## Investigating the Role of Maternal Sensitivity in the Impact of

## **Antenatal Stress on Infant Temperament**

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#### Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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#### OVERVIEW

#### Part 1: Literature Review

The first section of this thesis consists of a meta-analysis examining antenatal anxiety and depression as risk factors for developing postnatal depression. In total, 30 studies (31 separate samples) were included in the meta-analysis. Results indicated a medium to large effect size for antenatal depression as a risk factor for postnatal depression, and a medium effect size for antenatal anxiety as a risk factor. One significant predictor of effect sizes was found: effect sizes for studies with adjusted covariates were smaller than that for studies where covariates were not adjusted. The results highlight the importance of developing robust antenatal screening procedures, early interventions and treatments during the perinatal period.

#### Part 2: Empirical Paper

The empirical paper reports on a study examining the role that maternal sensitivity plays in the pathway between antenatal stress and infant difficult temperament, with a rarely studied population; young, economically disadvantaged mothers and babies. The study also investigated the potential mediating and moderating role of maternal sensitivity. Participants were included from a study of a community home-visiting programme at the 12 months' follow-up point. Data included maternal mental health variables (anxiety and depression), infant development (temperament) and maternal sensitivity. Video-recorded interactions were coded for maternal sensitivity. Results showed a significant association between antenatal depression and maternal sensitivity at 12 months. Further research is warranted to investigate the role of maternal sensitivity in a larger sample. The study was conducted in collaboration with my fellow D.Clin.Psy. student, Nathan Dowling (Dowling, 2018). See Appendix 2 for a breakdown of contributions.

#### Part 3: Critical Appraisal

The critical appraisal reflects upon the process of conducting the research presented in Part Two of this thesis. Firstly, the reasons for choosing the research topic are discussed. Then, the methodological issues arising from conducting the research are considered. The appraisal includes reflections on the complexities of the sample and concludes with personal reflections on the overall research process.

#### **IMPACT STATEMENT**

The research outlined in this thesis aimed to contribute to the ever-growing literature on maternal mental health. It has been widely acknowledged that maternal stress in the antenatal period has serious social and emotional consequences, both for the mother and child. The mother's mental health during pregnancy is documented to have an impact upon the unborn infant and the quality of their relationship, postnatally.

The meta-analysis detailed in this thesis highlights the need for robust screening procedures, early interventions and treatments during the perinatal period. Untreated maternal mental health has a long-lasting, detrimental impact on the mother, child and family. The aim of the literature review was to examine the risk factors for postnatal depression, with important clinical implications related to early identification, intervention and evidence-based treatment. Both antenatal depression and anxiety were found to be significant risk factors for postnatal depression, with a medium to large effect size and a medium effect size, respectively. The findings also showed that effect sizes for studies with adjusted covariates were smaller than that for studies where covariates were not adjusted.

The majority of published literature in the field of maternal mental health and infant outcome has focused on low-risk populations and there is a critical gap in our knowledge about the impact in high-risk samples. There is a need to consider the multiple disadvantages of high-risk mothers and the likely stresses they experience during the peripartum period, which will affect foetal and postnatal development. The study detailed in the empirical paper is one of the first to investigate the role of maternal sensitivity in the link between antenatal depression and infant outcome, in a sample of high-risk, vulnerable mothers. Unlike many studies in the current literature, this study controlled for postnatal maternal stress symptoms, to provide a valid test of the hypothesis that the effects of antenatal stress on infant outcome are not explained by concurrent maternal mental state at 12 months.

Research is currently unclear about the exact mechanisms for the effects of maternal stress on infants and focus has been directed towards foetal programming, specifically in relation to the impact upon the developing brain of the infant. The effects of stress during pregnancy on the mother's brain and behaviour are essentially unknown. This research found that antenatal depression was a significant predictor of postnatal maternal sensitivity, raising the question of how maternal mental health during pregnancy affects parenting. The findings in the empirical paper contribute to the start of emerging literature investigating the priming of the maternal brain.

The findings in this thesis have important implications for highlighting the need for continued efforts to fully understand and assess maternal mental health in the perinatal period, in order to target specific interventions and promote well-being in the mother and child.

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## PART 1: LITERATURE REVIEW

Antenatal depression and anxiety as risk factors for postnatal depression: a meta-analysis

#### Abstract

**Background:** Research into the risk factors for postnatal depression has increased substantially since the last review in 2004 by Robertson, Grace, Wallington and Stewart. Thus, an updated meta-analysis is warranted.

**Methods:** This meta-analysis provides a synthesis of the recent literature pertaining to antenatal anxiety and depression as risk factors for developing postnatal depression. Systematic electronic searches were conducted in order to identify relevant studies examining risk factors for postnatal depression. In total, 30 studies (31 separate samples) with 21,489 participants were included, and relevant data was extracted by the author. Meta-regressions were conducted on studies investigating antenatal depression as a risk factor for postnatal depression. These analyses were used to determine whether or not the effect size was conditional upon the time-point of postnatal measure, the use of a semi-structured or structured interview, or the adjustment of covariates in the analyses of the included studies.

**Results:** A significant combined effect of d = 0.744 was found for antenatal depression as a risk factor for postnatal depression, characterised as a medium to large effect. A significant combined effect of d = 0.591 was found for antenatal anxiety as a risk factor, characterised as a medium effect. Using meta-regression, only one significant predictor of the effect sizes was found: effect sizes for studies with adjusted covariates were smaller than that for studies where covariates were not adjusted.

**Conclusions:** The current meta-analysis confirms current findings that antenatal anxiety and depression are strong predictors of postnatal depression. The results are of significant clinical importance and highlight the need for robust antenatal screening procedures, early interventions and treatments during the perinatal period.

#### Introduction

The postpartum period is a demanding stage of a woman's transition into parenthood, requiring significant personal and interpersonal adaptation. It is characterised by a variety of changes, including; biological, physical, social, and emotional, which can be overwhelming. Unfortunately, women in the postpartum period can be vulnerable to a range of psychiatric disorders, such as; postpartum blues, depression, and psychosis, sometimes requiring hospitalisation (Rai, Pathak, & Sharma, 2015). Although there is a substantial amount of research documenting its negative effects, perinatal mental illness is under-diagnosed (Goodman et al., 2011; O'Hara & McCabe, 2013; Rai et al., 2015). Furthermore, the literature is lacking in definitive conclusions about the effectiveness of treatment approaches and there is limited availability of evidence-based treatment for postnatal depression (Dennis, 2004).

Postnatal depression is a major public health issue that can have a profound negative impact upon women, infants and families. Research into perinatal mental health highlights the importance of early screening, diagnosis, and management as critical parts of postpartum care. Due to the significant consequences of maternal prenatal and postnatal depression, research in the area is extensive. Since the previous review conducted in 2004 (Robertson, Grace, Wallington, & Stewart, 2004), the number of published studies on this topic has increased significantly, thus rendering an updated meta-analysis useful.

The National Institute for Health and Care Excellence (NICE; 2018) guidelines state that depression and anxiety are the most common mental health problems women experience during pregnancy. Around 12% of women experience depression and 13% experience anxiety at some point during the pregnancy (NICE, 2018). The current NICE guidelines for the assessment and treatment of postnatal depression highlight that anxiety disorders (including generalised anxiety disorder, obsessive– compulsive disorder, panic disorder, phobias, post-traumatic stress disorder and

social anxiety disorder) and depression are under-recognised throughout pregnancy and the postnatal period (NICE, 2018).

#### Antenatal anxiety and antenatal depression

As highlighted by the most recent review, the strongest predictors of postnatal depression are the experience of depression or anxiety during pregnancy or a previous history of depressive illness (Robertson et al., 2004). Two earlier metaanalyses had identified antenatal anxiety as a prominent risk factor for postnatal depression (Beck, 2001; O'Hara and Swain, 1996). Despite its role as a predictor being apparent in the literature, antenatal anxiety has arguably received little attention (Getch, 2011). The focus on antenatal anxiety is steadily increasing and it is documented by many as a clearly identified risk domain (Austin, Tully, & Parker, 2007; Heron, O'Connor, Evans, Golding, & Glover, 2004; Matthey, 2004; Matthey, Barnet, Howie, & Kavanagh, 2003). Interestingly, Matthey and colleagues (2003) highlighted that a previous history of an anxiety disorder (panic disorder, acute adjustment disorder with anxiety, and phobia) was a greater risk factor for postnatal depression than a history of a depressive disorder. Heron et al. (2004) assessed self-reported anxiety and depression and have shown that antenatal anxiety is a predictor of postnatal depression (at eight weeks and eight months), even after controlling for antenatal depression.

In contrast to antenatal anxiety, a vast amount of research has focused on antenatal depression as a predictor variable of postnatal depression. In addition, antenatal depression has been investigated for its potential mediational effects between some risk factors and postnatal depression. The results of Leigh and Milgrom's (2008) study revealed that each of their predictor variables for postnatal depression (income, history of abuse, major life events, antenatal anxiety, negative cognitive style, self-esteem and social support) was significantly mediated by antenatal depression.

#### Postnatal depression

Postnatal depression is classified in the Diagnostic and Statistical Manual of Mental Disorders (DSM, 5<sup>th</sup> ed.) as a major depressive episode with 'peripartum onset'. To meet the diagnostic criteria for postnatal depression, symptoms of a major depressive episode must be present for at least two weeks and a diagnosis is made when the depressive episode occurs before or after the birth of the child (American Psychiatric Association, 2013). Symptoms include depressed mood, anxiety and fear, feelings of guilt or inadequacy related specifically to the ability to care for the newborn baby, feelings of not being able to cope and irrational fears.

#### Measuring depression and anxiety

Depression is a serious mental health concern for mothers during the transition into parenthood, hence there is a need for reliable and valid screening instruments. Although it is argued that the gold standard for making a clinical diagnosis involves the use of a clinical interview, a review of screening tools for postpartum depression by Boyd and colleagues (Boyd, Le, & Somberg, 2005) found that the Edinburgh Postnatal Depression Scale (EPDS) is the most researched measure with moderate psychometric properties. The EPDS is a ten-item, self-report questionnaire, which was developed by Cox and colleagues as a screening tool for postnatal depression (Cox, Holden, & Sagovsky, 1987). It has been well validated as a measure of antenatal and postnatal depression in settings including; outpatient, home visits and at the six- to eight-week postpartum examination (Evans, Heron, Francomb, Oke, & Golding, 2001). There appears to be little consensus amongst researchers regarding the assessment of postnatal depression, and whether a formal diagnostic interview should be used in conjunction with self-report questionnaires, such as the EPDS.

When considering the optimal period for screening for postnatal depression, Boyd et al.'s (2005) review highlights that the ideal time period is at, or more than,

two weeks following childbirth. Postnatal depression can be distinguished from 'baby blues' or 'postpartum blues', which is a common experience of new mothers (Wisner, Parry, & Piontek, 2002). Research has suggested that 'postpartum blues' may last until two weeks post-delivery (O'Hara, 1987), and that the depressive component of postpartum blues tends to be more intense than the subsequent postnatal depressive symptomatology (Teissèdre & Chabrol, 2004). Similarly, O'Hara and Wisner (2014) report that postpartum depression is typically independent of 'the blues'.

The literature includes a range of time-points at which depression is measured in the pre and postnatal period, with some researchers assessing mothers on more than one occasion. A systematic review investigating screening for postnatal depression found that the timing of the screening was extremely variable, with ranges between 12 weeks of gestation to 36 weeks in the antenatal period and anything between five weeks and 12 months' post-birth (Austin & Lumley, 2003). Boyd et al. (2005) noted in their review that the diagnostic criteria for postnatal depression, including the time period, are not accepted by researchers or clinicians universally. As there is little or no consensus regarding the optimal time-period for assessing postnatal depression, comparisons are difficult to make and conclusions are hard to draw. This could complicate larger reviews or a meta-analysis, which seek to compare and investigate a collection of studies around the same topic. To date, there has been little focus on the impact of the time-point of assessing postnatal depression or its potential moderating role.

Some have argued that there are no specific tools that have been developed to measure antenatal anxiety (Ross, Evans, Sellers, & Romach, 2003). Instead, researchers typically use a self-report measure of anxiety called the State-Trait Anxiety Inventory (STAI; Spielberger, 1970). However, there is evidence to suggest that the EPDS can be a useful screening instrument for anxiety, due to it being highly correlated with anxiety measures, such as the STAI (Boyd et al., 2005; Brouwers, van Baar, & Pop, 2001). This may help to explain why little attention has previously been

paid to antenatal anxiety as a risk factor for postnatal depression, in comparison to antenatal depression. It is interesting to consider whether recent literature has advanced in the assessment of antenatal anxiety, using the EPDS and what current evidence says regarding the impact of antenatal anxiety on postnatal mental health.

#### Previous meta-analyses

As noted above, a large body of research has highlighted numerous risk factors for postnatal depression, including a previous history of depression, low levels of social support, depression and anxiety during pregnancy, and experiencing stressful life events during pregnancy or early puerperium (Robertson et al., 2004). In addition, several meta-analyses have been conducted to examine the research related to risk factors for postnatal depression, including over 100 studies and 12,000 participants (Beck, 1996; Beck, 2001; O'Hara & Swain, 1996; Robertson et al., 2004). In 1996, Cheryl Beck published a meta-analysis of 44 studies from the 1970s to the 1990s. Beck included eight predictor variables of postnatal depression, including antenatal depression, social support, a history of depression, life stress, childcare stress, maternity blues, marital relationship and antenatal anxiety. Results indicated a large effect size for the relationship between antenatal depression and postpartum depression was found to be in the range of a moderate effect size (r = 0.36).

O'Hara and Swain (1996) also published a meta-analysis on risk factors for postnatal depression. They found the strongest predictors of postnatal depression to be a history of psychopathology and psychological disturbance during pregnancy, low social support and poor marital relationship, and stressful life events. Lower socioeconomic status (SES) was a small yet significant predictor of postnatal depression. Beck (2001) then published an update to her earlier meta-analysis in 1996, which had synthesised the results of studies conducted mostly in the 1980s. Her updated investigation included 84 studies published in the 1990s. The results confirmed the findings of the previous meta-analysis and, in addition, revealed four new predictors of postnatal depression: self-esteem, marital status, socioeconomic status, and unplanned/unwanted pregnancy.

More recently, Robertson et al. (2004) conducted a review to synthesise the vast amount of research related to the predictors of postnatal depression. They reviewed two previous meta-analyses (detailed above), in addition to subsequently published studies. Their results confirmed the findings that the strongest predictors of postnatal depression are; depression during pregnancy, anxiety during pregnancy, experiencing stressful life events during pregnancy or the early puerperium, low levels of social support, and a previous history of depression (Robertson et al., 2004). Since this latest review, over 450 studies have been conducted and added to the significant amount of literature on this topic. Over half of these studies were cross-sectional and many used a qualitative approach to investigate risk factors. Amongst these studies were six systematic reviews and one meta-analysis. The majority of these reviews focused upon the prevalence of postnatal depression. Only one systematic review, which focused on risk for postpartum depression in rural women, reported on the inclusion of variables which had been controlled for in 'some, but not all,' of the studies (Villegas, McKay, Dennis, & Ross, 2011). These variables included age, income, level of social support and past psychiatric history.

An increasing number of studies being available means that there is an opportunity for further synthesis and room for the investigation of factors that might explain variation in effect sizes across studies (referred to in the meta-analytic literature as effect size moderators). Indeed, O'Hara and McCabe (2013) have highlighted the call for more research on the mediators linking risk factors with postnatal depression and moderators that affect any associations. There has been little or no attention paid to the impact of researchers controlling for covariates in their

analyses of risk factors for postnatal depression and, in fact, the most recent review in 2004 did not report on this.

#### The current review

The current meta-analytic review focused on antenatal depression and anxiety as risk factors for postnatal depression. The review was limited to studies conducted in Western countries, published since the most recent review in 2004 and which measured depressive symptoms in both the antenatal and postnatal periods.

A critical issue in the assessment of postnatal depression is establishing the optimal period to screen. It is understood that there are difficulties with screening for postnatal depression immediately after delivery, but there is some disparity across the literature about when data should be collected in the postnatal months. Measures of postnatal depression (including the EPDS) have been demonstrated to be useful for screening purposes at six weeks postpartum, yet some research has investigated up to 18 months' post childbirth (Boyd et al., 2005). It is also valuable to investigate whether the strength of the association between antenatal anxiety or depression and postnatal depression varies by data collection through a semi-structured or structured interview. Further, there are discrepancies across the literature in relation to researchers choosing whether or not to adjust for covariates in their analyses, warranting the inclusion of this in a meta-regression analysis.

The review investigated the role of potential methodological factors that can explain variation in effect sizes, including; the time-point of the measure of depression in the postnatal period, the use of a semi-structured or structured interview, and whether or not the researchers had adjusted for covariates in their analyses. Examining the role of these potential factors allows us to determine whether there is a risk that researchers might be over- or under-estimating the specific strength of the association between antenatal anxiety or depression and postnatal depression.

The present meta-analysis aims to contribute to our understanding of risk factors for postnatal depression and provide an update on this ever-expanding body of knowledge. Contributing to our understanding of risk factors for postnatal depression is clinically valuable as it highlights areas of need which can be targeted with suitable screening procedures and interventions.

This paper aimed to address the following questions:

- 1. Risk factors: what is the updated strength of the magnitude of antenatal anxiety and depression as risk factors for postnatal depression?
- 2. Is the effect size conditional upon the time-point of the measure of depression in the postnatal period, the use of a semi-structured or structured interview, or whether or not the researchers had adjusted for covariates in their analyses?

#### Method

A meta-analysis of peer-reviewed articles of antenatal risk factors for postnatal depression in female participants was conducted. Published literature was reviewed and details were extracted from the articles, including the time points of the assessment, location of the study, age of participants, and factors relating to other inclusion and exclusion criteria outlined below.

#### Search strategy

A systematic literature search was conducted using two electronic databases (PsycINFO and MEDLINE). Search terms included; baby blues, postpartum, postnatal, perinatal or maternal depression, predictor and risk or protective factor (see Appendix 1 for details). The searches were limited to articles that were published since the most recent review in 2004, written in English, using human subjects, published from peer-reviewed journals, included female participants and contained the search terms within the title, subject heading or abstract of the paper.

#### Inclusion/exclusion criteria

The following criteria were required for the paper to be included in the review:

- 1) The study was conducted between 2004 and 2017
- 2) Risk factors were explicitly defined and measured
- Depression or depressive symptoms were measured at a minimum of two time points; one in the prenatal and one in the postnatal period (defined as within the first 12 months following childbirth)
- Depression or depressive symptoms in the postnatal period were measured more than two weeks following childbirth, to avoid capturing 'postpartum blues' (Boyd et al., 2005; Robertson et al., 2004)
- The study was conducted in a Western country (defined as a country belonging to the Organisation for Economic Co-operation and Development, OECD)
- The results section provided the necessary quantitative data for the calculation of effect sizes

Non peer-reviewed articles, non-English published studies, book reviews, letters to the editor, comments, replies and animal studies were excluded. Studies were excluded if participants had another mood disorder or severe mental illness (e.g., bipolar disorder), which ensured that depressive symptoms were captured consistently across the studies. Studies were also excluded if they included participants under 18 years of age. As the aim of the current study was to examine a naturalistic relationship between potential antenatal risk factors and postnatal depression, randomised control trials and any studies which included a control group were excluded.

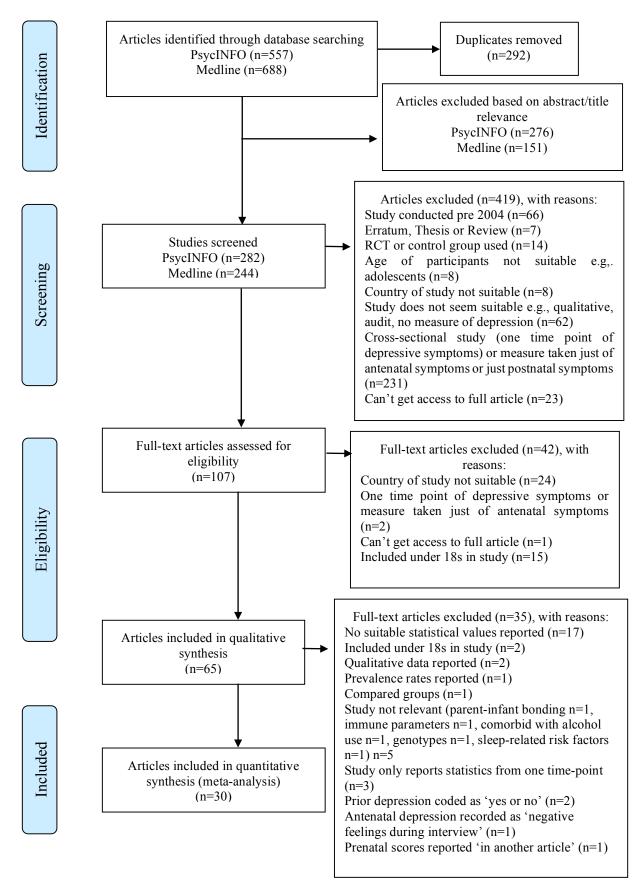
#### Screening and selection

Once duplicates were removed, 953 studies remained. All studies were screened for relevance by title and abstract and coded as either "yes" or "no" to define

eligibility. Abstracts of the potential studies were read and coded as either "yes", "no" or "maybe". The next stage involved gaining access to the full-text of the remaining 107 studies, where the exclusion and inclusion criteria were applied to the information written in the methods section. Studies were excluded due to factors including country of study, time point of measure taken and inclusion of participants under 18 years old. One study was excluded due to the full text being inaccessible. Sixty-five studies were then included in a qualitative synthesis, where the results section was read and once again checked against the criteria. Twenty-two studies were excluded on the basis of their not providing suitable statistical values in the results, including only reporting one time-point or only providing qualitative data. Two studies were excluded due to the inclusion of participants under the age of 18. The remaining eleven studies were excluded due to a lack of relevance to the aims of the current study (e.g., sleeprelated risk factors or a focus on genotypes). Thirty studies were selected for inclusion in this meta-analysis (see Diagram 1 overleaf).

### Diagram 1.

Consort diagram of the phases of the meta-analysis.



#### Data collection and extraction

Data was extracted directly from the results section of the included papers and recorded in a data extraction table. The following study characteristics were entered into the table: country of study, stage of antenatal measure of anxiety/depression or anxiety/depressive symptoms, stage of postnatal measure of anxiety/depression or anxiety/depressive symptoms, type of measure used, attrition rate, population mean age and standard deviation, sample size, year of publication, study design, parity, recruitment method and statistical method used. Finally, effect sizes were extracted and converted in standardised effect sizes (Cohen's d).

Several studies measured depression or depressive symptoms at multiple time points in the antenatal and postnatal periods. In order to fulfil the independence assumption for meta-analyses, data was extracted with a view to compute an average result, as only one effect size per outcome-construct per study should be included (Lipsey & Wilson, 2001).

#### Effect size calculation

The computer program, Comprehensive Meta-Analysis, was used to calculate the effect sizes from the various statistical values extracted from the included studies (CMA; Version 2; Borenstein, Rothstein, & Cohen, 2005). These included correlational and Odds Ratio values. All effect sizes were converted to the common metric of standardised mean differences (Cohen's d) prior to analysis.

In Verkerk et al.'s (Verkerk, Denollet, Van Heck, Van Son, & Pop, 2005) study, the Confidence Intervals (CI) required adjustment, as the lower interval was much larger than the upper (for mid-pregnancy depressive symptoms as a predictor for depression at 12 months postpartum: OR = 2.63, CI = 0.90-7.69). Thus, a more conservative upper CI limit was computed (matching the lower limit based on natural log values). It is also worth noting that in Zaers et al.'s (Zaers, Waschke, & Ehlert, 2008) study, the researchers conducted sequential multiple linear regression analyses, which included depressive symptoms whilst controlling for anxiety in late pregnancy, but not vice versa. Thus, the effect size for anxiety was substantially larger than that for depression, which is likely an artefact of the statistical analysis. In general, uncorrected effect sizes (i.e., without covariates) were used, but in some studies adjusted effect sizes were the only effect size reported, and hence were used as the best approximate effect size. In Sweeney and Fingerhut's (2013) study, the researchers included 'Established risk factors for postpartum depression (PDPI-R)' in their hierarchical multiple regression. This measure (Postpartum Depression Predictors Inventory– Revised) produces a combined score for several risk factors, of which prenatal depression is one. The reported analyses were therefore repeated with both these studies (Zaers et al. 2008; Sweeney & Fingerhut, 2013) removed to check the consistency of the meta-analytic findings.

#### Statistical procedures

Meta-analysis is a statistical technique used to estimate the mean and variance of underlying population effects from a collection of studies investigating in the same research topic (Field & Gillett, 2010). For this review, all major statistical analyses were performed using STATA software (Stata Corp, 2015). The first stage computed the overall effect size and significance, as well as a test of heterogeneity (the variation in study outcomes between studies). When heterogeneity is present in the studies under synthesis, it is appropriate to select a random effects model for computations, which is more conservative than a fixed effect model (Cooper, Hedges, & Valentine, 2009). Random effects models assume that the variability between the effect sizes across studies is due to sampling error plus the variability in the population of effects (Lipsey & Wilson, 2001). The current meta-analysis used random effects models for all analyses. The next stage involved a test of publication bias, which was first assessed by inspecting the funnel plot visually. The Egger test was then used to calculate the degree of bias illustrated in the funnel plot. Then, the 'trim

and fill' method (Duval & Tweedie, 2000) of imputing missing studies was employed. This procedure estimates the number of missing studies by 'trimming' the funnel plot until it is symmetrical and then 'filling' in each side of the funnel plot to make it symmetrical. An adjusted pooled effect size is then re-estimated. Subsequently, sensitivity analyses were conducted, in order to test the robustness of the data. The effects of potential outliers were examined by excluding studies which came close to three standard deviations from the mean and re-running the analysis. When sensitivity analyses show that the overall result is not affected by the different decisions that could be made during the review process, the results of the review can be regarded with a higher degree of certainty (Higgins & Green, 2011).

Finally, moderation analyses were performed, using random effects metaregression models. Conducting a meta-regression allows us to relate the size of effect to one or more characteristics of the included studies. Where heterogeneity exists between studies, it is appropriate to use random-effects models. Although multiple study characteristics are outlined above, only three meta-regression analyses were conducted. This limited the risk of Type 1 error. The meta-regression analyses were performed to determine whether or not the effect size was conditional upon the timepoint of postnatal measure, the use of a semi-structured or structured interview, or the adjustment of covariates in the analyses of the included studies. The time-point of the antenatal measure was not investigated due to the vast majority of studies reporting one time-point category of the 'third trimester'. Some characteristics of the studies were not investigated with moderation analyses due to a lack of rationale for doing so, including; country of study, mean age of participants, sample size, year of publication and design of study. Other characteristics were not included in a moderation analysis due to inconsistencies in reporting relevant information across the studies, including; parity, attrition rate and recruitment method.

#### Results

#### Corpus of studies

The literature search resulted in the inclusion of 30 studies and 31 separate samples in a meta-analysis of antenatal depression as a risk factor for postnatal depression. Nine of these studies were included in a meta-analysis of antenatal anxiety as a risk factor for postnatal depression. The included studies are summarised in Table 1.

#### Characteristics of included studies

Together, these studies had 21,489 participants. The sample size across the included studies varied considerably; Sweeney and Fingerhut's (2013) study had the smallest (N = 46) and Milgrom et al.'s (2008) study had the largest number of participants (N = 12,361). All of the studies were published between the years 2004 and 2016. The majority of the studies were conducted in the United States of America (n = 6), with the second most prevalent countries being Australia (n = 3), Germany (n = 6), with the second most prevalent countries being Australia (n = 3), Germany (n = 6), where (n = 6) and (n = 6), where (n = 6) are the second most prevalent countries being Australia (n = 6). = 3) and Japan (n = 3). Two each were conducted in Turkey, Portugal, Canada, South Korea and The Netherlands and one each in Spain, Italy, Mexico, Finland and France. The predominant method used to measure anxiety and depressive symptoms was the Edinburgh Postnatal Depression Scale (EPDS). Other studies used measures such as the Beck Depression Inventory (BDI), or the Center for Epidemiologic Studies Depression Scale (CES-D). Eight of the studies included a formal diagnostic assessment, using a structured or semi-structured interview, such as the Mini-International Neuropsychiatric Interview (M.I.N.I.) or the Structured Clinical Interview (SCID). Five of the included studies reported on relevant depression or anxiety statistics for multiple time points (e.g., three months, six months and 12 months postpartum) in their analyses (Barnum, Woody, & Gibb, 2013; Lara, Navarrete, & Nieto, 2016; Parker et al., 2015; Verkerk, Denollet, Van Heck, Van Son, & Pop, 2004; Verkerk et al., 2005). For these studies, an average score was computed for the metaanalysis. In the study by Akyuz et al., they provided relevant statistics in their analysis for both their fertile and infertile subgroup (conceived following treatment for infertility; Akyuz, Seven, Devran, & Demiralp, 2010). These statistics were included in the metaanalysis, separately.

# Meta-analysis results for antenatal depression as a risk factor for postnatal depression

Figure 1 illustrates a forest plot for antenatal depression as a risk factor for postnatal depression, showing an overall effect size<sup>1</sup> of d = 0.744 (95% Confidence Interval [CI] = 0.591-0.896, z = 9.57, p < 0.001). This is a medium to large effect size (Cohen, 1977). Heterogeneity between studies was large and statistically significant (Q = 418.44, df = 30, p < 0.001, l<sup>2</sup> = 92.8%,  $\tau^2$  = 0.126), which means that the variability across the effect sizes exceeds what would be expected based upon sampling error (Lipsey & Wilson, 2001).

#### **Publication bias**

Publication bias was first assessed visually by inspecting the funnel plot (see Figure 2). This appeared to show a publication bias, which was confirmed using Egger's test. The results provided evidence for publication bias (t = 6.09, p < 0.001). The Duval and Tweedie (2000) nonparametric 'trim and fill' method of accounting for publication bias in meta-analysis was used. The method estimates the number and outcomes of missing studies, and adjusts the meta-analysis to incorporate the theoretical missing studies. This method demonstrated that seven additional studies would be needed to reduce the asymmetry of the funnel plot (pooled adjusted estimate d = 0.602 [CI] = 0.463-0.741, p < 0.001). The imputed missing studies (highlighted with a box around the point) can also be seen in Figure 2.

<sup>&</sup>lt;sup>1</sup> As stated earlier, the meta-analysis was conducted with the exclusion of two studies, (Zaers et al. 2008; Sweeney & Fingerhut, 2013), which showed an overall effect size of d = 0.746

#### Sensitivity analyses

Z-Standardised effect sizes were computed for the studies in the metaanalysis. Only one study came close to three standard deviations (2.534). Re-running the meta-analysis, selecting out this study created an adjusted effect size of d = 0.710 (CI = 0.559-0.860, z = 9.25, p < 0.001). Heterogeneity between the studies remained significant (Q = 387.82, df = 29, p < 0.001,  $I^2$  = 92.5%,  $\tau^2$  = 0.117). The results indicate that the overall finding of a d = 0.744 effect size is robust.

#### Meta-regression analyses

For studies where the postpartum measure of depression was taken less than three months postpartum (n = 14), there was a significant effect (t = 5.99, p < 0.001, d = 0.676, SE = 0.113, CI = 0.432 - 0.920). For studies where the postpartum measure of depression was taken more than three months postpartum (n = 14), there was also a significant effect (t = 6.40, p < 0.001, d = 0.769, SE = 0.120, CI = 0.509 - 1.028). The analysis to test whether these two effect sizes were reliably different or not showed that they were not (ES difference = 0.09, SE = 0.16, t = 0.55, p = 0.58). Note that for three studies it was unclear in their results section which time-point their analyses related to (e.g., six weeks or six months postpartum), and hence these studies were excluded from the meta-regression analysis (Lara et al., 2016; Luoma, Korhonen, Salmelin, Helminen, & Tamminen, 2015; Martini et al., 2015).

For studies where the method included the use of a semi-structured or structured interview (n = 8), there was a significant effect (t = 3.73, p = 0.007, d = 0.577, SE = 0.155, CI = 0.211 - 0.943). For studies where the method did not include a formal diagnostic interview, but used questionnaires (n = 23), there was also a significant effect (t = 9.24, p < 0.001, d = 0.795, SE = 0.086, CI = 0.616 - 0.973). The analysis to test whether these two effect sizes were reliably different or not showed that they were not (ES difference = 0.22, SE = 0.17, t = -1.26, p = 0.22).

For studies where the researchers adjusted for covariates in their analyses (n = 15), there was a significant effect (d = 0.58, SE = 0.108, t = 5.37, p < 0.001). For studies where the researchers did not adjust for covariates in their analyses (n = 16), there was also a significant effect (d = 0.876, SE = 0.09, t = 9.51, p < 0.001). The analysis to test whether these two effect sizes were reliably different or not showed that there was a significant difference (ES difference = 0.309, SE = 0.14, t = 2.20, p = 0.036), with larger effects being found in studies that did not include covariates.

Author, Year (Country)	Time of Prenatal Assessment as Reported in Article	Time of Postnatal Assessment as Reported in Article	Time of Postnatal Assessment Extracted for Meta- Analysis	Sample Size (N)	Age (Mean and SD)	Measures Used
Akyuz et al., 2010 (Turkey)	Third trimester	4-6 weeks postpartum	4-6 weeks postpartum	156	infertile group 30.59yrs (SD=4.801) and fertile group 26.105yrs (SD=4.036)	BDI and PDSS
Austin et al., 2007 (Australia)	Third trimester	8 weeks postpartum	8 weeks postpartum	748	31.1yrs	STAI and EPDS
Barnum et al., 2013 (USA)	Third trimester	1 month and 2 months postpartum	Average computed	101	28.44yrs (SD = 6.39)	EPDS
Bolak et al., 2016 (Turkey)	Third trimester	3-6 months postpartum	3-6 months postpartum	87	29.30yrs, (SD = 4.30)	EPDS
Bos et al., 2013 (Portugal) Davey et al., 2011 (Canada)	Third trimester Third trimester	3 months postpartum 8 weeks postpartum	3 months postpartum 8 weeks postpartum**	272 1403	29.8yrs (SD=4.99)	BDI-II and DIGS EPDS (postpartum) and depression and anxiety subscales of the Kellner Symptom Questionnaire (SQ, antenatal)
Escriba-Aguir & Artazcoz, 2011 (Spain)	Third trimester	3 months and 12 months postpartum	One statistic reported for "postpartum depression"*	769		EPDS
Galanti et al., 2009 (USA) Goyal et al., 2009 (USA) Goyal et al., 2010 (USA)	Third trimester Third trimester Third trimester	12 weeks postpartum 3 months postpartum 1 month, 2 months and 3 months postpartum	12 weeks postpartum 3 months postpartum 3 months postpartum***	56 112 198	27.9yrs (SD=5.8) 32.5yrs (SD=4.6) In low income group 26.3yrs (SD=6.0) in high income group 32.6yrs (SD= 4.2)	BDI CES-D CES-D
Grussu & Quatraro, 2009 (Italy)	8-9 months pregnancy	6-8 weeks postpartum	6-8 weeks postpartum	297	32.5yrs (SD=3.9)	EPDS, PDPI-R and GHQ12

## **Table 1.**Summary of studies included in the meta-analysis.

Ikeda & Kamibeppu, 2013 (Japan)	8 <sup>th</sup> month of pregnancy	1 month postpartum	1 month postpartum	76	33.4yrs (SD=4.5)	PPDI-R-J and M.I.N.I.
Ikeda et al., 2014 (Japan) Kim et al., 2008 (South Korea)	Week 32 of pregnancy Week 24 of pregnancy	1 month postpartum 1 and 6 weeks postpartum	1 month postpartum 6 weeks postpartum**	84 60	33.4yrs (SD = 4.5)	EPDS and M.I.N.I. EPDS, BDI and BAI
Lara et al., 2016 (Mexico)	≥26 weeks of pregnancy	6 weeks and 6 months postpartum	Average computed**	210	29.5yrs (SD = 6.3)	PHQ-9, PDPI-R and SCID-I
Luoma et al., 2015 (Finland)	Third trimester	2, 6 months, 4-5 years, 8-9 years and 16-17 years post delivery	"Antenatal EPDS sum score 13 or more and EPDS anxiety subscore 6 or more"**	329	27.1yrs	EPDS
Maia et al., 2012 (Portugal)	Last trimester	3 months after delivery	3 months postpartum	386	30.08yrs (SD=4.205)	BDI-II and DIGS
Martini et al., 2015 (Germany)	Gestational weeks 10– 1), 22–24 weeks and 35–37 weeks	10 days, 2 months, 4 months, and 16 months postpartum	"After delivery"***	274		CIDI-V
Milgrom et al., 2008 (Australia)	"antenatally" mean = 25.1 weeks (SD = 9.0)	6 weeks postpartum	6 weeks postpartum**	12,361	30.3yrs (SD=5.6)	EPDS
Oddo-Sommerfeld et al., 2016 (Germany)	Third trimester	12 weeks postpartum	12 weeks postpartum**	266	32.35 yrs (SD = 4.46)	EPDS, BDI-V and STADI
Park et al., 2015 (South Korea)	Second and Third trimesters	4 weeks postpartum	4 weeks postpartum	153	31yrs (SD=3.99)	EPDS-K
Parker et al., 2015 (Australia)	36 weeks pregnancy	3 months postpartum	Average computed*****	756		EPDS, DASS and M.I.N.I.
Records et al., 2007 (USA)	Third trimester	2 months, 4 months, 6 months and 8 months postpartum	8 months postpartum****	139	27yrs (SD=5.2)	EPDS and CES-D
Sutter-Dallay et al., 2004 (France)	Third trimester	6 weeks postpartum	6 weeks postpartum**	497	29.6yrs (SD=4.2)	EPDS and M.I.N.I.
Sweeney & Fingerhut, 2013 (USA)	Third trimester	2 months postpartum	2 months postpartum	46	27.17yrs (SD=6.59)	EPDS and PDPI-R
Tachibana et al., 2015 (Japan)	Second trimester	1 month postpartum	1 month postpartum	1133	35.06yrs (SD=4.35)	EPDS
Verkerk et al., 2004 (Netherlands)	32 weeks' pregnancy	3 months, 6 months and 12 months postpartum	Average computed	90		EPDS and RDC

Verkerk et al., 2005 (Netherlands)	34 weeks' pregnancy	3 months, 6 months and 12 months postpartum	Average computed	277	30.8yrs (SD=4.1)	EPDS and RDC
Zaers et al., 2008 (Germany)	Late pregnancy	1-3days, 6 weeks and 6 months postpartum	6 months postpartum**	47	30.6yrs	EPDS
Zelkowitz et al., 2008 (Canada)	During pregnancy	2 months postpartum	2 months postpartum**	106	30.6yrs (SD=4.9)	EPDS

\* Escriba et al., "Subjects who participated at either phase 2 or 3 were included in the analysis".

\*\* Prenatal anxiety statistic reported

\*\*\* Extracted as only statistic reported

\*\*\*\* Chosen as study reported correlations between antenatal CES-D score and 8 months postpartum CES-D score

\*\*\*\*\* Average computed from four sets of statistics reported in study – they reported M.I.N.I. depression predictors (DASS depression at baseline), EPDS depression predictors (DASS baseline and EPDS baseline) and M.I.N.I. and EPDS predictors (DASS depression at baseline)

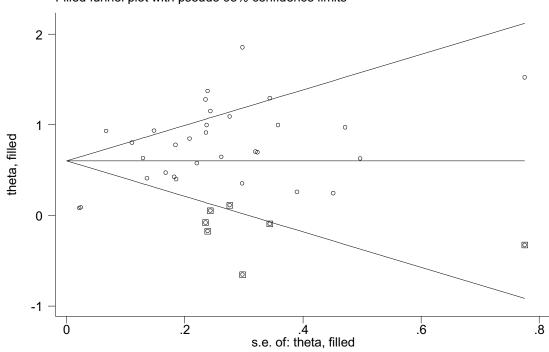
Abbreviations: BAI (Beck Anxiety Inventory), BDI (Beck Depression Inventory), BDI-V (Simplified Beck Depression Inventory), CES-D (Center for Epidemiologic Studies Depression Scale), CIDI-V (Composite International Diagnostic Interview for Women), DASS (Depression Anxiety Stress Scales), DIGS (Diagnostic Interview for Genetic Studies), EPDS (Edinburgh Postnatal Depression Scale), GHQ (General Health Questionnaire) M.I.N.I. (Mini-International Neuropsychiatric Interview), PDPI-R (Postpartum Depression Predictors Inventory-Revised), PHQ (Patient Health Questionnaire), SCID (Structured Clinical Interview for DSM-IV), STADI (State-Trait Anxiety Depression Inventory), STAI (State-Trait Anxiety Inventory), RDC (Research Diagnostic Criteria)

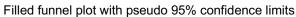
**Figure 1.** A forest plot of antenatal depression effect sizes and confidence intervals for each study included in the meta-analysis.

Study D		ES (95% CI)	% Weight
Akyuz et al., 2010 (fertile subgroup)		1.28 (0.82, 1.74)	3.34
Akyuz et al., 2010 (infertile subgroup)	<u>+</u>	- 1.29 (0.62, 1.97)	2.48
Austin et al., 2007	• i	0.09 (0.04, 0.14)	4.78
Barnum et al., 2013		1.00 (0.53, 1.46)	3.32
Bolak et al., 2016	· · · · · · · · · · · · · · · · · · ·	1.85 (1.27, 2.44)	2.82
Bos et al., 2013		0.41 (0.14, 0.67)	4.19
Davey et al., 2011		0.57 (0.14, 1.01)	3.46
Escriba & Artazcoz, 2011		0.40 (0.03, 0.76)	3.77
Galanti et al., 2009		0.63 (-0.35, 1.60)	1.62
Goyal et al., 2009		0.85 (0.44, 1.25)	3.57
Goyal et al., 2010		1.15 (0.67, 1.63)	3.27
Grussu & Quatraro, 2009		0.65 (0.13, 1.16)	3.11
keda & Kamibeppu, 2013		0.25 (-0.64, 1.13)	1.84
keda et al., 2014	-	1.53 (0.01, 3.04)	
Kim et al., 2008		0.42 (0.07, 0.78)	
_ara et al., 2016		0.91 (0.45, 1.37)	
_uoma et al., 2015		1.00 (0.29, 1.70)	
Maia et al., 2012		0.80 (0.59, 1.02)	
Martini et al., 2015		1.09 (0.55, 1.63)	
Milgrom et al., 2008		0.93 (0.80, 1.06)	
Oddo-Sommerfeld et al., 2016		0.63 (0.38, 0.88)	
Park et al., 2015		0.47 (0.14, 0.80)	
Parker et al., 2015	•	0.08 (0.04, 0.12)	
Records et al., 2007		0.78 (0.42, 1.14)	
Sutter et al., 2004		0.26 (-0.51, 1.02)	
Sweeney & Fingerhut, 2013		0.70 (0.07, 1.33)	
Fachibana et al., 2015	_ <u>_</u>	0.93 (0.64, 1.22)	
Verkerk et al., 2004		0.97 (0.05, 1.90)	
Verkerk et al., 2005		0.35 (-0.23, 0.93)	
Zaers et al., 2008	· · · · ·	0.70 (0.08, 1.33)	
Zelkowitz et al., 2008	· · · · · ·	1.37 (0.90, 1.84)	
Overall (I-squared = 92.8%, p = 0.000)	∲ ·	0.74 (0.59, 0.90)	
NOTE: Weights are from random effects analysis			
-3.04	0	I 3.04	

### Figure 2.

A funnel plot to explore publication bias, with 'filled' studies (boxed) to show the inclusion of theoretical missing studies.





# Meta-analysis results for antenatal anxiety as a risk factor for postnatal depression

Figure 3 illustrates a forest plot for antenatal anxiety as a risk factor for postnatal depression, showing an overall effect size of d = 0.591 (95% Confidence Interval [CI] = 0.316 - 0.867, z = 4.20, p < 0.001). This is classified as a medium effect size (Cohen, 1977). Heterogeneity between studies was statistically significant (Q = 71.72, df = 8, p < 0.001,  $l^2$  = 88.8%,  $\tau^2$  = 0.137).

#### **Publication bias**

Publication bias was first assessed visually by inspecting the funnel plot (see Figure 4). This appeared to show slight publication bias. The results of the Egger test provided no evidence for a publication bias (t = 1.20, p = 0.269). The Duval and Tweedie nonparametric 'trim and fill' method of accounting for publication bias in meta-analysis was used. The method estimates the number and outcomes of missing studies, and adjusts the meta-analysis to incorporate the theoretical missing studies. This method demonstrated that one additional study would be needed to reduce the asymmetry of the funnel plot (pooled estimate = 0.504 [CI] = 0.224 - 0.783, p < 0.001). The theoretical missing study (highlighted with a box around the point) can also be seen in Figure 4.

#### Meta-regression analyses

Meta-regression analyses were not conducted due to the small number of studies in the meta-analysis (n = 9).

#### Sensitivity analyses

Standardised effect sizes were computed for the studies in the meta-analysis. Only one study came close to three standard deviations (2.22). Re-running the metaanalysis, selecting out this study, created an adjusted effect size of d = 0.498 (CI = 0.235 - 0.762, z = 3.70, p < 0.001). Heterogeneity between the studies remained significant (Q = 58.91, df = 7, p < 0.001,  $I^2$  = 88.1%,  $\tau^2$  = 0.114). This indicates that the overall finding of a d = 0.591 effect size is robust.

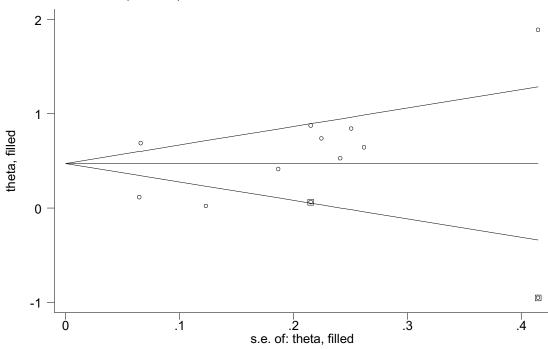
## Figure 3.

A forest plot of antenatal anxiety effect sizes and confidence intervals for each study included in the meta-analysis.

		%
	ES (95% CI)	Weight
- 2	0.84 (0.35, 1.33)	9.87
<b></b>	0.69 (0.56, 0.82)	13.95
	1.89 (1.08, 2.70)	6.39
	0.88 (0.45, 1.30)	10.76
-	0.02 (-0.22, 0.26)	12.95
-	0.11 (-0.01, 0.24)	13.96
	0.74 (0.30, 1.18)	10.52
	0.41 (0.05, 0.78)	11.48
	0.53 (0.05, 1.00)	10.12
$\diamond$	0.59 (0.32, 0.87)	100.00
		0.84 (0.35, 1.33) 0.69 (0.56, 0.82) 1.89 (1.08, 2.70) 0.88 (0.45, 1.30) 0.02 (-0.22, 0.28) 0.11 (-0.01, 0.24) 0.11 (-0.01, 0.24) 0.74 (0.30, 1.18) 0.41 (0.05, 0.78) 0.53 (0.05, 1.00)

## Figure 4.

A funnel plot to explore publication bias, with 'filled' studies (boxed) to show the inclusion of theoretical missing studies.



Filled funnel plot with pseudo 95% confidence limits

#### Discussion

The central aim of this meta-analysis was to investigate antenatal depression and anxiety as risk factors for postnatal depression. This review provides an update from the most recent synthesis (Robertson et al., 2004). A vast amount of literature has been dedicated to this area, and current research indicates that antenatal anxiety and depression are amongst the strongest predictors of postnatal depression. Drawing on data from 30 studies (31 separate samples), involving 21,489 mothers, a significant combined effect of d = 0.74 was found for antenatal depression as a risk factor for postnatal depression. Nine of these studies were further investigated in relation to antenatal anxiety as a risk factor for postnatal depression, producing a significant combined effect of d = 0.59. The findings reported in this analysis demonstrate a medium to large effect of antenatal depression and a medium effect of antenatal anxiety as risk factors for postnatal depression. Sensitivity analyses suggested the results of the current study were robust; potentially outlying effect sizes were removed and did not alter the overall effect size.

The results confirm the findings from previous reviews (Beck, 1996; O'Hara & Swain, 1996; Robertson et al., 2004). More specifically, Robertson et al. (2004) investigated five studies and found depression during pregnancy to have a 'strong/moderate' effect size of d = 0.75 (total number of subjects = > 3000) and anxiety during pregnancy was found to have a 'strong/moderate' effect size of d = 0.68 in six studies (total number of subjects = > 1100).

The results of the meta-analysis investigating antenatal depression revealed significant publication bias, a potential source of Type I error, which can exert a substantial influence on meta-analytic reviews. Publication bias arises when the likelihood of a study being published depends upon whether or not its results were statistically significant. For example, a study that does not show a significant effect might not be submitted for publication, whereas a similar study that reached significance is more likely to be published. Hence, publication bias might cause an

overestimation of the effect sizes in the meta-analysis. The current review utilised several tools to assess and correct for publication bias, including visually examining funnel plots, applying the 'trim and fill' method and conducting the Egger test. Although it is useful, the 'trim and fill' method has been criticised in the literature; some argue that it is inclined to under-correct for publication bias and may generate false positives on occasion (Carter & McCullough, 2014). More advanced technical methods have been created but they are typically only effective when the meta-analysis contains a relatively large number of studies (over 100; Field & Gillett, 2010). For antenatal anxiety, there was no evidence of publication bias. Heterogeneity between studies was also statistically significant. Reasons for heterogeneity can be related to clinical differences, methodological differences between studies or unknown study characteristics.

Further investigation is warranted to understand more about what methodological or population factors give rise to the significant heterogeneity observed between studies. It might be that the selection criteria of the current study were not strict enough, e.g., in relation to factors such as study design, which included; prospective longitudinal studies, prospective cohort studies and community based studies. It is also important to note that there was a distinct lack of consistency across the studies regarding the methods used to assess for depression and anxiety in the antenatal and postnatal period, and only eight of the studies included a diagnostic interview in their assessments. This lack of consistency added challenges to the collation of data in a meaningful and valid way, somewhat limiting the certainness of the findings. There were also marked differences in the risk factors assessed and the confounding variables that were controlled for in their statistical analyses. Such general limitations are reportedly also present in the wider body of literature (Lancaster et al., 2010).

Heterogeneity between studies somewhat constrains the scope of metaanalyses seeking to summarise the evidence for any particular risk factor. Although,

Higgins (2008) states that heterogeneity is to be expected in a meta-analysis and that any amount is acceptable, so long as there are sound criteria for eligibility and the data are correct. In the current meta-analysis, further examination of factors which could explain the significant heterogeneity would be beneficial, e.g. timing of the postnatal measurement. More specifically, further analyses to separate out the effects found in studies that measured postnatal depression before three months postpartum, from those that measured it after three months, may reduce the heterogeneity.

Whilst investigating antenatal depression as a risk factor for postnatal depression, the current meta-analysis examined the role of potentially important factors to explain variance in effect sizes, including; time-point of postnatal measure, the use of semi-structured or structured interview, and whether or not the researchers had adjusted for covariates in their analyses. Two of the three meta-regression analyses yielded non-significant results, most likely due to the relatively small number of studies included in each comparison (time-point n = 14, interview type n = 8). However, a significant difference was found between studies where the researchers had adjusted for covariates in their analyses, and those who did not. The effect size for studies with adjusted covariates was smaller than that for studies where covariates were not adjusted. This is an interesting finding, although the covariates controlled in analyses were variable across the studies. For example, Austin et al. (2007) controlled for the following variables in their analysis: past depressive episode, antenatal EPDS score, age, smoking, parity, education and marital status. Whereas Escriba-Aguir and Artazcoz (2011) controlled for the following variables: history of depression, employment during pregnancy, native country, age, couple's occupational social class and parity. In contrast, Verkerk et al. (2004) controlled for age, parity, education level and clinical depression during pregnancy, in their analysis.

#### Limitations

Although the current review shows evidence in line with the literature and findings from previous reviews, it is important to note the following limitations. The majority of studies included in this review utilised the EPDS as their measure of depression and anxiety, and whilst the EPDS has shown good validity, it may still be subject to response validity problems. Furthermore, the use of a supplementary diagnostic interview was not consistently observed amongst the studies. Secondly, some of the studies assessed for postnatal depression at multiple time points, which meant that an average was computed for the meta-analysis. This means that the meta-analysis could only reflect postnatal depression reported in the 'postnatal period' in general, rather than at specific time points across the first year. With a relatively small number of studies available in this review for examining antenatal anxiety as a risk factor, further analyses using meta-regression were not possible. As stated above, significant publication bias can infer a failure to obtain all or a representative sample of the population of studies on a topic (Sharpe, 1997). The current meta-analysis was limited to studies conducted in Western countries and published in English, meaning that the results are only generalisable to such populations. Also, the current study lacked the use of a quality assessment tool to further scrutinise the studies used in the final sample. Although, the assessment of quality is inherently a subjective process (Lancaster et al., 2010).

The current study aimed to update the literature from the most recent review conducted by Robertson and colleagues in 2004. As such, it is important to highlight some limitations of that review. The authors reported a very small sample of studies in relation to antenatal depression (five studies) and antenatal anxiety (six studies), in their findings. It is possible that the authors may have missed other relevant studies in the literature. The review by Robertson et al., also failed to report controlling for any covariates or degree of heterogeneity between the studies. Given these limitations, the current meta-analysis may have missed a significant portion of studies

that had been published since the more comprehensive review, conducted by Beck (2001).

#### Summary and future directions

The current meta-analysis provides further support for current research documenting that antenatal depression and anxiety are strong predictors of postnatal depression. The findings infer the need for robust screening procedures, early interventions and treatments during the perinatal period. The response to treatment for mental health problems in the perinatal period is reportedly good, however problems are often not identified and thus go untreated. It is evident that, if left untreated, women can continue to have lasting symptoms and the negative effect is shown in their children and families. Between 2006 and 2008, there were reportedly 1.27 maternal deaths per 100,000 birth deliveries in the United Kingdom, resulting from maternal mental health problems (NICE, 2018). Future directions for research could be focused on improving the identification of women who are at high risk of developing psychiatric disorders in the perinatal period. This would have a significant impact on the well-being of mothers and their families, and on service costs.

The ramifications of postnatal depression on the child and family are welldocumented in the literature, thus examining risk factors is of great clinical relevance. The majority of potential risk factors for postnatal depression, as outlined in the literature, can be ascertained during routine care in the perinatal period, thus highlighting the importance of educating all healthcare providers and developing robust screening procedures. The requirement for developing effective psychological interventions is also important. Currently, there is limited evidence for the effectiveness of treatments for anxiety disorders in pregnancy and thus there is a need for future research to focus on how interventions might be best adapted for use with women during their pregnancy. Challenges of the measurement of anxiety in the antenatal period have been noted; including common normative pregnancy-related worries and concerns and the possible confounding effects of the physical aspects of anxiety with the pregnant state (Austin et al., 2007). The fact that pregnancy is a time of physiological changes and variations in hormone levels causes questions to arise about the validity of measuring anxiety using symptom-based measures. The literature is indeed moving towards the development of measures of sources of anxiety, such as psychosocial stress (Johnson & Slade, 2003).

Despite the vast amount of evidence pointing to the feasibility of screening during the antenatal period, very little attention has been paid to conducting well-controlled trials of preventative interventions for postnatal depression (Brugha et al., 2000). Brugha and colleagues attempted to intervene with mothers in the antenatal period by reducing psychosocial risk factors, which had no impact on postnatal depression nor the reduction of risk factors (2000). It has also been noted that no screening tool has proved sufficient as an effective predictor of postnatal depression and attempts by different research groups have been elusive and the sensitivity and specificity of such studies has been poor (Austin & Lumley, 2003; Neiman, Carter, Van Sell, & Kindred, 2010). The treatment of anxiety and depression in mothers during the perinatal period is imperative to alleviate the deleterious effects on families and society, thus highlighting the importance of developing effective evidence-based treatments and interventions.

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## PART 2: EMPIRICAL PAPER

# Investigating the Role of Maternal Sensitivity in the Impact of

# **Antenatal Stress on Infant Temperament**

#### Abstract

**Aims:** This study aimed to expand knowledge about the pathways between antenatal stress and infant temperament, with a rarely studied population; young, economically disadvantaged mothers and babies. More specifically, the aim of the current study was to investigate the role that maternal sensitivity plays in the pathway between antenatal stress and infant difficult temperament at 12 months postpartum. The current study also investigated the potential mediating and moderating role of maternal sensitivity.

**Methods:** As part of a joint project, the current study involved participants from a study of a community home-visiting programme at the 12 months' follow-up point. The sample size included 98 participants for antenatal depression and anxiety baseline scores, 86 for overall postnatal maternal sensitivity and 95 for infant temperament scores at 12 months postpartum. Video-recorded interactions were coded for maternal sensitivity using the NICHD sensitivity scales. The data included maternal mental health variables (anxiety and depression), infant development (temperament) and maternal sensitivity. The data were analysed using a regression-based path-analytic framework, involving the principles of mediation and moderation analysis.

**Results:** Maternal antenatal anxiety and depression were not significantly correlated with infant temperament at 12 months. A significant negative correlation was found between antenatal depression and overall maternal sensitivity. A non-significant correlation was found between antenatal anxiety and overall maternal sensitivity. Neither antenatal depression nor anxiety were found to be significant independent predictors of infant temperament at 12 months. The results showed that antenatal depression was a significant independent predictor of maternal sensitivity, but antenatal anxiety was not. Maternal sensitivity did not mediate the pathway between

antenatal stress and infant temperament at 12 months. Maternal sensitivity did not moderate the effects of antenatal stress on infant temperament at 12 months.

**Conclusions:** This was one of the first studies to investigate the potential mediating or moderating role of the postnatal environment, using a high-risk sample. A significant association was found between antenatal depression and maternal sensitivity at 12 months, but further research is warranted to investigate the role of maternal sensitivity in a larger sample.

#### Introduction

Research findings are supportive of the idea that the antenatal phase involves sensitive periods and windows of development, where the infant is particularly vulnerable to the effects of an environment characterised by stressors or traumatic events (Talge, Neal, & Glover, 2007). Indeed, it has been widely established that the emotional state of a mother during pregnancy can have consequences for the unborn infant. A significant body of research exists suggesting that if a mother experiences antenatal stress, the infant is at a significantly higher risk of developing social, emotional and/or cognitive problems. This association has been demonstrated with respect to several different aspects of antenatal stress, including stressful life events (Bergman, Sakar, Glover, & O'Connor, 2008), anxiety symptoms (Van den Bergh & Marcoen, 2004), depressive symptoms (Goodman, Rouse, Long, Ji, & Brand, 2011), pregnancy-specific worries (Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003) and perceived stress (Berkowitz et al., 2003). These results have important clinical implications. If it is possible to reduce antenatal stress, this may have an important positive effect on infants' developmental outcomes.

Currently, the pathway between antenatal stress and infant outcomes is assumed to be related to exposure to maternal stress hormones causing alterations in foetal neurodevelopment, with potentially enduring consequences for later development in the infant. The effects of antenatal stress on infant development have been studied most systematically in animals. A large body of animal studies has suggested that exposure to stress during pregnancy has an impact on the infant, through maternal stress hormones being transmitted across the placenta, or due to an effect on uterine artery blood flow. However, it is also documented that the placenta is an effective barrier between the maternal and foetal hormonal environments in humans; thus the mechanisms that mediate the effect of antenatal stress on infant development remain to be fully elucidated (Van den Bergh, Mulder, Mennes, & Glover, 2005). Several hypotheses have been proposed to explain why

antenatal stress might impact infant development, including the foetal programming hypothesis. In this hypothesis, the developing HPA axis (hypothalamic-pituitaryadrenal axis) is adaptively sensitive to maternal stress hormones during critical periods of foetal development, as these may represent signals of a harsh future environment. This exposure may lead to adaptive alterations in the function and structure of the neural systems responsible for regulating both foetal and, later, infant behaviour and emotional responses to optimise development to likely future environmental circumstances. Although some evidence exists in support of this in a variety of animal species (Van den Bergh et al., 2005), limited evidence exists for thoroughly evaluating the foetal programming hypothesis in humans.

Studies have shown that maternal exposure to prenatal stressful life events is associated with difficult infant temperament (Austin, Hadzi-Pavlovic, Leader, Saint, & Parker, 2005; Davis et al., 2007; Henrichs et al., 2009; Huizink et al., 2003). Infant temperament has been defined as the "relatively consistent, basic dispositions inherent in the person that underlie and modulate the expression of activity, reactivity, emotionality, and sociability" (Goldsmith et al., 1987, p.524). Difficult infant temperament can be defined as a cluster of behaviours and affective states, characterised by withdrawal, irritability, intense reactions to stimuli, low adaptability to change, poor attention and distractibility (Franco, 2015). Infant temperament has also been referred to as having two dimensions: positive reactivity (soothability and activity) and negative reactivity (distress to limitations and fearfulness) (Garstein & Rothbart, 2003).

Austin et al. (2005) found that maternal trait anxiety was predictive of 'difficult' infant temperament at four or six months. Furthermore, this relationship was independent of concurrent depression. They defined 'difficult' infant temperament as high scores (> 3.14, 1 S.D. above the mean) on the easy-difficult continuous scale from the Short Temperament Scale for Infants (Austin et al., 2005). Similarly, Henrichs and colleagues (2009) demonstrated that maternal pre- and postnatal

anxiety were independently associated with perceived infant temperamental difficulties at six months, including fearfulness, sadness and negative affectivity. Davis et al. (2007) showed that prenatal maternal depression impacted upon infant temperament, specifically infant negative reactivity, and that this association remained significant even after controlling for postpartum maternal depression. Their sample included a population of 'well-educated' women. Huizink et al. (2003) found that increased maternal prenatal stress was associated with temperamental variation in infants at eight months. However, they note that their sample consisted of 'normal-risk' mothers and acknowledged the need for research involving a 'high-risk' population, such as low-SES (socio-economic status) pregnant women.

More recently, a review by Korja and colleagues summarised 32 studies and identified 23 which had demonstrated an association between maternal antenatal stress and a child's negative reactivity or self-regulation (Korja, Nolvi, Grant, & McMahon, 2017). The effect sizes for this association typically varied from low to moderate. Of the 21 studies involving parents' reports of child negative reactivity or self-regulation, the review identified 13 studies that found higher prenatal anxiety to be associated with maternal reports of more difficult infant temperament (in six studies), higher negative affectivity (in four studies) and reports of more crying (in three studies). Eight of the 21 studies did not find any association between antenatal anxiety and parent-reports of infant negative reactivity or self-regulation. Prenatal perceived and experienced maternal stress was examined in 11 studies. They found six studies which showed a significant association between maternal antenatal stress and parent reports of infant negative reactivity. In five of the 11 studies, prenatal stress was not related to parents' reports of infant negative reactivity (Korja et al., 2017). The authors acknowledged that, in the majority of the included studies, the mother's education level was deemed to be relative high and the effect of socioeconomic status was not controlled for in all the studies (22 of 32 studies). In addition, postnatal stress was only controlled for in two-thirds of the studies.

Importantly, some studies have shown that the association between antenatal stress and infant developmental outcomes is independent of the effects of maternal *post*natal depression and anxiety (Bergman, Sakar, O'Connor, Modi, & Glover, 2007; Talge et al., 2007; O'Connor, Heron, Golding, Beveridge, & Glover, 2002; Van den Bergh & Marcoen, 2004). Nevertheless, not all studies have controlled for *post*natal depression and anxiety.

Furthermore, as demonstrated in Talge et al.'s review (2007), the majority of studies have investigated this area of research using a sample characterised as 'low risk', including mothers deemed to have low or normal risk status (Davis et al., 2004; Huizink et al., 2003; Van den Bergh & Marcoen, 2004; Van den Bergh et al., 2005) or to have middle-income status (Field et al., 2003). In their review of 23 studies, Talge and colleagues identified only two studies which included a sample of women characterised as 'high risk', meaning low socio-economic status or low income (Copper et al., 1996; Dole, Savitz, Siega-Riz, McMahon, & Buekens, 2003). Both of these studies found that antenatal stress was associated with increased risk for preterm birth. Stress experienced by women classified as high risk is likely to be greater; thus warranting further attention and replication of the few studies in the current literature. High risk populations are also likely to be characterised by multiple disadvantages, which could affect foetal and postnatal development. Therefore, the effects of other stressors need to be understood.

As noted above, it is often assumed that antenatal depression affects infant outcomes directly via foetal development. However, mothers experiencing antenatal depression may experience a range of difficulties, particularly in relation to bonding and the quality of interaction with their infant in the postnatal period. This may explain the association between antenatal depression and infant outcome. There is limited research that has considered the relationship between antenatal depression (or indeed antenatal stress and anxiety) and the mother-infant dyad across the antenatal and postnatal period.

Another possibility is that the quality of the mother-infant relationship may moderate, rather than mediate, the relationship between antenatal depression and infant outcome. Bergman and colleagues investigated the moderating role of motherinfant attachment quality on the association between prenatal exposure to stress or anxiety and infant outcome (specifically, cognitive development). Their findings represent the first evidence in the human literature that the effects of exposure to elevated stress hormones *in utero* predicting infant cognitive is eliminated by a sensitive early-rearing environment (Bergman et al., 2010). Their sample was deemed to be 'normal risk' and therefore it is important for future research to focus on high-risk families, who are likely to have multiple disadvantages which may contribute to the relationship between antenatal anxiety and depression and infant outcome. The evidence looking at this potential moderating relationship is generally limited.

Interestingly, animal studies have shown that maternal care during early postnatal development can counteract detrimental effects of prenatal environmental stress, exerting long-lasting effects that modulate the behavioural phenotype of the offspring (Bergman, Sakar, Glover, & O'Connor, 2008; Del Cerro et al., 2010). Kaplan and colleagues reported that postnatal maternal depression and anxiety have been associated with disturbances in the quality of caregiving, specifically in parental sensitivity (Kaplan, Evans, & Monk, 2008). This association has been shown in both adult and adolescent mothers (Tarabulsy et al., 2005). Maternal sensitivity has been defined as "the extent to which the parent can consistently read and respond to the child's cues" (Kaplan et a., 2008, p.250), and has been described as a protective factor that moderates risk factors in early life and is a robust predictor of infant developmental outcomes (Burchinal, Lowe, Vandell, & Belsky, 2014). However, the research on this topic has predominantly focused on the postnatal period and there is little research in the human literature about whether the early caregiving

environment may either mediate or moderate the effect of antenatal stress and anxiety on child outcomes, such as infant temperament.

#### Rationale

The current study will investigate the role that maternal sensitivity plays in the pathway between antenatal stress and infant difficult temperament, with a specific focus on negative affect; a dimension of infant temperament that appears most consistently linked to antenatal stress. By using a sample of young, economically disadvantaged women and their babies, this investigation aims to expand knowledge about the pathway between antenatal stress and infant temperament, with a rarely studied population. This study will also be one of few studies to test the potential mediating or moderating role of the postnatal caregiving environment.

#### Research questions & hypotheses

- Do antenatal depression and anxiety predict infant temperament at 12 months, whilst controlling for postnatal anxiety and depression? We hypothesise that higher levels of antenatal depression and anxiety would lead to more difficult infant temperament, whilst controlling for *post*natal anxiety and depression.
- 2. Is postnatal maternal sensitivity associated with antenatal depression and anxiety? We hypothesise that postnatal maternal sensitivity would be negatively correlated with antenatal depression and anxiety, such that higher levels of depression and anxiety measured in the antenatal period would be associated with lower levels of maternal sensitivity in the postnatal period.
- Does maternal sensitivity mediate the association between antenatal stress and infant temperament? We hypothesise that that it will significantly mediate the common variance between antenatal stress and infant temperament scores.

4. Is there a moderating effect of maternal sensitivity? We hypothesise that higher postnatal maternal sensitivity decreases the impact of antenatal stress on infant temperament (negative affect) at 12 months.

#### Method

#### Setting

The current study took place in the context of a randomised clinical trial of a community home-visiting programme aimed at promoting young parents' reflective capacity, secure attachment, maternal mental health and infant outcomes. The programme was delivered in socio-economically disadvantaged areas of three sites in the United Kingdom. The current study was conducted in collaboration with another UCL Clinical Psychology doctoral student, Nathan Dowling. The unique contributions are detailed in Appendix 2.

#### Participants

To enter the study, participants had to meet the following eligibility criteria:

1. Inclusion criteria:

- Women expecting their first baby AND
- Aged 19 or under, OR aged between 20 to 25 and currently eligible for meanstested benefits (or someone they live with and depend upon such as a partner or parent, is eligible for means tested benefits) or live in a ward that fell below the 20<sup>th</sup> percentile for the national Indices of Multiple Deprivation.

#### 2. Exclusion criteria:

- Expectant mothers with a psychotic illness
- Expectant mothers with substance abuse disorders/ chronic drug dependence
- Expectant mothers with profound or severe learning disabilities
- Expectant mothers who would require the use of an interpreter

- Expectant parents with a life-threatening illness
- Expectant parents whose baby is expected to be born with a life threatening illness or profound disability

#### Sample size

The total sample size of the trial was 140 at the point of entry into the study in the third trimester of pregnancy. The sample for the current study was the 98 participants who had remained in the study at 12 months' post-partum, who had antenatal depression and anxiety baseline scores. Of these, there were 86 participants who had overall postnatal maternal sensitivity scores and 95 had infant temperament data at 12 months postpartum.

#### **Power calculation**

Based on results from a study by Bergman et al. (2008), we estimated that the main effect of antenatal stress would require between 40-90 participants for 80% at alpha = .05. The regression coefficient for the effect of antenatal stress in the Bergman study was .39, which would require 41 participants for 80% power with 4 covariates. Conservatively assuming the effect was half that size, a sample of 87 participants would be required for 80% power.

#### Recruitment

Recruitment for the clinical trial took place at three different locations in the UK. Participants were recruited from antenatal clinics in regional hospitals between 20 and 28 weeks' gestation. Participants for the current study consisted of the sample followed up at 12 months after the baby was born. Researchers visited participants in their homes to complete measures and conduct video-recordings of mother-infant interactions during a series of semi-structured tasks.

### Sample characteristics

The means and standard deviations of the demographic variables, including maternal age, infant age, maternal education level, ethnicity, marital status and household income, are shown in Table 1.

Sample demographics.	M (SD)	Range
Maternal age	22.19 (2.54)	16-27
Infant age	1.14 (0.19)	0.96-2.04
-	n	%
Education level		
None	10	10
GCSES/O-levels or equivalent	31	32
A-level or equivalent	11	12
NVQ, HND or equivalent	33	34
Degree	8	8
Postgraduate Degree	3	3
Ethnicity		
White	80	83
Asian	7	7
Black	6	6
Mixed	4	4
Co-habiting		
Yes	42	43
No	56	57
Household income		
Less than £10,000 pa	50	55
£10,000- £20,000 pa	18	20
£20,000 - £30,000 pa	14	15
£30,000- £50,000 pa	8	9
£50,000 - £70,000 pa	1	1

Table 1.Sample demographics.

*Note:* GCSE = General Certificate of Secondary Education/O-levels = Ordinary Level; A-Level = Advanced Level Certificate of Secondary Education; NVQ = National Vocational Qualification; HND = Higher National Diploma. Numbers do not add up to total N due to missing data.

#### Research design

The design for the current study was a correlational longitudinal study. The main independent variables (predictors) were antenatal depression and anxiety, measured at pregnancy (between 28-32 weeks' gestation). The dependent variables included infant temperament (negative affect) and maternal sensitivity, measured at 12 months postpartum.

We also included, as covariates, postnatal maternal symptoms of anxiety and depression to provide a strong test of the hypothesis that the effects of antenatal stress on infant temperament are not explained by concurrent maternal mental state at 12 months.

Although this study utilised data from a clinical trial, its remit was not to investigate treatment effects in any way. As the final waves of data collection of the trial are not yet complete, this study is unable to report any analyses involving treatment group, since the group assignments have not been un-blinded. However, the primary predictions concern relationships between pre-randomisation variables and outcome, and hence should be independent of group allocation, which was done at random and stratified by maternal antenatal depression.

#### Measures

Maternal mental health measures taken at pregnancy (between 28-32 weeks' gestation) and at 12 months postpartum:

The *State-Trait Anxiety Inventory (STAI)* is a 40-item, self-report questionnaire that assesses the presence and severity of current symptoms of anxiety and a generalised tendency to be anxious. The two subscales (20 items each) within this measure include the State Anxiety Scale (measuring current state of anxiety), using items that measure feelings of tension, worry and nervousness. The second subscale is the Trait Anxiety Scale, (measuring relatively stable aspects of 'proneness to be anxious'), including items measuring general states of confidence, security and

feeling calm. Respondents are asked to rate each item on the basis of a four-point Likert scale. Higher scores on both subtests indicates greater anxiety. It is a reliable and sensitive measure of anxiety, and strong evidence exists to confirm its construct validity (Spielberger, 1983).

The Edinburgh Post-Natal Depression Scale (EPDS) is a ten-item, self-report scale developed by Cox and colleagues to screen for postnatal depression (Cox, Holden, & Sagovsky, 1987). Respondents are asked to rate how often they have felt a particular way during the previous week, on a four-point scale. The EPDS assesses the common symptoms of depression and excludes somatic symptoms, such as changes in appetite or tiredness, which are normal experiences expected to occur in the postnatal period and thus it would not differentiate between depressed and non-depressed mothers (Murray & Cox, 1990). The validity of the EPDS has been well documented for measuring depression in the antenatal and postnatal periods (Cox et al., 1987; Evans, Heron, Francomb, Oke, & Golding, 2001).

#### Child development measure completed at 12 months:

The Infant Behaviour Questionnaire Revised (IBQ- R) is a widely used parentreport measure of infant temperament which requires parents to rate the frequency of specific temperament-related behaviours observed in their child (aged three to 12 months) over the past seven days, using a seven-point Likert scale. The original IBQ-R tool was a 191-item instrument. In an effort to reduce demands on mothers associated with participation in the study, researchers administered the 37-item 'very short form', which assesses three broad dimensions from the IBQ-R; Negative Affect/Emotionality, Positive Affectivity/Surgency, and Orienting/Regulatory Capacity (Putnam & Rothbart, 2006). Negative Affect is characterised by high positive loadings on Fear, Distress to Limitations and Sadness, and high negative loadings on Falling Reactivity. The very short form version of the IBQ-R has shown similar reliability to the IBQ-R and other temperament measures (Putnam & Rothbart, 2006).

#### Mother and infant dyad – measuring maternal sensitivity at 12 months:

In order to measure maternal sensitivity at 12 months postpartum, the mother was asked to complete six short tasks with their young child, which were video-recorded by study researchers during home visits. The recordings of each task were then coded using the well-validated Sensitivity Scales from the National Institute of Child Health and Human Development (NICHD) Study of Early Child Care and Youth Development (NICHD, 1997; see Appendix 3), with an additional set of coding scores for the entire video. For the purpose of this study, the NICHD scale was adapted to focus on ratings related to the mother; the child ratings originally present in the scale were omitted. Mothers were rated on each of the following subscales: Sensitivity to non-distress, Sensitivity to distress, Intrusiveness, Detachment/disengagement, Stimulation of development, Positive regard for the child, Negative regard for the child and Flatness of affect. Each of the subscales was scored using a four-point rating scale (1 = not at all characteristic to 4 = very characteristic).

Inter-rater reliability checks were carried out by an experienced research psychologist on 14 cases, which was approximately every fifth video. For all tasks, the intraclass correlations (ICC; average measure) total for maternal sensitivity was 0.84. For the coding scores of the whole video, the ICC was 0.84.

The tasks included free play without toys, completing a distracting questionnaire, reading a story-book, playing with a difficult toy, managing the with-holding of interesting toys and finally reading a book showing different attachment scenarios.

The first set of tasks focused on mother-infant interaction in the context of play. The mother was asked to play with the child as they normally would, without using toys. The next task was a procedure developed by Smith and Pederson (Smith & Pederson, 1988). In this task, the mother was asked to complete a distracting questionnaire, whilst the child was left to explore the room.

Two tasks were included in order to understand the specificity of effects of particular aspects of parental care for particular developmental outcomes, including behavioural problems. The first task involved focusing on reading a book together and the other task involved the child playing with a toy that is difficult to manipulate, with the mother being invited to join in after a few minutes. For the behavioural problems domain, a task was implemented whereby the child was not allowed to touch a set of three desirable toys after they were taken away and the mother was asked to assist the child in managing this, without using toys. Such a challenge has been found to be a good way of assessing the capacity of the mother to sensitively set limits and manage negative affect in the child.

Lastly, another book-reading task took place, in which the content of the book involved strong attachment-related scenarios. Mothers were invited to talk to the child about what was happening in the story and how the people in the pictures might have been feeling.

#### Ethical considerations

The current study took place in the context of a trial, which had received NHS ethics approval. All participants gave full written consent at the start of the study and were re-consented at the 12 months' follow-up point.

#### Data analysis procedures

The current study investigated the effect of antenatal stress on infant temperament, whilst controlling for other relevant characteristics. All statistical analyses were performed using IBM SPSS Statistics (Version 24). Data was assessed for normality. If skewness and kurtosis scores were not between  $\pm 1.96$ , the

Kolmogorov-Smirnov test or Shapiro-Wilk test was significant at p < .01, and the histogram appeared to deviate markedly from a normal distribution, data was judged to be non-normally distributed. In order to test for the assumptions of linearity, normality and homoscedasticity in the regression analyses, scatterplots and histograms were plotted and examined. Collinearity statistics tested for multicollinearity (if VIF value lies between 1-10, there is no multicollinearity) and the Durbin-Watson's test was carried out to test for auto-correlation of the data (if d = 2, there is no auto-correlation).

The overall maternal sensitivity score was calculated by computing a single latent variable on which all the individual sensitivity scores from each task loaded. This was done in order to obtain an overall maternal sensitivity score which best captured the variability in the individual sensitivity task scores. Maximum likelihood estimation was used to estimate a single factor model using the package Mplus Version 7.4. Regarding variables with missing data, the Expectation-Maximisation (EM) algorithm was used to impute values for missing data for the household income variable. The imputation was based upon maternal education level, occupational status and marital status.

As the study was looking at the mechanisms by which a variable transmits its effect to another, a regression-based path-analytic framework was used, involving the principles of mediation and moderation analysis (Hayes, 2013). Initial analyses tested the association between maternal antenatal anxiety and depression and infant temperament, controlling for covariates, using regression. Similarly, regression analyses tested the associations between maternal antenatal depression and anxiety and maternal sensitivity. To test moderation, we examined the interaction effect between antenatal stress and postnatal maternal sensitivity and whether or not such an effect was significant in predicting infant temperament at 12 months. Formal testing of the potential moderating effects of maternal sensitivity was conducted using hierarchical regression analyses, in which antenatal stress x postnatal sensitivity

variables were entered into the model after including main effects and any covariates. The potential mediating effects of maternal sensitivity was tested by using a linear regression analysis using bootstrapped tests of the indirect effect, following the process developed by Andrew Hayes (2013). The PROCESS macro developed by Hayes (2013) is a logistic regression path analysis modelling tool for SPSS. It generates an estimate of the direct and indirect effects in mediation models and conditional effects in moderation models, as well as bootstrap CI for inference.

## Results

The results are presented in five sections. The first section of the analysis outlines how the data were prepared and the assessment of the key variables for normality of distribution and outliers. The second section includes the descriptive statistics. Section three details the correlation analyses, which were conducted to determine associations between the predictor variables (antenatal depression and anxiety) and outcomes (infant temperament and overall maternal sensitivity). The fourth section reports the regression analyses used to examine whether the independent variables (antenatal anxiety and depression) were associated with infant temperament or maternal sensitivity, whilst controlling for potential covariates including postnatal anxiety and depression and demographic variables (maternal age, maternal education level, marital status and household income). The fifth and final section reports results from hierarchical multiple regressions used to test hypothesised mediating and moderating effects in relation to maternal sensitivity, antenatal stress and infant temperament.

# Data preparation and distributional checks on main study variables

The two measures of anxiety (STAI-state and STAI-trait) were standardised and mean scores were computed to represent overall 'antenatal anxiety'. Depression and anxiety are often referred to in combination as 'stress'. In order to examine the effect of 'antenatal stress' on the outcome variables, an average of participants' scores across measures of anxiety and depression was computed, by first standardising the EPDS, STAI-S (state) and STAI-T (trait) scores, and then calculating the mean. Scores were computed for a measure of maternal sensitivity from each of the tasks. The overall maternal sensitivity score was calculated by computing a single latent variable on which all the individual sensitivity scores from each task loaded. Using the package Mplus Version 7.4, the single factor model fit the data very well. The model chi-squared was 2.33 (4 df), p = .67 (RMSEA <.01; SRMR = .02). The standardised loadings ranged between .60 and .70 (all significant at <.001).

The task which involved mothers completing a questionnaire was not possible to code, due to the fact that the majority of the subtests in the chosen scale (NICHD) could not be applied to this task. i.e.. scorina the mother on detachment/disengagement when she was instructed to complete a questionnaire. Thus, this task was not included in our final analyses.

Before conducting the main analyses, the data was examined for outliers and for conformity with the assumption of normality. Normality of the variables was examined visually using histograms in addition to conducting the Kolmogorov-Smirnov (K-S) and Shapiro-Wilk tests. Maternal sensitivity and infant temperament were found to be normally distributed; tests of K-S and Shapiro-Wilk were nonsignificant (p > .001). No outliers were identified in the maternal sensitivity data and one was identified in the infant temperament data. This outlier was not excluded as it was decided that it represented clinically-relevant information. No transformations of the data were conducted.

# **Descriptive statistics**

The main independent variables (predictors) were antenatal depression and anxiety. The dependent variables were maternal sensitivity and infant temperament

(negative affect). Descriptive statistics were calculated for each variable (see Table 2). Using the recommended EPDS cut-off scores of 10 and 12 (Murray & Carothers, 1990), 12% of mothers were shown to be at moderate risk for clinical depression (Total score 10-12) and 25% of mothers were shown to be at high risk for clinical depression (Total score 13-30).

# Table 2.

,,,,,	Ν	Mean (SD)	Range
Antenatal depression (EPDS)	98	8.83 (5.46)	0-26
<sup>a</sup> EPDS total $\ge$ 10 <13	12		
<sup>a</sup> EPDS total $\ge$ 13	24		
Antenatal state anxiety (STAI-S)	98	34.20 (10.70)	21-65
Antenatal trait anxiety (STAI-T)	98	38.70 (10.87)	20-69
Maternal sensitivity (Attachment scenario)	86	10.34 (1.79)	6 - 14
Maternal sensitivity (Book reading)	86	11.85 (1.87)	7 - 17
Maternal sensitivity (Difficult toy)	85	11.78 (1.80)	7 - 15
Maternal sensitivity (Withhold toys)	81	10.65 (1.68)	7 - 15
Maternal sensitivity (Without toys)	85	10.54 (2.05)	7 - 15
Overall maternal sensitivity	86	10.31 (1.93)	7 - 17
Infant temperament (Negative affect)	95	4.17 (1.01)	1.5-6.5

Descriptive statistics - Means, standard deviations and ranges of scores of participants for the antenatal measures (predictors), maternal sensitivity (overall and for each individual task) and infant temperament at 12 months (outcomes).

Note: N=Number, SD=Standard Deviation, <sup>a</sup>Number of mothers with an EPDS cut-off score of >10 or >12

#### Correlation analyses

As expected, maternal depression and anxiety measured concurrently in the antenatal period were significantly correlated (EPDS and STAI r = .80, p < .01). In order to answer the first research question, we conducted a correlation analysis to test for association between antenatal depression and anxiety and infant temperament (negative affect). Contrary to expectations, the association between antenatal depression and to be small and non-significant (r = .19, p = .06). No association was found between antenatal anxiety and infant temperament (r = .14, p = .18). No significant correlation was found between antenatal anxiety and infant temperament (r = .17, p = .11). Correlations are reported in Table 3, including postnatal scores for descriptive purposes.

In order to answer the second research question, we conducted a correlation analysis between antenatal depression and anxiety and overall postnatal maternal sensitivity. A significant negative correlation was found between antenatal depression and overall maternal sensitivity (r = -.28, p < .05). However, there was no significant correlation found between antenatal anxiety and maternal sensitivity, (r = -.11, p =.30). No significant correlation was found between overall antenatal stress and maternal sensitivity (r = -.18, p = .10).

# Table 3.

Correlations between antenatal measures of depression (EPDS), anxiety (STAI), stress (mean scores of EPDS and STAI), and postnatal measures at 12 months of infant temperament (IBQ-R very short form) and overall maternal sensitivity.

Variables	1	2	3	4	5	6	7	8
Antenatal (predictors)								
1. Depression antenatal	-							
2. Anxiety antenatal	.80**	-						
3. Stress antenatal	.91**	.98**	-					
Postnatal (descriptive)								
4. Depression postnatal	.64**	.63**	.67**	-				
5. Anxiety postnatal	.58**	.68**	.68**	.78**	-			
6. Stress postnatal	.63**	.70**	.71**	.90**	.97**	-		
Postnatal (outcomes)								
7. Infant temperament (negative affect)	.19	.14	.17	.14	.17	.17	-	
8. Maternal sensitivity <sup>a</sup>	28*	11	18	16	03	08	.10	-

*Note:* \* *p* < .05; \*\* *p* < .01; <sup>a</sup> sensitivity factor based on sensitivity across all tasks in single factor confirmatory factor model (excluding the questionnaire task)

#### Regression analyses

Do antenatal depression and anxiety predict infant temperament at 12 months, whilst controlling for postnatal anxiety and depression?

In order to answer the first research question, a linear hierarchical regression analysis was conducted to test whether maternal antenatal depression and anxiety predicted infant temperament, whilst controlling for *post*natal depression and anxiety and other covariates.

In this regression analysis, infant temperament (negative affect) was included as the dependent variable. In the first model, maternal age, maternal education level, marital status and household income were included as a block of covariate variables. In the second model, postnatal depression and anxiety were entered as a block of variables as additional covariates. Antenatal depression and anxiety were entered into another block for the third model. Scatterplots and a histogram showed that the assumptions of linearity, normality and homoscedasticity were met. Collinearity statistics showed that there was no multicollinearity. The Durbin-Watson's test indicated no auto-correlation in the data (2.01).

The hierarchical multiple regression revealed that in model one, maternal age, maternal education level, marital status and household income did not contribute significantly to the regression model ( $F_{4,87} = .30$ , p = .88) and accounted for 1.3% of the variation in infant temperament. Introducing postnatal depression and anxiety as covariates accounted for an additional 5.2% of the variation in infant temperament, but this change was not significant, ( $\Delta F_{2,85} = 2.38$ , p = .10,  $\Delta R^2 = .05$ ). Introducing the antenatal variables in model three explained an additional 1.7% of variation in infant temperament. This change was also not significant ( $\Delta F_{2,83} = .78$ , p = .46,  $\Delta R^2 = .02$ ). When all of the variables were included in the model, neither antenatal depression

nor anxiety were significant independent predictors of infant temperament. Results are shown in Table 4<sup>2</sup>.

This hierarchical regression analysis was also run with antenatal anxiety and depression combined to represent 'antenatal stress'. Antenatal stress was not a significant predictor of infant temperament ( $\beta$  = .16, *t* = 1.04, *p* = .30).

<sup>&</sup>lt;sup>2</sup> An additional hierarchical regression analysis was run with no covariates entered into the model (as none were significantly associated with infant temperament). This analysis yielded a similar pattern of findings.

# Table 4.

emperament (N – 92).							
Variable	В	SE B	β	t	p value	R	$R^2$
Step 1						.12	.01
Maternal education	.04	.09	.05	.40	.69		
Household income	.08	.11	.08	.73	.47		
Marital status	.12	.22	.06	.56	.58		
Maternal age	00	.04	00	02	.99		
Step 2						.26	.07
Anxiety postnatal	.05	.19	.05	.27	.79		
Depression postnatal	.03	.03	.20	1.05	.30		
Step 3						.29	.08
Anxiety antenatal	01	.21	01	06	.95		
Depression antenatal	.03	.03	.19	.10	.32		

Summary of hierarchical regression analysis for variables predicting infant temperament (N = 92).

#### Is postnatal maternal sensitivity associated with antenatal depression and anxiety?

In order to answer the second research question, a linear hierarchical regression analysis was conducted to test whether maternal antenatal depression and anxiety predicted maternal sensitivity, whilst controlling for postnatal depression and anxiety and other covariates.

In the first model, maternal age, maternal education level, marital status and household income were included as a block of covariate variables. In the second model, postnatal depression and anxiety were entered as a block (as variables to control for), then antenatal depression and anxiety were entered into another block in the third model. A scatterplot and histogram showed that the assumptions of linearity, normality and homoscedasticity were met. Collinearity statistics showed that there was no multicollinearity. The Durbin-Watson's test indicated no auto-correlation in the data (2.29).

The hierarchical multiple regression revealed that in model one, maternal age, maternal education level, marital status and household income contributed significantly to the regression model ( $F_{4,79} = 2.53$ , p < .05) and accounted for 11.3% of the variation in maternal sensitivity. Household income was an independent predictor of maternal sensitivity ( $\beta = .28$ , t = 2.44, p < .05). Introducing postnatal depression and anxiety as covariates accounted for an additional 1.3% of the variation in maternal sensitivity, but this change was not significant, ( $\Delta F_{2,77} = .57$ , p = .57,  $\Delta R^2 = .01$ ). Introducing the antenatal variables in model three explained an additional 6% of variation in maternal sensitivity. This change was not significant ( $\Delta F_{2,75} = 2.76$ , p = .07,  $\Delta R^2 = .06$ ). When all of the variables were included in the model, antenatal depression was a significant independent predictor of maternal sensitivity ( $\beta = -.44$ , t = -2.35, p < .05). Results are shown in Table 5<sup>3</sup>.

<sup>&</sup>lt;sup>3</sup> An additional hierarchical regression analysis was run with the only significant covariate, household income, entered into step one. This analysis yielded a similar pattern of findings.

This hierarchical regression analysis was also run with antenatal anxiety and depression combined to represent 'antenatal stress'. Antenatal stress was not a significant predictor of maternal sensitivity ( $\beta$  = -.18, *t* = -1.09, *p* = .28).

# Table 5.

$\frac{36113111711}{110111} (11 - 0+).$							
Variable	В	SE B	β	t	p value	R	$R^2$
Step 1						.34	.11
Maternal education	.00	.09	.01	.05	.96		
Household income	.25	.10	.28	2.44	.02*		
Marital status	07	.22	04	33	.75		
Maternal age	.05	.04	.13	1.20	.24		
Step 2						.36	.13
Anxiety postnatal	.19	.19	.19	1.01	.32		
Depression postnatal	03	.03	19	-1.03	.31		
Step 3						.43	.19
Anxiety antenatal	.29	.20	.29	1.44	.16		
Depression antenatal	07	.03	44	-2.35	.02*		

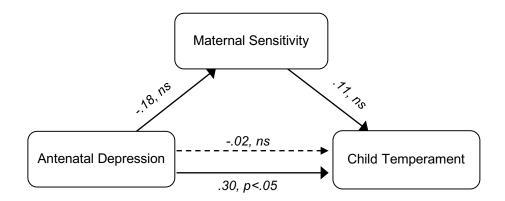
Summary of hierarchical regression analysis for variables predicting maternal sensitivity (N = 84).

*Note: \*p<*.05

#### Mediation analysis

In order to answer the third research question, a mediation analysis was conducted to test the hypothesis that the relationship between antenatal stress and infant temperament, at 12 months, is mediated by maternal sensitivity. As antenatal depression was shown to be significantly associated with maternal sensitivity (and not antenatal anxiety), we chose to include this in our mediation analysis. In order to confirm any mediating effects and assess for shared variance, a regression was conducted using the PROCESS macro (Hayes, 2013). The following variables were mean centred: antenatal depression and overall maternal sensitivity (Aiken, West, & Reno, 1991). As a significant independent predictor of maternal sensitivity, household income was entered in to the model as a covariate.

In the first part of the mediation model, the regression of antenatal depression on the potential mediator, maternal sensitivity was non-significant (b = -.18, t = -1.67, p = .10). The second part of the mediation process showed that the mediator (maternal sensitivity), controlling for antenatal depression, was not a significant predictor of infant temperament (b = .11, t = .99, p = .32). The third step of the analysis revealed that, controlling for the mediator (maternal sensitivity), antenatal depression was a significant predictor of infant temperament (b = .30, t = 2.76, p < .05). Finally, the mediation model showed that the indirect effect of antenatal depression on infant temperament, mediated by maternal sensitivity, was non-significant (b = .02, 95% CI [-.12, .01]). It was found that maternal sensitivity did not mediate the pathway between antenatal depression and infant temperament at 12 months, whilst controlling for household income. Results are depicted in Figure 1.



### Figure 1.

Mediational model of maternal sensitivity between antenatal depression and infant temperament. Note: Dotted line = indirect effect

#### Moderation analysis

Does maternal sensitivity have a moderating effect on the pathway between antenatal stress and infant temperament at 12 months?

Although a non-significant correlation was found between antenatal stress and infant temperament, it was still considered useful to conduct additional analyses. In line with the fourth research question, to investigate whether maternal sensitivity has a moderating effect on the pathway between antenatal stress and infant temperament, additional regression analyses were performed using the PROCESS macro (Hayes, 2013). To avoid potentially problematic multicollinearity, it has been recommended that the variables be mean centred when using moderation analysis (Aiken et al., 1991). The following variables were mean centred: antenatal depression and overall maternal sensitivity. As it was found to be a significant independent predictor of maternal sensitivity, household income was imputed as a covariate. Overall, the regression model was significant ( $F_{4,79} = 3.13$ , p = <.05). When the antenatal depression x postnatal maternal sensitivity interaction term was considered, the change in variance accounted for was minimal and non-significant ( $F_{1,79} = 2.68$ , p = .11,  $\Delta R^2$  = .03). Maternal sensitivity did not moderate the effects of antenatal stress on infant temperament at 12 months. Results are outlined in Table 6.

# Table 6.

Interaction of antenatal depression and maternal sensitivity predicting infant temperament at 12 months (N=84).

	Infant Temperament						
Variable	b	SE	t	p value	R	$\Delta R^2$	
Regression Model					.37*	.14	
Maternal sensitivity	.10	.11	.91	.37			
Depression antenatal	.32	.11	2.95	.00*			
Interaction	17	.11	-1.64	.11		.03	

*Note:* \**p*<.05; *Household income served as a covariate in this model.* 

#### Discussion

The current study was designed to investigate the role of maternal sensitivity in the pathway between antenatal stress and infant difficult temperament (negative affect). Although research has attempted to draw conclusions on the relationships between each of these factors, they have rarely been examined in existing studies simultaneously, nor with a young and economically disadvantaged sample. The key goals of the study were to investigate associations between antenatal stress (anxiety and depression) and infant difficult temperament at 12 months, and to investigate the potential mediating or moderating role of maternal sensitivity in this pathway.

# Main findings

As expected, the present study found that depression and anxiety, as measured in the antenatal period, were strongly and positively correlated. This finding is consistent with research in this area (Heron, O'Connor, Evans, Golding, & Glover, 2004; O'Connor, Heron, & Glover, 2002).

A significant negative correlation was found between antenatal depression and overall maternal sensitivity at 12 months. This relationship has received little attention in the literature and thus this finding is the first, to the author's knowledge. When we examined this association after controlling for postnatal depression the findings showed that household income was a significant strong independent predictor of postnatal maternal sensitivity, but antenatal depression remained a significant independent predictor of maternal sensitivity. However, it is possible that the significant association with depression that we found is not a reliable one, and that replication with a larger sample size may be warranted.

Contrary to our expectations, no association was found between antenatal anxiety and overall maternal sensitivity at 12 months. Similarly, when antenatal

depression and anxiety were combined to represent antenatal 'stress', no association was found with maternal sensitivity.

The relationship found between antenatal depression and maternal sensitivity, an important aspect of caregiving, raises the important prospect that the documented 'foetal programming' effects might be more complex than first thought. Although a number of studies on the influences of antenatal depression and anxiety on infant outcomes have controlled for the effects of postnatal depression and anxiety, there remains a critical gap in our understanding of the potential influence of parenting factors on the association between antenatal stress and infant outcomes (Kaplan et al., 2008). Thus far, studies reporting on this topic have rarely controlled for postnatal caregiving, and the current findings suggest that future research may need to consider this.

Contrary to predictions, the present study did not find any associations between the independent variables (antenatal depression, anxiety, or stress) and difficult infant temperament at 12 months. These findings are not consistent with previous research in this area (Austin et al., 2005; Davis et al., 2007; Henrichs et al., 2009; Huizink et al., 2003).

Despite these null findings, we still considered it worthwhile to test the hypothesis that the relationship between antenatal stress and infant temperament, at 12 months, is mediated by maternal sensitivity. Perhaps unsurprisingly, maternal sensitivity did not mediate the pathway between antenatal depression and infant temperament, at 12 months. Similarly, maternal sensitivity did not play a moderating role on the pathway between antenatal depression and infant temperament at 12 months.

It was interesting to note that an association between antenatal depression and infant temperament did come to light when maternal sensitivity was controlled for in the regression analyses. This might suggest that sensitivity accounts for some of the reasons why antenatal depression does not consistently predict infant

temperament; perhaps maternal sensitivity accounted for some of the noise in the relationship between antenatal depression and infant temperament, and this may explain why it did not show up when we controlled for maternal sensitivity. As these sorts of effects (where a univariate association is not present but becomes apparent when covariates are controlled for) are not always reliable, we are cautious about interpreting this effect, but it may add further weight to the argument that with a larger sample a reliable association (even a direct univariate one) may have been detected.

The lack of a robust association found between antenatal stress and infant outcome was surprising, given the large literature dedicated to this topic. The current literature focuses heavily upon the foetal programming hypothesis to explain the association. It is relevant to consider that our findings highlight the issue that the biological mechanisms of the foetal programming are not yet fully understood. Although it is an interesting hypothesis and one which has gathered attention and extensive investigation through animal studies, it has not been sufficiently studied in the human literature. The current findings highlight that there remains a gap in our understanding of this and further investigation, using human studies, is warranted. In addition, there is currently a wide variety of effect sizes being reported in the published literature with regards to antenatal stress and infant temperament. The association in our data was of a magnitude of r = .19 (p = .06) and may well have been significant in a larger sample.

Another possible reason for the lack of findings in the current study relates to the high-risk, disadvantaged sample of young women chosen to be the study population. As noted, the mothers and babies were from socio-economically disadvantaged areas in the United Kingdom. Such a sample has rarely been studied and, thus, there may be unknown population differences. These differences may have impacted upon our ability to identify any relationship between antenatal stress and infant outcome.

Furthermore, this sample was characterised by multiple risks and it is likely that many other stressors were being experienced, which this study did not account for. It may be worth considering the impact of childhood trauma, attachment relationships and the intergenerational transmission of parenting, on the participants' own parenting styles and levels of maternal sensitivity. For the mothers included in this study, this was their first child and therefore their first experience of parenthood. We know that the antepartum period places high demands on women and is characterised by a variety of changes, including; biological, physical, social, and emotional, which can be overwhelming. The psychological sequelae of the stress caused by these changes is likely to be exacerbated in such a vulnerable, impoverished sample. It might be that a greater understanding and control of confounding variables may lead to associations being found between antenatal stress and infant outcome.

Another possible reason for the lack of findings in the current study involves the measurement of the outcome, which relied upon maternal self-reports of infant temperament. It is possible that parental biases might have been involved during completion of the self-report questionnaire. In a study by Seifer et al. (2004), they conducted a comparison of parent-observer agreement under two conditions; own child or standard child. They found mothers to be less accurate when rating the temperament of their own children. The authors attributed this to systematic bias in parent reports of infant temperament (Seifer, Sameroff, Dickstein, Schiller, & Hayden, 2004). Furthermore, the infant outcome variable in the current study was measured at 12 months. It is plausible that the role of antenatal stress in predicting infant temperament may become more apparent at an older age. Thus, a longer period of follow-up might be warranted.

Given that foetuses develop rapidly during pregnancy and that development of particular processes and systems occurs at different points during pregnancy, the consequences of foetal exposure to stress on foetal development are likely to vary

depending on the timing of exposure within pregnancy (Martin & Dombrowski, 2008; O'Connor et al., 2003). The current study measured antenatal anxiety and depression between 28-32 weeks' gestation. Although Davis et al. (2007) found that prenatal stress during late gestation is a good predictor of difficult infant temperament, there is still a lot of uncertainty about the timing of the stress in pregnancy that will have the *most* effect on infant outcome. In the current literature, efforts to specifically understand the role of timing of antenatal stress have been complicated by differing outcomes and thus further research is needed.

It is also important to consider that the study took place in the context of an ongoing randomised control trial (RCT), where group allocation is not yet available, and thus it was not possible to control for this. Although the hypotheses relied on antenatal measures taken prior to allocation, and the groups were balanced with respect to antenatal depression (and therefore the results should not be unduly affected by treatment allocation), we cannot rule out the possibility that treatment related changes in the intervention group added noise to the measurements and therefore obscured real effects.

Lastly, the sample size warrants some acknowledgment. Although the sample size was deemed sufficient according to our power calculation, it still may have limited our statistical power to detect moderate to small effects. It is possible therefore that a true effect may have been overlooked due to low statistical power. The mediation and moderation analyses may have been limited by the sample size and resulting lack of power to detect interactions.

Although there are a number of strengths to this study, such as the longitudinal correlational design and the use of a rarely investigated, high-risk sample, there are some further limitations which require consideration. Firstly, as with any longitudinal study, attrition was an issue and this could potentially impinge on the findings discussed. Retention of the mother-infant dyads in the study was difficult to maintain over the 12-month period. Some of the mothers dropped out before the follow-up

assessment or did not give consent at the appointment for their interactions with their child to be video-recorded by the researcher. It is important to highlight here that the chosen study population was that of significantly disadvantaged women for whom participation in a research study may be difficult.

#### Implications and future directions

The findings of this study highlight the complexity of fully understanding the pathway between antenatal stress and infant outcome, when the postnatal caregiving environment is considered. The foetal programming hypothesis has so far been a strong contender in the research to explain the effects of antenatal stress on infant outcome. However, the remaining lack of conclusions drawn regarding the mechanisms underlying foetal programming precludes our ability to determine the most effective treatment and intervention options. If the postnatal caregiving environment has an impact on the pathway between antenatal stress and infant outcome, this will have important clinical implications. It may provide valuable information to help plan and implement effective interventions. The use of such interventions in routine clinical practice would help to reduce the burden of mental health problems and its social and emotional consequences, both for the mother and child. In order to further elucidate these implications, future research may benefit from controlling for the postnatal caregiving environment, so that the association between antenatal stress and infant outcome can be evaluated more thoroughly.

The finding that antenatal depression was a significant independent predictor of postnatal maternal sensitivity raises the question of whether depression in the antenatal period would be particularly important in affecting parenting. Indeed, only antenatal depression, and not postnatal depression, was associated with maternal sensitivity. There are a number of ways of thinking about how such a specific association might arise. Currently, the effects of pregnancy on the human brain are essentially unknown (Hoekzema et al., 2017). There is however some emerging research available with the aim of investigating neural plasticity in human mothers' brains. We know that, following birth, the brain and body of mothers undergo important changes to prepare the mother for her new role as a caregiver and to respond to infant-related cues. A study by Kim and colleagues (2010) identified structural changes in brain regions among human mothers during the first few postpartum months, and that these changes were predicted by a mother's positive perception of her baby at the first month postpartum. More specifically, they found an increase in the volume of grey matter in large regions of the prefrontal cortex, parietal lobe, and midbrain. The research highlights the postnatal period as a critical time for changes in certain brain regions, which may be important in the development of sensitive maternal behaviours (Kim et al., 2010).

The focus of this research into maternal brain changes has currently been on the early postnatal period and it may be that future studies could also take into account the antenatal period, too. Indeed, longitudinal studies starting in pregnancy, or even before conception, with follow-up into the postpartum period, may help determine whether the mother's brain is primed antenatally and has an effect on parenting behaviour (Kim, Strathearn, & Swain, 2016). Another possibility is that antenatal depression reflects a personal vulnerability that affects bonding in the early postnatal period, which in turn sets in motion less harmonious maternal-infant interactions thereafter, regardless of the future course of the mother's maternal depressive symptoms. Further work is needed to elucidate these different possibilities, as well as ascertain more generally whether antenatal depression is indeed more robustly associated with caregiving than postnatal depression.

Our results are a reminder of the need for continued efforts to assess maternal mental health throughout pregnancy in order to target specific interventions. The current study also highlights the need to further investigate these issues with a highrisk sample of women. In relation to the findings of the current study, replication is

needed on a larger scale to see whether the effect could generalise to other populations, too.

### Summary

In summary, this study was one of the first studies to investigate the potential mediating or moderating role of postnatal caregiving in the relationship between antenatal stress and infant development, using a high-risk sample. This rarely studied population is characterised by multiple stresses and the interaction of these with maternal mental health requires further investigation, using a larger sample. The current study found a significant association between antenatal depression and maternal sensitivity at 12 months. It raises important issues about whether changes in the antenatal period have potential priming effects on the mothers' brains, preparing them for the transition to parenthood, or on their capacity to bond effectively with the infant in the early postnatal period.

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PART 3: CRITICAL APPRAISAL

#### Introduction

The following is an appraisal of the empirical research presented in Part Two of this volume. The first section will detail my reasons for choosing the research topic. I will then consider the methodological issues arising from conducting the research, including; the data collection process, ethical considerations and challenges of the coding process. The next section details my reflections on the complexities of the sample. The critical appraisal will conclude with some of my thoughts on the overall research process.

#### Choosing the research topic

There were several factors which informed my decision to choose a project within the field of maternal mental health. Firstly, I wished to base my project on an idea which incorporated my interest in working with children and families; this being the area in which I gained the majority of my pre-training experience. Secondly, I had been given an opportunity to complete one of my placements in a specialist perinatal mental health service, during my third year of training. Throughout my six-month placement, I met a range of mothers suffering from postnatal depression; some with it being their first experience of mental health difficulties. The mothers exhibited a range of vulnerabilities and came from diverse cultural backgrounds. I thoroughly appreciated my clinical work with this population and gained insight into the potential for recovery and healing in the postpartum period. Subsequently, I was very keen to be involved when an opportunity arose to investigate maternal sensitivity, using data collected from an ongoing research trial with vulnerable mothers and infants.

# Methodological considerations

# Data collection process

The current study used data collected as part of a larger, ongoing randomised clinical research trial. I was aware of the daunting prospect of data collection, which

many of my fellow trainees were facing, and thus I felt a sense of relief that this was not a requirement of my chosen project. Nevertheless, conducting this project was not without its complexities. Not being involved in the collection of data meant that I had very limited control over the process. However, our access to support from researchers at the Anna Freud Centre, to liaise with about progress of the trial and to answer our many queries, was invaluable. One issue that arose quite early on in the data collection process was that the researchers in the three locations around the UK were experiencing difficulties in following up the participants. We heard that some mothers were not giving consent to be filmed at the 12 months' follow-up appointment and that others could not be contacted. As this was a longitudinal study, we could expect attrition to be an issue (Twisk & De Vente, 2002). Not being involved in the data collection process meant that we had to put our trust in the research team around the country to gather as much data as possible.

As the project was based upon having baseline data and follow-up data at 12 months, it was not feasible to have managed this on a large enough scale, within the restrictions of a doctoral thesis project. Thus, having contact with a research team based in three different locations around the UK created a pathway for us to gather a rich data source.

### Ethical reflections

A benefit of not collecting any additional data was that we had access to a large pool of data, without the need to re-apply for ethics. Again, having witnessed my fellow trainees go through this lengthy, painstaking process, I experienced relief at not having to complete this task myself. Nevertheless, I still feel it is an important and worthwhile exercise to reflect upon some of the ethical considerations of working with such a vulnerable population.

A crucial ethical issue with this study was maintaining the confidentiality of the video data, in which we invested a great deal of thought, as we were not able to

anonymise the videos. The sharing of video data between the researchers required careful planning and we were mindful of the highly sensitive nature of our data set. Furthermore, it is noted that longitudinal studies present greater issues in relation to threats towards an individual's right to privacy than most investigations using a cross-sectional design (Egeland, 1991). To help resolve this issue, the mothers reconsented at the 12 months' follow-up point for their data to be used.

Working with such a high-risk sample emphasised the importance of having researchers who were sensitive and understanding of the problems experienced by disadvantaged families. Interestingly, researcher characteristics can influence the process of building rapport with participants (Pezalla, Pettigrew, & Miller-Day, 2012). Although we did not have contact with the researchers directly, it was clear from the videos that they took an empathic, professional and flexible approach to engaging the sample of mothers and infants. The mothers and their young children were evidently treated as people, not as 'research subjects'.

### The coding process and challenges

Coding the mother-infant interactions in order to measure maternal sensitivity at 12 months was a time-consuming and lengthy process. Before we could obtain access to the videos from the ongoing RCT, an intensive training programme was conducted with myself, my joint-thesis partner and a researcher at the Anna Freud Centre. I was pleased with the amount of thought and planning that went into the development of the training process, which felt very collaborative. I was able to bring some insight from my prior experience of having completed training in the Keys to Interactive Parenting Scale (KIPS), another parent-infant video observation scoring tool (Comfort & Gordon, 2006). However, I also experienced the challenge of changing the direction of my thinking, with a new scale to learn and apply. Nevertheless, I appreciated this opportunity to further develop my skills in this method of evaluating behaviour. Whilst completing the training, I noted my tendency towards interpreting the mother-infant interaction and behaviours whilst wearing my 'clinical hat'. This was subsequently impeding my ability to focus on scoring the mothers from an objective perspective. I found myself being curious about the details of attachment behaviours between the mother and baby, which was not necessarily the focus of our task. It was an important learning experience for me to switch from wearing my 'clinical hat' to my 'research hat'.

The chosen scale for measuring maternal sensitivity was the NICHD sensitivity scales. At the start of the project, the utility of this measure was being determined by the research team involved in the ongoing RCT. Initially, the measure involved both mother and infant ratings. It became apparent through our training process, that the ratings for the mothers was much more relevant for our chosen research topics, and that including infant ratings was unnecessary. A collaborative decision was made to omit the infant rating subscales from the measure.

As part of the ongoing research trial, it was deemed beneficial to conduct the follow-up appointments with the mother-infant dyads in their home setting. However, there are some challenges worth noting from the coder's perspective. Firstly, some of the video quality was quite poor, due to the positioning of the camera in the room. At times, it was hard to see the faces of the mother and infant and thus a challenge to determine facial expressions or mood. Further, we were aware that the researchers had been given a script to read to participants regarding each of the tasks. It was apparent that this was not always done in the same way amongst the different researchers and thus mothers may not have fully understood the task requirements. This highlights some of the general difficulties of conducting large, longitudinal studies involving multiple researchers in separate locations, and the need for consistency with the method of data collection.

There were restrictions added to the filmed interactions in terms of context and time. The clips to be coded were an average of 35 minutes long, which are unlikely to be representative of the everyday and natural interactions between the

mother and infant. It was imperative for the ongoing research trial that the mothers were asked to interact with their young child for a limited amount of time, participating in activities that they might not have previously done to stimulate their child. We noted that several of the mothers experienced difficulty with some of the tasks requiring them to speak in English, which was perhaps not their first language. Some of the mothers seemingly felt comfortable to attempt to engage their child with the task in English, whereas others raised the issue with the researchers and subsequently spoke in their mother-tongue. This meant it was not always possible to understand fully the content of the conversations between the mother and child, thus important details or nuances may have been missed and not accounted for.

Another issue that arose during the process of coding the video interactions was that the mother ratings in the sensitivity scale were very hard to apply to the task involving the completion of a distracting questionnaire. It felt an unfair representation to rate the mother as severely detached and disengaged, when she had been instructed to complete the questionnaire in the same room as her infant. Following a discussion with some of the research team involved in the ongoing trial, it was decided that it was appropriate to score certain subscales as 'not applicable' in the case of the questionnaire task. As a consequence, we ended up with a significant amount of missing data for this task, which was subsequently excluded from the analysis.

# The complexities of our sample

With the time pressures of completing the coding of the videos, it was difficult to fully comprehend what it might be like to be a parent in such vulnerable circumstances and with complex histories. I would like to take this opportunity now, to reflect upon my observations of coding the interactions. Whilst conducting this research, I became increasingly mindful of the high level of impoverishment present in our study sample. The level of vulnerability of the majority of families was evident in the videos and this evoked feelings of sadness in me. Many of the home environments appeared neglected and were cramped and cluttered. During the data collection, I learned that some of the mothers had lost their children following care proceedings or had themselves, or their partners, been incarcerated. My previous experience of working as an assistant psychologist in the context of care proceedings gave me some insight into the ongoing stresses of some of the parents in our sample. It was possible that we might have lost some of the mothers at the higher end of vulnerability, by the time they were due to be followed up at 12 months postpartum. Indeed, "it is often those most in need who drop out of programs as a result of low motivation, poor skills and limited social support", (Furstenberg, Brooks-Gunn, & Morgan, 1987, p. 151). It has been noted that losses to the sample has potential for distortion in the findings, meaning that the most vulnerable participants may have been under-represented in the final sample, inferring possible bias within the sample (Fischer, Dornelas, & Goethe, 2001).

Upon reflection, I have considered some of the challenges that the young mothers may have faced during this study. Firstly, they may not necessarily have felt comfortable in letting unfamiliar people into their homes, with the addition of a camera, which could be perceived as quite imposing. It was inevitable that the mothers would be aware of being filmed and having a researcher present in their homes. Some of them were noticeably anxious during filming, despite the efforts to keep them calm and relaxed by the researchers. This may have led them to act unnaturally in their home environment, perhaps due to fear of judgement. Thus, this may not have been a true reflection of mother-infant interactions. Another challenge faced by the mothers was balancing the needs of their child with the requirements of the tasks. Some infants were observed to be very tired and others required feeding at points during the assessment, which would have inevitably impacted upon their emotional and physical states.

Although the video clips represented just a short space of time in comparison to their lives, it was clear to see how many of these mothers were distressed and

anxious. For some, this clearly impacted upon their interactions with their children. I frequently witnessed mothers becoming frustrated as well as some of the infants being highly distressed for the majority of the recorded interactions. During the recordings, I often saw cycles of increasing levels of uncooperative child behaviours (disengaging or in protest states) and maternal demands and irritability. Indeed, the co-occurrence of these negative maternal and infant interactive behaviours (confrontation or withdrawal) may fuel negative cycles of interaction (Leadbeater, Bishop, & Raver, 1996).

For a portion of the mothers, it was clear that the presence of the researcher in their home was used as an opportunity to share their stories, and through this we learned a bit more about their struggles. As stated by Chablani and Spinney (2011), there is value in engaging in purely social activity, including small-talk, with participants as a way of building trust. This idea is supported by Hammersley and Atkinson (1995), who note that conversations with participants, that are not directly related to the research, can be advantageous in establishing one's identity as a 'normal, decent' person (as cited in Chablani & Spinney, 2011). A balance is needed, to retain fidelity to the script and task procedures, whilst also maintaining rapport with participants to facilitate engagement.

With such a vulnerable sample of mothers, it is important to acknowledge that the barriers to engagement might be substantial. Many of our sample were living in the midst of a variety of high-risk situations, such as; unemployment, housing crises, poverty, court proceedings, social exclusion and isolation. Within these situations, it is relevant to consider the level of social support that the mothers have access to. With a focus on younger mothers, Logsdon and colleagues found that the level of social support was dependent upon the family structure, socio-economic status, threats to safety (including neighbourhood violence) and the mother's relationship with the father of her child (Logsdon, Gagne, Hughes, Patterson, & Rakestraw, 2005). In several of the videos, I witnessed a family member or partner present in the house.

However, more often than not, it was hard to ascertain the level of support each mother had in raising her child. Risk factors associated with impoverishment, such as; financial crises, relationship conflicts and lack of social support, have been shown to contribute to the quality of parent–child interactions (Leadbeater et al., 1996).

#### **Overall reflections**

There were several benefits to working collaboratively with a colleague on this research project. We were able to share the workload of coding the significant amount of video data we received, allowing us to include a larger sample of mothers in our final analyses. In addition, during our training programme, we were able to work jointly to understand the NICHD sensitivity scales and consult each other when it came to discrepancies. Working together allowed for collaborative problem-solving when issues arose, as well as mutual support throughout the project.

A number of the findings from the research detailed in the empirical paper were not statistically significant. I had concerns that my results did not match my expectations, and received a helpful reminder from my supervisor that 'this is how science works'. I learned an important skill of taking a step back and thinking about the reasons for our lack of significant findings. Although the findings were not what we expected, we found an association that raised some important questions and allowed us to think about recommendations for the future of research in this area.

# Conclusions

This critical appraisal highlights some of the specific challenges of the research process and methodological considerations. The experience of conducting this research project has been both challenging and very rewarding. It provided me with an opportunity to gain insight into working with high-risk, vulnerable families and enabled me to experience some of the challenges associated with studying this population. Key lessons learned were; the advantages and disadvantages of utilising

data from a larger trial, the challenges added by the complexities of a high-risk sample to methods of data collection and analysis, which may need to be adapted throughout the research process, and other relevant factors that may need to be considered when investigating such a vulnerable population.

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APPENDICES

# Appendix 1: Literature Review Search Terms

Med	line Search Terms:	
1	risk factors/ or protective factors/	718171
2	postpartum depression/	4523
3	baby blues.mp.	69
4	postnatal depression.mp.	2231
5	perinatal depression.mp.	456
6	maternal depression.mp.	1709
7	pregnancy depression.mp.	41
8	2 or 3 or 4 or 5 or 6 or 7	6704
9	1 and 8	1688
10	limit 9 to human	1687
11	limit 10 to ("0110 peer-reviewed journal" and english and human)	1567
	[Limit not valid in Ovid MEDLINE(R); records were retained]	
12	limit 11 to ("0110 peer-reviewed journal" and human) [Limit not valid in	1567
	Ovid MEDLINE(R); records were retained]	
13	limit 12 to last 15 years	1360
14	("postpartum depressi*" or "baby blues" or "postnatal depressi*" or	6125
	"perinatal depress*" or "maternal depressi*").mp. [mp=title, abstract,	
	original title, name of substance word, subject heading word, keyword	
	heading word, protocol supplementary concept word, rare disease	
	supplementary concept word, unique identifier, synonyms]	
15	((risk adj factor*) or (protective adj factor*) or PREDICTOR*).ti. or	662753
	((risk adj factor*) or (protective adj factor*) or PREDICTOR*).ab. or	
10	((risk adj factor*) or (protective adj factor*) or PREDICTOR*).sh.	1044
16	14 and 15	1344
17	12 and 16	688

Psy	cINFO Search Terms:	
1	risk factors/ or protective factors/	69173
2	postpartum depression/	4022
3	baby blues.mp.	42
4	postnatal depression.mp.	3361
5	perinatal depression.mp.	454
6	maternal depression.mp.	2593
7	pregnancy depression.mp.	62
8	2 or 3 or 4 or 5 or 6 or 7	7931
9	1 and 8	912
10	limit 9 to human	893
11	limit 10 to ("0110 peer-reviewed journal" and english and human)	734
12	limit 11 to ("0110 peer-reviewed journal" and human)	734
13	limit 12 to last 15 years	720
14	("postpartum depressi*" or "baby blues" or "postnatal depressi*" or	8803
	"perinatal depress*" or "maternal depressi*").mp. [mp=title, abstract,	
	heading word, table of contents, key concepts, original title, tests &	
	measures]	
15	((risk adj factor*) or (protective adj factor*) or PREDICTOR*).ti. or ((risk	187982
	adj factor*) or (protective adj factor*) or PREDICTOR*).ab. or ((risk adj	
	factor*) or (protective adj factor*) or PREDICTOR*).sh.	
16	14 and 15	1945
17	12 and 16	557

# Appendix 2: Details regarding each individual's contribution to the joint

research project

This research was conducted as part of a joint thesis project with my fellow D.Clin.Psy. student, Nathan Dowling (2018).

The training programme for coding of the videos of mother-infant interactions was undertaken collaboratively by myself and Nathan, with the guidance of a researcher at the Anna Freud Centre. Nathan and I sometimes met jointly with our shared supervisor, Professor Pasco Fearon, throughout the course of the research.

The videos for the maternal sensitivity variable were coded independently by myself and Nathan, from different locations. We each coded about half of the videos. Our scores were individually sent to a researcher at the Anna Freud Centre, who collated the data and monitored inter-rater reliability. Nathan and myself also scored approximately half of the questionnaires each, including the EPDS, IBQ and STAI.

Nathan's project aimed to investigate the association between postnatal depression and maternal sensitivity, whilst focusing upon individual tasks. The title of his thesis was 'Impact of Depression on Maternal Sensitivity to One-Year-Old Infants'.

The current project focused upon investigating the role of overall maternal sensitivity in the pathway between antenatal stress and difficult infant temperament at 12 months.

Both pieces of work included analyses of scores on measures of depression and maternal sensitivity. All analyses were completed independently.

# Appendix 3: Scale used to measure maternal sensitivity

(Not included for copyright reasons)