+	+	?
Vieten 2008	?	?	?	?	+	+	?
Woolhouse 2014	?	+	?	?	?	+	?

+ low risk of bias

? unclear risk of bias

- high risk of bias

Figure 3. Meta-analysis of mindfulness group interventions on self-report symptoms of anxiety

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Guardino 2014	39.47	6.7	21	37.35	11.51	20	43.5%	0.22 [-0.39, 0.84]	
Vieten 2008	35.4	9.1	13	35.6	8.4	18	32.3%	-0.02 [-0.74, 0.69]	
Woolhouse 2014	32.83	7.8	13	33	12.78	10	24.2%	-0.02 [-0.84, 0.81]	
Total (95% CI)			**47**			**48**	**100.0%**	**0.09 [-0.32, 0.49]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 2 (P = 0.85); I² = 0%

Test for overall effect: Z = 0.41 (P = 0.68)

-10   -5   0   5   10

Favours [experimental]   Favours [control]