Review article

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The impact of psychological distress during pregnancy on the developing fetus: biological mechanisms and the potential benefits of mindfulness interventions

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Abstract: The *in utero* environment plays an essential role in shaping future growth and development. Psychological distress during pregnancy has been shown to perturb the delicate physiological milieu of pregnancy, and has been associated with negative repercussions in the offspring, including adverse birth outcomes, long-term defects in cognitive development, behavioral problems during childhood and high baseline levels of stress-related hormones. Fetal epigenetic programming, involving epigenetic processes, may help explain the link between maternal prenatal stress and its negative effects on the child. Given the potential long-term effects of early-life stress on a child's health, it is crucial to minimize maternal distress during pregnancy. A number of recent studies have examined the usefulness of mindfulness-based programs to reduce prenatal psychological stress and improve maternal psychological health, and these are reviewed here. Overall, the findings are promising, but more research is needed with large studies using randomized controlled study designs. It remains unclear whether or not such interventions could also improve child health outcomes, and whether these changes are modulated at the epigenetic level during fetal development. Further studies in this area are needed.

Keywords: Epigenetics; mindfulness; pregnancy; stress.

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Introduction

Maternal psychological distress during pregnancy can adversely affect the development of the fetus, with accumulating evidence showing that it can have long-term negative effects on the health of the child. Although the mechanistic links between prenatal distress and the long-term health repercussions are yet to be fully elucidated, physiological changes that occur in response to distress could influence fetal programming. Fetal programming postulates that the fetus adapts to its *in utero* environment to maximize growth and development, but such adaptations can have long-term consequences post-natally [1].

Given the essential role that maternal health during pregnancy plays in the long-term health of the developing fetus, it is important to identify prenatal interventions that can reduce maternal distress. The most widely used interventions to date have incorporated mindfulness practices. Mindfulness is a state of mind that consists of focusing attention on the present moment without judgment and without engaging with unrelated thoughts or emotions [2]. The aim of mindfulness meditation training is to notice fully every thought, sensation, or emotion that arises, and then to "let go" of those distractions and focus attention on an object, such as the breath [3]. Mindfulness-based interventions have been associated with reduced perceived stress, anxiety and depression [4, 5], and may be useful in reducing maternal distress during pregnancy, possibly with longer-term health consequences for both the mother and child.

In this review, we describe some of the changes in prenatal maternal physiology that occur during stress

or stress-related mood disorders such as depression and anxiety, and summarize correlational and mechanistic evidence for the short- and long-term effects of prenatal stress on the child. We then discuss recent studies on the effects of prenatal mindfulness interventions as a means to reduce maternal stress during pregnancy. Given the successes of a number of prenatal mindfulness interventions, we believe it is important to further study prenatal mindfulness interventions in the context of not only the psychological benefits for the expecting mother, but also the epigenetic, behavioral and health outcomes in the child.

Physiology of maternal distress during pregnancy

The focus of this review is maternal distress during pregnancy, including high levels of psychological stress, anxiety and depressed mood. Psychosocial stressors are life experiences, such as the death of a family member, natural disasters, daily hassles and job-related situations [6], that necessitate coping behaviors by the individual experiencing them [7]. Pregnant women often experience stressors that are unique to their situation, such as prenatal screenings [7], concerns about infant health and development [7], or having an unwanted pregnancy [6]. Stress during pregnancy can be classified as acute (e.g. trauma) or chronic (e.g. daily hassles), and each type of stress has varying degrees of severity. Depression and anxiety are mood disorders, which are also relatively common during pregnancy [8]. They are considered stress-related disorders, with repeat or chronic stress a risk factor and similar disruption of the underlying physiologic stress response [9, 10].

The stress response is characterized by a host of classic "fight or flight" symptoms such as rapid heartbeat [11], and is coordinated by the neuroendocrine, vascular and immune systems [12] (Figure 1). It begins by the perception of a threat by the senses, and then the subsequent activation of the paraventricular nucleus (PVN) of the hypothalamus [13]. PVN cells produce corticotrophin releasing factor (CRF), which causes the anterior pituitary gland to secrete adrenocorticotropic hormone (ACTH) into the bloodstream [13]. ACTH stimulates the adrenal cortex to produce corticosteroids [13]. This mechanism is known as the hypothalamic-pituitary-adrenal (HPA) axis. CRF also leads to the activation of the sympathetic nervous system via the stimulation of the adrenal medulla chromaffin cells to produce epinephrine [13], which is released into the bloodstream. This mechanism is known as the sympathetic adrenomedullary (SAM) system [11].

Pregnancy represents a state of altered physiology (Figure 2), and in the presence of stress, there is a complex interplay between the internal maternal physiologic environment and the changes induced by the stress response. Prenatal distress has been shown to suppress the lymphocyte activity of the immune system [12], predispose the body to infection [15], and decrease progesterone levels [16]. It has also been shown to alter the cytokine balance [16], which is essential for a healthy pregnancy. Women

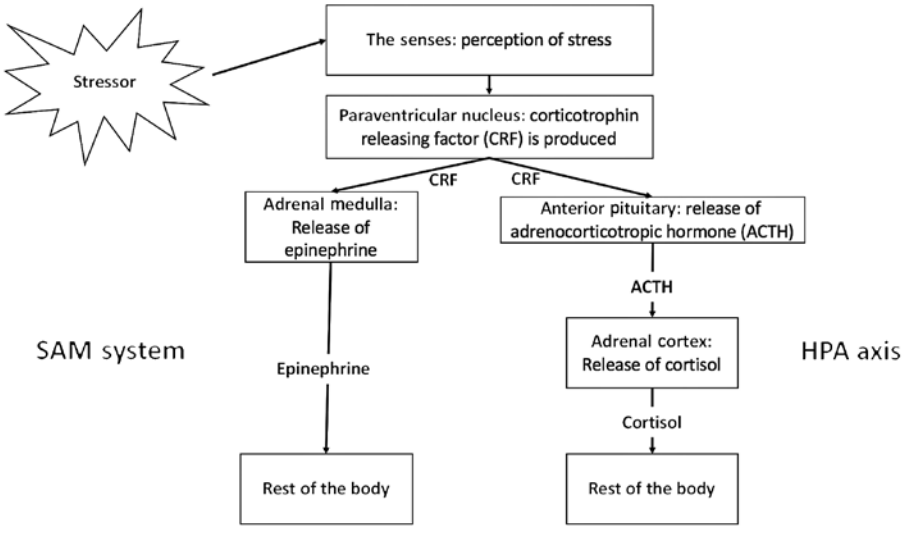

Figure 1: Two of the priniciple endocrine systems which are activated in response to a perceived stress: the sympathetic adrenomedullary (SAM) system and the hypothalamic-pituitary-adrenal (HPA) axis.

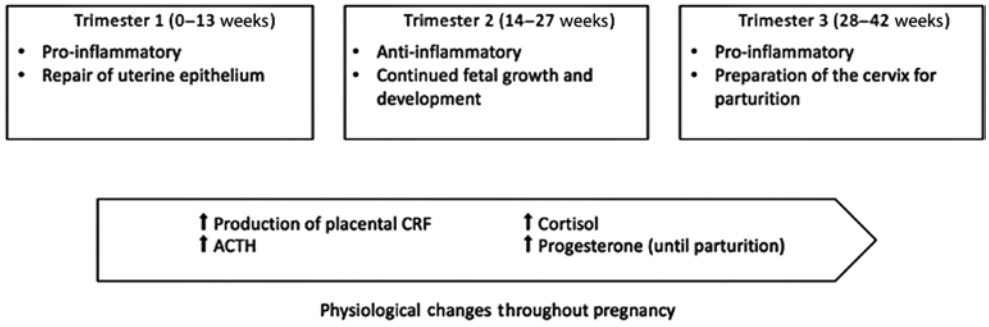

Figure 2: Pregnancy consists of three stages characterized by distinct physiological conditions [14].

experiencing prenatal distress have also been shown to have significantly higher circulating levels of ACTH, cortisol, and CRF than their non-stressed counterparts [7, 17]. These wide-ranging physiological changes that occur in the presence of distress can have major adverse effects on the *in utero* environment of the developing fetus.

Effects of maternal prenatal stress on the offspring

Animal models have provided a useful tool for examining the effects of maternal stress on the offspring. Overall, these studies have demonstrated that early-life stress can lead to dysregulation of the HPA axis, and behavioral changes in the offspring. Studies of rats exposed to prenatal restraint stress were found to display hyperactivation of the HPA axis, which persisted into adulthood and was associated with altered circadian rhythm. These animals also had high levels of anxiety and depression-like behaviors and impaired memory performance [18].

In addition to animal models, a number of human studies have linked maternal distress with adverse birth outcomes, including a greater risk of preterm birth, increased birth-related complications and lower birth weight, as well as longer-term health effects on the offspring [19–21]. Maternal distress during pregnancy may also cause long-term effects on the cognitive development of the infant, as well as leading to an increased risk of behavioral problems. High levels of self-reported anxiety and daily hassles in mid-pregnancy were associated with worse mental developmental in the infant at 8 months of age, and anxiety was also associated with delayed motor development [22]. Maternal antenatal depression has been associated with neurodevelopmental delays [22] and prenatal stress was inversely associated with mental development in toddlers [23]. A study of pregnant women during a natural disaster, found that those who experienced higher levels of perceived stress were more likely to have children with poorer mental development and language abilities at 2 years of age [24]. Older children are also more likely to have poorer attention and concentration if their mother experienced a major life event during pregnancy [25]. Severity of maternal depression during pregnancy has been associated with an increased likelihood of problematic behaviors in early childhood [26], and self-reported maternal anxiety and depression were associated with internalizing behaviors in young children [27, 28]. Both high levels of prenatal perceived stress and objective stress measures (i.e. death or severe illness of a close relative) have been linked to an increased risk of psychiatric disorders in mid childhood [29, 30].

A number of studies have demonstrated differential cortisol levels in children born to mothers with different types of prenatal distress. Prenatal anxiety has been positively associated with awakening and afternoon cortisol levels in offspring at 10 years of age [31], as well as a blunted cortisol response in the offspring at 14–15 years of age [32]. Young adults whose mothers had experienced a major negative life event during pregnancy had higher corticotropin (ACTH) and stress-induced cortisol levels than non-exposed offspring, as well as lower pre-test cortisol levels [29]. Some gender-specific associations have also been reported. A small study of cortisol response in preschool children showed that girls whose mothers were exposed prenatally to high levels of emotional complaints, had high cortisol levels under baseline and stress conditions, but no differences were observed in boys [30]. There is also some preliminary evidence that hormones other than cortisol may be affected in children with mothers who experienced prenatal distress. A study of the Chernobyl disaster showed that prenatal exposure in the second trimester specifically was associated with increased cortisol levels in adolescents, but was also associated with increased testosterone levels in females only [33]. Infants

born to mothers with high levels of prenatal anxiety and comorbid depression might also have lower dopamine and serotonin levels as well as lower vagal tone [34].

Proposed biological mechanisms: epigenetics

A number of studies have investigated possible mechanisms driving the association between prenatal maternal distress and later infant outcomes, and dysregulation of the HPA axis stress response has been implicated. It is hypothesized that fetal programming of the infant's HPA axis may play a clear role, and this is supported by the studies linking maternal stress with cortisol levels in children. Activation of the HPA axis following stress exposure leads to increased cortisol levels [35], which may result in increased exposure to the developing fetus. Indeed, elevated maternal cortisol levels during pregnancy have been predictive of infant temperament at 2 months of age [36], and high early morning values of cortisol in late pregnancy were associated with worse mental and motor development at 3 months [22]. However, other studies do not support an association between prenatal maternal cortisol and offspring learning and memory [25], and the link between maternal and fetal cortisol levels during pregnancy has not been clearly demonstrated [37]. It is also possible that other factors play a role, such as changes in uterine blood flow in stressed mothers and worse health behaviors, which could themselves influence fetal development.

While it remains unclear how exposures occurring during the crucial phase of early development can become biologically "embedded", epigenetic factors, which can regulate gene expression without altering the underlying DNA sequence, could be a mechanism by which these effects occur. The epigenome of the developing fetus may be particularly vulnerable to *in utero* exposures, with the loss and reprogramming of DNA methylation during embryogenesis. Indeed, a number of environmental exposures have been directly linked with a modified epigenetic profile in the neonate, and studies that have focused on stress during pregnancy are summarized below.

11-Beta-hydroxysteroid dehydrogenase type 2 (*HSD11β2*) is a barrier between maternal glucocorticoids and the fetal circulation that converts excess cortisol into cortisone [38] and serves as a protective role for the fetus [39]. Prenatal stress has been associated with the decreased expression of *HSD11β2* [39, 40] in the infant. If *HSD11β2* is not sufficiently expressed, cortisol can diffuse unchecked into the fetal circulation, and this may negatively affect growth and development. Although the precise mechanisms that connect decreased *HSD11β2* expression levels in infants with negative effects on growth and development have not yet been fully elucidated, correlative evidence exists. For example, Marsit et al. suggest that high levels of methylation at the *HSD11β2* promoter in infants is associated with intrauterine growth restriction, poor movement quality and hypertonia [40, 41].

Another gene that has been extensively studied in relation to maternal distress during pregnancy is the glucocorticoid receptor gene, *NR3C1* [40, 42]. The glucocorticoid receptor serves an essential function in the modulation of the HPA axis [43]. Its expression levels can decrease in chronically stressed individuals, leading to desensitization to cortisol's regulatory effect on the HPA axis [43], and thus perpetuating the physiological response to chronic stress. Studies have found that maternal prenatal perceived stress [42], depression [40] and anxiety [44] were all associated with higher levels of methylation of the *NR3C1* promoter in the infants. These epigenetic changes have been associated with low birth weight [42], lethargy and hypertonia [40], respectively. Other studies have also found increased levels of *NR3C1* DNA methylation in the offspring of mothers who experienced pregnancy-related anxiety, violence, or war exposure during pregnancy [45]. The large body of research on the methylation of *NR3C1* suggests that it could be another potential link between the mother's internal physiological environment during gestation and future developmental issues in the child (Figure 3).

The links between prenatal distress and DNA methylation of imprinted genes have also been studied. Imprinted genes are unique because they are only expressed from a single parental allele [46], so any methylation changes incurred *in utero* may have clinical significance with regards to the infant's growth and development. Vidal et al. [47] studied DNA methylation at maternally and paternally imprinted differentially methylated regions (DMRs) associated with nine different genes. Although there were no significant results for most of the genes they found that prenatal perceived stress was associated with a 2.8% increase in infant DNA methylation of the mesoderm specific transcript (*MEST)* DMR. The group suggests that this may be of clinical significance because *MEST* is maternally imprinted, and lack of *MEST* expression has been associated with the Silver-Russell syndrome, which causes growth retardation.

While much of the literature has focused on candidate genes, there have also been some epigenome-wide

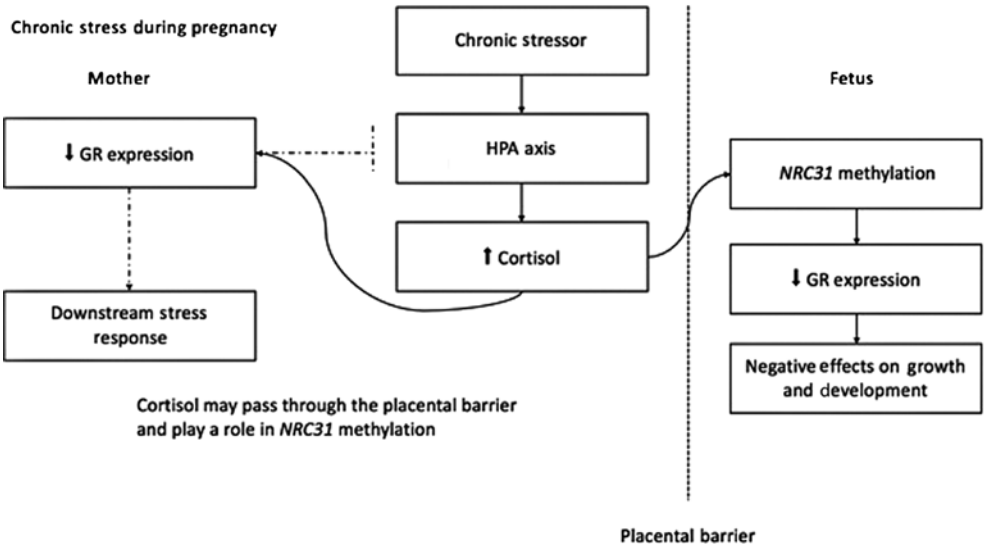

Figure 3: A simple model showing how chronic prenatal distress can impact the fetus, through changes in *NRC31* methylation.

association studies (EWAS) with mixed results. For example, a study by Rodney et al. [48] found that infants whose mothers had experienced severe war stress during pregnancy had 212 differentially methylated CpG regions in cord blood, compared to non-exposed control infants. Nemoda et al. [49] studied T lymphocyte methylation patterns in the neonatal cord blood of both infants whose mothers experienced prenatal depression and infants whose mothers did not experience prenatal depression. They found that infants in the prenatal depression group had 2520 differentially methylated CpG sites as compared to controls, and that 75.5% of these sites were hypomethylated. They also studied methylation in the postmortem hippocampi of adults whose mothers had a history of depression, and found that the DNA methylation patterns in the adult hippocampi overlapped with those in the neonatal T lymphocytes in 33 genes. This suggests that the epigenetic effects of prenatal depression on the child may be long term. A similar study by Non et al. [50] found 42 differentially methylated CpG sites in the neonatal cord blood of infants exposed to prenatal depression or anxiety as compared with controls, and suggest that some of these sites may be associated with genes that regulate transcription, translation, and cell division processes. Although there is substantial evidence suggesting that prenatal psychological stress, anxiety, and depression may be associated with the epigenetic profile of the newborn, not all EWAS support this notion. For example, a study of 201 mother-infant dyads found no significant correlation between maternal psychiatric diagnosis or depressive symptoms during pregnancy and gene-specific DNA methylation patterns in the neonatal cord blood of the infant [51]. The lack of consensus in the results of EWAS to date suggests that further research is warranted.

However, if the means through which maternal distress during pregnancy translates into long-term effects on the infant truly is via epigenetic mechanisms, it may be useful to study whether prenatal mindfulness-based stress reduction (MBSR) interventions may prevent or reverse those epigenetic changes before the damage is done. While there have been no studies to our knowledge on the effects of prenatal MBSR interventions on the epigenetic profiles of the infants, a number of studies have internally validated their mindfulness-based interventions as viable methods to reduce maternal prenatal psychological stress, anxiety, and depression.

Mindfulness interventions to reduce maternal prenatal stress

Mindfulness is the state of focusing attention on the present moment without judgment and without engaging with unrelated thoughts, beliefs, or emotions [2]. The goal is to fully notice every thought, sensation, or emotion that arises during practice, and to "let go" and return attention to the breath or another focus point [3]. Mindfulness has been shown to improve psychological attention control, emotion regulation, and self-awareness [52], and may thus have an effect on the cognitive appraisal of stressors. Trait mindfulness and mindfulness interventions have been shown to reduce both the grey matter of the amygdala [52] and the functional connectivity between the

amygdala and other regions of the brain that drive stress reactivity [53]. The amygdala is important for emotional processing in the brain, and plays a role in the initiation of the fight or flight response [53]. Preliminary research suggests that trait mindfulness can buffer SAM axis and HPA axis reactivity to acute stressors, thus decreasing the secretion of cortisol and catecholamines, which characterize the initiation of the fight or flight response [53]. Mindfulness interventions have been shown to increase parasympathetic nervous system activation, which counteracts the sympathetic fight or flight response in the presence of stressors [52, 53]. There is also evidence that mindfulness can normalize diurnal cortisol secretion [53], particularly in individuals with chronically high cortisol levels. However, studies on the effects of mindfulness on cortisol levels are not consistent [52]. In recent years, a number of studies on stress reduction in pregnant women have focused on interventions derived from the practice of mindfulness meditation (Table 1). Many included popular approaches, such as MBSR, which is a relaxation program developed by Kabat-Zinn [67], and mindfulness-based cognitive therapy (MBCT), which was developed by Segal et al. and intended to prevent relapse in individuals with depression [68]. A number of interventions also incorporated yoga practices or educational skill-building exercises geared toward the needs of pregnant women. The interventions typically ranged from 6 to 12 weeks in length and consisted of weekly sessions and practice at home.

Some studies have focused on pregnant women with pre-existing psychological conditions such as anxiety, depression, or bipolar disorder. Muzik et al. [62] studied the effects of a 10-week mindfulness yoga (M-Yoga) program as an alternative or complement to pharmaceutical treatment for pregnant women with clinical depression. Participants met weekly for 90 min to practice prenatal hatha yoga poses and mindfulness of the baby. They were given readings on mindfulness and were encouraged to practice at home. Overall, the program was associated with significant reductions in scores on both the Beck Depression Inventory-Second Edition (BDI-II) [69] and the Edinburgh Postnatal Depression Scale (EPDS) [70], both of which have been validated to measure the severity of symptoms of depression, such as loss of interest or feelings of worthlessness. Changes in mindfulness and maternal-fetal attachment were measured using the Revised Five Facet Mindfulness Questionnaire (FFMQ-Revised) [71] and the Maternal Fetal Attachment Scale (MFAS) [72], respectively, and there were significant improvements in each after the intervention. Dimidjian et al. [60] developed an 8-week Mindfulness-Based Cognitive Therapy Prenatal Depression (MBCT-PD) program for perinatal women with a history of clinical depression, but without a clinical diagnosis at the time of enrollment. The program was based on MBCT, with modifications specific to the perinatal period, such as education about pregnancy-related topics and increased attention to mindfulness practices designed specifically for pregnant women (e.g. "being with the baby"). It included formal mindfulness practices (e.g. sitting and walking meditation, body scan, etc.), informal mindfulness practices (e.g. mindfulness of daily activities), and cognitive behavioral skills practice. Participants met weekly for 2 h, and were provided DVDs for guided practice at home. The program resulted in significant improvements in symptoms of depression, based on the EPDS [70], which is frequently used to measure perinatal depressive symptom severity for both pregnant and postpartum women. Goodman et al. [64] developed the 8-week Coping with Anxiety through Living Mindfully (CALM) Pregnancy program, which was also an adaptation of MBCT, but specifically geared toward reducing anxiety and co-morbid symptoms in pregnant women with generalized anxiety disorder. The program was held for 2 h weekly and consisted of cognitive skills development, formal and informal mindfulness practices, and group discussions. Outside of the sessions, participants were asked to practice meditation daily for 30–40 min using audio recordings that were provided to them. During some weeks, the program also encouraged participants to practice a short 3-min mindfulness practice coined the "three-minute breathing space" three times per day or whenever they noticed unpleasant thoughts or feelings. Overall, the intervention was associated with significant reductions in clinical anxiety scores (Beck Anxiety Inventory, BAI) [73], worry scores (Penn State Worry Questionnaire, PSWQ) [74], and depression symptom severity (BDI-II) [69]. There were also significant improvements in self-compassion (Self-Compassion Scale, SCS) [75] and mindfulness (Mindfulness Attention Awareness Scale, MAAS) [76]. Miklowitz et al. [65] studied the effects of an 8-week program based on MBCT on perinatal women with a lifetime diagnosis of major depressive disorder, bipolar disorder, or cyclothymic disorder, with sub-threshold symptoms of depression at the time of enrollment. The program consisted of weekly 2-h sessions in which participants were exposed to a variety of mindfulness-related practices such as sitting meditation, mindful yoga, and body scan. They were also provided with readings about mindfulness and depression, and were encouraged to practice for 45 min at home each day with guided meditation CDs. The results indicated significant improvements in depression (BDI-II) [69] and mindfulness (FFMQ) [71].

Table 1: Studies investigating the effects of meditation programs during pregnancy.

Study	Intervention	Inclusion	Results from baseline to end of intervention	Sample size
Dunn et al. [54]	8-Week Mindfulness-Based Cognitive Therapy (MBCT) program	Pregnant women between 12 and 28 weeks' gestation at time of enrollment	Clinically reliable but non-significant decrease in stress (stress subscale of Depression, Anxiety, and Stress Scale, DASS-21) for ¾ of women in the intervention group	Intervention group: 4 Control group: 5
Beddoe et al. [55]	7-Week program designed to combine Iyengar yoga practice with MBSR	Healthy pregnant nulliparous women with singleton pregnancies between 12 and 32 weeks' gestation at time of enrollment	Significant reduction in stress (Perceived Stress Scale; PSS) and in trait anxiety (trait subscale of State-Trait Anxiety Inventory, STAI). Significant increase in average morning salivary cortisol	16
Duncan and Bardacke [56]	9-Week Mindfulness-Based Childhood and Parenting (MBCP) program	Late second or early third trimester pregnant women	Significant decrease in pregnancy-related anxiety (Pregnancy Anxiety Scale, PAS) and significant increase in mindfulness (Five Factor Mindfulness Questionnaire, FFMQ). Significant increase in positive affect (Positive and Negative Affect Scale; PANAS, and Differential Emotions Scale, DES). Significant decrease in negative affect (PANAS)	27
Carroll [57]	12-Week mindfulness-based prenatal yoga program	Second trimester pregnant women	Significant decrease in pregnancy-related stressors (PPP stressor subscale) and significant increase in mindfulness (FFMQ)	15
Vieten and Astin [58]	8-Week Mindful Motherhood program	Pregnant women at 12–30 weeks' gestation at enrollment and history of mood concerns for which they sought psychotherapy, counseling, or medication	Significant decreases in state anxiety (state subscale of STAI) and in negative affect (PANAS), compared to wait-list controls	Intervention group: 13 Control group: 18
Guardino et al. [59]	6-Week Mindful Awareness Practices (MAPS) program	Pregnant women at 10–25 weeks of gestation with a singleton pregnancy, experiencing high levels of perceived stress or pregnancy-specific anxiety	Significant improvements in state anxiety (state subscale of STAI), perceived stress (PSS), and mindfulness (FFMQ) for intervention group. Significant reductions in pregnancy related anxiety (Pregnancy Related Anxiety, PRA) and in pregnancy specific anxiety (Pregnancy Specific Anxiety, PSA) in intervention group	Intervention group: 24 Control group: 23
Dimidjian et al. [60]	8-Week Mindfulness-Based Cognitive Therapy – Prenatal Depression (MBCT-PD)	Pregnant women up to 32 weeks of gestation who meet criteria for prior major depressive disorder (MDD)	Significant improvements in depressive symptoms (Edinburgh Postpartum Depression Scale, EPDS)	49
Byrne et al. [61]	8-Week Mindfulness-Based Childbirth Education (MBCE)	Healthy, nulliparous pregnant women with singleton pregnancies between 18 and 28 weeks of gestation	Significant improvements in childbirth self-efficacy and birth outcome expectations (Childbirth Self-Efficacy Inventory, CBSI) and decreased fear of childbirth (Wijma Delivery Expectancy Questionnaire, WDEQ)	12
Muzik et al. [62]	10-Week mindfulness yoga (M-Yoga)	Primiparous pregnant women at over 26 weeks of gestation not taking psychotropic medications, with a score over 9 on the EPDS depression screen	Significant reductions in depressive symptoms (Beck Depression Inventory-second edition, BDI-II and EPDS). Significant improvements in mindfulness (FFMQ-Revised) and maternal-fetal attachment (Maternal Fetal Attachment Scale, MFAS)	18

Table 1 (continued)

Study	Intervention	Inclusion	Results from baseline to end of intervention	Sample size
Woolhouse et al. [63]	6-Week "MindBabyBody" program	Non-randomized study: pregnant women identified as at-risk for perinatal stress, depression, or anxiety Randomized controlled trial (RCT): all English-speaking pregnant women booked to give birth at a given hospital	Significant improvements in depressive symptoms (DASS-21 and CES-D), state anxiety (STAI state subscale), and mindfulness (awareness and describing subscales of FFMQ) for the non-randomized study participants. Significant reductions in anxiety (DASS-21 anxiety subscale) and mindfulness (observing and describing subscales of FFMQ) for both control and intervention participants in the randomized controlled study	20 for non-randomized study 32 for randomized controlled study (15 for control group and 17 for intervention group)
Goodman et al. [64]	8-Week CALM pregnancy program, which is designed to counter anxiety in pregnant women	Pregnant women with GAD or prominent symptoms of generalized anxiety at 1–20 weeks' gestation at time of enrollment	Significant improvements in anxiety (Beck Anxiety Inventory, BAI), worry (Penn State Worry Questionnaire, PSWQ), depression (BDI-II), self-compassion (Self-Compassion Scale, SCS), and mindfulness (MAAS)	23
Miklowitz et al. [65]	8-Week MBCT program	Pregnant women up to 32 weeks' gestation, within 1 year postpartum, or not pregnant but actively trying to conceive, with a lifetime diagnosis of major depressive disorder, bipolar disorder, or cyclothymic disorder with sub-threshold symptoms of depression at time of enrollment	Significant improvements in depression (BDI-II) and mindfulness (FFMQ) for women with major depressive disorder and bipolar disorder	32
Zhang and Emory [66]	8-Week Mindful Motherhood program	Pregnant women with singleton pregnancies at 12–31 weeks of gestation, self-identified as African Americans	Significant positive correlation between number of sessions attended by participants and mindfulness (Toronto Mindfulness Scale, TMS). Significant negative correlation between number of sessions attended and both intensity of pregnancy-related hassles (hassle intensity subscale of Pregnancy Experience Scale – Brief Version, PES) and reactive salivary cortisol response	Intervention group: 16 Control group: 17

MBCT = mindfulness-based cognitive therapy, MBCP = mindfulness-based childhood and parenting, CALM = coping with anxiety through living mindfully, GAD = generalized anxiety disorder.

Other studies have examined the usefulness of mindfulness interventions among otherwise healthy women, and some studies have actively excluded women with pre-existing medical conditions or mental illnesses. For example, a study by Beddoe et al. [55] used a 7-week mindfulness yoga program which combined Iyengar yoga (which is based on postures and careful alignment) with MBSR. Participants met weekly to practice sitting mindfulness meditation, progressive relaxation, and postural yoga. By the end of the program, there were significant reductions in Perceived Stress Scale (PSS) [77] scores, which measure the extent to which an individual experiences situations as uncontrollable or unpredictable. There were also significant reductions in trait anxiety, as measured by the trait subscale of the state-trait anxiety inventory (STAI) [78]. Interestingly, there was a significant overall increase in the average morning salivary cortisol after the intervention. Because cortisol levels have been shown to increase in concentration in the body over the course of a pregnancy, that may be a potential explanation for those results. A 12-week mindfulness-based prenatal yoga program studied by Carroll [57], which consisted of weekly group yoga sessions and two focus groups, was associated with a significant decrease in pregnancy-related stressors, based on the prenatal psychosocial profile (PPP) [79] stressor subscale, which measures current stressors and hassles related to pregnancy. Moreover, there was a significant increase in mindfulness, based on the FFMQ, which is subdivided into items that measure mindfulness, attention, awareness, non-judging, and non-reactivity. The 9-week Mindfulness-Based Childbirth and Parenting (MBCP) program developed by Duncan and Bardake [56] included formal mindfulness meditation practice and education on pregnancy-related topics for 3 h each week. Outside of the sessions, participants were asked to practice meditation for 30 min per day for 6 days each week, and were provided with guided meditation recordings, readings, and a workbook. There was also a 7-h silent retreat day. The program was associated with significant reductions in pregnancy-related anxiety (Pregnancy Anxiety Scale, PAS) [80] and negative affect (Positive and Negative Affect Scale; PANAS) [81]. Results also suggested significant improvements in mindfulness (FFMQ) and positive affect, based on both the PANAS and the Differenfial Emotions Scale (DES) [82]. Byrne et al. [61] developed the 8-week Mindfulness-Based Childbirth Education (MBCE) program, which combined mindfulness meditation with education about childbirth. Participants met weekly for 2 h and 30 min, and were also encouraged to practice meditation each day using audio recordings. After the intervention, there were significant improvements in childbirth self-efficacy and birth outcome expectations (Childbirth Self-Efficacy Inventory, CBSI) [83], and in fear of childbirth (Wijma Delivery Expectancy Questionnaire, WDEQ) [84].

Only a handful of studies have included a control group when assessing intervention effectiveness. Vieten and Astin [58] developed an 8-week program called the "Mindful Motherhood" which combined aspects of MBSR, MBCT, and consisted of education on topics specific to pregnancy, group discussions, and experiential exercises. There was a focus on awareness of the baby and belly during the body scan meditation practices, and the program included prenatal yoga as part of the mindful moving component. Participants were given a compact disc with guided meditation, and were encouraged to practice for 20 min each day. All women had a history of mood concerns, and those assigned to the intervention group had significantly lower levels of state anxiety (state subscale of STAI) and negative affect (PANAS) compared to the wait-list control group. Zhang and Emory [66] replicated the "Mindful Motherhood" program, and studied its effects on pregnant African-American women. There was a significant positive correlation between number of sessions attended by participants and their mindfulness scores, based on the Toronto Mindfulness Scale (TMS) [85]. There was a significant negative correlation between number of sessions attended and both intensity of pregnancy-related hassles (based on the hassle intensity subscale of Pregnancy Experience Scale Brief Version; PES) [86] and reactive salivary cortisol response. A pilot study by Woolhouse et al. [63] used a similar 6-week program (MindBabyBody) which combined the MBSR, MBCT, and MBCP programs. The program was geared specifically toward the needs of pregnant women, and consisted of formal and informal mindfulness practices at the weekly 2-h sessions. It was piloted in both a non-randomized trial with women considered to be at risk for perinatal stress, depression, or anxiety, and a randomized controlled trial (RCT) open to all pregnant woman (where control-group women received a standard level of care). Significant improvements in depressive symptoms (measured by the depression subscale of the Depression, Anxiety, and Stress Scale, DASS-21 [87]; and the Center for Epidemiological Studies Depression Scale, CES-D [88]) and state anxiety (state subscale of STAI) measures were observed in the non-randomized study participants. There were also significant reductions in anxiety (anxiety subscale of Depression, Anxiety, and Stress Scale, DASS-21) for both control and intervention participants in the randomized controlled study. A small pilot study by Dunn et al. compared the effectiveness of an 8-week MBCT program

administered to 10 women (nine of whom had preexisting stress or a history of psychiatric illness) on psychological measures of well-being, compared to a group of 10 control women without a history of mental health problems [54]. The main themes covered by the program included awareness, embracing the present, shared group experiences, and more. There was a clinically reliable but non-significant decrease in stress (stress subscale of depression, anxiety, and stress scale, DASS-21) for 3/4 of the women in the intervention group. However, most women showed no improvements in anxiety, depression (subscales of DASS-21), or mindfulness (MAAS). Guardino et al. [59] conducted a larger RCT with 24 intervention participants and 23 controls with high levels of anxiety and perceived stress at the time of enrollment. Intervention participants were assigned to a 6-week MBSR program that was not pregnancy-specific, while control participants were mailed a copy of a book with general information about what to expect during and after pregnancy. The program met weekly for 2 h, and consisted of both lectures and mindfulness practice. Participants were asked to practice meditation at home each day, and were given a compact disc with guided meditations. Participants in both the intervention and control groups had significant improvements in measures of mindfulness (FFMQ), perceived stress (PSS), and state anxiety (state subscale of STAI).

Overall, despite large heterogeneity in the design of these studies, in terms of the participant inclusion and exclusion criteria, the length and nature of the interventions, and the stress measures and other outcomes assessed, the findings of these studies are promising and suggest that mindfulness-based programs may be viable and effective interventions to reduce stress, anxiety, and depression in pregnant women. An important limitation of these findings to date, however, is that the studies have been very small (almost all <50 subjects), and it can be difficult to replicate the results of studies that are underpowered. Also, most studies have failed to consider selection bias in recruitment and to include an appropriate control group which would ensure any effects observed are likely to be the direct result of the intervention, rather than other external factors.

Conclusion

Psychological stress, depression, and anxiety during pregnancy can influence fetal development and have long-term consequences on the child's health. Reducing distress during pregnancy could thus be beneficial for both mother and child. A number of small studies have shown that prenatal mindfulness-based interventions are associated with reduced perceived stress, anxiety, and depression in expectant mothers, which can help promote a healthy pregnancy and *in utero* environment. To date however, very few studies have examined the potential benefits of prenatal mindfulness on child developments or later health outcomes but one study showed that meditation during pregnancy was associated with better child temperaments [89]. To our knowledge, no study has yet drawn a link between prenatal mindfulness interventions, changes in the epigenetic profile of the offspring, and long-term effects on the child, but further studies in this area are warranted. Such evidence-based research is needed to determine whether prenatal mindfulness interventions are useful tools to support the wellbeing of the expectant mother, but also to promote the short- and long-term health of the child.

Author's statement

Conflict of interest: Authors state no conflict of interest.

Material and methods: Informed consent: Informed consent has been obtained from all individuals included in this study.

Ethical approval: The research related to human subject use has complied with all the relevant national regulations, and institutional policies, and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

References

[1] Barker DJ. The fetal and infant origins of adult disease. Br Med J. 1990;301:1111. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1664286&tool=pmcentrez&rendertype=abstract. Accessed November 18, 2015.

[2] Epel ES, Puterman E, Lin J, Blackburn E, Lazaro A, Mendes WB. Wandering minds and aging cells. Clin Psychol Sci. 2012;1:75–83.

[3] Epel E, Daubenmier J, Moskowitz JT, Folkman S, Blackburn E. Can meditation slow rate of cellular aging? Cognitive stress, mindfulness, and telomeres. Ann N Y Acad Sci. 2009;1172:34–53.

[4] Astin JA. Stress reduction through mindf ulness meditation. Psychother Psychosom. 1997;66:97–106.

[5] Hofmann SG, Sawyer AT, Witt AA, Oh D. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. J Consult Clin Psychol. 2010;78:169–83.

[6] Howerton CL, Bale TL. Prenatal programing: at the intersection of maternal stress and immune activation. Horm Behav. 2012;62:237–42.

[7] Coussons-Read ME, Lobel M, Carey JC, Kreither MO, D'Anna K, Argys L, et al. The occurrence of preterm delivery is linked to

pregnancy-specific distress and elevated inflammatory markers across gestation. Brain Behav Immun. 2012;26:650–9.
[8] Lee AM, Lam SK, Sze Mun Lau SM, Chong CSY, Chui HW, Fong DYT. Prevalence, course, and risk factors for antenatal anxiety and depression. Obstet Gynecol. 2007;110:1102–12.
[9] Powers SI, Laurent HK, Gunlicks-Stoessel M, Balaban S, Bent E. Depression and anxiety predict sex-specific cortisol responses to interpersonal stress. Psychoneuroendocrinology. 2016;69:172–9.
[10] Belvederi Murri M, Pariante C, Mondelli V, Masotti M, Atti AR, Mellacqua Z, et al. HPA axis and aging in depression: systematic review and meta-analysis. Psychoneuroendocrinology. 2014;41:46–62.
[11] Kemeny ME. The psychobiology of stress. Curr Dir Psychol Sci. 2003;12:124–9.
[12] Wadhwa PD, Culhane JF, Rauh V, Barve SS. Stress and preterm birth: neuroendocrine, immune/inflammatory, and vascular mechanisms. Matern Child Health J. 2001;5:119–25.
[13] Black PH. Stress and the inflammatory response: a review of neurogenic inflammation. Brain Behav Immun. 2002;16:622–53.
[14] Mor G, Cardenas I, Abrahams V, Guller S. Inflammation and pregnancy: the role of the immune system at the implantation site. Ann N Y Acad Sci. 2011;1221:80–7.
[15] Coussons-Read ME, Okun ML, Schmitt MP, Giese S. Prenatal stress alters cytokine levels in a manner that may endanger human pregnancy. Psychosom Med. 67:625–31.
[16] Parker VJ, Douglas AJ. Stress in early pregnancy: maternal neuro-endocrine-immune responses and effects. J Reprod Immunol. 2010;85:86–92.
[17] Wadhwa PD, Sandman CA, Garite TJ. The neurobiology of stress in human pregnancy: implications for prematurity and development of the fetal central nervous system. Prog Brain Res. 2001;133:131–42.
[18] Darnaudéry M, Maccari S. Epigenetic programming of the stress response in male and female rats by prenatal restraint stress. Brain Res Rev. 2008;57:571–85.
[19] Grigoriadis S, VonderPorten EH, Mamisashvili L, Tomlinson G, Dennis CL, Koren G, et al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. J Clin Psychiatry. 2013;74:e321–41.
[20] Staneva A, Bogossian F, Pritchard M, Wittkowski A. The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: A systematic review. Women Birth. 2015;28:179–93.
[21] Jarde A, Morais M, Kingston D, Giallo R, MacQueen GM, Giglia L, et al. Neonatal outcomes in women with untreated antenatal depression compared with women without depression: a systematic review and meta-analysis. JAMA psychiatry. 2016;73:826–37.
[22] Huizink AC, Robles de Medina PG, Mulder EJH, Visser GHA, Buitelaar JK. Stress during pregnancy is associated with developmental outcome in infancy. J Child Psychol Psychiatry. 2003;44:810–8.
[23] Bergman K, Sarkar P, O'Connor TG, Modi N, Glover V. Maternal stress during pregnancy predicts cognitive ability and fearfulness in infancy. J Am Acad Child Adolesc Psychiatry. 2007;46:1454–63.
[24] Laplante DP, Barr RG, Brunet A, Galbaud du Fort G, Meaney ML, et al. Stress during pregnancy affects general intellectual and language functioning in human toddlers. Pediatr Res. 2004;56:400–10.
[25] Gutteling BM, de Weerth C, Zandbelt N, Mulder EJH, Visser GHA, Buitelaar JK. Does maternal prenatal stress adversely affect the child's learning and memory at age six? J Abnorm Child Psychol. 2006;34:789–98.
[26] Nulman I, Koren G, Rovet J, Barrera M, Pulver A, Streiner D, et al. Neurodevelopment of children following prenatal exposure to venlafaxine, selective serotonin reuptake inhibitors, or untreated maternal depression. Am J Psychiatry. 2012;169:1165–74.
[27] de Bruijn ATCE, van Bakel HJA, van Baar AL. Sex differences in the relation between prenatal maternal emotional complaints and child outcome. Early Hum Dev. 2009;85:319–24.
[28] O'Connor TG, Heron J, Glover V. Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. J Am Acad Child Adolesc Psychiatry. 2002;41:1470–7.
[29] Entringer S, Kumsta R, Hellhammer DH, Wadhwa PD, Wüst S. Prenatal exposure to maternal psychosocial stress and HPA axis regulation in young adults. Horm Behav. 2009;55:292–8.
[30] de Bruijn ATCE, van Bakel HJA, Wijnen H, Pop VJM, van Baar AL. Prenatal maternal emotional complaints are associated with cortisol responses in toddler and preschool aged girls. Dev Psychobiol. 2009;51:553–63.
[31] O'Connor TG, Ben-Shlomo Y, Heron J, Golding J, Adams D, Glover V. Prenatal anxiety predicts individual differences in cortisol in pre-adolescent children. Biol Psychiatry. 2005;58:211–7.
[32] Van den Bergh BRH, Van Calster B, Smits T, Van Huffel S, Lagae L. Antenatal maternal anxiety is related to HPA-axis dysregulation and self-reported depressive symptoms in adolescence: a prospective study on the fetal origins of depressed mood. Neuropsychopharmacology. 2007;33:536–45.
[33] Huizink AC, Bartels M, Rose RJ, Pulkkinen L, Eriksson CJP, Kaprio J. Chernobyl exposure as stressor during pregnancy and hormone levels in adolescent offspring. J Epidemiol Community Health. 2008;62:e5–e5.
[34] Field T, Diego M, Hernandez-Reif M, Schanberg S, Kuhn C, Yando R, et al. Pregnancy anxiety and comorbid depression and anger: effects on the fetus and neonate. Depress Anxiety. 2003;17:140–51.
[35] Herbert J. Cortisol and depression: three questions for psychiatry. Psychol Med. 2013;43:449–69.
[36] Davis EP, Glynn LM, Schetter CD, Hobel C, Chicz-Demet A, Sandman CA. Prenatal exposure to maternal depression and cortisol influences infant temperament. J Am Acad Child Adolesc Psychiatry. 2007;46:737–46.
[37] Talge NM, Neal C, Glover V. Antenatal maternal stress and long-term effects on child neurodevelopment: how and why? J Child Psychol Psychiatry. 2007;48:245–61.
[38] Kajantie E, Dunkel L, Turpeinen U, Stenman UH, Wood PJ, Nuutila M, et al. Placental 11 beta-hydroxysteroid dehydrogenase-2 and fetal cortisol/cortisone shuttle in small preterm infants. J Clin Endocrinol Metab. 2003;88:493–500.
[39] O'Donnell K, O'Connor TG, Glover V. Prenatal stress and neurodevelopment of the child: focus on the HPA axis and role of the placenta. Dev Neurosci. 2009;31:285–92.
[40] Conradt E, Lester BM, Appleton AA, Armstrong DA, Marsit CJ. The roles of DNA methylation of *NR3C1* and *11β-HSD2* and

exposure to maternal mood disorder in utero on newborn neurobehavior. Epigenetics. 2013;8:1321–9.
[41] Marsit CJ, Maccani MA, Padbury JF, Lester BM. Placental 11-beta hydroxysteroid dehydrogenase methylation is associated with newborn growth and a measure of neurobehavioral outcome. PLoS One. 2012;7:e33794–e33794.
[42] Mulligan C, D'Errico N, Stees J, Hughes D. Methylation changes at NR3C1 in newborns associate with maternal prenatal stress exposure and newborn birth weight. Epigenetics. 2014;7:853–7.
[43] Palma-Gudiel H, Córdova-Palomera A, Eixarch E, Deuschle M, Fañanás L. Maternal psychosocial stress during pregnancy alters the epigenetic signature of the glucocorticoid receptor gene promoter in their offspring: a meta-analysis. Epigenetics. 2015;10:893–902.
[44] Mansell T, Vuillermin P, Ponsonby A-L, Collier F, Saffery R; Barwon Infant Study Investigator Team, et al. Maternal mental well-being during pregnancy and glucocorticoid receptor gene promoter methylation in the neonate. Dev Psychopathol. 2016;28:1421–30.
[45] Turecki G, Meaney M. Effects of the social environment and stress on glucocorticoid receptor gene methylation: a systematic review. Biol Psychiatry. 2016;15:87–96.
[46] Li E, Beard C, Jaenisch R. Role for DNA methylation in genomic imprinting. Nature. 1993;366:362–5.
[47] Vidal AC, Benjamin Neelon SE, Liu Y, Tuli AM, Fuemmeler BF, Hoyo C, et al. Maternal stress, preterm birth, and DNA methylation at imprint regulatory sequences in humans. Genet Epigenet. 2014;6:37–44.
[48] Rodney NC, Mulligan CJ. A biocultural study of the effects of maternal stress on mother and newborn health in the Democratic Republic of Congo. Am J Phys Anthropol. 2014;155:200–9.
[49] Nemoda Z, Massart R, Suderman M, Hallett M, Li T, Coote M, et al. Maternal depression is associated with DNA methylation changes in cord blood T lymphocytes and adult hippocampi. Transl Psychiatry. 2015;5:e545.
[50] Non AL, Binder AM, Kubzansky LD, Michels KB. Genome-wide DNA methylation in neonates exposed to maternal depression, anxiety, or SSRI medication during pregnancy. Epigenetics. 2014;9:964–72.
[51] Schroeder JW, Smith AK, Brennan PA, Conneely KN, Kilaru V, Knight BT, et al. DNA methylation in neonates born to women receiving psychiatric care. Epigenetics. 2012;7:409–14.
[52] Tang Y-Y, Hölzel BK, Posner MI. The neuroscience of mindfulness meditation. Nat Rev Neurosci. 2015;16:213–25.
[53] Creswell JD, Lindsay EK. How does mindfulness training affect health? A mindfulness stress buffering account. Curr Dir Psychol Sci. 2014;23:401–7.
[54] Dunn C, Hanieh E, Roberts R, Powrie R. Mindful pregnancy and childbirth: effects of a mindfulness-based intervention on women's psychological distress and well-being in the perinatal period. Arch Womens Ment Health. 2012;15:139–43.
[55] Beddoe AE, Paul Yang C-P, Kennedy HP, Weiss SJ, Lee KA. The effects of mindfulness-based yoga during pregnancy on maternal psychological and physical distress. J Obstet Gynecol Neonatal Nurs. 2009;38:310–19.
[56] Duncan LG, Bardacke N. Mindfulness-based childbirth and parenting education: promoting family mindfulness during the perinatal period. J Child Fam Stud. 2010;19:190–202.
[57] Carroll L. The impact of mindfulness-based prenatal yoga on maternal stress during pregnancy. 2014. http://scholarworks.csustan.edu/handle/011235813/690. Accessed January 11, 2016.
[58] Vieten C, Astin J. Effects of a mindfulness-based intervention during pregnancy on prenatal stress and mood: results of a pilot study. Arch Womens Ment Health. 2008;11:67–74.
[59] Guardino CM, Dunkel Schetter C, Bower JE, Lu MC, Smalley SL. Randomised controlled pilot trial of mindfulness training for stress reduction during pregnancy. Psychol Health. 2014;29:334–49.
[60] Dimidjian S, Goodman SH, Felder JN, Gallop R, Brown AP, Beck A. An open trial of mindfulness-based cognitive therapy for the prevention of perinatal depressive relapse/recurrence. Arch Womens Ment Health. 2015;18:85–94.
[61] Byrne J, Hauck Y, Fisher C, Bayes S, Schutze R. Effectiveness of a Mindfulness-Based Childbirth Education pilot study on maternal self-efficacy and fear of childbirth. J Midwifery Womens Health. 59:192–7.
[62] Muzik M, Hamilton SE, Lisa Rosenblum K, Waxler E, Hadi Z. Mindfulness yoga during pregnancy for psychiatrically at-risk women: Preliminary results from a pilot feasibility study. Complement Ther Clin Pract. 2012;18:235–40.
[63] Woolhouse H, Mercuri K, Judd F, Brown SJ. Antenatal mindfulness intervention to reduce depression, anxiety and stress: a pilot randomised controlled trial of the MindBabyBody program in an Australian tertiary maternity hospital. BMC Pregnancy Childbirth. 2014;14:369.
[64] Goodman JH, Guarino A, Chenausky K, Klein L, Prager J, Petersen R, et al. CALM Pregnancy: results of a pilot study of mindfulness-based cognitive therapy for perinatal anxiety. Arch Womens Ment Health. 2014;17:373–87.
[65] Miklowitz DJ, Semple RJ, Hauser M, Elkun D, Weintraub MJ, Dimidjian S. Mindfulness-based cognitive therapy for perinatal women with depression or bipolar spectrum disorder. Cognit Ther Res. 2015;39:590–600.
[66] Zhang H, Emory EK. A mindfulness-based intervention for pregnant African-American women. Mindfulness (N Y). 2015;6:663–74.
[67] Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. Gen Hosp Psychiatry. 1982;4:33–47.
[68] Segal ZV, Williams JMG, Teasdale JD. Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse. New York, NY, USA: Guilford Press, 2002. https://books.google.com/books/about/Mindfulness_based_Cognitive_Therapy_for.html?id=_QJ3cQT5UpsC&pgis=1.
[69] Beck AT, Steer RA, Ball R, Ranieri W. Comparison of Beck depression inventories -IA and -II in psychiatric outpatients. J Pers Assess. 1996;67:588–97.
[70] Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150:782–6.
[71] Baer RA, Smith GT, Hopkins J, Krietemeyer J, Toney L. Using self-report assessment methods to explore facets of mindfulness. Assessment. 2006;13:27–45.
[72] Cranley MS. Development of a tool for the measurement of maternal attachment during pregnancy. Nurs Res. 1981;30:281–4.

[73] Beck AT, Steer RA. Manual for the beck anxiety inventory. San Antonio: The Psychological Corporation; 1990.
[74] Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn State Worry Questionnaire. Behav Res Ther. 1990;28:487–95.
[75] Neff K. The Development and validation of a scale to measure self-compassion. Self Identity; 2003.
[76] Brown KW, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol. 2003;84:822–48.
[77] Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24:385–96.
[78] Spielberger CD. State-Trait Anxiety Inventory. In: *Corsini Encyclopedia of Psychology*. Vol; Hoboken, NJ, USA: John Wiley & Sons, Inc.; 2010.
[79] Curry MA, Burton D, Fields J. The prenatal psychosocial profile: a research and clinical tool. Res Nurs Health. 1998;21:211–9.
[80] Levin JS. The factor structure of the pregnancy anxiety scale. J Health Soc Behav. 1991;32:368.
[81] Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol. 1988;54:1063–70.
[82] Boyle GJ. Reliability and validity of Izard's differential emotions scale. Pers Individ Dif. 1984;5:747–50.
[83] Lowe NK. Maternal confidence for labor: development of the childbirth self-efficacy inventory. Res Nurs Health. 1993;16:141–9.
[84] Wijma K, Wijma B, Zar M. Psychometric aspects of the W-DEQ; a new questionnaire for the measurement of fear of childbirth. J Psychosom Obstet Gynaecol. 1998;19:84–97.
[85] Lau MA, Bishop SR, Segal ZV, Buis T, Anderson ND, Carlson L, et al. The toronto mindfulness scale: development and validation. J Clin Psychol. 2006;62:1445–67.
[86] Dipietro JA, Christensen AL, Costigan KA. The pregnancy experience scale–brief version. J Psychosom Obstet Gynecol. 2008;29(4):262–7.
[87] Lovibond P. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther. 1995;33:335–43.
[88] Eaton WW, Muntaner C, Smith C, Tien A, Ybarra M. Center for Epidemiologic Studies Depression Scale: Review and revision (CESD and CESD-R). In: Maruish ME, editor. The use of psychological testing for treatment planning and outcomes assessment. 3rd ed. Mahwah, NJ: Lawrence Erlbaum; 2004:363–77.
[89] Chan KP. Prenatal meditation influences infant behaviors. Infant Behav Dev. 2014;37:556–1.