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A systematic review of longitudinal studies investigating the association between early life maternal depression and offspring ADHD.

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Abstract

Objective: The systematic review sought to understand the relationship between maternal depression and later ADHD in children. **Method:** Three databases were used to identify the studies (Medline, Web of Science and PsychInfo) resulting in 1,223 studies being screened and fourteen articles being included in the review. **Results:** The majority of studies (N = 11) reported a significant relationship between maternal depression (across both prenatal and postnatal periods) and ADHD symptoms in children. This relationship remained significant when temperament, or past ADHD symptoms were controlled for. Several methodological issues were identified including; overreliance on maternal report and parental ADHD not being accounted for in most studies. **Conclusion:** The review adds to the literature regarding the temporal relationship between maternal depression and the development of ADHD in children, and thus supports the case for improving access to mental health services for mothers as a preventative strategy in the development of child psychopathology.

Depression refers to a collective term for several depressive disorders, such as Major Depressive Disorder, and Persistent Depressive Disorder. Common symptoms across all depressive disorders include sadness, irritable moods, difficulties with motivation, fatigue and poor concentration (American Psychiatric Association, 2013). Maternal depression has been consistently associated with the development of psychopathology in children, related to rates of both internalising and externalising disorders (Goodman et al., 2011). Prevalence rates of prenatal depression are estimated to be between 17% and 25%, with some evidence that rates of prenatal depression are increasing over time (Pearson et al., 2018). Postnatal depression is estimated to affect around 17% of mothers (Shorey

et al., 2018), with women twice as likely as men to experience depression during their lifetime (Kuehner, 2017). Maternal depression has been frequently reported to be associated with child physical and mental health, and wellbeing (Ahun et al., 2021; Gelaye et al., 2016; Liu et al., 2017; Rogers et al., 2020; Korhonen et al., 2012; Leiferman, 2002; Turney, 2011).

This review seeks to focus on the longitudinal association between early life maternal depression (defined within this review as occurring within the first 10 years of a child's life to cover the pre-adolescent period) and Attention Deficit Hyperactivity Disorder (ADHD), which is one of the most commonly diagnosed childhood psychiatric disorders. ADHD refers to a collection of symptoms of inattention (including difficulties with sustained attention, following instructions and organisational skills) and hyperactivity and impulsivity (including fidgeting, restlessness, and difficulties in turn taking) (American Psychiatric Association, 2013). It is estimated that around 5% of children meet criteria for ADHD, with a further 5% displaying sub-diagnostic threshold levels of attention/hyperactivity problems that nevertheless cause impairment in function. ADHD is two to three times more commonly reported in males than females (Sayal et al., 2018).

ADHD has a significant genetic component, with a recent meta-analysis by Faraone & Larsson (2019) reporting a 74% heritability estimate, based upon family, twin and adoption studies. It has been found that some environmental factors, such as maternal tobacco and alcohol use, interact with genetic risk and are associated with increased rates of ADHD (Palladino et al., 2019). Maternal stress in pregnancy has also been shown to be more prevalent during the gestation periods of children with ADHD, compared to their healthy siblings, with some evidence that this effect is mediated by genetic factors (Grizenko et al., 2012).

ADHD difficulties in early childhood are associated with increased rates of substance use and poorer academic performance in adolescence (Barkley et al., 1990; Sayal et al., 2015), and increased prevalence of mood, substance use and antisocial behavior disorders in adulthood (Biederman et al., 2012). It is therefore important to better understand what specific factors contribute towards the development of ADHD, so that rates of ADHD symptomatology can be reduced to mitigate against longer term negative outcomes. One such avenue is considering the impact of the familial environment upon children's development of ADHD.

Socioeconomic status (SES) is a broadly relevant environmental factor in that low SES is associated with a 1.85 – 2.21 increase in rates of ADHD, although this increase is likely to be confounded by multiple other risk factors associated with low SES (Russell et al., 2016). Low SES has been associated with greater risk of experiencing Adverse Childhood Experiences (ACEs) (Walsh, McCartney, Smith and Armour, 2019). ACEs have been found to be significantly associated with ADHD, with children with ADHD having a higher number of ACEs than children without ADHD (Brown et al., 2017). Jimenez et al., (2017), reported a dose-response relationship, with greater number of ACEs associated with more severe ADHD symptomatology, controlling for early life ADHD symptoms. Although the ACEs research is informative for public health interventions, it lacks sophistication in terms of understanding specific pathways to development of ADHD. Maternal depression, for example, comes under the broad ACE of "household mental illness"; understanding its specific role in the development of ADHD would have implications for both service development and intervention with individual families.

There are multiple mechanisms through which maternal depression may be considered to confer risk for offspring ADHD, including shared genetic risk for ADHD (Powell et al., 2021), intrauterine mechanisms (e.g. Seckl & Holmes, 2007), and exposure to risk factors for ADHD which are associated with higher rates of maternal depression, such as smoking (Thakur et al., 2013). Further, maternal depression has long been associated with negative parental behavior (Lovejoy et al., 2000) that can impact upon a child's behavior, including ADHD symptoms. Maternal depression has also been reported to alter attachment styles and patterns (Lefkovics et al., 2014; Meuti et al., 2015), with attachment insecurity associated with externalising behavior difficulties in children (Guttmann-Steinmetz & Crowell, 2006), including ADHD (Storebø et al., 2013) and the highly comorbid Oppositional Defiant Disorder (ODD) (Theule et al., 2016). Further, in a genetically controlled study examining samples of adopted children only (one cross-sectional sample and one longitudinal sample) and controlling for biological mother's ADHD symptoms, Harold and colleagues found evidence for early child disrupted behavior influencing later parental depression and hostility, which in turn contributed to later child ADHD symptoms (Harold et al., 2013).

A recent meta-analysis and systematic review by Cheung et al. (2018) reported a moderate positive relationship between maternal depression symptoms and ADHD symptoms in child-mother dyads (Cheung et al., 2018). However, as the review mainly included cross-sectional studies (i.e., examining the co-occurrence of maternal depression in children with ADHD), it could not conclude whether maternal depression was a causal mechanism in the development of ADHD. The current review aims to expand on this review by assessing the longitudinal relationship between maternal depression and ADHD. Longitudinal designs which attempt to control for likely confounding variables are pivotal in understanding the association between maternal depression and offspring ADHD over time.

The aims of the current review were threefold: (i) To assess the relationship between maternal depression and ADHD, and whether the presence of early life maternal depression is significantly associated with later diagnosis of ADHD or symptoms of ADHD; (ii) To assess whether there are differential effects for prenatal and postnatal depression; and (iii) To consider potential confounding variables which may impact upon any reported relationship between maternal depression and ADHD.

Methods

The systematic review was conducted in reference to the guidance set out in the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines (Moher et al., 2009). A registered protocol of the review was not published, prior to the commencement of the review.

Search Procedures

The search procedure covered articles published from 1809 through to December 2019 through systematic searching of three electronic databases: Medline; PsychInfo; and Web of Science. Search terms were utilised in a database-specific manner utilising key terms which related to the three core concepts (maternal depression, ADHD, childhood). The search utilised maternal depression terms (prenatal OR pre-natal OR maternal or mother* OR post-partum OR postpartum OR post-natal OR postnatal AND depression OR depressive* OR postpartum dep*). These search terms were combined with the child specific terms (offspring OR child* OR bab* OR infant* OR adolescen* OR teen* OR young people OR young person*) and terms related to ADHD (adhd or attention deficit* or attention-deficit*). Search terms related to older children e.g. adolescen*, were included in order to

include papers which followed up children into adolescence from an early age. Key terms were exploded to include related terms. Upon completion of the systematic literature search, the reference sections of each included study were reviewed to identify any additional publications which met the inclusion/exclusion criteria. A single reviewer was utilised to conduct the search process and select the papers based on a pre-defined criteria.

Inclusion/Exclusion Criteria

All studies assessing maternal depression and childhood ADHD or Attention Deficit Disorder (ADD) were considered for inclusion. Only studies written in English and published in peer-reviewed journals were included in the review process. Study designs were defined as longitudinal if they had a follow up period of six months or more. Both prospective and retrospective designs were suitable for inclusion in the review. Studies which did not include a validated measure of maternal depression or childhood ADHD were excluded from the review. Many studies included a measure of "externalising" constructs, such as those contained within the Childhood Behavior Checklist (CBCL) (Achenbach & Rescorla, 2000). These studies were only included if they reported ADHD-related subscales (e.g. "hyperactivity"). Study designs were required to report the association between maternal depression and childhood ADHD, or ADHD symptomatology. Only children between 0 -10 years of age at the first follow up time point were included.

Maternal depression was defined as any period of depression experienced by mothers during the first ten years of a child's life, assessed by validated depression measures including structured clinical assessment tools and validated questionnaire measures. ADHD was similarly defined when it was assessed by validated questionnaires and/or structured clinical assessment tools. Studies which identified cohorts solely based upon ICD or DSM codes within medical records were excluded, as they did not fulfil this criterion. In line with the focus of the review upon early childhood, studies were only included in the current review if participants' first follow up time point was ≤10 years of age.

The PRISMA flow diagram below in Figure 1 details the review process.

(INSERT FIGURE 1)

(INSERT TABLE 1)

Overview of Studies

There were 1,223 studies that were identified during the systematic review, following the searches and deduplication of articles. Out of these studies, 112 were screened and 98 articles excluded due to not meeting the inclusion criteria of the review. Fourteen studies were therefore selected for inclusion in the systematic review. Primary reasons for exclusion included: no measure of maternal depression or ADHD; utilising externalising measures only; no validated measures utilised (e.g. studies reliant on ICD or DSM coding in clinical records); design that was not longitudinal; and no reported analysis of the relationship between maternal depression and ADHD. Study characteristics are reported in Table 2, with study results reported in Table 3. A meta-analysis was not conducted as the included studies were too heterogeneous in terms of the population studied (in terms of the age range of the children), how and when maternal depression was defined and measured, the specific covariates considered, and the statistical analysis approach. Due to this heterogeneity, a narrative synthesis approach was taken that aimed to consider possible reasons for differential findings across the studies.

(INSERT TABLE 2 AND TABLE 3)

Results

Study characteristics of the selected papers are reported in Table 2. The study publication dates were between 2006 – 2019. All included studies utilised prospective designs. Fifty percent of the studies were published within the past five years, further strengthening the case for this review in light of the Cheung et al. (2018) review undertaken relatively recently which did not include several of these studies. All fourteen papers came from high-income countries as defined by the World Bank (World Bank, 2020). The papers originated from eight different countries: Canada; United Kingdom; Netherlands; United States of America; Israel; Lithuania; Greece; and Finland. The studies examined eleven different cohorts; three studies utilised the UK based Avon Longitudinal Study of Parents and Children (ALSPAC) Cohort, two utilised the Generation R Cohort from the Netherlands, and two utilised the Canadian Quebec Longitudinal Study of Child Development cohort.

Quality Assessment

Studies were assessed utilising the Critical Appraisal Skills Programme (CASP) guidelines for assessing the quality of Cohort Studies (CASP, 2018). This framework does not provide a specified scoring criteria or system. Therefore, a unique scoring system was devised based on the CASP criteria and is reported in Table 1 (maximum score = 24). Studies were graded into high (19 - 24), medium (13 - 18) and low (\leq 12) quality categories. Quality rating reliability was assured by a postgraduate researcher as an independent reviewer. A random sample of papers (25%) were selected for review by the independent reviewer, who was blinded to the original quality assessment ratings. Ratings were then compared to the category assessments of the first author: high, medium or low quality. Agreement on category definition was very high (100%), the mean discrepancy in numerical scores was 1 (SD =1).

The main methodological problems relating to lower ratings were: insufficient blinding to exposure for outcome measures, due to the majority of studies utilising parental rated measures of ADHD; limited identification of confounds, particularly paternal psychopathology and maternal ADHD symptoms; significant follow up drop out; and bias within samples towards those of higher SES, income or educational backgrounds. An overview of the quality assessment process is displayed in Table 1.

Design

All studies were prospective longitudinal designs in accordance with the inclusion criteria. The majority of studies (N = 11) utilised maternal depression as a primary exposure measure, though for three studies (Apter-Levy et al., 2013; Breaux & Harvey, 2019; Choenni et al., 2019) maternal depression was not the primary focus of the study. Thirteen studies focused exclusively on early childhood (<10 years of age), whilst one study, included due to measurement of ADHD at earlier time points, followed up children until 17 years of age (Vergunst et al., 2019). The earliest initial follow up assessment of ADHD, or ADHD symptoms such as hyperactivity, was 17 months (Galera et al., 2011; Jusiene et al., 2015).

Participants

Sample size (in terms of number of mother-child dyads) ranged from 156 (Apter-Levy et al., 2013) to 5,722 (Van Batenburg-Eddes et al., 2013). A significant number of studies did not report ethnicity data. For those that did, White European/American was consistently the most frequent demographic recruited. Samples skewed towards parents with higher levels of reported educational attainment. Six studies reported mean maternal age. These ranged from 25.9 (Vergunst et al., 2019) to 38.6 years (Apter-Levy et al., 2013) . For large scale cohort studies (ALSPAC, Generation R and Quebec Longitudinal Study of Child Development), samples were representative of the local population.

Measures

The majority of studies (N = 13) utilised self-report questionnaires for assessing maternal depression, with the exception of one study which utilised the Structured Clinical Interview for DSM-III (Ashman et al., 2008). Five studies measured maternal depression across both prenatal and postnatal time points (Koutra et al., 2017; Leis et al., 2014; Park et al., 2018; Van Batenburg-Eddes et al., 2013; Wolford et al., 2017). Prenatal depression was measured across gestation points ranging from 12 weeks (Jusiene et al., 2015) to 32 weeks (Koutra et al., 2017; Leis et al., 2014). Maternal depression after birth was assessed at a significant range of time points, from 6 weeks post birth (Park

et al., 2018) to 11 years (Leis et al., 2014). Five studies assessed maternal depression at a single time point (Barker et al., 2012; Choenni et al., 2019; Galera et al., 2011; Romano et al., 2006; Vergunst et al., 2019). Three studies assessed prenatal depression at multiple time points (Leis et al., 2014; Park et al., 2018; Wolford et al., 2017), with a further seven studies assessing depression in the postnatal period across multiple time points (Apter-Levy et al., 2013; Ashman et al., 2008; Breaux & Harvey, 2019; Jusiene et al., 2015; Leis et al., 2014; Park et al., 2018; Wolford et al., 2017).

All studies utilised some element of parental assessment of child ADHD. Three studies also incorporated teacher rated measures (Ashman et al., 2008; Leis et al., 2014; Vergunst et al., 2019). One study utilised self-report measures when the children were aged 10 (Vergunst et al., 2019). There was a significant range in the age at which ADHD or ADHD symptomatology was assessed; from 17 months of age (Galera et al., 2011) to 17 years of age (Vergunst et al., 2019).

Main findings and Synthesis

Association between Maternal Depression at Different Timepoints and Later Child ADHD

The majority of studies (N = 13) reported a significant positive temporal association between maternal depression and child ADHD assessed via prospective longitudinal designs. Only one study (Park et al., 2018) did not detail such an association. The relationship between maternal depression and later offspring ADHD remained in the three studies that used non-maternal informants for ADHD symptoms (Ashman et al., 2008; Leis et al., 2014; Vergunst et al., 2019).

The timing of when maternal depression occurs is important in understanding any longitudinal relationships it has with ADHD. For example, relationships between post-birth maternal depression and ADHD might be partly due to the impact of having a child with ADHD-related temperament problems on maternal depression, whereas any relationship between prenatal depression and later ADHD is less likely to be due to confounding factors, such as child temperament. Five studies examined maternal depression across the pre and postnatal periods (Koutra et al., 2017; Leis et al., 2014; Park et al., 2018; Van Batenburg-Eddes et al., 2013; Wolford et al., 2017). No studies examined solely prenatal depression. Three of these studies reported evidence of unique associations

between both prenatal and postnatal depression and later ADHD symptoms (Koutra et al., 2017); Leis et al., 2014; Wolford et al., 2017). The age of the children in these studies at follow up ranged from 3 to 11 years.

Van Batenburg-Eddes et al., (2013), who utilised both the Generation R and ALSPAC cohorts; with a combined sample size of 5,722 mother-child dyads (CASP Rating = 22, "High Quality"), assessed the link between prenatal depression and attention/hyperactivity symptoms, encompassing postnatal depression as a key covariate. In both cohorts, a temporal relationship between prenatal depression and later attention problems was found, however this relationship only remained in the ALSPAC cohort following controlling for covariates. It is possible that the differences across cohorts are attributable to which specific covariates were accounted for, the specific measures of ADHD symptomatology used, or the specific timepoints when maternal depression and ADHD were measured.

In the final study to assess depression during pre and post-natal timepoints, Park et al., (2018), reported that children of mothers who reported decreasing depressive symptoms over time, had lower ADHD symptom scores, compared to children of mothers who had consistently low depressive symptoms. ADHD symptoms also did not differ between increasing and low trajectory groups. This paradoxical result should however be interpreted with caution due to the small sample sizes described in the increasing and decreasing trajectory groups (N = 27 and N = 15 respectively), meaning that their analyses were likely to be underpowered.

The remainder of the studies examined in this review assessed maternal depression solely after birth, and did not report any prenatal measures. Five of these studies utilised trajectory modelling designs to assess the impact of maternal depression over time (Ashman et al., 2008; Galera et al., 2011; Jusiene et al., 2015; Romano et al., 2006; Vergunst et al., 2019). A further four studies examined maternal depression following birth and ADHD using alternative longitudinal designs (Apter-Levy et al., 2013; Barker et al., 2012; Breaux & Harvey, 2019; Choenni et al., 2019). Overall, five studies controlled for child temperament, or child ADHD symptoms at an earlier time point (Barker et al., 2012; Galera et al., 2011; Jusiene et al., 2015; Romano et al., 2006; Vergunst et al., 2019). All of these studies reported a significant relationship over time between maternal depression

and offspring ADHD, hence providing evidence that associations between maternal depression and later ADHD are not simply as a result of the child's challenging behavior causing increases in maternal depression.

Covariates

Parental ADHD

Parental ADHD is a potential confounding variable in any purported relationship between parental depression and child ADHD, both in terms of its co-occurrence with depression and the potential impact on parenting (and therefore child's externalizing problems), and as a potential marker of genetic risk. Parental ADHD was measured in only two out of fourteen studies in the current review (Breaux & Harvey., 2019; Wolford et al., 2017). Breaux & Harvey., (2019), reported that when parental ADHD was accounted for within depression models, the effect of maternal depression on child ADHD was no longer significant. Wolford et al., (2017), in contrast reported a significant effect, controlling for the presence of maternal ADHD symptoms. There were several differences in the study design which may account for these differences including, the period of maternal depression focused on in the study, how maternal symptoms of ADHD were operationalised within the design, and the incorporation of paternal ADHD symptoms in the Breaux and Harvey study.

Maternal and Paternal Psychopathology

Understanding parental psychopathology in this context is pivotal to understanding the relationship between maternal depression and ADHD, as it allows for the controlling of shared genetic risk factors. Three studies included broader measures of maternal psychopathology, other than ADHD or depression (Galera et al., 2011; Van Batenburg-Eddes et al., 2013; Vergunst et al., 2019). Van Batenburg-Eddes et al. (2013) reported measures of maternal and paternal anxiety and depression. Models were adjusted for paternal depression or anxiety during pregnancy, and later depression and anxiety in both the Generation R and ALSPAC cohorts. Only in the ALSPAC cohort did a significant association between maternal depression and later ADHD remain. Despite this finding, there were no significant differences between maternal and paternal depression and anxiety on child ADHD, offering little support to hypothesized intrauterine mechanisms.

Galera et al. (2011) and Vergunst et al. (2019), both utilising the Quebec Longitudinal Study of Child Development cohort, reported significant associations between maternal depression and high symptom trajectories for hyperactivity-impulsivity and inattention, controlling for parental self-reported conduct disorder or antisocial personality disorder in childhood. Parental antisocial behavior in adolescents was found to be a significantly related to high trajectories in Galera et al. (2011), but not Vergunst et al. (2019), who examined trajectories over a longer time period. The difference between the results in these two studies implies that the effect of parental antisocial behavior on ADHD symptoms may diminish over time.

A further study recorded paternal depression and anxiety but did not include these factors as a covariate when examining the relationship between maternal depression and child psychopathology (Apter-Levy et al., 2013).

Parenting

Seven studies examined parenting, either as a main outcome variable or a covariate (Ashman et al., 2008; Breaux & Harvey., 2019; Choenni et al., 2019; Galera et al., 2011; Jusiene et al., 2015; Romano et al., 2006; Vergunst et al., 2019). Ashman et al. (2008) incorporated parenting stress as a measure within the contextual risk index. This index significantly mediated the effect of maternal depression on externalising-ADHD. However, there was no evidence from the other six studies that parenting factors mediated the relationship between maternal depression and offspring ADHD. Specifically, Galera et al., (2011) and Vergunst et al., (2019), examined coercive parenting, overprotection, self-efficacy, hostile-reactive parenting, and parental impact. The relationship between maternal postnatal depression and trajectories of high levels of hyperactivity-impulsivity and inattention remained after controlling for these variables. Romano et al., (2006), examined parenting practices, focusing on positive interaction and parental hostility. Hostile parenting independently increased the risk of high persistent hyperactivity significantly, but did not impact on the relationship between postnatal depression and persistent hyperactivity. Jusiene et al., (2015), examined maternal self-efficacy, maternal attitudes towards an infant, and maternal responses to negative emotions. High self-reported maternal self-efficacy was associated with high levels of attention and behavior regulation, but the relationship between maternal depression and their child's attention and behavior

regulation problems remained after controlling for these parenting variables. Choenni et al., (2019), utilised parenting as a main outcome measure, but did not report any significant correlations between maternal depression and positive or negative discipline, or maternal sensitivity. Maternal sensitivity, but not maternal negative and positive discipline, was reported to be associated with later ADHD symptoms, controlling for concurrent attention, executive function and ODD symptoms. Lastly, Breaux & Harvey., (2019), incorporated both self-reported and observational parenting measures assessing; parental warmth, parental laxness; and parental overreactivity. Overreactive parenting was associated with later child ADHD symptoms, which remained significant after controlling for parent ADHD symptoms. Both Choenni et al., (2019) and Breaux & Harvey., (2019) did not report an analysis of whether parenting factors impacted upon the significant relationship between maternal depression and offspring ADHD.

Discussion

This is the first systematic review to consider longitudinal studies specifically in the area of maternal depression and later ADHD. The review sought to synthesise the literature examining the relationship between maternal depression and later offspring ADHD, to assess whether there are differential effects for prenatal and postnatal depression, and to consider the factors which may impact upon any reported relationships. Largely these aims were achieved by the present review.

The findings in relation to these aims will now be summarised in turn. For the first aim, the majority of studies (N=13) reported a significant association of maternal depression (prenatal and/or postnatal) with offspring ADHD utilising longitudinal designs, and in 11 of these studies, these effects remained when controlling for relevant confounding variables. Study quality was generally of medium to high quality based on the CASP criteria (CASP, 2018). Where a significant effect of maternal depression was not found (N=1), there was no evidence to suggest that the study was of a higher quality than those studies which did find effects (the lack of findings could potentially be explained by a lack of power to detect significant effects). Hence, this systematic review is a first and important synthesis of the literature which offers some evidence of a potentially causal effect of

maternal depression on child ADHD, although it is acknowledged that in spite of the longitudinal designs included, causal inferences are still tentative given that the studies were not experimental (Tryon, 2018).

There was considerable diversity in the type of study covered in the review, with several studies involving trajectory modelling designs (Ashman et al., 2008; Galera et al., 2011; Jusiene et al., 2015; Romano et al., 2006; Vergunst et al., 2019), and several others utilising large cohort models (Barker et al., 2012; Leis et al., 2014; Van Batenburg-Eddes et al., 2013). This variety of designs enabled the review to consider the relationship between maternal depression and the development of ADHD symptoms in offspring over time, as well as utilising high powered designs, which were representative of local populations. A notable strength of the papers reviewed studying depression occurring post-birth, was the consideration of child temperament or early life ADHD symptoms as a covariate. This considerable confound did not appear to alter the relationship between maternal depression and ADHD, indicating that the relationship between maternal depression and later ADHD is not simply as a result of the child's challenging behavior causing increases in maternal depression. Hence, this review builds on the recent meta-analysis and systematic review by Cheung et al. (2018), which reported cross-sectional co-occurrence rates of depression in children with ADHD.

The present review provided evidence for the association of maternal depression across both the prenatal and postnatal periods with ADHD. Regarding the second aim, the review did not find conclusive evidence to suggest that either prenatal or postnatal depression is a stronger predictor of later ADHD. Few studies controlled for both prenatal and postnatal depression. Some studies found that both prenatal depression, and depression occurring post-birth were independent predictors of later ADHD (Koutra et al., 2017; Wolford et al., 2017). Another study reported a relationship for prenatal depression controlling for postnatal depression, but did not report whether postnatal depression was an independent predictor, controlling for depression occurring in the prenatal period (Leis et al., 2014). The largest study assessed by the review by Van Batenburg-Eddes et al., (2013), found that in the Generation R but not ALSPAC cohort, the effect of prenatal depression was significantly mediated by postnatal symptoms of depression and anxiety, but did not report if postnatal depression was an independent predictor separately. It is important to note that whilst some of the potential

causal mechanisms behind maternal depression and ADHD associations may be equally shared across prenatal depression and postnatal depression (e.g. shared genetic risk of depression or psychopathology), other mechanisms may be unique to each period of depression. Evidence from the prenatal stress literature suggests that prenatal stress can have significant effects upon a wide variety of areas including changes in neural pathways between the amygdala and prefrontal cortex, and altered hypothalamo-pituitary-adrenal (HPA) axis functioning (Van den Bergh et al., 2017). Pathways in postnatal depression in contrast may be derived through other factors, such as increased exposure to contextual risk factors (Ashman et al., 2008). The complexity of these shared and independent factors in the potential pathways between prenatal and postnatal depression and later child psychopathology, may explain the somewhat mixed findings regarding the timing of maternal depression in contributing to the development of ADHD.

In relation to the third aim of the review, a number of factors other than child temperament were considered as potential covariates that might explain the temporal relationship between maternal depression and later offspring ADHD. Of note, the review found few studies that measured parental ADHD, Parental psychopathology other than ADHD or depression was reported in several studies. Notably parental history of conduct disorder or antisocial personality disorder in childhood did not account for the relationship between maternal depression and high symptom trajectories for hyperactivity-impulsivity and inattention in two studies (Galera et al., 2011; Vergunst et al., 2019). Parenting factors were a further frequent covariate, but in only one study was there evidence that they accounted for the relationship between maternal depression and ADHD (Ashman et al., 2008).

Gaps in the Evidence Base Uncovered by this Review

There were several areas of methodology for which several significant limitations were apparent, which weigh against this review offering full support of maternal depression as a causal factor in the development of ADHD. Firstly, the majority of the studies were based solely on informant measures. Only three studies out of fourteen utilised teacher reports to measure ADHD symptoms, and only one design included self-report, raising the risk of bias. Despite the common limitation of many studies relying solely on mothers as informants, in the three studies that utilised

other informants, a significant effect between maternal depression and later ADHD was found in two out of three of these studies (Leis et al., 2014; Vergunst et al., 2019), indicating that this limitation does not significantly detract from the conclusions of this review. Some literature has proposed that mothers with depression may be more prone to appraising their children's behavior more negatively, compared to mothers who are not depressed. The Depression Distortion Hypothesis, proposed by Richters & Pellegrini, (1989), predicts that parental depression related to cognitive distortions may alter appraisals of child behavior. Madsen et al., (2020), reported that not only was the association between maternal depression and ADHD stronger when reported by mothers rather than teachers, the Strength and Difficulties Questionnaire (SDQ) was almost twice as likely to predict future ADHD difficulties, in the children of mothers who experienced depression. Mechanistic studies have also reported a relationship between maternal psychopathology and higher ratings of inattention. Haack et al., (2017), found that this relationship is mediated in part by higher levels of cognitive errors, in parents with depression and ADHD symptoms, resulting in higher ratings of child ADHD by parents.

Secondly, within the studies identified during the review, there was a notable paucity of studies which controlled for maternal, or paternal ADHD symptoms. This limitation is significant as the absence of this factor as a covariate limits the inferences which may be made, as there is substantial potential for reported associations to be confounded by residual shared genetic risk of ADHD between mothers and children, with ADHD heritability estimated to be as high as 74% (Faraone & Larsson, 2019). Furthermore, there is evidence that adults with ADHD experience a high level of comorbidity with depression, with 35 -50% of adults with ADHD experiencing at least one episode of depression during their lifetime (Sobanski, 2006). In the studies reviewed, there was also a lack of assessment of other facets of parental psychopathology, which may also account for externalising disorders, such as history of conduct disorder or current antisocial personality disorder, both of which are highly comorbid with ADHD and therefore also possibly share genetic risk (McGough et al., 2005; Storebø & Simonsen, 2016).

Moreover there is increasing recognition of a single generalised psychopathology construct or "p factor" (Caspi et al., 2014), underlying all forms of psychopathology, which is also observed in child and adolescent samples (Allegrini et al., 2020), as well as genomic and neural components

which are found across psychiatric disorders (Sprooten et al., 2021). Therefore, controlling solely for parental externalising disorders is likely to underestimate shared genetic factors. Gene-environment correlations in parent-child designs, also confound the association between maternal depression and ADHD; due to the influence of parental genetics factors on the home environment.

The lack of regular inclusion of these covariates in the studies reviewed, means that we are unable to draw strong conclusions from the literature about whether maternal depression is an "environmental" causal predictor or ADHD, or whether the significant observed relationships between maternal depression and ADHD are due to unmeasured genetic risk.

Thirdly, samples within the current review were all drawn from high income countries as defined by the World Bank (World Bank, 2020), and were all based within Europe or North America, with the exception of one study from Israel (Apter-Levy et al., 2013). Similarly, within these samples, cohorts tended to be drawn from populations of higher SES, educational background and married or co-habiting couples. There are therefore limitations as to the generalisability of the studies due to both country and demographic factors.

Fourthly, whilst the majority of studies reported a longitudinal association between maternal depression and offspring ADHD, the mechanisms behind this association were not clearly delineated. The most commonly discussed mechanism of risk was the transmission of risk for ADHD through intrauterine mechanisms. Several potential mechanisms were not comprehensively covered. Notably parenting practice was not significantly considered within the literature which is likely to significantly interact with maternal depression in the development of a child's externalising behavior difficulties, including ADHD (Reising et al., 2013). Moreover, no studies in the current review controlled for attachment, or considered attachment as a mediator, despite evidence of an association between attachment styles and externalising behavior within the existing literature (Storebø et al., 2013). Similarly recent literature has highlighted ACEs as a significant factor, where a dose-response relationship has been reported between child ACEs and ADHD symptoms (Jimenez et al., 2017). Whilst maternal depression would be encompassed within the definition of an ACE, it is possible that maternal depression may confer greater risk of exposure to other ACEs and in turn increase the risk of offspring ADHD.

Implications for Clinical Practice

Although not fully conclusive due to the gaps in the evidence base discussed, this review certainly raises the possibility that intervening to treat maternal depression across both pre and postnatal periods, could be a relevant factor in preventing the development of ADHD in offspring. As outlined in the introduction, ADHD has considerable costs to both individuals and society. This review therefore offers support to the importance of funding perinatal mental health support services, which are often very under-resourced even in developed nations (Bauer et al., 2014.). Therefore, there is a significant argument to be made that early interventions in maternal depression are important from both a health economic and public health standpoint, with significant evidence for interventions which can effectively treat depression present within the existing literature (Cuijpers et al., 2020). Existing reviews and meta-analyses provide evidence that interventions for parental depression is associated with improved parenting and/or child mental health (Cuijpers et al., 2015, Goodman et al., 2018, Letourneau et al., 2017). Furthermore, the review would also support the integration of parental mental health interventions into neurodevelopmental services, of which there is increasing evidence of efficacy (Chronis-Tuscano et al., 2013; Parand et al., 2010; Sharif et al., 2015).

Future Research Directions

Future research should build upon several of the limitations of the current literature identified by the current review. As highlighted by Madsen et al., (2020), measurement of child ADHD should draw on measures taken from multiple informants, to minimise potential bias from maternal reporting in this context, which may be influenced by maternal depression (Haack et al., 2017). The review also highlights that future research into the link between maternal depression and ADHD should consider maternal ADHD symptoms as a potential confounding variable. Similarly, as highlighted previously, few studies included measures of paternal psychopathology. Adding these covariates, would significantly improve the generalisability of findings. This research would be strengthened further by the use of behavioural genetics studies e.g. twin, adoption and children of twin designs, which would allow for more adequate control over shared gene-environment factors, than parent-child

designs alone (McAdams et al., 2014). Generalisability of findings would be enhanced by the use of non-western samples, in conjunction with cohorts which are more socioeconomically representative.

Strengths and Limitations of the Present Review

The present review has a number of strengths and limitations. A notable strength of the paper was the focus on longitudinal designs which considered important confounding factors such as early life temperament or early ADHD symptoms. The criteria of the review to include only studies which utilise validated measures of ADHD and depression, further strengthens the validity of the study, ensuring that there are accurate measures, and reducing the risk of bias from studies based upon unvalidated tools or unstructured clinical judgements. The review can also be considered to be systematic and replicable.

There are nevertheless several limitations of the review. Due to the heterogeneity of studies reviewed, a meta-analysis was not possible. Whilst the current review focused upon papers utilising validated measures to assess maternal depression or ADHD, this criterion meant that several large scale population based studies using clinical coding designs were ruled out. Secondly, the review focused narrowly upon maternal depression and did not consider studies which examined solely the relationship between paternal depression and ADHD, limiting the scope of implications of the review.

A large proportion of the literature also focused solely upon wider concepts than ADHD, namely the concept of externalising disorders, which ADHD is encompassed within, and are highly correlated with ADHD. This meant that a portion of the literature in this area was omitted. Relatedly, depression is highly correlated with other forms of psychopathology, most notably anxiety disorders (Mansell & McEvoy, 2017) but this was not considered in the present review. It is not clear from the review how other forms of maternal psychopathology relate to offspring ADHD.

Conclusion

This review provides important initial evidence suggesting an association between maternal depression and later ADHD assessed across both prenatal and postnatal periods, which remained when controlling for symptoms of earlier ADHD and child temperament. This review advances the

literature in terms of informing about the temporality of the association between maternal depression and children's ADHD. There were however several factors which restrict the generalisability of results, most notably the predominance of reliance upon potentially biased maternal reports of ADHD symptoms, and limited consideration in the literature of potential genetic confounding factors. The study however provides sufficient justification for health care commissioners to consider the potential benefit of effective mental health care treatment for mothers, with downstream effects upon child mental health.

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Figure 1.

PRISMA Flow Diagram

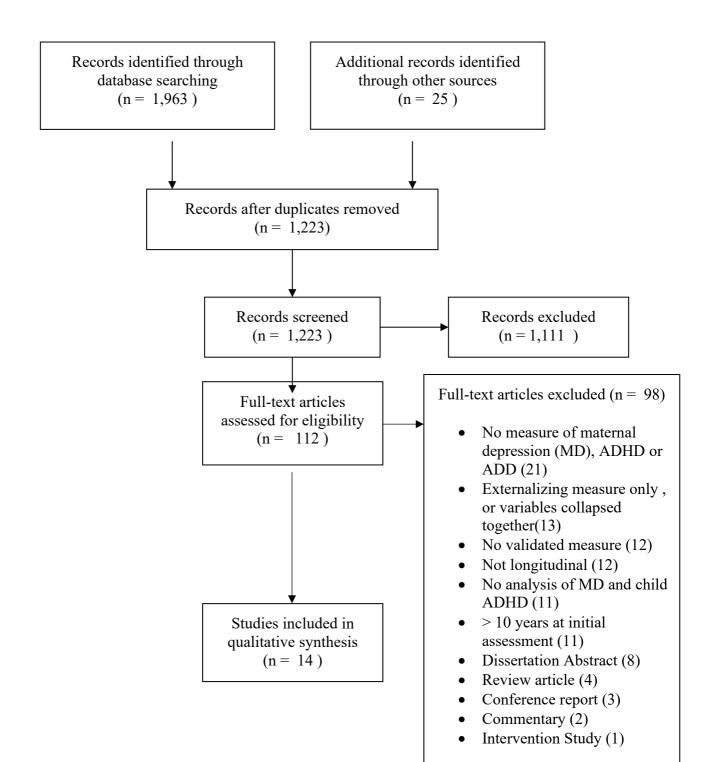


Table 1. *Quality Assessment of studies utilising the CASP framework*

	Apter- Levy et al. (2013)	Ashman et al. (2008)	Barker et al. (2012)	Breaux et al. (2019)	Choenni et al. (2019)	Galera et al. (2011)	Jusiene et al. (2015)	Koutra et al. (2017)	Leis et al. (2014)	Park et al. (2018)	Romano et al. (2018)	Van Batenburg- Eddes et al. (2013)	Vergunst et al. (2019)	Wolford et al. (2017)
1. Does the study address a clearly focused issue?	1	2	2	2	2	2	2	2	2	2	2	2	2	2
2. Was the cohort recruited in an acceptable way?	0	1	2	1	2	2	1	2	2	1	2	2	2	2
3. Was the exposure accurately measured to minimise bias?	2	2	2	2	2	2	2	2	2	2	2	2	1	2
4. Was the outcome accurately measured to minimise bias?	2	1	1	1	1	1	1	1	2	1	1	1	1	1
5. Have the authors identified all important confounding factors?	0	1	1	1	1	1	1	1	1	1	1	2	2	1

	Apter- Levy et al. (2013)	Ashman et al. (2008)	Barker et al. (2012)	Breaux et al. (2019)	Choenni et al. (2019)	Galera et al. (2011)	Jusiene et al. (2015)	Koutra et al. (2017)	Leis et al. (2014)	Park et al. (2018)	Romano et al. (2018)	Van Batenburg- Eddes et al. (2013)	Vergunst et al. (2019)	Wolford et al. (2017)
6. Was the follow up of subjects complete enough?	1	1	1	1	1	2	1	2	1	2	1	1	2	1
7. What are the results of the study?	1	1	2	1	1	2	2	2	2	1	2	2	2	2
9. Do you believe the results?	0	1	2	1	1	2	2	2	2	1	2	2	2	2
10. Can the results be applied to the local population?	1	1	2	2	1	2	1	1	2	0	2	2	2	2
11. Do the result of the study fit with other available evidence?	1	2	2	2	1	2	2	2	1	1	2	2	2	2
12. What are the implications of the study for practice?	1	1	2	2	1	2	1	1	2	1	2	2	2	2
Total score (maximum = 24)	11	15	21	17	15	22	18	20	21	15	21	22	22	21
Quality rating	Low	Medium	High	Medium	Medium	High	Medium	High	High	Medium	High	High	High	High

Table 2. Study Characteristics (N = 14)

Study	Location & Study Name	Participants and Study (e.g. ALSPAC)	Mean Maternal Age in Years (SD)	Measures (Maternal Depression and Child ADD/ADHD)	Informants on child outcome	CASP Quality Rating
Apter- Levy et al. (2013)	Israel (study name not specified).	156 mother-child dyads	38.66 (4.40)	Depression: Beck Depression Inventory (BDI) administered at childbirth, 6 months, 9 months and 6 years. ADHD: Development and Well-Being Assessment (DAWBA) at 6 year follow up.	Parents	11
				ADHD: Development and Well-Being Assessment (DAWBA) at 6 year follow up.		
Ashman et al. (2008)	USA, Adjustment to Parenthood Study.	159 mother-child dyads	31.1 (4.54)	Depression: Structured Clinical Interview for DSM-III (SCID); Center for Epidemiological Studies Depression Questionnaire; and a modified version of the Longitudinal Interval Follow Up Questionnaire. Measures were administered when their children were 14 months, 24 months, 3.5 years, 4.5 years, and 6.5 years of age.	Parents and teachers	15
				ADHD: Diagnostic Interview Schedule for Children IV - Parent version; Child Behavior Checklist (CBCL) and the Child Adaptive Behavior Inventory (CABI). Teachers completed the Achenbach Teacher Report Form, CABI, ADHD rating Scale and the Child Behavior Scale peer subscales at age 6.5.		
Barker et al. (2012)	UK, ALSPAC.	7429 mother-child dyads.	Not reported	Depression: Edinburgh Postnatal Depression Scale (EDPS) at 21 months. ADHD: DAWBA assessment at 7-8 years of age.	Parents	21
Breaux et al. (2019)	USA, (study name not specified).	258, mother-child dyads.	Not reported	Depression: The Millon Clinical Multiaxial Inventory–III at each time annually (4 time points from the child age of 3 - 6)	Parents	17
	specifica).			ADHD: National Institute of Mental Health Diagnostic Interview Schedule for Children–Fourth Edition at age, 3, 4, 5 and 6.		

Study	Location & Study Name	Participants and Study (e.g. ALSPAC)	Mean Maternal Age in Years (SD)	Measures (Maternal Depression and Child ADD/ADHD)	Informants on child outcome	CASP Quality Rating
Choenni et al. (2019)	Netherlands, Generation R.	584 mother-child dyads	31.9 (SD = 3.7)	Depression: Brief Symptom Inventory at age 3. ADHD: Conners Parent Rating Scale-Revised: Short Form (CPRS- R:S) administered at age 8.	Parents	15
Galera et al. (2011)	Canada, Quebec Longitudinal Study of Child Development.	2120 mother-child dyads (2057 used to model hyperactivity- impulsivity and inattention trajectories)	Not reported	 Depression: Center for Epidemiological Studies Depression Scales (CES-D) (abbreviated version) at 5 months. ADHD: Interviewer computerised questionnaire (comprising questions from the CBCL, Ontario Child Health Study Scales and Preschool Behavior Questionnaire) completed when children were 1.5, 2.5, 3.5, 4.5, 5, 6 and 8 years of age. 	Parents	22
Jusiene et al. (2015)	Lithuania (study name not specified).	281 mother-child dyads	Not reported	Depression: EDPS scale at 3 and 6 months, and 3 years after childbirth. ADHD: CBCL - at age 18 months, 2 years and 4 years.	Parents	18
Koutra et al. (2017)	Greece, Rhea study.	642 mother-child dyads.	Not reported	Depression: EDPS at 28-32 weeks of gestation and postnatally at 8 weeks postpartum. ADHD: Attention Deficit Hyperactivity Disorder Test and the Strength and Difficulties Questionnaire (SDQ) at 4 years of age.	Parents	20
Leis et al. (2014)	UK, ALSPAC.	2,891 mother-child dyads	Not reported	Depression: EPSD at 18 and 32 week gestation, 8 weeks, and 8 months postpartum and childhood (21, 33, 61 and 73 months, and 11 years of age.) ADHD: SDQ - collected at child age 10 by teacher and age 11 by mother report.	Teacher and Parent (Parent report at 11 years of age)	21

Study	Location & Study Name	Participants and Study (e.g. ALSPAC)	Mean Maternal Age in Years (SD)	Measures (Maternal Depression and Child ADD/ADHD)	Informants on child outcome	CASP Quality Rating
Park et al. (2018)	Canada (study name not specified).	191 mother-child dyads.	Not reported	Depression: Hamilton Depression Rating Scale (HAMD) and the EDPS during 2nd and 3rd trimesters, 6 weeks, 3 months, 6 months and 10 months. BDI was used at 3 year follow up and the EDPS at 6 year follow up.	Parents	15
				ADHD: The MacArthur Health and Behaviour Questionnaire at age 6.		
Romano et al. (2006)	Canada, The National Longitudinal Survey of	2946 mother-child dyads	Not reported	Depression : CES-D at cycle 1. Child aged (0 - 23 months) ADHD: Hyperactivity symptoms measured by CBCL at cycle 2, 3 and 4. (age 2 - 7)	Parents	21
	Children and Youth (NLSCY).			ADID. Hyperactivity symptoms incastical by CBCL at cycle 2, 3 and 4. (age 2 - 7)		
Van Batenburg-	Netherlands / UK,	Generation R, n = 2,280 and ALSPAC,	Generation R:	Generation R:		
Eddes et al. (2013)	Generation R/ALSPAC	n = 3,442. (mother-child dyads)	31.7(SD= 3.9)	Depression: Brief Symptom Inventory at 20 weeks gestation and repeated when the child was aged 3.		
	IVALSI AC		3.7)	ADHD: CBCL at child age 3, attention subscale.		22
			ALSPAC:	ALSPAC:	Parents	22
			29.3(SD= 4.4)	Depression: EDPS at 18 weeks of pregnancy and at 33 months.		
				ADHD: SDQ at child aged 4 years. Hyperactivity/inattention subscale		

Study	Location & Study Name	Participants and Study (e.g. ALSPAC)	Mean Maternal Age in Years (SD)	Measures (Maternal Depression and Child ADD/ADHD)	Informants on child outcome	CASP Quality Rating
Vergunst et al. (2019)	Canada, Quebec Longitudinal Study of Child Development.	1374 mother-child dyads	25.9 (SD = 4.9)	Depression: CES-D completed at 5 months. ADHD: Combined early childhood behaviour scale including items from the CBCL, Ontario Child Health Study Scales and the Preschool Behaviour Questionnaire. Assessment at age 15 and 17 were made using the Mental Health and Social Adaptation Assessment for Adolescents.	Parents, Teachers and Self- report.	22
Wolford et al. (2017)	Finland, Prediction and Prevention of Pre-eclampsia and Intrauterine Growth Restriction (PREDO)	1,779 mother-child dyads.	31.9 (SD not reported)	Depression: CES-D biweekly up to 14 times during pregnancy. Depressive symptoms were also reported using the BDI at 3 and 6 year follow up. ADHD: Conners Hyperactivity Index at age between 3 to 6 (mean = 3.8)	Parents	21

Table 3. *Study results*

Study	Analysis	Covariates	Results	Limitations
Apter-Levy et al. (2013)	MANCOVA and Chi-square test comparison between chronically depressed and never- depressed mothers and their children	Salivary Oxytocin OXTR Genotype Mother and Child Behaviours Paternal emotional distress Child social outcomes	Significant between-group difference between children of chronically depressed mothers compared to never-depressed mothers and diagnosis of ADHD.	Sample: Limited solely to married/cohabiting parents. Exclusion of common co-morbidities (e.g. anxiety). Sample highly educated (80% - college level) Measures/Design: Parents sole informants. Limited co-variates accounted for. Effects are for two divergent cohorts - limited evidence about depression trajectories. No measures for broader parental psychopathology/ADHD.
Ashman et al. (2008)	Latent growth mixture models with MANOVA analysis	Stressful life events Social support Parenting stress Relationship adjustment ECG Heart rate	Trajectories of decreasing and stable mild depression was related to increased hyperactivity and attention problems in children compared to non-depressed mothers. The effect of maternal depression on externalising-ADHD behaviours was significantly mediated by contextual risk factors. Maternal depression had a significant impact upon child frontal brain activity, but this did not significantly mediate the association between maternal depression and child ADHD.	Sample: Primarily European- American ethnicity. Excluded serious mental health problems, and/or alcohol/substance use difficulties. No measure of paternal mental health or parental ADHD.
Barker et al. (2012)	Logistic regression	Socioeconomic status Living conditions Family risk factors Early parenthood Educational attainment Substance Use Forensic history	There was a significant effect of maternal depression (when child =1.5 years) on child diagnosis of ADHD at age 7.5 without controlling for the cumulative risk index. When the risk index was added and assessed this resulted in a 41% decrease in externalising disorders although ADHD was not analysed separately.	Sample: 95% Caucasian. Measures/Design: Parents sole informants. ADHD not assessed separately when controlling for risk index. Paternal psychopathology not assessed.

Study	Analysis	Covariates	Results	Limitations
Breaux et al. (2019)	Regression analysis	Past ADHD symptoms (child), Co-morbid ODD, parental ADHD. Parental laxness Parental overreactivity Parental Warmth	There was initial evidence for a bidirectional relationship between maternal depression and child ADHD, as assessed by yearly follow up between the ages of 3 -6 year. For paternal depression the effect was unidirectional, with child ADHD predicting increased rates of paternal depression. When parental ADHD symptoms were entered into the depression model neither child ADHD, nor parental depression reported significant effects.	Measures/Design: Parents sole informants. Multiple models utilised but not clearly integrated.
Choenni et al. (2019)	Linear regression analysis	Maternal depression Maternal harsh parenting Child attention Executive function difficulties	Bivariate correlation between maternal depressive symptoms at age 3 and childhood ADHD symptoms at age 8, was statistically significant. This did not control for covariates as maternal depression was not a primary risk factor within the study.	Sample: Highly educated cohort. Ethnicity not reported. Measures/Design: Parents sole informants. No measure of general maternal psychopathology and/or ADHD. Maternal depression only utilised as covariate. Analysis: maternal depression not analysed as unique predictor.
Galera et al. (2011)	Group-based trajectory modelling and logistic regression.	Infant Temperament Methylphenidate exposure Premature Birth Low Birth Weight Alcohol/Substance Use/Smoking during pregnancy Family structure Low maternal education	Maternal depression when child aged 5 months was significantly related with trajectories of high levels of hyperactivity-impulsivity and/or attention, controlling for covariates.	Sample: Ethnicity not reported. Measures/Design: Parents sole informants. Hybrid measure utilised combining items from different instruments to assess ADHD. No measure of parental ADHD.

Study	Analysis	Covariates	Results	Limitations
Galera et al (2011) cont.		Maternal age at birth of child Household income Family dysfunction Parenting Paternal psychopathology		
Jusiene et al. (2015)	Latent class modelling	New-born Health Infant Problem Behaviours Maternal attitudes towards infant care. Maternal self efficacy Maternal responses to children's negative emotions	Maternal postnatal depression was found to be an additional risk factor for stable high attention and behavior regulation problems trajectories vs decreasing attention and behavior regulation problem trajectory, accounting for covariates.	Sample: Highly educated. Majority married. Relatively small sample. Measures: Parents sole informants. CBCL utilised as measure of attention and behavior regulation. No measure of paternal mental health. Maternal ADHD not assessed.
Koutra et al. (2017)	Multivariate analysis	Maternal age at delivery Maternal education Smoking status Working status Child sex Prematurity Breastfeeding duration Pre-school attendance TV watching Birth order Number of children in family Quality of assessment	Maternal prenatal depressive symptoms were related to higher scores in Hyperactivity subscale. Maternal postnatal depressive symptoms were associated with higher scores in almost all subscales of ADHD (except Inattention). High levels of maternal postnatal depression (EPDS≥13) were associated with increased scores in Hyperactivity, Inattention and Impulsivity subscales and the Total ADHD Index, accounting for covariates within the analysis. The effects of postnatal depression on ADHD symptoms were more pronounced in children whose mothers smoked during pregnancy.	Sample: Excluded mothers with history of previous psychiatric disorder. Measures: Parents sole informants. No measures of paternal psychopathology or maternal ADHD.

Study	Analysis	Covariates	Results	Limitations
Leis et al. (2014)	Bivariable linear regression.	Marital status, Maternal age at birth, Child birthweight, Child gender, Maternal educational attainment Cigarette smoking during pregnancy Alcohol use during pregnancy	Prenatal depression was associated with increased total child emotional and behavioural difficulties. Prenatal depression was also significantly associated with teacher and maternal reported hyperactivity controlling for other periods of depression or anxiety and sociodemographic variables. Elevated symptoms of comorbid prenatal depression and prenatal anxiety did not predict greater increases in offspring emotional/behavioural problems, than prenatal depression alone.	Sample - Homogenous ethnicity (98.9% = Caucasian) Measures: Parents sole informants. No measure of paternal psychopathology. No measure of maternal or paternal ADHD.
Park et al. (2018)	Multivariable linear regression analyses	Child sex Age Gestational age at birth Birth weight Prenatal SSRI exposure Maternal history of depression Maternal education Maternal minority status	Maternal depressive symptom trajectories were unrelated to children's internalizing and externalizing symptomatology at age 6. Children whose mothers reported a decreasing trajectory of depressive symptoms over time had lower reported levels of ADHD symptoms, than those whose mothers had consistently few depressive symptoms. ADHD symptomatology did not differ between children of mothers in the increasing and low trajectory groups.	Sample: High risk sample. High rate of drop out. Small sample size. Measures: Parents sole informants. No measure of maternal ADHD or paternal psychopathology.
Romano et al. (2006)	Semiparametric group mixture model to estimate trajectories, followed by logistic regressions.	Maternal age Parenting practices Family dysfunction Child Temperament Smoking and substance use Birth Weight	Postnatal depression, assessed between the ages of 0 -23 months, increased the risk of high and persistent hyperactivity significantly after accounting for sociodemographic and psychological covariates.	Sample: Homogenous ethnicity (88.5% - Caucasian) Measures: Parents sole informants. No measure of maternal ADHD. No paternal psychopathology measures. No measure of other ADHD related constructs - e.g. inattention.

Study	Analysis	Covariates	Results	Limitations
Van Batenburg- Eddes et al. (2013)	Logistic regression	Generation R: Maternal education Parental anxiety Maternal smoking and alcohol use during pregnancy Family Income Child ethnicity Child gender Child birth weight ALSPAC: Parental anxiety Maternal education Family income Ethnicity Maternal smoking and alcohol use during pregnancy Child gender Child birth weight	Prenatal depression was associated with child attention problems at age 3 in both ALSPAC and Generation R Cohorts. Controlling for maternal anxiety and depression after birth, prenatal depression was no longer associated with later child attention problems in the Generation R cohort. ALSPAC reported statistically significant associations for prenatal anxiety and depression when controlling for the same variables. However, there was no significant difference between paternal and maternal symptoms, in their relationship to later child attention problems.	Measures: Parents sole informants. No measure of maternal or paternal ADHD.
Vergunst et al. (2019)	Group-based trajectory modelling.	Methylphenidate use Child IQ Child Temperament Birth weight Parental tobacco, alcohol and drug use during prenatal and postnatal periods SES Family income Parental education Family structure Family dysfunction	Postnatal depression assessed at 5 months, was a significant risk factor which predicted high-symptom trajectories of hyperactivity—impulsivity and inattention, after controlling for covariates.	Measures: Use of a composite measure utilising items from a number of instruments. No measures of parental ADHD.

Study	Analysis	Covariates	Results	Limitations
Vergunst et al. (2019) cont.		Mother-child interaction Parenting Parental Psychopathology		
Wolford et al. (2017)	Latent profile analysis and logistic regression analysis	Maternal history of physician diagnosed depression Maternal ADHD problems Maternal age at delivery Antidepressant use Psychotropic medication use Smoking during pregnancy Parity (primiparous vs. multiparous) Chronic Hypertension Type I Diabetes Gestational length Birthweight Child sex Family structure Maternal alcohol use Maternal education	Prenatal depressive symptoms displayed a significant association with symptoms of ADHD at age 3, controlling for covariates including further symptoms of depression and maternal ADHD. There was an additive effect of postnatal depression to later child symptoms of ADHD.	Sample: Ethnicity not reported. Measures: Parents sole informants. No measure of paternal psychopathology