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## **Prenatal Stress & Socioemotional Outcomes in School-Aged Children: A Meta-Analytic Review**

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Prenatal Stress & Socioemotional Outcomes in School-Aged Children: A Meta-Analytic  
Review

A Dissertation

Presented in Partial Fulfillment of the Requirements for the Degree of

Doctor of Philosophy in Child-Clinical Psychology

Department of Psychology

College of Science and Health

DePaul University

Chicago, IL

By

Michelle A. Gilchrist, M.A.

July 2021

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### Biography

Michelle Anne Gilchrist was born and raised in Rochester, New York. She graduated from Pittsford Sutherland High School in 2003, received her Bachelor of Art's degree in Psychology from the University of Rochester 2007, and her Master of Arts in Clinical-Psychology from DePaul University in 2017. She completed her APA- accredited pre-doctoral clinical psychology internship program at Duke University Medical Center in 2021.

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### Abstract

Prenatal stress has been linked to a myriad of adverse obstetric, infant, and childhood outcomes. Several prospective studies have linked maternal stress and distress during pregnancy with long-term neurocognitive, behavioral, and emotional consequences for the offspring, including decreased cognitive abilities as well as symptoms of Attention Deficit/Hyperactivity Disorder (ADHD), depression, and anxiety. However, limited conclusions on the influence of type of stressors and the magnitude of the effect of prenatal stress on specific developmental trajectories can be drawn due to variation in study design and measured outcomes. This meta-analysis synthesized the state of the current literature and quantified the effects of prenatal stress on internalizing, externalizing, and ADHD symptoms among children ages 5 to 18. The current study also evaluated whether pregnancy specific (e.g., type of stressor), sociodemographic (e.g., child gender), and methodological factors (e.g., reporter of child outcome) moderated the association between prenatal stress and outcomes in school-aged children.

A total of 29 studies met full inclusion criteria for data analysis. A small positive effect was observed between prenatal stress and internalizing ( $r = .15$ ), externalizing ( $r = .13$ ), and ADHD ( $r = .18$ ), symptoms in school aged youth. Moderator analysis indicated effect sizes were stronger in younger women whose children were experiencing internalizing symptoms.

Findings suggest maternal stress during pregnancy is associated with offspring emotional and behavioral developmental outcomes in school aged children and adolescents. Improvement in the operationalization of sociodemographic variables is needed to continue to explore alternative characteristics that could contribute to this association.

## Introduction

Early adverse life experiences and exposure to toxic stress are associated with a variety of negative physical and mental health outcomes. Evidence suggests that the teratogenic effects of stress exposure can begin as early as fetal development (Van den Berg, Mulder, Mennes, & Glover, 2005) and extend well into adulthood (Heim & Binder, 2012; Shonkoff et al., 2012). Several prospective studies have linked maternal depression, anxiety, and stress during pregnancy with a range of adverse neurocognitive, behavioral, and emotional outcomes for offspring throughout development (King & Laplante, 2005; O'Conner et al., 2003; Van den Bergh & Marcoen, 2004). All of which have been associated with increased risk for academic challenges in school-aged children (DeSocio & Hootman, 2004), as well as employment failure (Greenberg, Domitrovich, & Bumbarger, 2001), and mental and physical health problems during adulthood (Smith et al., 2004). In addition, high levels of psychosocial stress are commonly reported throughout pregnancy (Kingston et al., 2012; Stone et al., 2015; Woods et al., 2010), such that understanding the effects of maternal prenatal stress on offspring development can significantly contribute to public health efforts.

It is important to study the long-term impact of prenatal stress in school aged children as it is a critical point in social, cognitive, and behavioral development. Studies assessing the effects of prenatal stress consistently document connections to numerous adverse psychosocial outcomes in school aged children. However, study findings differ regarding the kinds of stress (i.e., trauma, life events, depression, anxiety) that impact child outcomes, the timing that makes these effects most noxious, and the domains of child development that are negatively affected. The limited number of studies focused on school-aged children and methodological differences make study comparison difficult. Given these confounds a meta-analysis is needed to

quantitatively synthesize the results of studies evaluating the effects of prenatal stress on child behavioral and mental health outcomes.

### **Stress during the perinatal period**

Pregnancy and childbirth are a time of great physiological, psychological and social change for women. Studies have consistently shown that a sizeable proportion of women experience significant affective symptoms or stress during the perinatal period (O'Hara & Swain, 1996; Robertson et al., 2004), likely a result of these biological and psychological changes, as well as environmental changes in preparation for childbirth.

Prenatal stress is a term used within the literature which actually includes a broad range of distinct phenotypes, including stress, anxiety and depression. It encompasses the perceived or emotional challenges experienced by women during pregnancy that impede their ability to effectively cope and increase risk for maladaptive emotional or behavioral responses (Gunnar & Quevedo, 2007; Nast et al., 2013). Definitions of prenatal stress used within studies commonly include daily life hassles and acute stressful events (e.g., minor financial changes, transportation difficulties), chronic environmental challenges (e.g., poverty, racism) and general subjective levels of stress (e.g., how often events have been unpredictable or overwhelming, inability to handle general problems) (Davis & Sandman, 2012; DiPietro et al., 1996; Hobel, Goldstein, & Barrett, 2008). Research in this area has often operationalized "stress" using questionnaires of global perceptions of stress, chronic and acute stressful events (Hobel, Goldstein, and Barrett, 2008), or focusing specifically on relational conflict (Bogat, 2006; Martinez-Torteya et al., 2014), experiencing natural or manmade disasters (e.g., World Trade Center attacks, Hurricanes and tropical storms) (Yehuda et al, 2005; Kinney et al., 2008), as well as bereavement and loss (Li et al., 2009). Many studies have also used maternal mood as an indicator of prenatal stress,

including pregnancy related anxiety, depression and anxiety symptoms, or mental health diagnoses (O'Connor et al., 2002).

Numerous studies have found that a majority of pregnant women report moderate to high levels of stress during pregnancy and that they experience, on average, 1-3 stressful life events during pregnancy, including relational conflict, financial instability or homelessness, and family illness or loss (Kingston et al., 2012; Stone et al, 2015). To illustrate, in a longitudinal study of 1,522 pregnant women receiving antenatal care in the United States, 78% of the sample reported mild to moderate levels of perceived stress related to monetary changes, interpersonal difficulties (i.e., peer and family conflict and intimate partner violence), loss, and general feelings of being overwhelmed (Woods et al., 2010).

Prenatal mental health symptomatology has been linked to a myriad of obstetric, infant, and child outcomes. While maternal mental health symptoms may reflect a short-term emotional response to temporary stressors (i.e., increased demands in personal or professional life) they are also likely to emulate more persistent attributes unrelated to environmental characteristics. Therefore, a more nuanced understanding of maternal distress is needed to clearly identify factors that could contribute to negative child outcomes (Glover, 2011; O'Connor, Monk, & Fitelson, 2014).

Mood disorders, such as anxiety and depression, typically affect women at a disproportionate rate compared to men (Cook et al., 2004). Furthermore, there is compelling evidence that women are more vulnerable and at risk of developing psychiatric disorders during their reproductive years (Beck & Barnes, 2006; Cook et al., 2004). It is estimated that 8 to 25% of women will experience a mood disorder at some point during pregnancy (Cook et al., 2004; Kim et al., 2014; Seng et al., 2010; Vesga-Lopez et al., 2008). While depression is the most

commonly studied mood disorder, anxiety and PTSD are also commonly reported during and after pregnancy (Altshuler, Hendrick, & Cohen, 2000; Cook et al., 2004; Schetter & Tanner, 2012). Furthermore, a bidirectional relationship has been observed between the development of mental health symptoms and reported stress. For instance, it has been noted that women who report high rates of stressful life events are at an elevated risk for developing mental health symptoms (Kingsbury et al., 2018). In addition, others have described mental health symptoms contributing to increased levels of perceived stress in pregnancy. For example, Woods and colleagues (2010) observed that women with depression and panic disorder were 7-10 times more likely to report elevated stress levels compared to women experiencing other psychosocial stressors during pregnancy. Therefore, research studies often use symptoms of depression and anxiety as indicators of distress and prenatal stress (Glover, 2011; Talge, Neal & Glover, 2007; Van den Bergh, Mulder, Mennes, & Glover, 2005).

Research suggests that prenatal stress not only impacts women's physiological and psychological well-being but can also have significant long-term effects for offspring development. Developmental and adaptive programming models are commonly used to explain the relation between early life experience and subsequent health outcomes in adulthood, including exposures during fetal development (O'Donnell, Glover, Barker, & O'Connor, 2014). Programming models propose exposure to prenatal teratogens (i.e., maternal nutrition, psychopathology, and exposure to psychosocial stressors) results in developmental adaptations that, in the long term, increase vulnerabilities and effect offspring's future health outcomes (Barker, Eriksson, Fosen, & Osmond, 2002; Harville, Xiong, & Buekens, 2010; Talge, Neal & Glover, 2007; O'Donnell, Glover, Barker, & O'Connor, 2014).

Initial work focused on nutritional deficits in pregnancy as an indicator of negative birth outcomes, specifically low birthweight, which has been proposed as a causal factor for cardiovascular and metabolic problems in adulthood (Barker & Osmond, 1986; Barker et al., 2002; Gluckman, Hanson, & Beedle 2007). Programming models have now expanded to include various other psychosocial and environmental stressors that could contribute to physiological changes during fetal development. Proposed mechanisms via which prenatal stress can disrupt fetal development include: a. decreased uterine blood flow; b. changes in placenta functioning (i.e. altered glucocorticoids levels); and/or c. epigenetic influences that result in changes in offspring gene expression through DNA methylation (Kinney et al., 2008; Glover, 2011). While direct causal relationships have yet to be determined, current literature strongly suggests stress throughout pregnancy is linked to birth complications, infant temperament and regulation, as well as increased risk for negative physical and mental health outcomes in school aged children and adolescents (Grote, et al., 2010; Korja, Nolvi, Grant, & McMahon, 2017; Glover & the ALSPAC study Team, 2003).

### **Prenatal Stress and Early Developmental Outcomes**

Studies have evaluated a broad spectrum of stressors ranging in perceptual differences (objective vs. subjective), levels of severity (mild to severe), and duration of exposure (chronic vs acute) (Glover, 2014), with converging results that suggest suggesting significant deleterious effects on a variety of obstetric, infant, and child outcomes.

#### ***Obstetric outcomes***

Current literature indicates the impact of environmental stressors may be detected during pregnancy through the alteration of fetal neurodevelopmental functioning, including variability in fetal heart rate and motor activity. These studies indicate that fetuses of highly stressed women

were more like to exhibit increased fetal heart rate variability and higher percentage of fetal movement compared to women exposed to less stress (Van den Berg, Mulder, Mennes, & Oosterlaan, 2005). Alterations of fetal physiological characteristics are considered markers for negative temperament during infancy, such as increased fussiness, negative reactivity, and difficulty with emotion regulation (DiPietro, Hodgson, Costigan, & Johnson, 1996; Werner et al., 2007).

Additionally, various maternal stressors have also been linked to obstetric (e.g., preeclampsia, hyperemesis, spontaneous abortion) and birth (e.g., preterm birth, low birth weight, small head circumference) complications (Lazinkski, Shea, & Steiner, 2008; Grote et al., 2010; Hobel, Goldstein, & Barrett, 2008). For example, Dole and colleagues (2003) found high levels of pregnancy-specific anxiety as well as perception of gender and racial discrimination and living in unsafe neighborhoods, increased risk for preterm birth by 1.5 to 2-fold. In turn, multiple obstetric and neonatal outcomes (e.g., gestational age, birthweight and head circumference) have been linked to cognitive impairment in children (Bhutta et al., 2002; Neubauer, Voss & Kattner, 2008).

### ***Infant Outcomes***

During infancy, prenatal stress has been associated with negative temperament, sleep disturbances, increased fearfulness, as well as cognitive and motor delays (Davis et al, 2004; Bogat et al., 2006; Buitelaar et al., 2003). For example, a prospective study with 170 mother-infant dyads, found pregnancy specific anxiety predicted attention regulation and perceived stress predicted difficult behavior at 3 months old and attention regulation at 5 months (Huizink et al., 2002). In a second prospective study of twenty-two mother-infant dyads, infants whose mothers had elevated prenatal depression and anxiety scores, displayed higher negative reactivity

when exposed to novel stimuli (Davis et al., 2004). Additionally, researchers found that infants, as early as 12 months old, exposed to prenatal violence exhibit disruptions in patterns of attachment as well as disturbances in eating and sleeping patterns, common reactions to trauma in early development (Bogat et al., 2006; Levendosky et al., 2011). Importantly, early outcomes, such as temperament and reactivity, contribute to the child's self-regulatory abilities and problems in these domains increase risk for mental health symptoms during childhood (Korja, Nolvi, Grant, & McMahon, 2017).

### **Long-Term Outcomes of Prenatal Stress on Children and Adolescents**

While a large subset of the literature has focused on obstetric and infant outcomes, evidence also supports links between prenatal stress and changes in cognitive functioning, as well as increases in negative behavioral and emotional developmental trajectories throughout childhood and adolescence (King & Laplante, 2005; Van den Bergh & Marcoen, 2004; O'Connor, Heron, Golding, Glover & the ALSPAC study Team, 2003). It is commonly accepted that prenatal stress has long-term consequences on child and adolescent development. However, variability in findings has made integration and summarization of potential deleterious effects challenging. Commonly, studies report inconsistencies in findings in regards to the detriment of type and timing of prenatal exposure on various outcomes. Furthermore, challenges arise in evaluating the potency of the effects of prenatal stress and its contribution to specific child and adolescent behaviors. The current study aims to address some of these gaps in the literature by attempting to characterize the types of stressors that are most strongly linked with specific behavioral and mental health outcomes in school-aged children



### ***Prenatal Stress and Attention Deficit Hyperactivity Symptoms***

Neurodevelopmental disorders, like ADHD, begin early in life and often inhibit the child's academic, social, and occupational functioning. ADHD is characterized by patterns of inattention, hyperactivity, and impulsive behaviors (American Psychiatric Association, 2013). It is reported that ADHD affects 2 to 8.7% of school-aged children (ages 4-17), with a higher prevalence among boys (1.5-11.8%; Merikangas, Nakamura, & Kessler, 2009). While there is a large genetic component of developing ADHD, with heritability rates as high as 70-80%, there is also evidence of environmental factors contributing to symptom expression at varying developmental periods (Brikell et al., 2015; Larsson et al., 2014).

There is a growing literature documenting the associations between prenatal stress and ADHD symptoms in exposed offspring across development. Prenatal emotional stress, stressful life events, maternal bereavement, and exposure to natural disasters have been linked to increased hyperactivity and poor impulse control (Campbell, Shaw & Gilliom, 2000; Lui et al., 2004; McIntosh et al., 1995). These behaviors are key symptoms or commonly associated features of ADHD. Additionally, exposure to high levels of maternal anxiety during pregnancy has been prospectively linked to increased ADHD symptoms in children between the ages 4-15 including difficulties with attention, impulsivity (O'Connor et al., 2002, 2003; Van den Bergh & Marceon, 2004) and decreased performance on cognitive tasks (Van den Bergh et al., 2005).

Furthermore, Manzari and colleagues (2019), conducted a meta-analysis on prenatal stress and other neurodevelopmental disorders in offspring, and found a significant overall association between prenatal stress and ADHD. In this case, children of mothers with high levels of stress during pregnancy were 1.72 times more likely to develop ADHD than those not exposed. Subgroup analysis from this study showed the relationship between prenatal stress and

ADHD varied based on outcome reporter (i.e., parent report compared to clinical interview) and type of maternal stressor, such that the association became non-significant when using clinical records. In comparison, authors also reported a significant relationship between maternal report of subjective prenatal stress and the development of ADHD but not objective prenatal stress. Thus suggesting, variability in group difference that could contribute to the overall relationship between ADHD and prenatal stress.

Gender of the baby, as well as timing and severity of the exposure may play a key contributing factor in inconsistent findings. Several studies have identified boys being at a higher risk for developing ADHD following exposure to prenatal stress (Li et al., 2009; Zhu et al., 2015). For example, a nation-wide population-based cohort study in Denmark ( $N = 37, 275$  children) by Li and colleagues (2009), found that boys of mother's who lost a spouse or child due to unexpected death were 37% more likely to develop ADHD. In comparison, girls in this study had the same risk for developing ADHD regardless of their mother's prenatal exposure to death. Variation in timing has also made it hard to draw conclusions about sensitive periods of development. Studies on bereavement stress have demonstrated increased risk of developing ADHD when death occurred in the 3<sup>rd</sup> trimester (Class et al., 2014; Li et al., 2009). However, Zhu and colleagues (2015), reported higher rates of ADHD in boys whose mothers were exposed to severe stressful life events in the 2<sup>nd</sup> trimester.

### ***Prenatal Stress and Externalizing Symptoms***

Externalizing symptoms are categorized as a group of disruptive behaviors in which the child is influencing their outward environment and are generally indicated through non-compliance or defiance, and aggression (Campbell, Shaw & Gilliom, 2000; Liu et al., 2004). These behaviors are key symptoms or commonly associated features of Oppositional Defiant

Disorder and Conduct Disorder. While these behaviors are considered normative early in development, children who present them more frequently and intensively than their peers are more likely to experience long-term negative physical and mental health symptoms (Smith et al., 2004). It is reported that externalizing disorders affect 2.7 to 8% of school-aged children (ages 4-17), with a higher prevalence among boys, and these youth have an elevated risk for negative developmental trajectories well into adulthood (Danielson et al., 2020; Merikangas, Nakamura, & Kessler, 2009). Developmental models suggest that behavioral disorders impair cognitive development (i.e., decision making) (Fanti & Henrich, 2010) and negatively impact academic performance (DeSocio & Hootman, 2004) and social interactions (Greenberg, Domitrovich, & Bumbarger, 2001). Over time, the culmination of negative social feedback, cognitive distortions of self, and lack of appropriate coping strategies increase the risk for subsequent delinquent behavior (i.e., truancy, substance use) during adolescence, and can affect occupational outcomes and the development of other mental health symptoms in adulthood (Greenberg, Domitrovich, & Bumbarger, 2001).

Exposure to violence (Martinez-Torteya et al., 2014) or other stressful events (Huizink et al., 2007), maternal psychopathology (Van den Bergh & Marcoen, 2004), and psychosocial stress (Ramchandi, Richter, Norris, & Stein, 2010) during pregnancy have all been linked to behavioral difficulties and externalizing symptomology in children ranging in age from 4-16 years old. Specifically, children exposed to prenatal stress exhibit more aggressive behaviors (Hay et al., 2010). For example, in a longitudinal study with children from an urban community in South Africa, maternal prenatal family stress (i.e., fighting between family members, family member with a drug problem or disability) predicted child behavior problems at 4 years old (Ramchandi et al., 2010). Similarly, maternal prenatal anxiety and disaster exposure (i.e.,

Chernobyl disaster) has been identified to increase risk of externalizing problems in cohorts of 4–5-year-olds (O'Connor et al., 2002), 7- 8-year-olds (O'Connor et al., 2003; Van den Bergh & Marcoen, 2004) and 14-year-olds (Huiznick et al., 2007). For example, in a large community sample of mothers and children, high levels of maternal anxiety late in pregnancy were linked to behavioral problems (e.g., conduct problems) in 4–5-year-olds and 7–8-year-olds after controlling for obstetric complications, socioeconomic status (SES), and maternal postpartum depression (O'Connor et al., 2002; O'Connor et al., 2003).

### *Prenatal Stress and Internalizing Symptoms*

Internalizing symptoms tend to be directed inward, with individuals expressing more withdrawn, anxious, depressed, or inhibited behaviors (Liu et al., 2004). Internalizing symptoms are commonly associated with depression and anxiety disorders, with a prevalence ranging from 2.2 to 9% among 4- to 17-year-old youth (Merikangas, Nakamura, & Kessler, 2009). Children with internalizing symptoms are twice as likely to develop mood disorders and anxiety in adulthood (Bittner et al., 2007). They are also at an elevated risk for other adverse psychosocial outcomes including substance abuse, suicidal behavior, poor academic achievement, and unemployment (Fergusson & Woodward, 2002).

Prenatal maternal psychopathology and perceived stress are commonly associated with the development of depression and anxiety symptoms in their offspring. Elevated emotional problems have been consistently reported in cohorts of 6- to 9-year-olds exposed to higher-than-average maternal perceived stress, depression, and anxiety during pregnancy (Davis & Sandman 2012; O'Connor et al., 2002). O'Connor and colleagues (2003) reported antenatal anxiety as a significant predictor of emotional disturbance in a cohort of 6-year-olds, even after controlling

for additional risk factors (i.e., obstetric risk, psychosocial risk, and subsequent exposure to maternal psychopathology).

Similarly, adolescents who were exposed to prenatal stress and natural disasters in utero have reportedly a 2-4-fold increased risk for developing depression compared to their same-age peers (Huizink et al. 2007; Pawlby et al., 2009). Results from a population-based twin study in Finland showed youth exposed to the Chernobyl Disaster in utero reported higher lifetime prevalence of depressive symptoms and increased likelihood of major depressive disorder as compared to the non-exposed group, even after controlling for age, SES, and gender (Huizink et al., 2007). Huizink and colleagues (2007) concluded differences in symptom presentation were more likely due to perceived maternal stress rather than exposure to radiation, as participants did not exhibit adverse birth outcomes commonly associated with radiation exposure. Similarly, Pawlby and colleagues (2009) reported a 4.7-fold increase of developing depression at 16 years old if the adolescents' initial exposure to maternal depression was *in utero* when compared to adolescents whose mothers did not experience depression during pregnancy.

However, these findings are complicated by a lack of studies that account for additional exposures to other environmental stressors on the development of child psychopathology. Several studies report mediating effects of additional environmental stressors, most notably maternal mental health symptoms across development, on the connection between prenatal stress and child mental health outcomes (Pawlby et al., 2009; Rice et al., 2010). In a sample of 474 women who underwent *in vitro* fertilization, Rice and colleagues (2010) reported current (but not prenatal) maternal psychopathology symptoms, significantly predicted child mood symptoms in genetically related and unrelated mother-child dyads. The cumulative and differential effects of maternal mood may also contribute to the development of mental health symptoms in children.

Pawlby and colleagues (2009) noted the risk between developing depression at 16 and exposure to prenatal depression became non-significant when accounting for subsequent exposures to maternal depression across childhood. Furthermore, positive parenting practices and quality of attachment has been shown to predict more positive outcomes for children exposed to early stressful life events, suggesting that the caregiving environment can have a protective effect after prenatal stress exposure (Bergman, Sarkar, Glover, & O'Connor, 2008; Glover, 2011; Grant, McMahon, Reilly, & Austin, 2010). More research is needed to disentangle the effects of prenatal exposures and subsequent postnatal experiences.

Taken together there is a growing body of evidence that indicate significant associations between prenatal stress and adverse child and adolescent outcomes. However, methodological differences have made comparisons between studies difficult. Integration and summary of findings of studies that focused on different stressors and evaluated various developmental outcomes, in conjunction with analysis of the effects associated with variations in study methodology, are needed to better understand the effects of prenatal stress on school aged youth.

### **Environmental and Research Factors Contributing to the Relation Between Prenatal Stress and Child and Adolescent Outcomes: Proposed Moderators**

Studying the impact of the perinatal period on both women and their children is complex. A broad range of physiological, psychological, and environmental processes interact to influence developmental trajectories. Methodological limitations have made it challenging to identify nuanced environmental and individual characteristics that contribute to the development of specific outcomes as a result of prenatal exposures. Further exploration on the impact of (1) type of stress (psychosocial, physiological, psychological), (2) timing of exposure, (3)

sociodemographic characteristics, and (4) study design is needed to better understand the effects of prenatal stress on child and adolescent outcomes.

### *Characteristics of Prenatal Stress as Moderators*

Timing of exposure during pregnancy has been implicated in reported differences between type of stressor and potential outcome. Brain development begins within weeks of conception and continues into adolescence. There are vulnerable periods in which environmental characteristics can significantly impact offspring physiological and brain development (Zeanah, 2019). For instance, Buss and colleagues (2010), reported high pregnancy-specific anxiety (i.e., fear of labor, fear of pregnancy outcome) in mid gestation, was associated with grey matter volume in prefrontal cortical regions in a prospective cohort of children ages 6-9 years old. This association was not observed for children exposed to high pregnancy-specific anxiety later in pregnancy (25-31 weeks' gestation).

Similar associations have been reported between prenatal environmental stressors and child psychosocial outcomes. Exposure to environmental stressors in the first trimester has been associated with negative birth outcomes and later development of schizophrenia (Khashan et al., 2008; Lederman et al., 2004; Van Os et al., 1998), while exposure in 2<sup>nd</sup> and 3<sup>rd</sup> trimester has been linked to ADHD and other behavioral problems (Class et al., 2014; O'Connor et al., 2003), such as defiance and aggression.

Additionally, there is little literature on which forms of stress may have a greater impact on child development. For example, Davis and Sandman (2012) noted pregnancy-specific anxiety independently predicted child anxiety in comparison to other maternal stressors (i.e., perceived stress, depression, and general anxiety) during pregnancy. On the other hand, Barker and colleagues (2011) reported maternal prenatal and postpartum depression as more significant

predictors of child maladjustment than maternal anxiety. Furthermore, how a stressor is perceived may also contribute to its impact on women and their children. For example, experiencing a major life event may contribute to increased anxiety during pregnancy ultimately leading to the development of psychopathology (Schetter & Tanner, 2012). Given the variability in the prenatal stress literature surrounding type and timing of exposure it is critical to explore these characteristics as specific moderators of the effects of prenatal stress on child outcomes.

### ***Sociodemographic Moderators***

Several demographic characteristics have been identified in the literature as influencing the relation between prenatal stress and various outcomes. Specifically, other meta-analyses have reported location of study and SES as significantly moderating the relationship between prenatal stress and developmental outcomes (Buffa et al., 2018; Grote et al., 2010; Madigan et al., 2018). For example, women experiencing prenatal depression were at an elevated risk for negative birth outcomes if living in developing countries or were of lower SES in the United States (Grote et al., 2010). As a result, similar moderating variables were accounted for in the current meta-analysis.

Additionally, the current meta-analysis focused on the effects prenatal stress on internalizing, externalizing, and ADHD symptoms, but this relationship may vary depending on children's developmental stage. Studies assessing the developmental trajectories of internalizing disorders report stability of symptom presentation across childhood with a slight elevation in adolescents (Bongers, Koot, Van der Ende, & Verhulst, 2003; Twenge & Nolen-Hoeksema, 2002). Comparatively, developmental trajectories of externalizing symptoms appear to decrease throughout childhood and adolescence (Bongers, Koot, Van der Ende, & Verhulst, 2003; Leve, Kim, & Pears, 2006), although different trajectories have been reported based on symptom



reporter (i.e., parent versus teacher report; Keiley, Lofthouse, Bates, Dodge, & Pettit, 2003). Given developmental differences in children kindergarten – 12<sup>th</sup> grade, child age will also be assessed as a potential moderator.

### ***Methodological Moderators***

Limitations in methodology and the operationalization of key variables limit our understanding of the effects of prenatal stress exposure on child and adolescent outcomes, which makes identifying consistent developmental patterns challenging. For example, the current prenatal stress literature generally focuses on early developmental outcomes (0-3 years old) and less on school-aged outcomes. Additionally, difference in reporter of child outcome (i.e., parent-, self-, teacher-, clinical report) has been proposed to influence the association between prenatal stress and long-term child outcomes (Manzari et al., 2019). The reliance on self-report measures in this type of study design increases risk of reporter bias (Lev-Wiesel, 2009). Furthermore, variable type may impact the identified association. For example, the effect of maternal prenatal depression had a larger effect size on birth outcomes when measured categorically compared to continuously (Grote et al., 2010). In addition, Tarabulsy and colleagues (2014) noted that studies using retrospective reporting of symptoms had greater effect sizes than prospective studies in their sample. Finally, current psychopathology, stress, and timing of assessment have all been shown to potentially influence reporter reliability (Tarabulsy et al., 2014). Identifying and describing methodological characteristics that may positively or negatively impact reported findings within the prenatal stress literature can help address previously identified limitations and improve future study design allowing for more robust connections to be made between prenatal exposures and adverse child and adolescent outcomes.

### **Rationale and Aims for the Current Study**

To date, synthesis of the prenatal stress literature has primarily focused on birth outcomes and early child development. Meta-analyses have linked prenatal stress (i.e., anxiety, depression, and life events) with negative birth outcomes (i.e., preterm birth, low birthweight, inter uterine growth restriction (Bussières et al., 2015; Ding et al., 2014; Grote et al., 2010). Additionally, a small but significant effect size was documented between maternal prenatal stress and early child cognitive development in meta-analysis (Tarabulsky et al., 2014). Also, a systematic review linked prenatal stress and anxiety with emotional and self-regulation difficulties in the first two years of life, suggesting a continued negative influence of *in-utero* exposure on subsequent child development (Korja, Nolvi, Grant, & McMahon, 2017). To our knowledge, no meta-analysis has been conducted to quantify the effect of prenatal stress on the internalizing, externalizing, and ADHD symptoms of school age children and adolescents. Determining the magnitude of the influence of prenatal stress on offspring outcomes in childhood and adolescents is an important next step in our understanding its long-term effects.

Meta-analysis is a useful tool that expands upon a systematic review by providing quantitative analysis of the relationship between targeted variables. It is considered a more rigorous and valid study design than other qualitative reviews. Borenstein and colleagues (2009) argue meta-analysis is useful to address issues of sample size, specifically combining studies with small sample size and ultimately lower statistical power. Additionally, meta-analyses address issues of heterogeneity when attempting to draw conclusions between studies with diverse samples and research methodologies, thus helping explain results within the context of multiple studies (Borenstein et al., 2009). A meta-analysis that evaluates the effects of prenatal stress on child and adolescent internalizing, externalizing, and ADHD symptoms can make

significant contributions to the current literature, providing a rigorous and valid interpretation and summary of published and unpublished data, and more power in conclusions based on the pooled samples of multiple studies, as compared to the findings of individual studies.

A meta-analysis will also help provide context to explain individual findings and identify modifiers that contribute to different patterns of findings (Borenstein et al., 2009). While most forms of prenatal stress appear to negatively impact development, specific types of exposure appear to influence outcomes differently. For instance, two meta-analyses identified pregnancy specific anxiety as having a stronger influence on birth outcomes, specifically gestational age (Bussieres et al., 2015; Staneva, Bogossian, Pritchard, & Wittkowski, 2015), while objective life events during pregnancy was a stronger predictor of cognitive development in another meta-analysis (Tarabulsky et al., 2014), as compared to pregnancy-specific anxiety or perceived stress. Further exploration of the literature is needed to identify the role of different prenatal exposures on later developmental outcomes, specifically for school aged children.

Identifying potential moderators of the negative influence of prenatal stress exposures would help to clarify developmental trajectories for various child and adolescent outcomes. For example, commonly identified limitations by researchers focus on methodological challenges including study design and reporter bias. In the perinatal stress literature, many studies rely on self-report of single reporters, primarily the child's maternal caregiver, when assessing childhood outcomes. Informant bias is commonly discussed as a study limitation documenting the connection between previous experience and mental health symptoms on influencing current maternal perceptions about oneself as well as their child's behavior (Levendosky et al., 2016; Lev-Wiesel, 2009). A meta-analysis will allow for exploration of how differences in study

design influence the magnitude between prenatal stress and specific outcomes and provide recommendation for future data collection.

This meta-analysis seeks to synthesize previous research and quantify the effect of prenatal maternal stress on child and adolescent internalizing, externalizing, and ADHD symptoms. In addition, this study seeks to provide a better understanding of the differential effects of specific types of stressors, as well as stressor-related, demographic, or methodological differences that may heighten or buffer the reported effects of prenatal stress. This meta-analysis extends previous work that has only looked at specific types of prenatal stress and has only summarized effects related to birth and infant outcomes. The research aims are:

1. To determine the overall effect of prenatal stress on child and adolescent internalizing, externalizing, and ADHD symptoms.
2. To evaluate whether stressor characteristics, specifically type of exposure, will moderate the effect of prenatal stress on child and adolescent neurocognitive, behavioral, and emotional outcomes.
3. To identify other moderators (i.e., child age, SES) that could contribute to differences in the effect sizes reported.

### **Methods**

The current study followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines, including the information flow chart (Figure 1. PRISMA Flow Diagram Detailing the Search Strategy) reported below. PRISMA guidelines were developed to assist in the appraisal of the literature, reporting of findings, and to decrease report bias of systematic reviews and meta-analyses (Moher, Liberati, Tetzlaff, & Altman, 2009).

### **Literature Search and Article Selection**

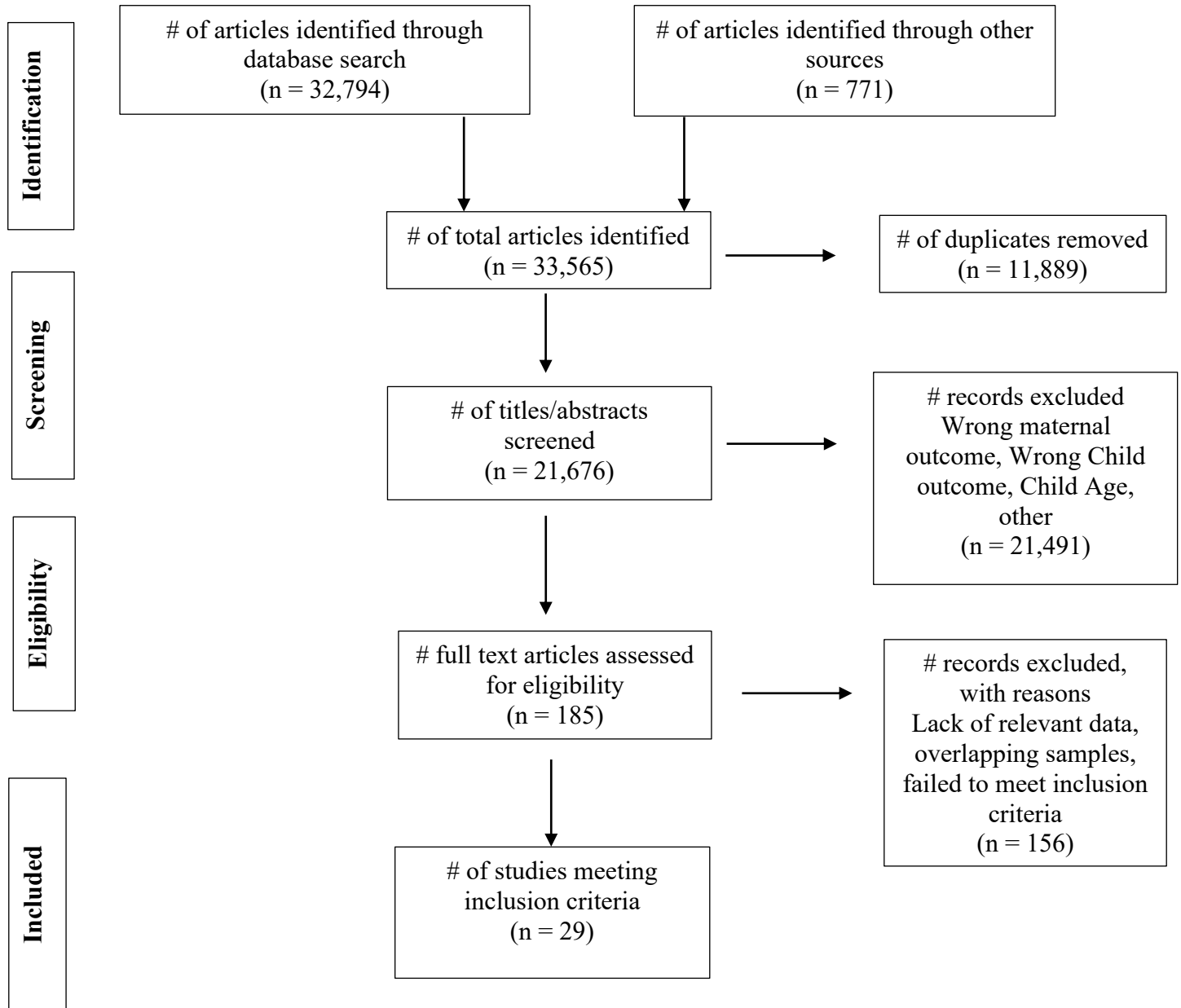
Articles were identified for review using major databases such as *PsychInfo*, *Pubmed*, *Cinahl*, and *Science Direct*. The search was limited to publications written in English between 1900 – 2019, using key words such as: “prenatal”, “pregnancy”, “antenatal”, “stress”, “distress”, “psychopathology”, “mood disorders”, “depression”, “anxiety”, “PTSD”, “Intimate Partner Violence”, “partner abuse”, “trauma”, “childhood”, “child development”, “school age”, “adolescents”, “behavior problems”, “socioemotional problems”, “externalizing disorders (including ADHD, CD, ODD)”, “Autism Spectrum Disorder”, “Internalizing Disorder (including depression, anxiety, PTSD).” Sixteen total searches were run using the combined terms, see Appendix A for example of full electronic search strategy. The search was supplemented with a manual search of reference lists from past reviews or other relevant meta-analysis (DiPietro et al., 2004; Glover et al., 2014; Murray et al., 2020; Shay-Zapfen & Bullock, 2010). To minimize selection bias, we attempted to collect unpublished manuscripts, such as dissertations identified through databases (i.e., *Dissertation Direct*) as well as through professional conferences (e.g., International Society for Traumatic Stress Studies).

### **Inclusion Criteria**

To be included, a study needed to meet the following criteria. First, studies must only contain human subjects. Second, studies must evaluate the relationship between maternal prenatal stress or psychopathology and negative child behavioral or emotional outcomes (i.e., ADHD symptoms, externalizing symptoms, or internalizing symptoms). Assessment of prenatal stress, perceived stress, and psychopathology were included if evaluated by self-report questionnaires, clinician administered interviews, health records, or observations. Studies that relied solely on maternal physiological measures (e.g., maternal cortisol) were excluded.

Additionally, articles were excluded if they evaluated prenatal toxins (e.g., lead), nicotine, and drug or alcohol exposure as the primary predictor variable. Third, studies must include at least 1 prospective stress assessment of the mother during pregnancy. Studies using retrospective (postnatal) measurements of stress were excluded. Fourth, the children identified in the study needed to be of school age, between kindergarten and 12<sup>th</sup> grade. Normative ages for school age children range from 5-18 years old, therefore studies were included if the mean age described fell within this range. Fifth, the assessment of child outcomes were included if they were conducted using self-, or parent-report questionnaires, clinician administered interviews, as well as health or school records. Finally, only English language articles were included.

**Figure 1.** PRISMA Flow Diagram Detailing the Search Strategy.



## **Coding Procedures**

Article coding was split into three phases: 1. title and abstract coding, 2. full-paper coding, and 3. obtaining measures and effect sizes. The author and a team of 6 undergraduates served as coders for the first phase of coding. The author trained the undergraduate students to code for inclusion as a function of 4 main characteristics 1. timing of stressor (i.e., occurring during pregnancy) 2. the operationalization of the maternal prenatal stressor (including type and measurement), 3. the operationalization of child outcome (including type and measurement), and 4. child age. For training purposes undergraduates recorded information on the previously described inclusion/exclusion variables in an excel spreadsheet. Ten studies were then randomly selected and coded by research personnel independently (Cooper, 2017). Discrepancies were discussed and agreement was met between coders. Following this meeting, coders were given 10 additional articles to establish interrater reliability. Interrater agreement ranged from 77.14 % – 98.57%, with a mean agreement of 86.43% (SD = 8.51 %). If the coder failed to meet 85% interrater reliability with the primary author in their first attempt, they were given a subsequent 10 articles to code. All coders met reliability within the first 2 attempts.

Following coder training, all articles were uploaded to Covidence, a purchased online systematic review management system, used to manage, sort, and review title/abstract as well as full texts (Covidence, 2014). In the software, an inclusion/exclusion template was created based on the previously described characteristics. All articles were double coded. Articles that were unclear and difficult to code were presented at weekly team meetings to discuss the decision-making process and reach consensus. Where consensus could not be reached, the author made the final determination/resolution. Phase 1 of the screening and selection process identified



33,565 references from the total data sources used. Of those, 11,889 were duplicate references and were removed. The titles and/or abstracts of 21,676 were coded and 21,491 excluded.

Phase 2 of the screening process consisted of obtaining full text versions of the remaining 185 articles for further review. A coding manual was created a priori to extract relevant study and outcome level information from all articles and manuscripts. Information collected in the coding manual included study characteristics (i.e. year of publication, journal, etc.), evaluation of methodology (i.e. sample characteristics, location of study, research design), predictor variables (e.g. types of prenatal stress), outcomes measured (e.g. internalizing or externalizing problems), statistical outcomes (e.g. means/standard deviations, correlations, or odds ratios), and coder characteristics (e.g. date coded, length of time spent coding; Cooper, 2017). An electronic version of the coding manual was created in Qualtrics XM, an online survey software, see Appendix B. Three of the original 6 undergraduate coders were selected to help with full text coding. All articles were double coded then consensus coded by the author.

Phase 3 consisted of obtaining measures of association and effect sizes. Attempts were made to contact authors in case of insufficient or missing information. During this stage, 156 of 185 studies were excluded either because there was insufficient information to calculate the effect size or because studies reported on subjects from common datasets.

## **Independence of Study Results**

### ***Longitudinal Data***

A violation of independence occurs when multiple articles are published using samples from a common dataset (Card, 2012). When studies reported different subsets of a larger sample then the following steps were taken in an effort to minimize loss of data and maintain the assumption of independence: 1. The article assessing the most variables of interest (i.e., maternal

prenatal stress and the child outcomes) was included; 2. The articles with the most time points (if the same number of time points assessed include articles with the largest sample). 3. If the number of variables of interest are the same, include the article with the largest sample size.

### ***Effect Sizes from Multiple Measures***

Independence can also be violated when multiple measures of the same construct are reported in one study. When multiple measures were present in the study the following steps were taken to assure independence was maintained. First each measure was evaluated to determine the relevance to the central hypothesis based on the pre-identified inclusion/exclusion criteria. If all measures met criteria, then an average effect size was computed. Based on Card's (2012) recommendation if the effect size was typically transformed, such as  $Z_r$ , then they should be averaged.

### **Data Analysis**

The data were analyzed using the Comprehensive Meta-Analysis Software v. 3 (CMA; Borenstein, Hedges, Higgins, & Rothstein, 2013). Effect sizes were derived from Pearson Correlation Coefficient,  $r$ , which is a useful index to determine the strength and direction of association between continuous variables (Card, 2012; Ellis, 2010). Generally, correlation coefficients in a population are skewed, as such the  $r$ -index was converted to z-scores using the Fisher's transformation ( $Z_r$ ) before combining or comparing effect sizes.  $Z_r$  was then translated back to the  $r$ -index for interpretation and reporting (Borenstein, Higgins, & Rothstein, 2009; Card, 2012).

Inferential models, like fixed-effect models or random-effect models, are commonly used to compare differences between observed and expected variance between the assessed phenomena. Fixed-effects models assume variation between studies is reflective of the sample of

participants and therefore random. In comparison, random-effects models account for study-level variance as influencing the relationship between variables. Random-effects models frequently utilize larger confidence intervals than fixed-effects models and are considered the more conservative approach (Egger, Davey Smith, & Phillips, 1997). It is recommended that the research question and the context of the literature be used to determine the chosen model. Specifically, random-effects models are considered more appropriate for samples with significant heterogeneity and “research [that] takes place in a real-world context” (Cooper, 2017, p. 248).

For this study a random effects model was used to estimate the mean effect size between prenatal stress and youth socioemotional outcomes, to account for both within- and between-study variance.  $Q$  and  $I^2$  were computed to assess heterogeneity of effect sizes. In the random effects model, a significant  $Q$ -test statistic indicates sufficient variability in effect size for subsequent analyses to be conducted in an attempt to identify or explain sources of variability (Borenstein et al., 2009; Card, 2012). The  $I^2$  statistic accounts for the proportion of the variance in the reported effect size that is a result of variance between studies. Thus, heterogeneity as a result of study characteristics and its contribution to observed variance is frequently measured using the  $I^2$  statistic (Borenstein et al., 2009; Card, 2012; Cooper, 2017).  $I^2$  is reported as a percentage, the higher the percentage the higher the variability between effect sizes.

Moderation analyses were conducted when evidence of heterogeneity was found. Proposed moderators, described above, were derived from theory and previous empirical literature. Categorical moderators (i.e., study location) were analyzed using subgroup analysis similar to ANOVA. To account for imprecise estimates of small subgroups, subgroups were pooled and then analyzed with a random effects model (Borenstein et al. 2011). If significant

differences were detected post hoc analysis, like a Fisher's Least Significant Difference test in ANOVA, was conducted to determine significant subgroup differences. Conversely, meta-regression analyses were used to examine the effect of continuous moderators (i.e., maternal race/ethnicity) in the relation between prenatal stress and youth psychosocial outcomes. Meta-regression is similar to a multiple regression, in which effect sizes are evaluated as criterion variables and study characteristics are the predictors (Cooper, 2017; Shelby & Vaske, 2008).

Meta-analyses are often restricted by the quality and completeness of the primary research reviewed. Publication bias, due to the tendency to publish statistically significant findings, is a commonly identified limitation in meta-analysis research. To reduce the effect of the publication bias, funnel plots will be evaluated and the "trim and fill" method will be applied (Duval & Tweedie, 2000; Sterne, Becker, & Egger, 2005). Funnel plots are a visual tool that estimates study effects in comparison to study size. The "trim and fill" method is an algorithm using the funnel plot that estimates the number of studies missing in analysis due to asymmetric formation of the plots. Ultimately this approach yields a more symmetric funnel plot and is considered a more valid estimate of the overall effect (Duval & Tweedie, 2000). Additionally, a fail-safe N will be calculated. A fail-safe N estimates the number of missing studies with null findings needed to make the reported effect size insignificant (Rosenthal, 1991; Sterne, Becker, & Egger, 2005).

## **Results**

### **Descriptions of Studies**

Of the 185 identified studies, 53 correlation coefficients ( $r$ 's) were extracted from 29 articles. Articles were composed of 27 published manuscripts and 2 unpublished dissertations. Study and sample information for these articles are presented in Table 1. The sample sizes of

studies ranged from 54 to 41,608 mother-child dyads. Included studies were published between 2004 and 2020. Cohorts of women who participated in the identified studies were recruited between 1959 and 2011.

Studies varied in the country of origin, study design, and sample characteristics (see Table 1). Ten studies were conducted in North America, fifteen studies in Europe (i.e., England, Finland, Netherlands), two in Australia, and one each in Africa and South America.

Several longitudinal cohorts with overlapping datasets were identified including; Avon Longitudinal Study of Parenting and Children (ALSPAC), Finish Family Competence Study (FFC), Mater University of Queensland, Norwegian Mother and Child Cohort Study, South Long Child Development Study, The French Eden Mother-Childbirth Cohort. Of the original 185 number of studies, 25 (13.5%) included data from the ASLPAC study. Steps to minimize violation of independence were taken (see methods section) and ultimately 5 ALSPAC studies were included in the current analysis (Bolea-Alamanac et al., 2019; Flouri et al., 2020; Quarini et al., 2016; Capron et al., 2015; O'Donnell et al., 2014). The same method was used for all other identified longitudinal cohorts with multiple eligible studies. Of these, 7 of the 14 identified were included in the current analysis.

Mother's age ranged from 21.2 to 38.1 years. 66.9% identified of the women identified as White/Caucasian. Maternal education was used as the primary index of SES with 42.8% of the women reported having high school equivalence or below. Sixteen studies evaluated mental health symptoms (i.e., anxiety and depression), five stress/distress, three trauma, and five combined mental health symptoms and stress, as indicators of prenatal stress. Most (89.7%) studies utilized self-report measures to evaluate stress during pregnancy.

At the outcome assessment, child age ranged from 5 - 18 years old. Due to the variance in reporting, child age was split into developmental categories (i.e., early childhood, middle childhood, and adolescence, see Table 2). About half (55.2%) of the included studies provided data on multiple outcomes (i.e., both internalizing and externalizing symptoms), and separate effect sizes were created for each outcome. Regarding youth psychosocial outcomes, internalizing symptoms were measured in 23 articles, externalizing symptoms were measured in 19 articles, and ADHD symptoms were measured in 11 articles. Information was collected by child-report ( $n = 5$ ), parent-/teacher-report ( $n = 18$ ), clinical interview/health records ( $n = 4$ ), or a combination of reporters (i.e., parent and child or parent and teacher;  $n = 2$ ).

**Table 1.** Sample Characteristics of Studies Included in the Meta-Analysis (*k* = 29)

<b>Study<sup>+</sup></b>	<b>N</b>	<b>Year of Recruitment</b>	<b>Continent</b>	<b>Child Age Group</b>	<b>Prenatal Stress Type</b>	<b>Reporter</b>	<b>Child Outcome Measure</b>	<b>Reporter</b>
Betts et al., 2014	3,925	1981-1984	Australia	Adol.	Combo	Self	Externalizing, Internalizing	Child
Bolea-Alamanac et al., 2019	3,605	1991-1992	Europe	Adol.	Mental Health Symptoms	Self	ADHD	Parent
Capron et al., 2015	4,303	1991-1992	Europe	Adol.	Mental Health Symptoms	Self	Internalizing	Child
Clavarino et al., 2010	298	1981-1983	Australia	Multi	Mental Health Symptoms	Self	ADHD	Parent
Davis & Sandman, 2012	178	--	N. America	EC	Mental Health Symptoms	Self	Internalizing	Parent
Davis et al., 2020	74	--	N. America	Adol.	Stress/Distress	Self	Internalizing	Child
Eichler et al., 2017	204	2005-2007	Europe	EC	Mental Health Symptoms	Self	Externalizing, Internalizing	Parent

**Table 1 (con't).** Sample Characteristics of Studies Included in the Meta-Analysis (*k* = 29)

Study <sup>+</sup>	N	Year of Recruitment	Continent	Child Age Group	Prenatal Stress Type	Reporter	Child Outcome Measure	Reporter
Faleschini et al., 2019	1,125	1999-2002	N. America	Mid	Mental Health Symptoms	Self	Externalizing, Internalizing, ADHD	Parent
Flouri et al., 2020	4,264	1991-1992	Europe	Multi	Stress/Distress	Self	Internalizing	Child
Glynn et al., 2018	407	--	N. America	Multi	Mental Health Symptoms	Self	Internalizing	Child
Hartman et al., 2019	41,608	1999-2009	Europe	EC	Combo	Self	Externalizing, Internalizing	Parent
Hentges et al., 2019	1,992	2008-2011	N. America	EC	Combo	Self	Externalizing, Internalizing	Parent
Isaksson et al., 2017	358	2002-2012	Africa	Mid.	Trauma	Self	Externalizing, Internalizing	Parent
Jones et al., 2019	63	1998	N. America	Mid.	Stress/Distress	Self	Externalizing, Internalizing	Parent
Loomans et al., 2011	3,446	2003-2004	Europe	EC	Mental Health Symptoms	Self	Externalizing, Internalizing, ADHD	Combo (Parent & Teacher)
Martinez-	119	--	N.	Mid.	Trauma	Self	Externalizing,	Parent



Torteya et al.,  
2016

America

Internalizing,  
ADHD

**Table 1 (con't).** Sample Characteristics of Studies Included in the Meta-Analysis (*k* = 29)

Study <sup>+</sup>	N	Year of Recruitment	Continent	Child Age Group	Prenatal Stress Type	Reporter	Child Outcome Measure	Reporter
Martini et al., 2010	102	1995	Europe	Adol.	Stress/Distress	Self	Externalizing, Internalizing, ADHD	Clinical Inter.
Maxwell et al., 2018	1,711	1959-1966	N. America	Mid.	Combo	Narrative	Externalizing, Internalizing	Parent
Morin, 2005	85	1998	N. America	EC	Combo	Self	ADHD	Teacher
O'Donnell et al., 2014	7,944	1991-1992	Europe	Mid.	Mental Health Symptoms	Self	Externalizing, Internalizing, ADHD	Parent
Pawlby et al., 2009	127	1986	Europe	Adol.	Mental Health Symptoms	Clinical Inter.	Internalizing	Clinical Inter.
Perera et al., 2013	248	2000-2003	Europe	EC	Stress/Distress	Self	Externalizing, Internalizing, ADHD	Parent
Phihlakoski, 2012	908	1985	Europe	Adol.	Mental Health Symptoms	Self	Externalizing,	Parent
Plant et al., 2013	116	1986	Europe	Multi	Mental Health Symptoms	Clinical Inter.	Externalizing	Clinical Inter.

**Table 1 (con't).** Sample Characteristics of Studies Included in the Meta-Analysis (*k* = 29)

Study <sup>+</sup>	N	Year of Recruitment	Continent	Child Age Group	Prenatal Stress Type	Reporter	Child Outcome Measure	Reporter
Quarini et al., 2016	7,959	1991-1992	Europe	Adol.	Mental Health Symptoms	Self	Internalizing	Clinical Inter.
Silva et al., 2019	614	2013-2014	S. America	EC	Trauma	Self	Externalizing	Parent
Van den Bergh & Marceon, 2004	72	--	Europe	EC	Mental Health Symptoms	Self	Externalizing, Internalizing, ADHD	Combo (Parent & Child)
Van Der Waerden et al., 2015	1,178	2003-2005	Europe	EC	Mental Health Symptoms	Self	Externalizing, Internalizing, ADHD	Parent
Warren, 2004	54	1992-1993	N. America	EC	Mental Health Symptoms	Self	Externalizing, Internalizing	Parent

EC = Early Childhood; Mid. = Middle Childhood; Adol. = Adolescence; Multi = Combination of Ages; <sup>+</sup> See Appendix B for reference numbers and citations for all studies used in the current meta-analysis

<b>Table 2. Study and Sample Characteristics of Eligible Studies (<i>k</i> = 29)</b>		
<b>Participant Characteristics</b>	<b>k (<i>n</i>)</b>	<b>%</b>
Child Gender*		
Male	51,059	
Female	48,626	
Child Age (Developmental Category) <sup>+</sup>		
Early	11	37.9%
Middle	6	20.7%
Adolescents	8	27.6%
Mixed	4	13.8%
Maternal Education*		
Average High School education or below		42.8%
Maternal Age*		
Mean/SD	29.7 (3.4)	
Maternal Race/ Ethnicity*		
% White/Caucasian		66.9%
<b>Study Characteristics</b>		
Location		
North American	10	34.5%
Europe	15	51.7%
Other	4	13.8%
Child Outcome		
Internalizing	22	75.9%
Externalizing	19	65.5%
ADHD	11	37.9%

\*Number of Studies Missing Information; Child Gender (n=2); Maternal Education (n=10); Maternal Age (n=12); Maternal Race/Ethnicity (n=15); <sup>+</sup> Developmental Category Age Ranges (years); Early - 5-8; Middle - 9 – 11; Adolescents - 12 – 18.

### **Prenatal Stress and Child/Adolescent Psychosocial Outcomes**

The first aim of this meta-analysis was to calculate the magnitude of the relationship between prenatal stress and child/adolescent psychosocial outcomes. Due to concerns of dependence, separate effect sizes were calculated (reported in Pearson's correlation ( $r$ )) for each child/adolescent outcome. A meta-analysis, using a random effects model, was conducted for each youth outcome independently (Van den Noortgate, 2012; i.e., internalizing symptoms, externalizing symptoms, and ADHD symptoms). The summary of effect sizes between prenatal stress and child/adolescent psychosocial outcomes is presented in Table 3. Extreme outliers were identified if "the study's confidence interval did not overlap with the confidence interval of the pooled effect (Harrier et al., 2021)." One study was identified and removed from internalizing symptom analysis.

The overall effect size for the relationship between prenatal stress and youth internalizing symptoms ( $k = 22$ ,  $N = 82,546$ ) was  $r = 0.149$  (CI: [0.110 - 0.187]). The  $I^2$  value was 92.18, indicating that 92% of the variation across studies is due to heterogeneity rather than chance (Higgins and Thompson, 2002). The  $Q$  statistic indicated significant heterogeneity in this sample ( $Q$  ( $df = 21$ ) = 268.47,  $p < .001$ ). This suggests a small positive effect between prenatal stress and child and adolescent internalizing symptoms. In other words, increased prenatal stress is associated with higher internalizing symptoms in school age children and adolescents.

A similar result was observed between prenatal stress and youth externalizing symptoms with an overall effect size of  $r = 0.133$  ( $k = 19$ ,  $N = 70,112$ , CI: [0.103 - 0.164]). 81.28% of the variation across these identified studies was due to heterogeneity rather than chance. The  $Q$  statistic indicated significant heterogeneity in this sample ( $Q$  ( $df = 18$ ) = 96.159,  $p < .001$ ). Results indicate a small positive effect between prenatal stress and child and adolescent

externalizing symptoms, where higher prenatal stress is associated with higher externalizing symptoms in school age children and adolescents.

Finally, there was a significant overall effect between prenatal stress and ADHD symptoms in school aged children and adolescents ( $k = 11, N = 18,222, r = 0.179, CI: [0.149 - 0.208]$ ). Results indicate a small positive effect between prenatal stress and child and adolescent ADHD symptoms, where higher prenatal stress is associated with higher ADHD symptoms in school age children and adolescents. However, the  $Q$  statistic was non-significant ( $Q (df = 10) = 16.691, p = .081$ ), suggesting moderation analysis are not indicated. The mean effect size and confidence interval and the effect size for each of the individual studies are represented visually for each outcome in forest plots (Figure. 2 - 4).

**Table 3.** Summary of Effect Sizes for Prenatal Stress and Child/Adolescent Psychosocial Outcomes

<b>Outcome Category</b>	<b><i>k</i></b>	<b>Mean ES</b>	<b>95% CI</b>	<b><i>z</i></b>	<b><i>Q</i></b>	<b><i>I</i><sup>2</sup></b>
Internalizing Symptoms	22	0.149	0.110 - 0.187	7.39***	268.47***	92.18
Externalizing Symptoms	19	0.133	0.103 – 0.164	8.44***	96.16***	81.28
ADHD Symptoms	11	0.179	0.149 - 0.208	11.63***	16.69 <sup>+</sup>	40.09

*Note.* \*\*\* $p < .001$ ;  $k$  = Number of Studies; ES = Effect Size; CI = Confidence Interval;  $Q$  = Significance Test for heterogeneity;  $I^2$  = Percentage of variance among effect sizes due to heterogeneity.  
<sup>+</sup>  $p = 0.081$ ; approaching significance

### Forest Plot - Prenatal Stress and Internalizing Symptoms

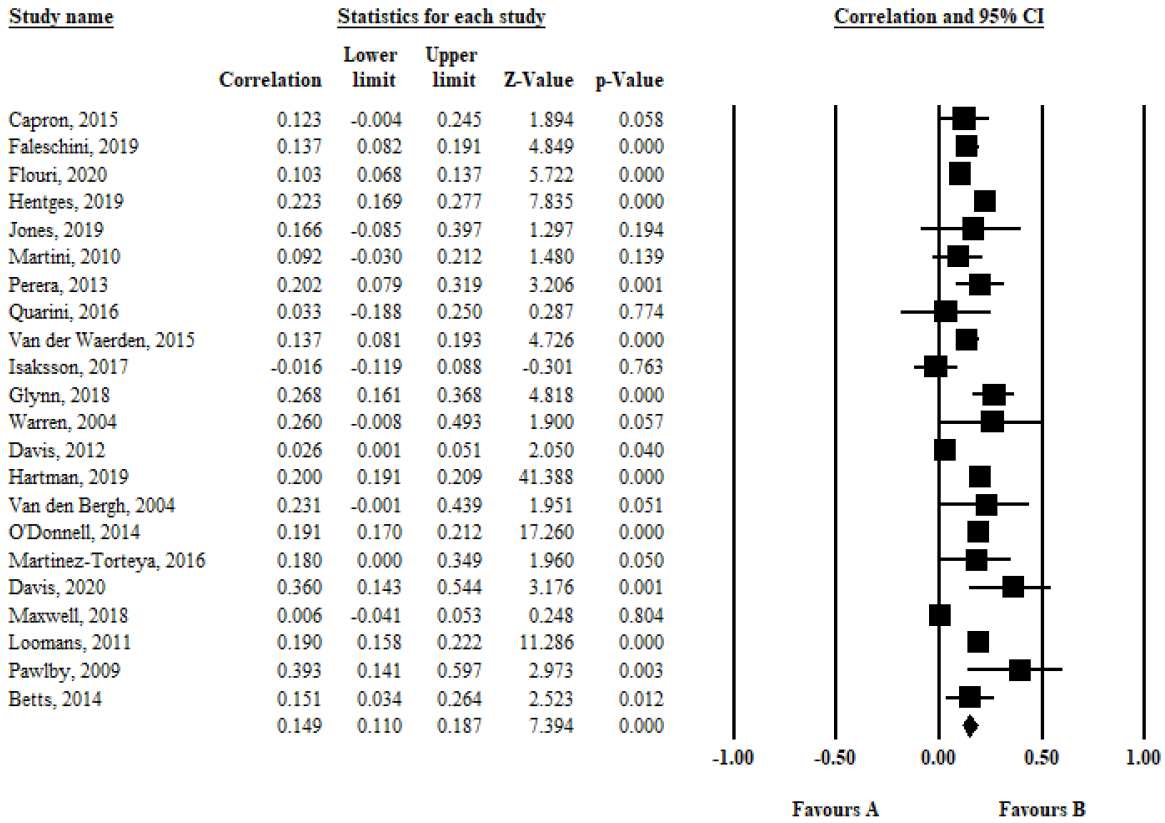


Figure 2. Effect sizes (represented as *r*'s) and 95% CI's are indicated for each study included in the meta-analysis. Black squares indicate individual studies. The black diamond represents the overall effect size for the association between prenatal stress and internalizing symptoms of school aged children/adolescents.

### Forest Plots - Prenatal Stress and Externalizing Symptoms

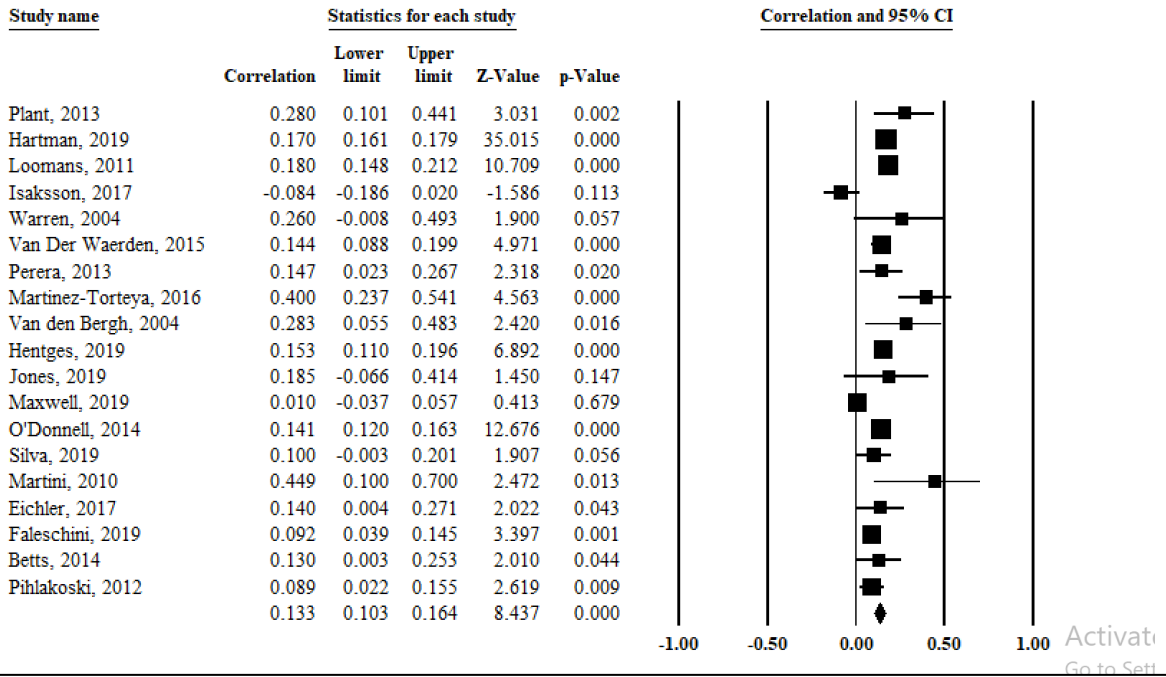


Figure 3. Effect sizes (represented as *r*'s) and 95% CI's are indicated for each study included in the meta-analysis. Black squares indicate individual studies. The black diamond represents the overall effect size for the association between prenatal stress and externalizing symptoms of school aged children/adolescents.

### Forest Plot - Prenatal Stress and ADHD Symptoms

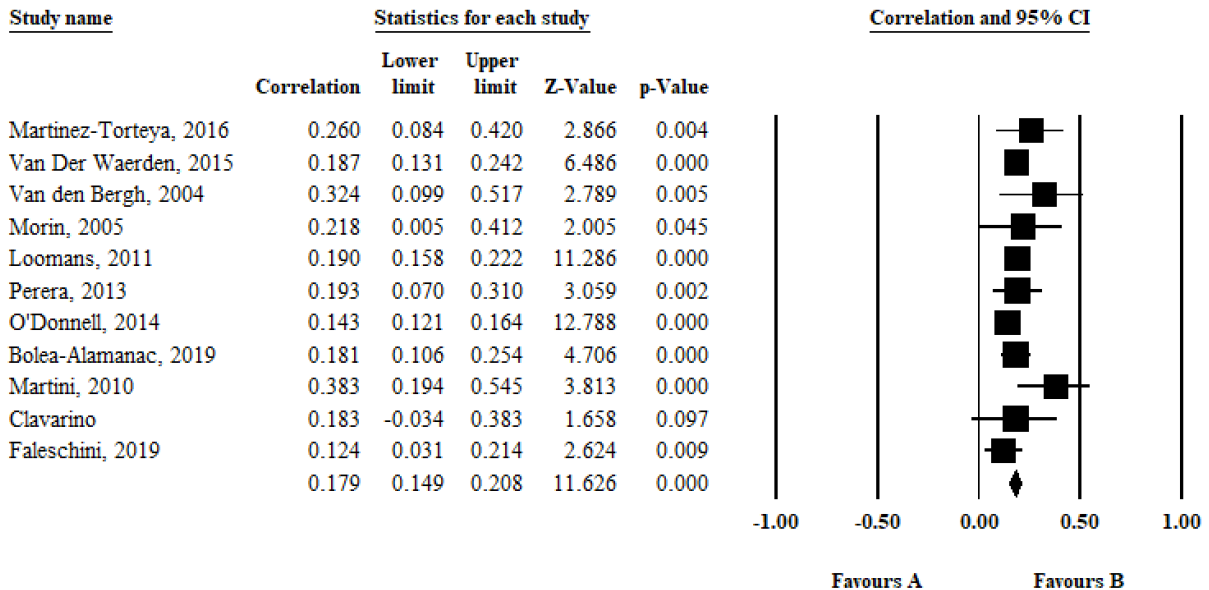


Figure 4. Effect sizes (represented as *r*'s) and 95% CI's are indicated for each study included in the meta-analysis. Black squares indicate individual studies. The black diamond represents the overall effect size for the association between prenatal stress and ADHD symptoms of school aged children/adolescents.

## **Moderation Analyses**

### ***Categorical Moderation Analyses***

To address the second and third aim of the study, characteristics of prenatal stress (i.e., type of stressor), sociodemographic characteristics (i.e., child age, maternal education), and study design (i.e., study location, reporter of child outcome) were examined as moderators. As noted in Table 3, the  $Q$  statistic indicated significant heterogeneity in the effect sizes for prenatal stress and both youth internalizing and externalizing symptoms. Similarly, the  $I^2$  indicated high magnitude of variability in heterogeneity for all effect sizes except for the relation between prenatal stress and ADHD symptoms. Therefore, moderation analysis was conducted only on the association between prenatal stress and internalizing and externalizing symptoms. All identified moderators were examined for all effect sizes except between prenatal stress and ADHD symptoms. Categorical subgroups with less than four articles were excluded from moderator analyses. To account for imprecise estimates of small subgroups, when subgroups analysis was conducted, within group estimates were pooled to increase accuracy, and then analyzed with a random effects model instead of a fix-effects model, as described in Borenstein et al. 2011.

### **Categorical Moderator Analysis for Prenatal Stress and Internalizing Disorders.**

Recruitment year, study location, reporter for child outcome, prenatal stress type, as well as child age (described by developmental category) all yielded non-significant group differences. Table 4 presents the results of all categorical moderator analyses for the relationship between prenatal stress and internalizing symptoms, conducted as described above.



**Table 4.** Results of categorical moderator analysis for *Internalizing Symptoms*

Category	<i>k</i>	Mean ES	95% CI	<i>Q</i> , <i>p</i> -value
<b>Recruitment Year</b>				
1959-1999	10	.128	0.63 - 0.192	1.02, <i>p</i> = 0.31
2000's	7	0.166	0.130 - 0.202	
<b>Study Location</b>				
Europe	11	0.164	0.122 – 0.205	0.74, <i>p</i> = 0.39
North America	9	0.136	0.086 – 0.184	
<b>Reporter for Outcome</b>				
Self-Report (Child)	17	0.177	0.096 - 0.186	0.55, <i>p</i> = 0.46
Other	5	0.141	0.093 – 0.259	
<b>Prenatal Stress Type</b>				
Psychopathology	11	0.162	0.101 – 0.221	0.35, <i>p</i> = 0.56
Stress/Distress	7	0.132	0.050 – 0.212	
<b>Child Age</b>				
Early Childhood	9	0.165	0.074 – 0.253	1.04, <i>p</i> = 0.60
Middle Childhood	5	0.097	-0.025 - 0.216	
Adolescence	6	0.165	0.074 - 0.253	

*Note.* *k* = Number of Studies; ES = Effect Size; CI = Confidence Interval; *Q* = Significance Test for Heterogeneity; \**p* < .05. \*\**p* < .01. \*\*\**p* < .001

**Categorical Moderator Analysis for Prenatal Stress and Externalizing Disorders.** Similarly, moderation analysis of recruitment year, study location, prenatal stress type, and child age (by developmental category) were non-significant. Table 5 summarizes results of all moderator analysis with categorical moderator variables for the relationship between prenatal stress and externalizing symptoms conducted as described above. Reporter of child outcome had insufficient categories (i.e., at least 4 cases) to complete moderation analysis.

**Table 5.** Results of categorical moderator analysis for *Externalizing Symptoms*

Category	<i>k</i>	Mean ES	95% CI	<i>Q</i> , <i>p</i> -value
<b>Recruitment Year</b>				
1959-1999	8	0.133	0.64 - 0.201	0.004, <i>p</i> = 0.95
2000's	9	0.131	0.096 - 0.164	
<b>Study Location</b>				
Europe	10	0.158	0.125 – 0.191	2.28, <i>p</i> = 0.13
North America	6	0.144	0.067 – 0.161	
<b>Reporter for Outcome</b>				
Parent-Report	14	--	--	Insufficient sample size
Other	3	--	--	
Parent + Other Reporter	2	--	--	

**Table 5 (con't).** Results of categorical moderator analysis for *Externalizing Symptoms*

Category	<i>k</i>	Mean ES	95% CI	<i>Q</i> , <i>p-value</i>
<b>Prenatal Stress Type</b>				
Psychopathology	9	0.148	0.102 – 0.194	0.28, <i>p</i> = 0.60
Stress/Distress	6	0.125	0.049 – 0.199	
<b>Child Age<sup>+</sup></b>				
Early Childhood	9	0.169	0.160 – 0.177	2.67, <i>p</i> = 0.10
Middle Childhood	6	0.100	0.016 – 0.182	

*Note.* *k* = Number of Studies; ES = Effect Size; CI = Confidence Interval; *Q* = Significance Test for Heterogeneity; \**p* < .05. \*\**p* < .01. \*\*\**p* < .001; <sup>+</sup>Child Age was split between 2 developmental categories due to lack of studies in the adolescence categories (n=3).

**Continuous Moderation Analysis**

The current study utilized meta-regression analysis to estimate the impact of continuous study moderators on the relationship between prenatal stress and child/adolescent socioemotional outcomes (i.e., internalizing and externalizing symptoms). Meta-regression analysis was performed on continuous moderators with a minimum of 10 studies available for each variable (Fu et al., 2011).

Maternal race (percentage Caucasian/White), maternal age (mean age), child gender (percentage male), and socioeconomic status as measured by maternal education (percent of women with equivalent high school completion or lower) were coded as continuous variables to be entered into meta-regression models to determine their potential moderating effect on the relation between prenatal stress and child/adolescent internalizing and externalizing symptoms.

Table 6 and Table 7 presents a summary of the results for all continuous moderator analysis of

the association between prenatal stress and internalizing and externalizing symptoms respectively.

#### **Continuous Moderator Analysis for Prenatal Stress and Internalizing Disorders.**

Maternal race was measured by computing the percentage of Caucasian/White women in each sample. Percent of Caucasian/White women ranged from 0% (a non-white sample) to 100% (all Caucasian/White sample), with the average of 65.2%. Nine studies failed to report data on maternal race/ethnicity. Results showed no significant moderation of maternal race/ethnicity on the relationship between prenatal stress and child/adolescent internalizing symptoms ( $b = 0.115$ ,  $SE = .087$ ,  $Z = 1.32$ ,  $p = .19$ ).

Average maternal age ranged from 21.2 to 38.1, with the mean age of 29.9 years. Seven studies failed to report data on maternal mean age. Results showed a significant moderation by average maternal age ( $b = -0.001$ ,  $SE = .006$ ,  $Z = -2.10$ ,  $p = 0.04$ ), such that studies with higher mean age reported a weaker relationship between prenatal stress and child/adolescent internalizing symptoms. Forty-four percent of the relationship between prenatal stress and child internalizing symptoms can be explained by the average maternal age of the study.

Child gender was measured by computing the percentage of males in each sample. Percent of male youth ranged from 43.7% to 57.4%, with an average of 51.2%. Two studies failed to report data on child gender. Results showed no significant moderation of youth gender on the relationship between prenatal stress and child/adolescent internalizing symptoms ( $b = 0.671$ ,  $SE = 0.641$ ,  $Z = 1.05$ ,  $p = .30$ ).

Socioeconomic status was measured by computing the percentage of mothers with the equivalence of a high school education or less. For European studies this was classified “has no A levels” (MacKinnon, et al. 2018). Nine studies failed to report data or did not have comparable data. Percent of women with the equivalence of a high school education or below ranged from

13.4% - 80.3% (M = 39.5 %). Results showed no significant moderation of maternal education on the relationship between prenatal stress and child/adolescent internalizing symptoms ( $b = 0.121, SE = 0.171, Z = .71, p = .48$ ).

**Table 6.** Results of Continuous moderator analysis for *Internalizing Symptoms*

<b>Outcome Category</b>	<b><i>k</i></b>	<b><i>b</i></b>	<b>SE</b>	<b>95% CI</b>	<b><i>Z</i></b>	<b><i>R</i><sup>2</sup></b>
Maternal Education	13	0.121	0.171	-0.215 - 0.457	0.71	0.00
Maternal Race	14	0.115	0.087	-0.056 – 0.286	1.32	0.26
Mean Maternal Age	15	-0.001*	0.006	-0.026 – -0.009	-2.10	0.44
Child Gender	20	0.671	0.641	-0.585 – 1.927	1.05	0.11

Note.; \* $p < .05$ . \*\* $p < .01$ . \*\*\* $p < .001$ ;  $k$  = Number of Studies;  $b$  = Slope ES = Effect Size; CI = Confidence Interval

**Continuous Moderator Analysis for Prenatal Stress and Externalizing Disorders.**

Percent of Caucasian/White women ranged from 0% (a non-white sample) to 100% (all Caucasian/White sample), with the average of 61.5%. Seven studies failed to report data on maternal race/ethnicity. Results showed no significant moderation of maternal race/ethnicity on the relationship between prenatal stress and child/adolescent externalizing symptoms ( $b = 0.115, SE = .081, Z = 1.42, p = .16$ ).

Average maternal age ranged from 21.2 to 32.8, with the mean age of 29.3 years. Seven studies failed to report data on maternal mean age. Results showed no significant moderation of maternal age on the relationship between prenatal stress and child/adolescent externalizing symptoms ( $b = -0.005, SE = 0.009, Z = -0.52, p = 0.60$ ).

Child gender was measured by computing the percentage of males in each sample. Percent of male youth ranged from 46.0% to 57.4%, with an average of 51.2%. Two studies

failed to report data on child gender. Results showed no significant moderation of youth gender on the relationship between prenatal stress and child/adolescent externalizing symptoms ( $b = -0.001$ ,  $SE = 0.78$ ,  $Z = -0.00$ ,  $p = 1.0$ ).

As previously described, socioeconomic status was assessed through maternal education status. Seven studies failed to report data or did not have comparable data. Percent of women with the equivalence of a high school education or below ranged from 8.5% - 80.3% ( $M = 43.4\%$ ). Results showed no significant moderation of maternal education on the relationship between prenatal stress and child/adolescent externalizing symptoms ( $b = -0.038$ ,  $SE = 0.131$ ,  $Z = -0.29$ ,  $p = 0.77$ ).

**Table 7.** Results of Continuous moderator analysis for *Externalizing Symptoms*

<b>Outcome Category</b>	<b><i>k</i></b>	<b><i>b</i></b>	<b>SE</b>	<b>95% CI</b>	<b><i>Z</i></b>	<b><i>R</i><sup>2</sup></b>
Maternal Education	12	-0.038	0.131	-0.295 - 0.218	-0.29	0.00
Maternal Race	12	0.115	0.081	-0.044 – 0.273	1.42	0.00
Mean Maternal Age	12	-0.005	0.009	-0.023 – 0.013	-0.52	0.00
Child Gender	17	-0.001	0.78	-1.528 – 1.525	-0.00	0.01

*Note.*; \* $p < .05$ . \*\* $p < .01$ . \*\*\* $p < .001$ ;  $k$  = Number of Studies;  $b$  = Slope ES = Effect Size; CI = Confidence Interval

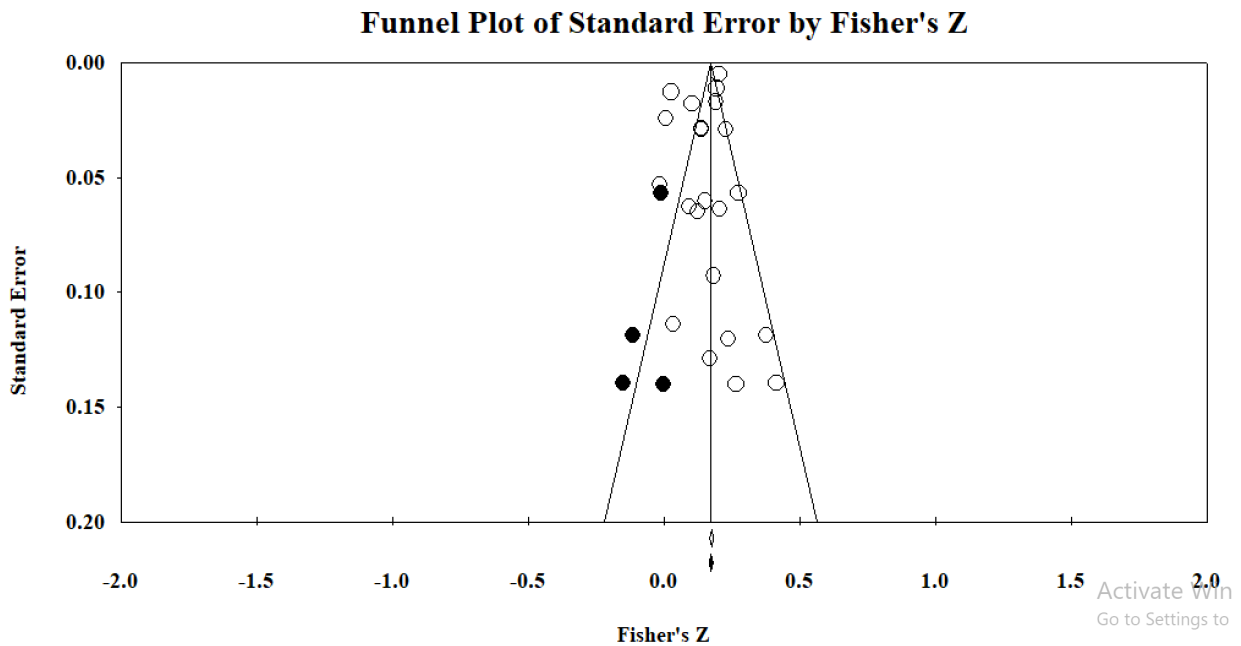
### **Publication Bias**

Meta-analysis are often restricted by the quality and completeness of the primary research reviewed. Publication bias, due to the tendency to publish statistically significant findings, is a commonly identified limitation in meta-analysis research. Publication bias analyses were run separately for each child outcome variable.

**Funnel Plots**

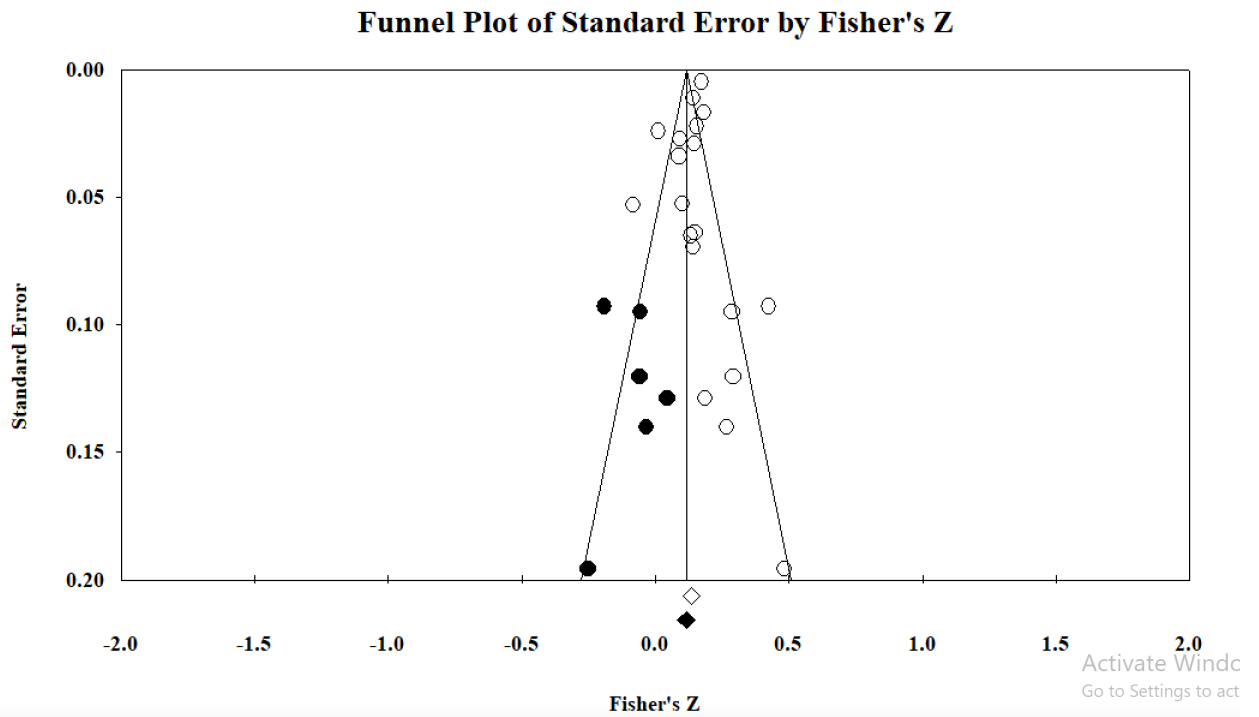
Funnel plots are a visual tool that estimates study effects in comparison to study size. If studies are distributed symmetrically about the combined effect, publication bias is thought to be absent. When samples are concentrated at the bottom of the plot towards one side of the mean, it is assumed publication bias is present. Figures. 5-7 present the funnel plots for each of the youth outcomes. To assess the potential effect of publication bias, funnel plots were evaluated (Sterne, Becker, & Egger, 2005; Duval & Tweedie, 2000). Taken together, these results and those below seem to suggest some publication bias but not enough to negate the findings.

**Figure 5.** Funnel Plot - Internalizing Symptoms

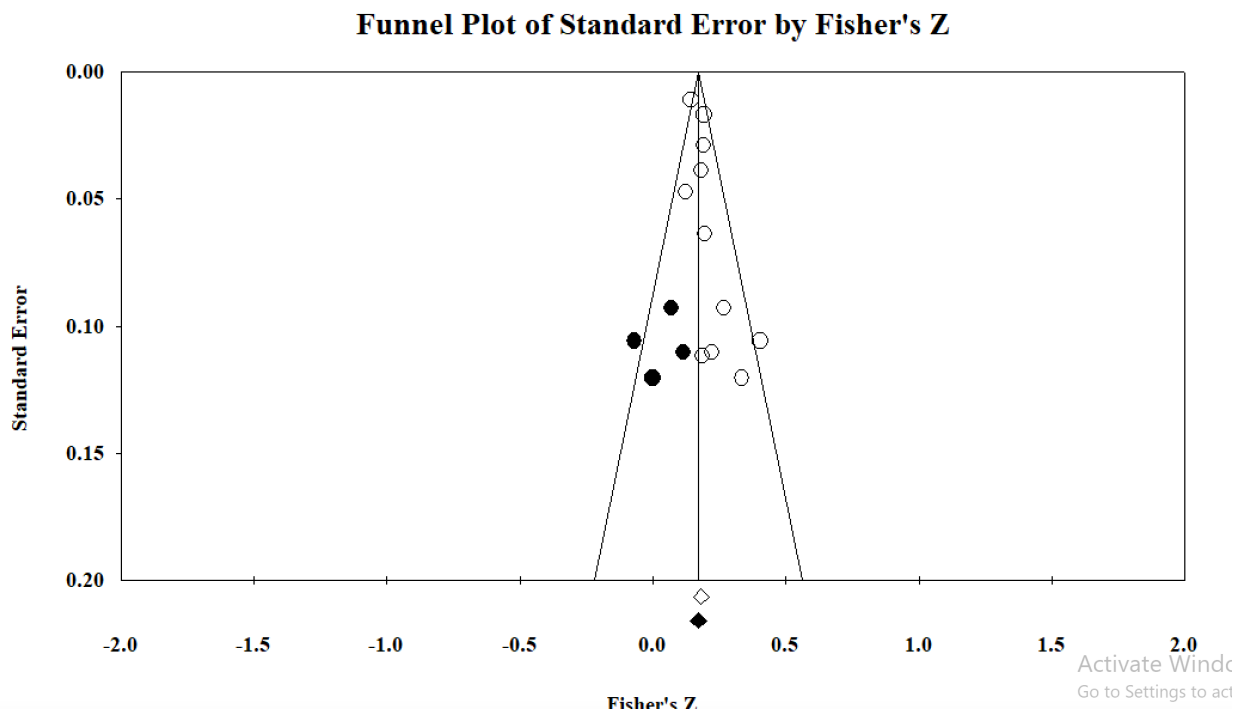


Note: The y-axis on the funnel plot represents the standard error, and the x-axis represents the effect size. White circles indicate studies that were included in the meta-analysis, and black circles indicate values to adjust for asymmetry in the funnel plot. The white diamond at the bottom of the funnel plot represents the observed mean effect size, and the black diamond represents the adjusted mean effect size.

**Figure 6.** Funnel Plot - Externalizing Symptoms



**Figure 7.** Funnel Plot - ADHD Symptoms



Note: The y-axis on the funnel plot represents the standard error, and the x-axis represents the effect size. White circles indicate studies that were included in the meta-analysis, and black circles indicate values to adjust for asymmetry in the funnel plot. The white diamond at the bottom of the funnel plot represents the observed mean effect size, and the black diamond represents the adjusted mean effect size.



**Duval and Tweedie's Trim and Fill**

The "trim and fill" method is an algorithm using the funnel plot that estimates the number of studies missing in analysis due to asymmetric formation of the plots. Ultimately this approach yields a more symmetric funnel plot and is considered a more valid estimate of the overall effect (Duval & Tweedie, 2000).

**Internalizing Symptoms.** The trim and fill method analysis conducted to evaluate publication bias on articles evaluating the relationship between prenatal stress and internalizing symptoms in children suggest that 4 studies are missing. See Figure 5 for a funnel plot with these 4 imputed samples (filled circles). Under a random effects model, Cohen's  $r$  and 95% confidence interval for the combined studies is 0.149 (.110 to .187). Using Trim and Fill, the imputed Cohen's  $r$  estimate is 0.131 (.092 to .168).

**Externalizing Symptoms.** In the current analysis, the trim and fill method suggests that 6 studies are missing. See Figure 6 for a funnel plot with these 6 imputed samples (filled circles). Under a random effects model, Cohen's  $r$  and 95% confidence interval for the combined studies is 0.133 (.103 to .164). Using Trim and Fill, the imputed Cohen's  $r$  estimate is 0.114 (.082 to .146).

**ADHD Symptoms.** When evaluating the analysis for the relation between prenatal stress and ADHD symptoms the trim and fill method suggests that 4 studies are missing. See Figure 7 for a funnel plot with these 4 imputed samples (filled circles). Under a random effects model, Cohen's  $r$  and 95% confidence interval for the combined studies is 0.179 (.149 to .208). Using Trim and Fill, the imputed Cohen's  $r$  estimate is 0.168 (.137 to .200).

**Fail-Safe  $N$** 

A fail-safe  $N$  estimates the number of missing studies with null findings needed to make the reported effect size insignificant (Rosenthal, 1991; Sterne, Becker, & Egger, 2005).

***Internalizing Symptoms.*** The meta-analysis assessing prenatal stress and internalizing symptoms of children and adolescents incorporates data from 22 studies, producing a z-value of 26.12 and a corresponding p-value less than 0.001. The Fail-Safe N = 3,887, which means that 3,887 null studies (mean correlation  $r = 0$ ) would need to be located and included in order for the combined p-value to exceed 0.05. More conservatively estimated, when the alpha level was set to 0.01 (instead of 0.05), analysis yielded a FSN of 2,241.

***Externalizing Symptoms.*** As reported in the above results, the meta-analysis evaluating prenatal stress on externalizing symptoms of children and adolescences incorporates data from 19 studies, which yields a z-value of 22.76 and corresponding p-value less than 0.001. The Fail-Safe N = 2,543, which means that 2,543 null studies (mean correlation  $r = 0$ ) would need to be located and included in order for the combined p-value to exceed 0.05. More conservatively estimated, when the alpha level was set to 0.01 (instead of 0.05), analysis yielded a FSN of 1,465.

***ADHD Symptoms.*** The meta-analysis evaluating prenatal stress on ADHD symptoms had the fewest number of studies. The analysis incorporates data from 11 studies, which yields a z-value of 16.31 and corresponding p-value less than 0.001. The Fail-Safe N = 751, which means that 751 null studies (mean correlation  $r = 0$ ) would need to be located and included in order for the combined p-value to exceed 0.05. More conservatively estimated, when the alpha level was set to 0.01 (instead of 0.05), analysis yielded a FSN of 430.

## Discussion

Research studies have consistently demonstrated a link between maternal prenatal stress and adverse obstetric and infant outcomes. In addition, there is an evolving literature showing that exposure to prenatal stress has long-term neurocognitive, behavioral, and emotional consequences for offspring, including symptoms of ADHD, depression, and anxiety that persist well into the school-age years. However, variation in sample sizes, study design and measure outcome has made it challenging to evaluate the role of maternal prenatal stressor characteristics on different developmental trajectories, particularly in school aged children. This meta-analysis aimed to synthesize the state of the current literature and quantify the effects of prenatal stress on internalizing, externalizing, ADHD symptoms among children ages 5 to 18. Further, it evaluated whether pregnancy specific (e.g., type of stressor), sociodemographic (e.g., child gender), and methodological factors (e.g., reporter of child outcome) moderate the association between prenatal stress and outcomes in school-aged children. Although previous meta-analyses have been conducted (e.g. Madigan et al., 2018; Manzari et al., 2019; Silva et al., 2018; Su et al., 2020; Tirumalaraiu et al., 2020) they have focused on 1.) a single *specific* type of stressor, rather than including multiple types or 2.) have relatively small follow-up periods, so that results are pertinent to early childhood or early adulthood or 3.) have included retrospective studies, which introduce recall bias to the results. To our knowledge, this is the first meta-analysis to evaluate the literature on maternal prenatal stress, that includes *multiple* types of stressors, and examines *long-term* behavioral and mental health outcomes that specifically affect older school-aged children.

### **Meta-analytic findings and preliminary moderation results**

The present meta-analysis included 29 prospective studies to examine the association between prenatal stress and the emotional as well as behavioral functioning of school age children. As 55% of studies reported on multiple child outcomes simultaneously (i.e., internalizing, externalizing, and ADHD symptoms), each outcome was analyzed separately. Overall, the results provide additional support for the hypothesis that prenatal stress deleteriously affects child socioemotional and behavioral outcomes. Furthermore, our findings extend prior research by demonstrating that negative effects persist into later childhood, namely the school-aged period. Additionally, moderation analysis was conducted to evaluate whether theoretical and methodological factors could impact the association between prenatal stress and child/adolescent outcomes. Contrary to expectations, this analysis yielded only one significant relationship, with average maternal age at birth moderating the association between prenatal stress and youth internalizing symptoms.

### ***Internalizing Symptoms***

The results of the current meta-analysis found a statistically significant association between prenatal stress and internalizing symptoms in school-aged youth. This is consistent with the results of other more limited meta-analyses that have established a long-term relationship between a specific type of prenatal stressor and internalizing symptoms. For instance, Silva and colleagues (2018) established an increased risk of internalizing problems (i.e., depressed mood and anxiety) in a group of children, ranging in age from 10 months old to 16 years old who had been exposed to prenatal violence. Similarly, prenatal maternal mood, specifically depression, has also consistently been linked to the development of depression in the offspring across childhood/adolescent and into adulthood (Su et al., 2020; Tirumalaraiu et al., 2020). In sum,

results from the present study are line with previous work (Silva et al., 2018; Su et al., 2020) that has demonstrated an association between prenatal stress and the risk of developing internalizing symptoms across childhood.

Furthermore, the findings from the current study add to the literature by establishing an association between prenatal stress and internalizing symptoms in school age children, 5-18 years old. The majority of previous research has focused on either younger children, specifically under the age of 4, or older adolescents and adults. A better understanding of this relationship is critical as recent reports suggest that approximately 3.2 million adolescents in the U.S will experience at least one depressive episode between the ages of 12-17 years old (National Institute of Mental Health, 2019). Understanding how prenatal experiences could contribute to the development of internalizing symptoms in this age group is essential to the continued development of early interventions that could potentially alter symptom trajectories.

***Significant Moderation Results: Maternal Age***

Average maternal age was the only hypothesized moderator that significantly contributed to the association between prenatal stress and internalizing symptoms, such that effect sizes were stronger in younger women. This result is consistent with prior findings that younger maternal age is linked to pregnancy complications and adverse obstetric outcomes (Caroland & Frankowska, 2011; de Vienne et al., 2009) as well as later developmental outcomes including academic problems and behavioral difficulties (Tearne, 2015; Saha et al., 2009). A recent systematic review suggests the relationship between maternal age and offspring depression may be curvilinear, with increased risk found both for the youngest and oldest mothers across studies (Su et al., 2020).

Why might younger maternal age pose a risk factor for children? One possible explanation is that maternal age serves as a proxy for other demographic variables that have been shown to predict child outcomes. For example, elevated socioeconomic status and income as well as higher educational achievement are commonly associated with women who have children later in life (Martin, 2004; Tearne, 2015). Additionally, there is evidence of increased pregnancy preparedness (Nelson et al, 2004) as well as positive parenting behaviors (i.e., maternal supportiveness) in women of older maternal age (Barnes et al., 2014; Tearnes, 2015). As such, the current findings may reflect the connection between maternal age and other psychosocial variables, which we could not explore in the current analysis, thus highlighting a need to continue to examine psychosocial variables that may impact the association between prenatal stress and emotional and behavioral outcomes of school aged children.

### *Externalizing Symptoms*

Similar to internalizing symptoms, a small but significant association between prenatal stress and externalizing symptoms in school-aged youth was established. This is consistent with other meta-analyses that describe a long-term association between various types of prenatal stressors (i.e., maternal distress, intimate partner violence exposure, and maternal mental health symptoms) and behavioral challenges (i.e., aggressive behavior and delinquency) across childhood and adolescence (Kingston & Tough, 2014; Rogers et al., 2020; Silva et al., 2018). These results highlight the enduring impact of prenatal stress on childhood behavioral outcomes. This continues to be an important area of investigation, as 7.4 million children in the United States have a diagnosed behavior problem, and the most prevalent group being diagnosed are school age children 6-11 years old (Centers, 2021). This has significant clinical and developmental implications as children identified with behavior problems in school are more

likely to have continued additional academic, social, and mental health challenges (Masten et al. 2005; Montes et al., 2012).

Additionally, this study expanded the literature by testing for different effect sizes as a function of different types of behavioral difficulties. Other meta-analyses, (i.e., Silva et al., 2018) have included hyperactivity or impulsivity in the categorization of externalizing symptoms. In the current analysis, we examined each of these outcomes separately to determine if there was a difference in association between prenatal stress and each of these types of behavior.

### ***ADHD Symptoms***

Finally, there was a small but significant association between prenatal stress and ADHD symptoms in school-aged children and adolescents. This finding is consistent with a similar meta-analysis by Manzari and colleagues (2019), which reported children of mothers with high levels of prenatal stress were more likely to develop ADHD than those not exposed. However, the current analysis revealed less heterogeneity on the association between prenatal stress and ADHD symptoms than reported by Manzari and colleagues (2019). This finding suggests less variability in effect sizes across identified studies in the current analysis and potentially a more robust association than previously reported. This difference could be a result of the more stringent inclusion criteria of the current analysis, like the inclusion of only prospective studies. Prospective studies are considered methodologically more rigorous than retrospective studies, which often rely heavily on the participants recall of the past and have more difficulty controlling for confounding variables (Hess, 2004). Reliance on maternal recall of pregnancy experiences have been shown to be skewed by current life events (i.e., child diagnoses) or maternal mood, that may negatively impact perceptions of child behavior (Fergusson et al., 1993; Grizenko et al., 2012). To our knowledge, this is the first meta-analysis to explore this

association using only prospective studies. However, only 11 studies were identified in the current analysis, highlighting a continued need for well-designed longitudinal studies that evaluate ADHD symptoms as an outcome.

### ***Moderation Analysis: Stressor Type***

The second aim of the study was to evaluate whether stressor characteristics, specifically type of exposure, would moderate the association between prenatal stress and emotional or behavioral outcomes. In the current analyses, the type of prenatal stressor did not moderate the association between prenatal stress and internalizing or externalizing symptoms in school aged youth.

In the current study, initial article coding utilized five categories to describe the prenatal stressor. However, there were too few studies in some of these categories (i.e., trauma, daily hassles) to conduct a subgroup analysis. Additionally, studies frequently combined stressors making it challenging to group articles by stressor type. As a result, subgroup analysis of the type of stressor was limited to the categories of *prenatal stress* (i.e., perceived stress or distress, stressful life events) and *maternal mental health symptoms*. The inability to adequately group studies by stressor type may contribute to the lack of findings.

This is one of the few, if only, studies to explore diversity in prenatal stressor phenotypes without excluding any stressor types. Other authors have restricted the scope of their meta-analyses to a particular prenatal stressor which has allowed them to explore variations within those stressor types. For example, Bussieres and colleagues (2015), reported that pregnancy specific anxiety was the strongest predictor of negative birth outcomes while Madigan and colleagues (2018) reported a significantly larger effect size associated with maternal prenatal depression than anxiety in childhood developmental outcomes. Still further, Manzari et al.



(2019) showed significant differences in the effect of perceived compared to objective prenatal stress in child developmental outcomes. Although the current study sought to more broadly address potential variability in the impact of stressor type, the lack of consistency in categorization as well as a dearth of studies assessing objective stressors made it difficult to draw inferences on how types of prenatal stress may have varying effects on offspring. In effect, prenatal stress is a highly complex and not well-defined construct. The current study continues to highlight the need to develop consistent measurement and methodology that would allow for comparison between prenatal experiences on different child developmental outcomes.

### ***Other theoretical and methodological moderators***

The third aim of this study was to identify other moderators that might contribute to differences in the effect sizes reported. Except for maternal age, none of the other identified moderators (i.e., child age or gender, maternal race/ethnicity or education, reporter of child outcome, year of recruitment, or study location) explained between-study heterogeneity in the association between prenatal stress and internalizing or externalizing symptoms in school aged youth.

It should be noted that moderation analysis was frequently limited by the available data within each study. Child age, maternal race/ethnicity, reporter of child outcome, year of recruitment were challenging to group due to differences in study reporting. When reporting these variables, studies frequently provided different sample characteristics (i.e., means and standard deviations, percentages or ranges). Additionally, studies would combine variables to create one outcome or composite outcome variable, making it challenging to group by individual characteristics. Furthermore, there were times where variables needed to be combined to create one effect size for our study, to ensure the independence of the data points used. As a result,

there was either insufficient or small sample sizes when attempting to evaluate group differences in all of these variables. These findings of methodological discrepancies may explain why prior meta-analyses of studies of prenatal stress have also failed to find moderation effects for these variables. More consistent reporting of sociodemographic variables would facilitate testing for potential moderators of the relationship between prenatal stress and youth outcomes.

Other variables examined in this study have emerged as significant moderators in other meta-analyses. In particular, previous meta-analyses have demonstrated a marginally significant to significant moderation effect of socioeconomic “risk” (which included maternal education within the categorization) on the association between prenatal stress and various child developmental outcomes (Bussieres et al., 2015; Madigan et al., 2018). But, very few meta-analyses exploring the association between prenatal stress and child developmental outcomes have used education (years of education or level of education attained) as the primary indicator of SES. Taken together these findings may suggest that maternal education alone may not have a moderating effect but rather a combination of psychosocial risk factors when acting together may influence this association.

This interpretation fits with a plethora of literature linking socioeconomic status to disparities in prenatal and postpartum healthcare. It is often reported that mothers from economically disadvantaged backgrounds are less likely to access and receive prenatal care and are at increased risk for health complications (i.e., birth complications, or mental health symptoms; Blumenshine et al., 2010; Goyal, Gay & Lee, 2010). Also, socioeconomic status, like poverty, has been linked to a variety of adverse outcomes in children starting at a very early age.

Thus, differences in findings across studies may be due to the inconsistency with which SES is reported as a construct. Class status (i.e., working class, middle/low class), income,

employment status, maternal age, and education are commonly identified variables of SES. Studies also frequently create composite variables that combine theoretical indicators of SES to indicate high and low risk characteristics. These methodological differences make it challenging to choose a sample characteristic that could be consistently used to measure this variable. In the current study, the most consistent indicator of SES reported was maternal education, with 26 out of 29 studies reporting some variation of this variable. Nonetheless, significant variability existed in how maternal education was reported. Some studies reported average education in years while others identified percentages of academic completion (i.e., those with a high school diploma, those with less than a high school diploma, those with advanced education). Again, this highlights the need for more consistent reporting between studies. Improvement in methodological constructs would help simplify study comparison or allow for researchers to identify which combination of variables put children at higher risk.

Child gender, as reported by percentage of males, did not moderate the association between prenatal stress and child/adolescent internalizing or externalizing symptoms. This is consistent with the meta-analysis by Madigan and colleagues (2018), who also found no moderating effect of gender on the association between prenatal depression and anxiety and child socioemotional development. This is surprising given the frequently reported gender differences on child emotional and behavioral outcomes. It is often reported that girls experience higher rates of internalizing problems, while boys have a higher rate of externalizing problems (Center, 2021; Ihle et al., 2002; Rescorla et al., 2012).

The consistent lack of gender differences across meta-analyses may indicate uniform effects of prenatal stress on boys and girls. Alternatively, the findings may hide contrasting gender differences that wash each other out across contexts and development. For instance,

prenatal stress may predict more negative outcomes for younger boys and for older girls (Leadbeater et al., 1999; Sutherland & Brunwasser, 2018; Telzer & Fuligini, 2013). Future studies should continue to explore various developmental and environmental factors that could contribute to the association between prenatal stress and child/adolescent emotional and behavioral challenges.

Finally, study location also did not emerge as a significant moderator. Due to the lack of geographical diversity reported, there were insufficient numbers per subgroup to run moderation analysis for internalizing and externalizing symptoms in non-Westernized countries. For this reason, the current analysis for location was split between studies conducted in North America and Europe, with no moderating effect found on the association between prenatal stress and internalizing or externalizing symptoms. This finding highlights that a large percentage of research on prenatal stress is conducted in Westernized countries whose outcomes may be different from those in other parts of the world. Previous studies have shown significant moderating effects on the association between prenatal depression and negative birth outcomes by country location, with a stronger association in those living in developing countries (Grote et al., 2010).

The exclusion of retrospective studies may have contributed to the lack of geographical diversity in the current sample. In a scoping review on prenatal stress and child development in low- and middle-income countries, Buffa and colleagues (2018), found that studies in low- and lower-middle income countries represented 15% and 25% of the studies reviewed respectively. In their review, Buffa and colleagues found six studies that analyzed prenatal stress and childhood behavioral outcomes in non-Western countries, five with a significant relationship reported. Only one of these studies utilized a prospective design, highlighting a bias in the

research to Western or more economically advantaged countries in this particular sample. There is clearly a need for studies that explore the effects of prenatal stress in more economically and culturally diverse locations.

### **Strengths and Limitations of the Current Meta-Analysis**

#### ***Limitations***

Meta-analytic results from the current study should be interpreted in the context of several limitations. For example, we were unable to evaluate the role of timing and chronicity of maternal prenatal stress on youth socioemotional outcomes. While there have been increased efforts to evaluate stress across pregnancy there continues to be a lack of understanding of the impact of these experiences in older children and adolescents. Although several longitudinal studies were identified in the current meta-analysis, there were not sufficient studies that provided detailed enough information to use timing of exposure as a moderating variable. Frequently authors collapsed stress scores across pregnancy. Additional research is needed to explore the impact of timing of exposures is needed to understand whether there are critical periods during pregnancy that could have the largest impact on child development.

Additionally, we were unable to evaluate the role of genetics or postpartum experiences on the development of socioemotional difficulties in school age children. Developmental models of stress suggest multiple pathways for how prenatal exposure may lead to long term negative outcomes (Talge et al., 2007), and that children can be buffered from the negative experiences of prenatal stress through mechanisms such as increased caregiving and secure attachment; (Bergman et al., 2008; Glover, 2011; Grant, McMahon, Reilly, & Austin, 2010). Additional research is needed to integrate process research with studies of prenatal stress to understand what mediating mechanisms link prenatal stress with negative outcomes among school-age children

and what moderators might help break that connection. McLean et al., 2021; O'Connor et al., 2003; Pawlby et al., 2009; Rice et al., 2019

### *Strengths*

Despite several limitations, the current meta-analysis had many strengths. First this meta-analysis exclusively focused on prospective studies to address the enduring association between prenatal stress and emotional and behavioral outcomes in children and adolescents. Using prospective studies has the major benefit of avoiding recall bias which provides support for potential causal influences.

Secondly, the current study contributes to the existing literature by providing evidence for a robust and persistent association between prenatal stress and internalizing and externalizing symptoms in youth. Specifically, we have established that this association extends to the school age period, by focusing on children ages 5-18 years old. Thirdly, to our knowledge this is the first study to attempt to tease apart difference in stress phenotype. Previous meta-analyses have generally focused on specific prenatal stressors (i.e., prenatal IPV exposure or prenatal mental health) on varying child outcomes. Due to individual study reporting, there were limited conclusions that could be drawn for the data available again highlighting a need for future research in this area.

Finally, there were efforts to minimize publication bias through searching of the grey literature including dissertation databases and searching of reference lists and conference presentations. Several authors provided unpublished correlations in response to our email request about the published articles. Furthermore, post-hoc analyses were conducted to assess potential effects of publication bias and to ensure that study findings remained robust to these effects.

### **Implications and Future Directions of the Current Meta-Analysis**

The results of this study in conjunction with the existing literature show a robust connection between prenatal stress and negative child outcomes. Review and analysis of the literature within this study also highlight the need to improve how we operationalize variables in the prenatal stress literature. A consensus on how to collect and label relevant variables is needed to be able to draw more precise conclusions on the role of prenatal stress on child/adolescent outcomes. Additionally, SES is a commonly identified construct impacting this association however, lack of consistency in reporting makes it difficult to draw definitive conclusions on its impact. A common set of clearly defined demographic variables should be included in all studies to make sample comparison easier. Future studies should incorporate multiple, clearly defined, SES factors as well as non-income based predictors of poverty that could contribute to the relationship between prenatal stress and child and adolescent outcomes.

There is also a need to continue to follow children and their families longitudinally well into the school age years and to test for mediating and moderating processes that explain how and for whom and under what conditions prenatal stress is most influential. Such studies would also facilitate the identification of protective variables that help youth withstand the negative effects of prenatal stress. Together, such data would further elucidate risk and resiliency factors in childhood that contribute to mood and behavior symptom presentation in school age children. Additional research in non-Westernized countries is also needed to better understand the impact of prenatal experiences in other countries.

Finally, from a clinical and public health perspective, findings from this study augment the current literature and amplify the message that prenatal maternal health is a major public health concern that warrants continued support by investing in targeted prevention and

intervention efforts. Evaluation of maternal stress should be a routine part of prenatal and postpartum care. Integrating maternal wellness measures into routine child physician appointments could allow for continued monitoring of maternal stress. Early detection of maternal stress and improved interventions would contribute to decreasing symptom presentation during childhood and beyond.



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**Appendix A. Example of Search Strategy**

( pregnancy or pregnant or prenatal or antenatal or antepartum or expectant mother )

AND

( stress, psychological OR distress OR psychopathology OR mood disorders OR depression OR anxiety OR post traumatic OR posttraumatic OR PTSD OR intimate partner violence OR domestic violence OR partner abuse OR trauma OR "daily life hassles" )

AND

( child\* OR adolescents OR adolescence OR youth OR teenager OR teen OR "school age" )

AND

( Autism OR autistic OR ADHD OR attention deficit OR oppositional defiant disorder OR conduct disorder OR ((externaliz\* OR internaliz\*) (behavior OR disorders OR symptoms)) OR ((child\* OR neuro\* OR cognitive) OR (development\* OR behavior\* OR disorders)) )

**Appendix B. Study Eligibility Screen Form**

# Data collection form

**General Information**

Study ID	
Date form completed ( <i>dd/mm/yyyy</i> )	
Name/ID of person extracting data	
Reference citation	
Country of Study	
Language of Study	
Study author contact details	
Publication type ( <i>e.g. full report, abstract, letter</i> )	
Original, Peer Reviewed article	
Notes:	

**Study eligibility**

Study Characteristics	Eligibility criteria <i>(Insert inclusion criteria for each characteristic as defined in the Protocol)</i>	Eligibility criteria met?			Location in text or source ( <i>pg &amp; ¶/fig/table/other</i> )
		Yes	No	Unclear	
Type of study	Prospective Study? (Y/N) See end of document for definition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	If Not Prospective study; Identify study type:  1. Included as prospective study 2. Included as other study design 3. Excluded	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Methodology	Identify Type of Stressor Evaluated:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

	<ol style="list-style-type: none"> <li>1. Stress/Distress</li> <li>2. Daily life hassles</li> <li>3. Psychopathology (Depression, anxiety, PTSD)</li> <li>4. Trauma</li> <li>5. Natural Disasters</li> </ol> <p>Exclude – Prenatal Toxin exposure, drug and alcohol exposure.</p>		
	<p>How was maternal stressor measured?</p> <ol style="list-style-type: none"> <li>1. Self-report measures</li> <li>2. clinician administered interviews</li> <li>3. health records</li> <li>4. observations</li> <li>5. maternal physiological measures (e.g., maternal cortisol)</li> </ol>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
	<p>Identify Child behavioural or emotional outcome:</p> <ol style="list-style-type: none"> <li>1. Neurocognitive Disorders/Cognitive</li> <li>2. Externalizing Disorders</li> <li>3. Internalizing Disorders</li> <li>4. Disruptive Behaviors</li> </ol>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
	<p>How was child outcome measured?</p> <ol style="list-style-type: none"> <li>1. self-, parent-, or teacher-report questionnaires</li> <li>2. clinician administered interviews,</li> <li>3. health or school records</li> <li>4. observations</li> </ol>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Participants	<p>Target Population</p> <p>_Kids age 5-18 years old</p>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
<p>INCLUDE <input type="checkbox"/></p>		<p>EXCLUDE <input type="checkbox"/></p>	
Reason for exclusion			
Notes:			

**Appendix C. Qualtrics XM Coding Manual**

**Prenatal Stress - Dissertation**

---

**Start of Block: Study Identifying Information**

Q1 Study ID

---

Q2 Study Title

---

Q3 Year of Publication

---

Q4 APA Formatted  
Citation

---

Q5 Publication Type

- Peer Reviewed Journal Article (1)
- Dissertation (2)
- Book (4)
- Other (3)

-----

Q37 Language of Article

- English (1)
  - Other (EXCLUDE) (2)
- 

Q6 Aim of the Study

\_\_\_\_\_

-----

Q38 Does the study still fit inclusion criteria?

- Include (Continue to Next Section) (1)
- Exclude (Continue to FINAL Inclusion/Exclusion Criteria Section) (2)

**End of Block: Study Identifying Information**

---

**Start of Block: Predictor Variables (Pregnancy Variables - Needed for Inclusion/Exclusion)**

Q8 Did Stressor Occur During Pregnancy

- Prenatal Only (1)
  - Prenatal & Postpartum (2)
  - Postpartum Only (EXCLUDE) (3)
  - No Prenatal Variable (EXCLUDE) (4)
-

Q9 Type of Stressor Evaluated (Check all that Apply)

- Stress/Distress (1)
- Daily Life Hassles (2)
- Psychopathology/Mental Health Symptoms (3)
- Trauma (4)
- Natural Disasters (5)
- Grief/Loss (7)
- Nicotine/Alcohol (8)
- Drug Exposure (i.e Cocaine) (9)
- Other (11)

---

*Display This Question:*

*If Type of Stressor Evaluated (Check all that Apply) = Other*

Q 9.1 (If other) Indicate other Stressor identified

---

Q9.2 Number of stressors evaluated: (Based on the number of boxes checked above)

---



Q10 What instrument was used to measure maternal stressor? (Name all)

---

Q11 How was the stressor measured?

- Self-Report (1)
- Clinician administered interviews (2)
- Health Record (3)
- Observations (4)
- Maternal Physiological Measures (e.g., cortisol) only (EXCLUDE) (5)
- Multiple Assessments Used (6)

*Display This Question:*

*If How was the stressor measured? = Multiple Assessments Used*

Q11.1 If Multiple Assessments Used: (Check all that apply)

- Self-Report (1)
- Clinician Administered Interviews (2)
- Health Records (3)
- Observation (4)
- Maternal Physiological Measures (5)

Q12 Type of Variable - How was the stressor variable identified?

- Continuous Variable (1)
  - Categorical Variable (2)
  - Mixed/Multiple Types of Measurement (3)
- 

Q13 Timing of Stressor During Pregnancy

- 1st Trimester Only (1 - 12 Weeks Gestation) (1)
  - 2nd Trimester Only (13 - 26 Weeks Gestation) (2)
  - 3rd Trimester Only (27+ Weeks Gestation) (3)
  - Combination/Other (Explain) (4)
  - Not Identified (5)
- 

*Display This Question:*

*If Timing of Stressor During Pregnancy = Combination/Other (Explain)*

13.1 Combination Explain - Timing of Prenatal Stressor During Pregnancy

---



---

Q14 Does the study still fit inclusion criteria?

- Include (Continue to Next Section) (1)
- Exclude (Continue to FINAL Inclusion/Exclusion Criteria Section) (2)

**End of Block: Predictor Variables (Pregnancy Variables - Needed for Inclusion/Exclusion)**

---

**Start of Block: Outcome Variable (Child Variables Needed for Inclusion/Exclusion)**

Q15 Was there a child outcome measured in this study?

- Yes (1)
- No (2)

Q22 Child Age By Category

- Under 5 Years Old (1)
- 5 - 18 Years Old (2)
- Older than 18 Years old (3)
- Mixed (If Yes: Indicate Age Range Next) (4)
- Unsure/Not identified (5)

*Display This Question:*

*If Child Age By Category = Mixed (If Yes: Indicate Age Range Next)*

Q23 If Mixed Category Selected Indicate Age Range Below

---

Q17 Child Age

	Mean (1)	Standard Deviation (2)	Median (4)	Range (5)	Specified Group in Study (6)
Child Age (1)					
Child Age 2 (5)					
Child Age 3 (6)					
Child Age 4 (7)					

-----

Q107 Describe how child age is reported if different from above.

\_\_\_\_\_

-----

Q39 Child Behavioral & Emotional Outcomes Evaluated

- Neurocognitive Disorders (i.e. Autism) (1)
- Cognitive Outcomes (i.e. Language, IQ) (2)
- Externalizing Disorders (i.e. ADHD, ODD, CD) (3)
- Externalizing Symptoms/Disruptive Behaviors (i.e. Aggression, Hyperactivity) (4)
- Internalizing Disorders (i.e. Depression, Anxiety, PTSD) (5)
- Internalizing/Mood Symptoms (6)
- Multiple Behavioral & Emotional Outcomes Evaluated (7)

*Display This Question:*

*If Child Behavioral & Emotional Outcomes Evaluated = Multiple Behavioral & Emotional Outcomes Evaluated*

Q40 If Multiple Behavioral & Emotional Outcomes Evaluated: Indicate Which

- Neurocognitive Disorders (i.e. Autism) (1)
- Cognitive Outcomes (i.e. Language, IQ) (2)
- Externalizing Disorders (i.e. ADHD, ODD, CD) (3)
- Externalizing Symptoms/Disruptive Behaviors (i.e. Aggression, Hyperactivity) (4)
- Internalizing Disorders (i.e. Depression, Anxiety, PTSD) (5)
- Internalizing/Mood Symptoms (6)

Q19 Name all Child Variables Measured (Instruments)

---

-----

Q20 How was the child's behavior (outcome measure) assessed?

- Self Report (1)
  - Other Reports (i.e. Parent/Teacher) (2)
  - Clinician Administered Interviews (3)
  - Health or School Records (4)
  - Observation (5)
  - Physiological Measures (e.g., cortisol) only (EXCLUDE) (6)
  - Multiple Assessments Used (7)
- 

*Display This Question:*

*If How was the child's behavior (outcome measure) assessed? = Other Reports (i.e. Parent/Teacher)*

Q20.1 For Other Reports:

- Parent (1)
  - Teacher (2)
  - Both (3)
- 

*Display This Question:*

*If How was the child's behavior (outcome measure) assessed? = Multiple Assessments Used*

Q20.2 If Multiple Assessments Used: (Check all that Apply)

- Self Report (1)
- Other Reports (i.e. Parent/Teacher) (2)
- Clinician Adminstered Interviews (3)
- Health or School Records (4)
- Observation (5)
- Physiological Measures (e.g. cortisol) (6)

-----

Q77 Type of Variable - How was the child variable identified?

- Continuous Variable (1)
- Categorical Variable (2)
- Mixed/Multiple Types of Measurement (3)

-----

Q21 Does the study still fit inclusion criteria?

- Include (Continue to Next Section) (1)
- Exclude (Continue to FINAL Inclusion/Exclusion Criteria Section) (2)

End of Block: Outcome Variable (Child Variables Needed for Inclusion/Exclusion)

---

Start of Block: Study Methodology

Q7 Prospective Study?

- Yes (1)
- Maybe/Unsure (2)
- No (3)

-----

Q115 Is a longitudinal cohort identified?

- Yes (1)
- No (2)

*Skip To: Q116 If Is a longitudinal cohort identified? = Yes*

-----

Q116 If yes, what is the name of the cohort

\_\_\_\_\_

-----

Q66 Did the study have an experiment and control group?

- Yes (1)
- No (3)

-----

Q67 Describe Groups Identified in the study

\_\_\_\_\_

-----



Q68 Do ANY of the groups fit Inclusion Criteria

- Yes (1)
- Maybe (2)
- No (3)

Q79 Reported Sample Size

\_\_\_\_\_

*Display This Question:*

*If Prospective Study? = Yes*

Q80 Does study report change in sample size (attrition or subsets analyzed)

- Yes (4)
- No (5)

*Display This Question:*

*If Does study report change in sample size (attrition or subsets analyzed) = Yes*

Q81 Describe change in sample size or attrition rate

\_\_\_\_\_

Q69 Include/Exclude

- Include (Continue to Next Section) (1)
- Exclude (Continue to FINAL Inclusion/Exclusion Criteria Section) (2)

**End of Block: Study Methodology**

Start of Block: Maternal Descriptive Characteristics

Q49 Final Number of Women who Participated

Q32 Maternal Age

	Mean (1)	SD (2)
Maternal Age (1)		

Q41 Maternal Age Reported In Alternative Way (Describe)

Q33 Average Income

	Mean (1)	Standard Deviation (2)
Average Income (1)		

Q43 Income Reported Differently (Describe)

---



---

Q34 Education (Categorical)

	Frequency (1)	Percentage (2)
Less than High School (1)		
High School/High School Equivalency (2)		
Some College (4)		
College Degree or Higher (5)		

---

Q42 Average Education

	Mean (1)	Standard Deviation (2)
Average Years of Education (1)		

Q105 Describe how education reported if different from above?

Q35 Race Ethnicity

	Frequency (1)	Percentage (2)
White (1)		
Black/African American (2)		
Hispanic/Latino (3)		
Asian/Pacific Islander (5)		
American Indian/Native Alaskan (6)		
Biracial/Multiracial (7)		

Q106 Describe how Race/Ethnicity is reported if different from above.

---

End of Block: Maternal Descriptive Characteristics

---

Start of Block: Covariates Measured

Q49 Where other obstetric variables measured?

- Gestational Age (1)
- Birth Weight (2)
- Maternal Smoking/Drinking (3)
- Other (4)

---

*Display This Question:*

*If Where other obstetric variables measured? = Other*

Q108 Describe Other

---

---

Q50 Was Maternal Postpartum Psychopathology Measured

- Yes (1)
  - No (2)
  - Unsure (3)
-

Q51 Was Maternal Parenting Measured

- Yes (1)
- No (2)
- Unsure (3)

Q52 Were child exposure to stressful life events measured? (Anytime in lifetime postpartum)

- Yes (1)
- No (2)
- Maybe (3)

Q53 List all covariates and how measured (what instruments were used?)

\_\_\_\_\_

**End of Block: Covariates Measured**

**Start of Block: Child Descriptive Characteristics**

Q46 Total Number Children Participating

\_\_\_\_\_

Q47 Total Number Children/Families Lost to Follow up (Describe Attrition)

\_\_\_\_\_

Q44 Child Sex/Gender (Frequency/Percentage)

	Frequency (1)	Percentage (2)
Male (1)		
Female (2)		
Other (3)		

-----

Q109 Describe Gender/Sex if described differently than above.

\_\_\_\_\_

-----

Q50 Child Race/Ethnicity

	Frequency (1)	Percentage (2)
White (1)		
Black/African American (2)		
American Indian or Alaska Native (3)		
Asian (4)		
Native Hawaiian or Pacific Islander (5)		
Other (6)		

-----

Q110 Describe if Race/Ethnicity is described differently than above

\_\_\_\_\_

-----



Q75 Education (Categories)

- Preschool (1)
- Elementary School (2)
- Middle School/Junior HS (3)
- High School (4)

---

Q76 How was Education of Child described (if at all)

---

**End of Block: Child Descriptive Characteristics**

---

**Start of Block: Study Location**

Q55 Country

---



---

Q56 City, State (if provided)

---



---

Q57 Location Description

- Urban (1)
- Suburban (6)
- Rural (2)
- Multi-site Study (4)
- Can't Tell (7)

---

Q59 Describe Multi-site Location

---

End of Block: Study Location

---

Start of Block: Test Statistics

Q82 Was an effect size reported? (Cohen's d) (Effect size is a quantitative measure of the magnitude of a phenomenon)

Yes (1)

No (2)

---

Q83 What was the direction of the effect of the maternal stressor on the the childhood outcome?

Positive (1)

Negative (2)

---

Q84 Information for each maternal stress variable measured

	Mean (1)	SD (2)	Sample size (n) (4)	Name Stressor (i.e. EPDS) (5)
Maternal Stressor # 1 (1)				
Maternal Stressor # 2 (2)				
Maternal Stressor# 3 (4)				
Maternal Stressor #4 (5)				

-----

Q85 Identify the maternal stressors labeled in the table above:

\_\_\_\_\_

-----

Q86 Information for each child outcome variable

	Mean (1)	SD (2)	Sample Size (n) (3)	Name Child variable (i.e IQ) (4)
Child Outcome # 1 (1)				
Child outcome #2 (2)				
Child Outcome #3 (3)				
Child Outcome #4 (4)				

-----

Q87 Identify the child outcome variable labeled in table above:

\_\_\_\_\_

-----

Q64 (Information about the null hypothesis significance test) Main Test Statistics Used In Analysis

- Correlation (1)
- Regression (2)
- Moderation (3)
- Mediation (4)
- Structural Equation Modeling (5)
- ANOVA (7)
- Odds Ratio (8)
- Other/Multiple (9)

-----

Q65 Describe Tests Statistics used in the Article

\_\_\_\_\_

-----

Q88 Value of the independent t-statistic or square root of F-Test on one-factor ANOVA

\_\_\_\_\_

-----

Q89 Degrees of freedom for test (in the denominator) for independent t-statistic or square root of F-Test on one-factor ANOVA

\_\_\_\_\_

-----

Q90 p-value from test (for independent t-statistic or square root of F-Test on one-factor ANOVA)

---

Q91 Dependent t-statistic

---

Q92 Degrees of Freedom for test statistic (in denominator) (for dependent t-statistic)

---

Q93 p value from test (for dependent t-statistic)

---

Q94 F-Statistic (when included in a multifactor ANOVA)

---

Q95 Degrees of Freedom in denominator of F-Test (when included in a multifactor ANOVA)

---

Q96 p-value from F- Test (when included in a multifactor ANOVA)

---

Q97 # of variables in multifactored ANOVA

---

Q98 If correlation completed what was the r- value

---

Q99 P-value from correlation test

---

Q113 Regression analysis

	Insert Value Given in Article (1)
Standardized Regression Coefficient (Beta) (1)	
Standard deviation of DV (2)	
Unstandardized Regression Coefficient (B) (3)	
Standard deviation of DV (4)	

---

Q114 P-value in regression analysis

---

Q104 OTHER Or Multiple tests indicated: If other statistic reported not indicated here describe below

---

Q105 OTHER or Multiple Tests indicated: Describe test statistic/p-value (Ex:  $Z = 4.4, p < 0.001$ )

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Q102 Is more information needed?

Yes (1)

No (2)

Q111 Describe any questions or concerns or other confusion.

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End of Block: Test Statistics

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Start of Block: Final Inclusion/Exclusion Criteria

Q60 More information needed \*\*contact author\*\*

Yes (9)

No (10)



Q61 Author email

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Q62 Final Inclusion/Exclusion

- Include (1)
  - Exclude (2)
  - More information needed (4)
- 

Q63 Reason for Exclusion

- Wrong Predictor Variable (Maternal/Pregnancy) (1)
  - Wrong Outcome Variable (Child) (2)
  - Language (3)
  - Methodology (4)
  - Other (5)
- 

*Display This Question:*

*If Reason for Exclusion = Other*

Q78 If Excluded for Other reasons (Describe)

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**End of Block: Final Inclusion/Exclusion Criteria**

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**Start of Block: Coding and Coder Characteristics**

Q70 Coder Name

- Michelle Gilchrist (1)
- Meg Nair (2)
- Leslie Castillo (4)
- Abby Bushnell (5)
- Other (6)

Q71 Date Coded

\_\_\_\_\_

Q73 When did you code this Article?

- 12:00 AM - 5:59 AM (1)
- 6:00 AM - 11:59 AM (4)
- 12:00 PM - 5:59 PM (2)
- 6:00 PM - 11:59 PM (3)

Q72 In minutes, how long did it take you to code this study?

\_\_\_\_\_

Q74 Notes: Provide any notes about the study or concerns you have regarding your codes

\_\_\_\_\_

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**End of Block: Coding and Coder Characteristics**

**Appendix D. References Included in Meta-Analysis**

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