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The Correlation Between Maternal Postpartum Depression and Child Psychopathology

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List of Abbreviations

Full Name	Abbreviation
Dizygotic Twins	DZ
Gene by Environment	GxE
Socioeconomic Status	SES
Monozygotic Twins	MZ
Odds Ratio	OR

Maternal Psychopathology

Full Name	Abbreviation
Alcohol Abuse Disorder/Alcoholism	AAD
Antisocial Personality Disorder	ASPD
Conduct Disorder	CD
General Anxiety Disorder	GAD
Major Depressive Disorder	MDD
Panic Disorder	PD
Postpartum Blues	PPB
Postpartum Depression	PPD

Child Psychopathology

Full Name	Abbreviation
Attention Deficit and Hyperactivity Disorder	ADHD
Child and Adolescent Psychiatric Assessment	CAPA
Conduct Disorder	CD
Oppositional Defiant Disorder	ODD
Separation Anxiety Disorder	SAD

Abstract

Background: Postpartum depression (PPD) is a phenomenon that affects nearly 10-15% of pregnancies in the US. It is characterized by depressed mood or anhedonia and lasting for more than 2 week. PPD changes how moms interact with family members and child rearing behavior. Depression is a phenomenon that is also known to affect the psychopathology of children. However, the specifics of how postpartum depression impacts children remains controversial. Many studies do not control for major depressive disorder which makes it difficult to disentangle the impact depression has within the first year of life. Furthermore, other PPD risk factors may be confounding the effect PPD has on child psychopathology.

Aims:

1. Identify risk factors for PPD in the areas of: A) birth outcomes, B) prenatal behaviors, C) maternal mental health, and D) SES
2. Identify associations between PPD and child psychopathology
3. Identify associations between relevant child psychopathology (identified in aim 2) and select PPD risk factors (identified in aim 1).
4. Determine the GxE interaction for select birth outcomes and select child psychopathology.

Methods: This is a retrospective cohort study from the Virginia Twin Study of Adolescent Behavioral Development (VTSABD). There were 855 moms included for analysis with 7.46% reporting PPD and 1710 relevant twin pairs.

Results:

1. PPD was associated with: A) child fretting and staying with other family members, B) drinking alcohol during pregnancy, C) major depressive disorder and panic disorder, and, D) marital satisfaction
2. PPD was associated with ADHD and conduct disorder with the main driver being ADHD.
3. ADHD was linked to: A)fretting and staying with other family members, B) drinking alcohol at least once per week C) postpartum depression and alcoholism, and D) low income and low familial education
4. Twin Correlations reveal that fretting and ADHD is driven by genetics. Staying with other family members is driven by the environment. PPD increases genetic heritability of children's ADHD.

Discussion: Having postpartum depression increases the odds that children have ADHD by increasing the genetic variance.

Chapter 1: Background

Postpartum Depression Disorder (PPD) and Prevalence

Pregnancy and childbirth is often a wonderful and rewarding process for many women. However, it can also be a scary one filled with anxiety and unforeseen obstacles. With maternal mortality on the rise, prevention and identifying underlying causes is key (MacDorman et al., 2016). One of these underlying causes of maternal mortality is PPD and suicide (Oates, 2003).

Many changes in the body occur during pregnancy which bring forth and exacerbate underlying mental health issues. These mood and cognition changes can lead to issues such as postpartum blues, depression, and psychosis (Ohara, 1987).

Postpartum blues (PPB) is the least severe depressive disorder occurring after pregnancy and is often termed “baby blues”. PPB is a psychological phenomenon of a depressed mood. It usually has an immediate onset after birth and affects 60-80% of women (Henshaw, 2003). This phenomenon usually resolves on its own within 1-2 weeks.

Postpartum Psychosis is the most severe mental health disorder, often requiring hospitalization. It occurs in less than .2% of women (Natasha, et al. 2017). Psychosis usually peaks around 4 weeks after delivery and symptoms include paranoia, mood shifts, hallucinations, delusions and suicidal/homicidal thoughts (Earls, 2010; Kahn, Wilson, & Wise 2005).

Postpartum depression (PPD) is a serious psychiatric disease that affects between 10-15% of women (Seyfried & S. M. Marcus, 2003; Natasha. et al., 2017). Postpartum depression is an episode of major depressive disorder (MDD) whose onset is usually between 6 weeks and 3 months after giving birth, but can happen anytime within a year of birth. The peak time for a

major episode of PPD is usually around 6 weeks postpartum and minor episodes usually occur within months two and three (kahn et al., 2002). Mothers diagnosed with PPD must meet the diagnostic criteria for lifetime MDD and occur during the postpartum period.

To be diagnosed with PPD/MDD, women must have at least 5 of the following symptoms: depressed mood, loss of pleasure (anhedonia), fatigue, loss of interest, insomnia, poor concentration, feelings of worthlessness/guilt, or recurring suicidal thoughts. At least one of those symptoms must be a depressed mood or anhedonia (American Psychiatric Association, 2013)**.** Additionally, women must experience these symptoms for more than 2 weeks.

Postpartum depression (PPD) has more than just physiological consequences for the mother. Children of depressed mothers suffer from various physiological, social, and economic consequences. PPD impacts how the mother interacts with family members and their newborns (Wijngaarden, Schene, & Koeter, 2004; Letourneau, Tramonte, & Willms, 2013). Additionally, These children are more likely to have emergency department visits and sick visits during their lifetime. They, also, are less likely to utilize well-child visits. This creates a larger economic burden on healthcare systems and the families using them (Sills et al., 2007). Not only is there an economic impact, but an impact on child development as well. Offspring of depressed mothers are more likely to experience cognitive problems and depression (Conroy, et al., 2012). In addition, children of PPD mothers are at greater risk of abuse and neglect (Earls, 2010). With the severity of impact that PPD has on mothers and their family, identifying causes and later risk in children is important in mediating their impact and helping women through this difficult period.

Risk Factors for Postpartum Depression

Many risk factors for PPD have been identified in previous studies to help predict mothers at highest risk for developing the mental health disorder. These risk factors usually fall into one of three categories: A) birth outcomes and complications, B) medical and mental health history, or 3) social and environmental factors.

Birth Outcomes and Complications: Birth outcomes and complications have shown small associations with PPD. These complications often induce additional stresses in the mother and increase their risk of PPD (Silverman et al., 2017). Obstetric complications during pregnancy such as: caesarean section, instrumental delivery, premature delivery, and excessive bleeding intrapartum are all considered small risk factors for PPD (Roberson et al., 2004). A possible reason for this is that mothers who had cesarean sections (c-section) waited longer to hold their babies for the first time and hold them for less time. They also tend to have a less positive view about the baby and pregnancy. Additionally, mothers interact with their children less once they are home during the first 5 months. However, mothers who undergo c-section after pregnancy are more likely to be fatigued and may account for the decreased stimulation with children (Dimmatea et al., 1996). Conversely, other studies found no correlation between c-section and PPD (Carter, Frampton, & Mulder 2006; Hutton, et al. 2015).

Other birth outcomes, like hospitalizations, neurological deficits and low-birth weight can also increase the risk of PPD (Ghaedrahmate et al. 2017;Mathisen et al., 2013; Barkmann et al 2015, Helle N, et al. 2015, Silverman et al., 2017). Gestational age is another factor that seems to play a minor role in PPD, however, the literature is mixed on its role and if the relationship is direct or indirect (Drewett, Blair, & Emmett, 2004; Nielson et al.,2005; Silverman et al. 2017,)

Medical and Mental Health history: Some factors that lead to PPD cannot be prevented. However, identifying women with these risk factors is important in making sure they are well supported through their natal period. A previous diagnosis of major depressive disorder (MDD) is one of the largest predictors of PPD in women (Ghaedrahmate et al. 2017; Lanchester, et al. 2010). Additionally, MDD and anxiety disorders are often tied together. Because of this, anxiety disorders are often seen to have a large predictive value on PPD as well. However, previous anxiety disorders can also lead to other postpartum mental health complications such as severe prenatal and postpartum anxiety onsets (Natasha et al. 2017; Opp. et al., 2009; Milgrom et al., 2008). Other predictive factors include personality disorders (like obsessive-compulsive personality disorder) and bipolar disorders, however these are more predictive of psychosis (Akman et al., 2007).

Mothers with a history of substance use and abuse also have higher rates of PPD than their non-substance using counterparts. Alcohol abusers see higher rates of PPD. Furthermore, it is estimated that smoking increases the incidence of PPD by 1.7 times (Kahn, Wilson, & Wise, 2005; Dagher & Shenassa 2012). However, it is unclear whether or not this pattern is tied to maternal mental health and undiagnosed issues or is a unique factor contributing to PPD (Katon, Russo, & Gavin, 2014; Homish et al., 2004).

Medical complications before and during pregnancy can also create an increased risk for PPD. For women previously diagnosed with MDD, there is an even greater risk for PPD if they have gestational diabetes or if they are of an older age during the pregnancy. For women without a previous diagnosis of MDD, risk factors for PPD included being a younger age, having a

cesarean section (c-section), and premature birth (Silverman et al., 2017). However, these complications were often minor and the largest predictor remains previous mental health history.

Social and Environmental factors: Not only do birth outcomes, birth complications and health history play a role in predicting postpartum depression, but social and environmental factors as well. Low-income mothers have higher rates of postpartum mothers than do their higher earning counterparts (Kahn, Wilson, & Wise, 2005). Links between low income families, rates of PPD are as high as 25% (Rafferty, Mattson, Earls, Yogman, & , 2018). Employment status and education are also seen as contributing factors to PPD, with the highest rates of PPD being seen in low-income and unemployed groups (Huang, et al. 2015, Miyake, et al. 2015). However, the effect of income was only seen as a small one in comparison to other risk factors (Robertson et al., 2004)

A mother's social support system also plays a role in the development of PPD. Mothers that lack community ties and single mothers often struggle more with PPD than those who are married and with a partner who supports the pregnancy (Opp. et al., 2009). Younger mothers are often the most likely to struggle with these issues and are, therefore, more likely to have PPD.

Child's temperament may also be another environmental factor that plays a role in mothers' PPD. If the child has trouble interpreting cues, is overly fussy or has trouble sleeping, there may be an increase in PPD (Rafferty, 2018). In an observational study of children, those with depressed mothers cried more. As the children aged, reports of crying and depression decreased (Milgrom, 1995). This research was reconfirmed later in which an association was found between PPD and fussiness (Quist et al., 2019). Research has also found that PPD mothers

are less responsive to children's cues and interact with them less (Schuetze & Zeskind 2001). This may account for the increase in crying behavior.

The Association between Postpartum Depression and Internalizing Behavior

One set of cognitive problems that children of depressed mothers may have is internalizing issues. Internalizing behavior describes an inappropriate self-regulation of mood and emotion that is directed inward. Manifestations of internalizing behaviors include depression, anxiety, social withdrawal and somatic problems. There have been several studies that have investigated the link between PPD and internalizing problems, but the results have been mixed. In 2011, a study of 708 mothers found that depression incidence was higher in offspring up to 16 years of age. However, they failed to control for MDD (Murray, et al., 2011). Subsequent studies have continued to find an association between PPD and internalizing behavior even when controlling for other maternal psychopathology (Verbeek, et al., 2012). A year later, a study of low SES offspring in the UK, replicated this finding. However, the moms' depression was by self report and not by diagnosis (Pearson, et al., 2013).

Despite these positive results, other papers have found other maternal psychopathology, such as anxiety, to explain child internalizing outcomes rather than PPD (Barker, Jaffee, Uher, & Maughan, 2011). Additionally, several studies that controlled for mothers' MDD, saw no association between internalizing behaviors and PPD. Instead, MDD was a better predictor of depression in children (Halligan et al, 2007; Hay, 2008; Naicker et al., 2012; Mars et al. 2012; Pawlby, 2009).

The Association between Postpartum Depression and Externalizing Behavior

In addition to PPD's associations with children and adolescent internalizing behaviors, there have been many studies exploring the link between PPD and externalizing behaviors. Externalizing behaviors are unhealthy emotionally processing behaviors directed outwards towards the environment, such as stealing and destruction of property. Common diagnoses included in the category of externalizing would be: Attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder (CD), substance abuse disorders and antisocial personality disorder (ASP).

The research on development of these externalizing problems due to PPD has been mixed. In a 2003 study, researchers found that PPD after birth increased the risk of violent behavior in children. However, they failed to control for MDD and the sample size was relatively small (Hay et. al, 2003). Subsequent studies from the same group found externalizing problems went away when controlling for MDD in mothers, however, decreased IQ remained (Hay, Pawlby, Waters, & Sharp, 2008). Additionally, some studies have found sex affects to be important. In a 2012 study, research found externalizing behaviors and PPD to be correlated in male offspring by self-report (Korhonen, Luoma, Salmelin, & Tamminen, 2012). In addition, several studies have found correlations between PPD and children's CD and ODD (Hay et al. 2003, Mars et al. 2012). There are many reasonings for these results. For example, because PPD may affect a mother's ability to bond with the baby, children are more at risk for developing insecure attachment which is associated with conduct disorder and other externalizing behavior problems (Earls, 2010). However, Despite these positive correlations, several others have found

no association between externalizing behavior and PPD (Hay et al. 2008, Halligan et al. 2007, Murray et al. 2011, Agnafor et al. 2013; 2011, Mars et al. 2012). In fact, in a 2011 study, a negative correlation was observed (2011, Alvarez).

Postpartum Depression Risk Factors and the Impact on Child Psychopathology

Risk factors for postpartum depression may also be common risk factors for internalizing and externalizing behavior in children. This section will explore the three areas of risk factors for mothers' PPD (1. Birth Outcomes and Complications, 2. Maternal Medical and Mental Health History, and 3. Social and Environmental Factors) and their interactions with child psychopathology.

Child Birth Outcomes and Complications: Birth complications that affect the mother's PPD have limited effects on child psychopathology. In the previous section, some studies found an interaction between cesarean sections and PPD. However, this effect does not seem to extend to internalizing and externalizing behaviors in children by the time they were nine years old (Robson et al., 2015). Furthermore, delivering breech or via emergency cesarean does not increase likelihood of neurological defects in children (Whyte et al., 2004). Hospitalization was another outcome that may cause increased odds of getting PPD. However, like the previous complications, length of hospitalization does not affect children internalizing or externalizing problems (Benish-Weisman, Kerem, Knafo-Noam, & Belsky 2015)

Unlike other complications, preterm birth/low birth weight, are factors that affect both PPD and child psychopathology. Babies of extremely low birth weight (<1000g) are more likely to have ADHD, internalizing and externalizing problems, and conduct disorder but not

oppositional defiant disorder during childhood. However, the strength of these associations disappear through adolescence, with the exception of internalizing behaviors (Mathewso, et al., 2017). For children of very low birthweight (<1500 g), child behavioral outcomes were less severe, but still presented with difficulties in academic achievement, attention problems and internalizing behavior problems (Aarnoudse-Moens et al., 2009). Furthermore, problems with internalizing behavior and attention can continue on into adulthood (Hack et al., 2005).

Parental Mental Health: Maternal psychopathology is a major risk factor for future mental health disorders in children. One of the largest risk factors for PPD is MMD, which also alters childrens' outcomes. Mothers with major depressive disorder increase the risk for adolescent depression and suicide. (Foster, Garber and Durlak, 2007; Weissman et al., 1987; Wiessman et al., 1992). However, some studies have shown that fathers are the more important determining factor of children's internalizing behavior (Connell & Goodman, 2002).

Maternal mental health also increases risk of externalizing behaviors. Mother's with MDD have children with an increased risk of having conduct disorder, having issues in school, and dealing with substance abuse (Weissman et al., 1987, Weisman et al., 1992). Furthermore, mother's substance abuse, depression, anxiety, antisocial personality disorder (ASP), schizophrenia and bipolar all increase the chances of a child's externalizing problems. While father psychopathology also plays a role, the mothers impact is much stronger (Connell & Goodman, 2002).

Substance abuse is another area that affects both PPD and child psychopathology. Previous studies have demonstrated that maternal alcohol abuse predicts externalizing behaviors in 5th graders when controlling for MDD in low-income families (Conners-Burrow, et al. 2012).

Additionally, More specifically, children of heavy maternal drinkers were more likely to have conduct disorder and ADHD than light drinkers and abstainers (Kendler et al., 2013; Torvik et al., 2011). A possible reasoning for this is that alcohol plays an environmental role in CD and a genetic one with ADHD (D'Onofrio, et al. 2007). For example, the maternal drinking behavior coincides with a harsher parenting style that leads to externalizing (Conners-Burrow, et al. 2012).

The effects of paternal substance abuse on child outcomes is mixed. Some studies have found a small effect on internalizing behaviors and insignificant in externalizing behaviors (Connell & Goodman, 2002). Other studies have shown no effect between fathers alcohol abuse on internalizing or externalizing behavior in children (Fitzgerald et al., 1993; Rognmo et al., 2012).

Smoking is another behavior that may be associated with both PPD and children's behaviors. Like alcohol abuse, several studies have demonstrated an effect between maternal smoking and externalizing behavior and not internalizing behavior (Stene-Larsen, Borge, & Vollrath 2009; Williams et al., 1998). Furthermore, smokers from low-income backgrounds are also associated with conduct disorder (Brion et al., 2010).

Some studies have found links between smoking and internalizing behavior. For example, a study that followed mothers who quit smoking before pregnancy saw a decrease in externalizing problems in their children. However, their increase in the chance of exhibiting internalizing behaviors remained, suggesting the link between smoking and internalizing behaviors may be due to genetic factors rather than biological changes that occur before pregnancy (Dolan et al., 2016). Afterall, smoking during pregnancy can be an indicator of other

mental health problems, such as depression, anxiety and ASPD (Moylan et al., 2015). Therefore it may be these mental health disorders mediating child behavior outcomes rather than smoking.

Familial Social Factors: One of the shared social risk factors for PPD and child psychopathology is the SES of the parents. Previous research has shown that lower SES is related to increases in anxiety, depression, conduct disorder and adhd. The reason being is that poverty can lead to lower-quality physical environment, maternal emotional unresponsiveness, and fewer stimulating experiences contribute significantly to internalizing behaviors and externalizing behaviors (Eamon, 2000). These mental health diagnoses, especially those of externalizing behaviors, were more likely to have lower educational achievement (Meich et al., 1999). Hoeverver, some research has not found a link between SES and internalizing behavior (Conger et al., 1999; McLoyd, 1998). Instead, internalizing problems is likely mediated by some other factor such as altered parenting, marital status and increases in violence (Conger et al., 2002, Miech et al., 1999)

It is also notable that past research has found the relationship between SES to be non-linear. In other words, those from low income backgrounds compared to middle-income are hit the hardest. But rates of mental health disorders between middle and high income earners was modest or non-existent (Hudson, 2005). Despite having an increase in mental health symptomatology, low-income communities have less services than higher income ones due to logistical, attitudinal, and systemic barriers (Santiago et al., 2012). The lack of access for low income parents may cause additional problems for the children of these families.

Hypotheses and Aims

The first aim of this paper is to investigate the relationship between PPD risk factors like, Birth Outcomes, Mental Health History, and Social and Environmental impacts, and confirm their predictive values on postpartum depression. Based on the research there is expected to be an impact of birth outcomes, such as c-section, gestational age, low-birthweight, IQ, and fussiness, on postpartum depression. In addition to these variables, an exploratory analysis with 40+ outcome variables was also included (see appendix A).

The next step in this aim is to look at the association between prenatal behaviors and their impact on MDD. Because of the association between drinking, smoking and depression, it is expected that all of these factors will increase the likelihood of PPD.

The third step in this first aim is to look at the association between lifetime maternal mental health and PPD. It is expected that a mental health diagnosis of major depressive disorder (MDD) will have a major predictive value on PPD. Additionally, because of the association between MDD, general anxiety disorders and alcohol abuse, it is expected that these will also have predictive value on PPD.

Finally, in step four of this first aim, we look at how social and economic factors impact PPD. The economic factors include mothers' education, father's education and income levels. We expect to confirm findings of past research papers that socioeconomic status (SES) will increase the likelihood of PPD. Social factors investigated included marital happiness and positive feelings of the marriage in the future. We expect to confirm previous studies that found that marital satisfaction predicts PPD.

The second aim of this paper is to investigate the correlation between postpartum depression in mothers and the effects on the internalizing and externalizing behaviors of children. The internalizing behaviors to be reviewed include: major depression, overanxious disorder**,** and separation anxiety. The externalizing behaviors include: Oppositional Defiance Disorder (ODD), Conduct Disorder (CD), and Attention Deficit and Hyperactivity Disorder (ADHD). There is an expectation that PPD will have a unique impact on child's psychopathology over and above MDD for both internalizing and externalizing behaviors.

The third aim of this paper is to see how relevant psychopathology, identified in the second aim, correlates with selective PPD risk factors, identified in the first aim of this paper. It is expected that some birth complications, such as low birth weight, will lead to increases in externalizing behaviors.

Next, we explore how gestational behaviors, such as smoking and alcohol consumption during pregnancy impacts child development. It is expected that these behaviors will increase relevant internalizing and externalizing behaviors.

In part 3 of the third aim, the impact of familial mental health on child psychopathology is explored. We expect maternal mental health to have a stronger impact than patneral, given the past literature. We also expect that maternal PPD to be the main mediating effect on child psychopathology once all other maternal psychopathology is considered as a covariate.

Finally, an analysis will be done to consider the role social and environmental factors plays on relevant child psychopathology. Because mental health is negatively affected by social determinants of health, income and education should also play a role in a child's mental health**.** Additionally, marital discord may also have a small effect.

The last aim of this study is to identify the GxE effect of PPD on relevant birth outcomes as well as, the GxE effect of different environments on relevant child psychopathology.

Summary of Aims

Aim 1: To determine the association between PPD and:

1A) Birth Outcomes

1B) Prenatal Behaviors

1C) Maternal Mental Health

1D) SES

Aim 2: To determine the association between postpartum depression and child psychopathology: controlling for lifetime history of major depression.

Aim 3: To determine the relationship between PPD risk factors and Selected Child Psychopathology

Aim 4: To determine the GxE of selected traits via Twin Analysis

Chapter 2: Methods

Survey Data

This is a retrospective cohort study of postnatally depressed and nondepressed mothers and their children. PPD data was measured retrospectively at least 8 years after giving birth. To classify as having PPD, Mothers had to have major depression symptoms (according to the DSM IV) within one year after child birth and they had to last more than 2 weeks. There were 855 moms included for analysis with 7.46% reporting PPD.

Lifetime report of other parental psychopathology was also determined. These included: major depression disorder, antisocial personality disorder, alcoholism and panic disorder. This was done by a structured clinical interview for the DSM-III-R diagnosis. The interviews were performed by a psychiatric diagnostician (Kendler, 1992).

Table 1: Parental Psychopathology

Mothers Psychopathology	
Lifetime Depression	587 (44.30%) n=1325; 5 missing
Postpartum Depression (Wave 2)	67 (7.84%) n=855; M=22
General Anxiety Disorder	172 (12.95%) n=1328; M=2
Panic Disorder	60 (4.63%) n=1295; 35 missing
Antisocial Personality	42 (3.17%) n=1324
Alcoholism	73 (5.51%) n=13.26; 4 missing
Any Mental Health Diagnosis	650 (48.87%) n=1330
Fathers Psychopathology	
Depression	291 (29.94%) n=972; 8 missing
General Anxiety Disorder	66 (6.76%) n=976; 4 missing
Panic Disorder	14 (1.46%) n=957; 23 missing
Antisocial Personality	77 (7.91%) n=973; 7 missing
Alcoholism	186 (19.14%) n=972; 8 missing
Any Mental Health Diagnosis	347 (35.44%) n=979; 1 missing

Table 1: This table describes the prevalence of mothers psychopathology and fathers psychopathology in the data set.

Data for the twins was taken from waves 1-4 of the Virginia Twin Study of Adolescent Behavioral Development (VTSABD) was used for analysis. VTSABD contains psychological assessments of parents and twins from ages 8 to 17 years of age in four waves. The data was collected between 1974 and 1983 which each wave was completed in 1½ intervals. There was not enough data from minority groups collected, so they were excluded from the study leaving an entirely caucasion sample. The data set contained 1457 families and 2814 children (Eaves et al., 1997; Moore et al., 2019).

Table 2: Description Juvenile Twins

Overall	1457 Twins Pairs; 2814 Twins
Sex	
Male	1557 (53.8%)
Female	1338 (46.2%)
Missing	19
Zygosity	
MZ	378 (52.5%)
DZ	342 (47.5%)
Missing	15

Table 2: Sex and zygosity break down of the twins in the data set

The measures of child psychopathology that were focused on included: major depressive disorder, anxiety disorders, conduct disorder, oppositional defiant disorder, and attention deficit hyperactivity disorder. These were measured by the Child and Adolescent Psychiatric Assessment (CAPA) which is an interview-based diagnostic tool to measure clinical severity of symptoms to make a psychiatric diagnosis according to DSM-IV. To measure child psychopathology, parental reports of symptoms were all collected (Table 3). However, the mother's report is the focus of this paper.

Table 3: Child Psychopathology by Wave

Mother's Rating of the Child	**All Waves**	**Wave 1**	**Wave 2**	**Wave 3**	**Wave 4**
Depression	43 (0.73%) n=5877; M=672	12 (0.46%) n=2633; 238 missing	18 (0.94%) n=1923; 164 missing	8 (0.77%) n=1039; M=210	5 (1.54%) n=325; M=60
OverAnxious Disorder	360 (6.05%) n=5946; M=646	153 (5.83%) n=2625; 246	115 (5.96%) n=1931; 156	67 (6.34%) n=1057; M=192	25 (7.51%) n=333; M=52
Separation Anxiety Disorder	92 (1.55%) n=5941; M=651	39 (1.44%) n=2701; 170 missing	31 (1.57%) n=1972; M=115	9 (0.83%) n=1084; M=165	1 (0.29%) n=345; M=40
Conduct Disorder	75 (1.24%) n=6114; M=478	42 (3.17%) n=1324	15 (0.76%) n=1982; M=105	17 (1.57) n=1086; M=163	5 (1.45%) n=345; M=40
Oppositional Defiance Disorder	156 (2.57%) n=6068; M=524	63 (2.37%) n=3663; missing 2663	42 (2.12%) n=1978; M=109	39 (3.61%) n=1080; M=169	12 (3.46%) n=347; M=38
Attention Deficit and Hyperactivity Disorder	149 (2.49%) n=5986; M=606	66 (2.47%) n=2671; 200 missing	41 (2.15%) n=1911; M=176	33 (3.11%) n=1062; M=187	9 (2.63%) n=342; M=43
Fathers' Rating of ADHD	50 (1.39%) n= 3590; M=3002	28 (1.34%) n=2089; 782 missing	22 (1.47%) n=1501; M=1501	xxx	xxx

Table 3: This table reports the prevalence of child psychopathology of a child adolescent life. From ages 8-17.

In addition, mothers were asked about their prenatal behaviors, early medical outcomes and development of the twins. Prenatal behaviors included drinking and smoking during pregnancy (Table 4). There were over 50 child outcomes and developmental questions were asked about the twins. These included birth-weight, birth complications, hospitalization, etc (S.Table 1).

Table 4: Prenatal Behaviors

	Incident #
Took Tranquilizers, Antidepressants, or Sleeping Pills	25 (1.89%) n=1323; M=7
Smoked During Pregnancy	322 (24.36%) n=1322; M=8
Smoked >10 Days during pregnancy	77 (5.82%) n=1322; M=8
Drank During Pregnancy	36 (2.71%) n=1292; M=2
Drank <1/week	21 (1.63%) n=1292; M=2
Drank at Least 1/week	11 (0.85%) n=1292; M=2
Drank Most Days	5 (0.38%) n=1292; M=2

Table 4: This table measures the prevalence of smoking and drinking in this dataset. 24.36% of the sample was smothers and only 2.71% of mothers reported drinking.

Data Analysis

Data analysis method for aim #1: To determine the association between PPD, child psychopathology and: 1a) Birth Outcomes, behaviors and complications, 1b) Prenatal substance use behaviors, 1c.) Familial mental health diagnosis, and 1d) Social and Economic Factors.

From the data set, only data from mothers who filled out the postpartum depression survey was included (n=855) and their children's data (n=1910). To find the relationship between postpartum depression and birth outcomes a bivariate linear regression in SAS was used**.** The code used in SAS was PROC GENMOD which is an extension of traditional linear

regressions, however the model takes into account the non-independence of the twin data. During these anaylses, MDD was always held as a co-variate along with child sex, unless otherwise noted. The regression reports back and odds ratio which is the chance that a given outcome (child psychopathology/birth variable) occurs given a particular exposure (PPD), compared to the chance of the outcome occurring in the absence of that exposure (Szumilas, 2010). This procedure was also used to find the association between PPD and prenatal substance use, as well as, PPD and familial mental health diagnosis. Social and economic factors explored were continuous variables. Therefore, the PROC GENMOD statement was modified to accept continuous multivariate responses.

Data analysis method for aim #2: To determine the association between PPD and child psychopathology while controlling for MDD

From the VTSABD data all four waves of children's data was collected or until children turned 18 were included so that outcomes could be measured over the adolescent lifetime. Children's psychopathology was measured by the mother's account of symptoms and a positive diagnosis. Internalizing measures used included depression and anxiety. Externalizing measures used were conduct disorder, ADHD, and oppositional-defiant disorder. Mothers Lifetime depression (MDD) and PPD was measured using the mother's self report of symptoms and DSM IV diagnosis. To find the relationship between postpartum depression and children's psychopathology a linear regression in SAS was used as described in the aim 1 section**.** MDD and sex were used as co-variates.

Data analysis method for Aim #3: To determine the relationship between PPD risk factors and Selected Child Psychopathology

The procedure described in aim one is repeated here. Instead of looking at PPD however, relationships with ADHD were explored. Co-variates included conduct disorder and child sex unless otherwise noted.

Data analysis method for aim #4: To determine the Gene by Environment effects of select birth variables and ADHD.

Twin studies are a common way to determine Gene-Environmental (GxE) interaction on a population level (Evans & Martin, 2000). They are based upon the degree of similarity between monozygotic twins/identical twins (MZ) and dizygotic twins/fraternal twins (DZ). Estimates of heritability, shared, and non-shared environmental yields estimates of heritability to explain whether individual differences in a specific phenotypic trait are attributable to genetic and environmental influences. The twin design is based on the fact that monozygotic (MZ) twins share 100% of their genes and dizygotic (DZ) twins share 50% of their genes. By comparing the concordance between twin pairs, research can determine if a trait is genetic or environmental. If the DZ twins had less than 50% correlation in comparison to the MZ twins, that suggests that the phenotype being measured is influenced mainly by genetics. However if the DZ correlation is greater than 50% of the MZ correlation, that suggests that the environment is largely at play. An example is shown in Figure A (Sahu & Prasuna, 2016).

Phenotype 1 represents a perfect correlation where in MZ twins 50% or the homogeneity is due to genes and 50% is due to the shared environment. The 20% difference in the MZ twins is due to non-shared environments. The DZ correlation is a perfect half of the MZ correlation, suggesting genes and environment are equally at play. Phenotype 2, represents a phenotype that is largely genetic since the DZ correlation is less than one-half the MZ correlation. Phenotype 3 represents a phenotype that is due largely to environmental factors.

Furthermore, the genetic heritability of a trait can determined using the formula: h=2x (MZ-DZ). For example, calculating the heritability of phenotype 3 would be as follows: h=2x(0.7-0.6)=.020 or 20%.

The MZ and DZ twins were compared in SAS using either PROC FREQ for bivariate variables and taking the tetrachoric correlation, such as fretting, or using PROC CORR for multivariate variables, such as ADHD behaviors, and taking the pearson correlation.

Figure A: Example of Twin Analysis

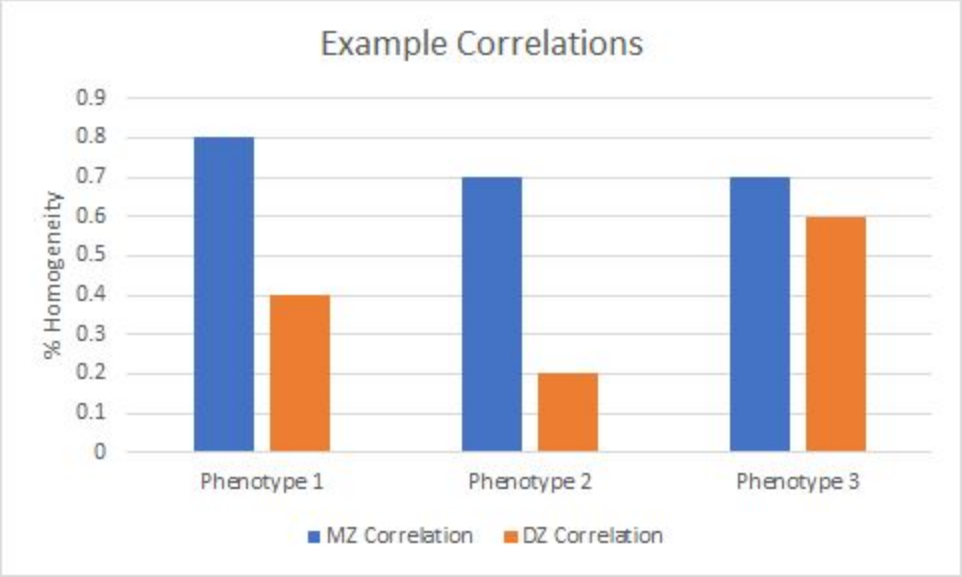


Figure A: This a sample figure to explain twin correlations.

To investigate the more complex underlying mechanisms between associations, gene by environmental (GxE) interaction analysis was done between PPD and child outcomes. A GxE interaction describes a differing effect of genotype on a person in differing environments or a differing environmental impact on a person given different genotypes (Ottman, 2008). Additionally, a gene by environmental (GxE) impact can be determined by stratifying a given outcome by a particular environment and then calculating to see if there is a difference in

heritability (Dick, 2011, Knopik et al., 2005). GXE interaction was determined for fretting and the interaction with PPD. In addition, a GxE analysis done for ADHD and PPD and alcoholism.

Chapter 3: Results

Aim 1: To determine the association between PPD and: 2A) Birth Outcomes, 2B) Prenatal Behaviors, 2C) Maternal Mental Health 2D) SES

Aim 1A: To Determine the Association between PPD and Birth Outcomes: In this section the relationship between birth variables and their correlation with PPD was analyzed. Birth outcomes include birth complications (like breech birth and c-section), complications with the twins (like incubation of twins, needing a blood transfusion, having a congenital abnormality, etc), and bonding indicators with the twin (like frequency of crying of babies or if the baby was difficult to love or comfort). This analysis also included some developmental outcomes, such as indicating when a baby said first words or phrases, when they began walking, if the children were ever held back, IQ etc. Finally, this data set also included time the babys spent apart from mom or dad, including if the child was adopted or spent more than a week with non-immediate family members. Supplemental Table 1 lists all the variables in the analysis while Table 5 shows select variables that were associated with either PPD (p-values <0.05) or MDD (p-values <0.05).

Only two variables were correlated with PPD. They included reports of fretting (excessive crying) (O.R.=2.25, p-value=0.0111) and the child staying with other family members (O.R.=2.93, p-value=0.0219). MDD was associated with breech birth, the baby being unresponsive to sight or sound, the child being difficult to love, and the child having encephalitis/meningitis.

Table 5: Relationship Between PPD and Birth Outcomes

	Odds Ratio of PPD (95% confidence interval)	P-value for PPD	Odds Ratio of MDD (95% confidence interval)	P-value for MDD
Breech Birth	1.0784 (0.3557-3.2688)	0.8939	**0.6315 (0.4154-0.9600)**	**0.0315**
Unresponsive to sight and sound	2.8111 (0.9856-8.0180)	0.0533	**3.2808 (1.3165-8.1754)**	**0.0108**
Fretting	**2.2486 (1.2029-4.2034)**	**0.0111**	0.8604 (0.6093-1.2152)	0.3934
Difficult to love	0.8648 (0.1839-4.0677)	0.8541	**13.7558 (2.9881-63.3242)**	**0.0008**
Had Encephalitis/meningitis	0.7958 (0.959-6.6067)	0.8325	**6.9794 (1.3698-35.5616)**	**0.0193**
Staying with other family	**2.9295 (1.1685-7.3447)**	**0.0219**	1.2579 (0.6748-2.3450)	0.4702
Being apart from father	.7145 (0.2818-1.8120)	0.4790	**2.3640 (1.5059-3.7110)**	**0.0002**

Table 9: This table describes the increased odds of having PPD as a result of these Birth Outcomes. Covariates in this analysis included MDD and sex. Fretting (OR=2.25, p=0.01) and staying with other family members (OR=2.93, p=0.02) increased the odds of having postpartum depression. All other variables listed were associated with MDD. No sex differences were seen.

It should be noted that over 50 variables were considered in this unbiased review of the birth variables (Supplemental Table 1). This suggests that a Bonferroni correction should be done with adjusted p-values. The new significant p-value was 0.001. Using this strict p-value means that none of these birth variables should be considered significant in this analysis. Therefore, it would be unsurprising if future studies on these variables found different outcomes or other variables, such as income or domestic violence was played a confounding role.

Aim 1B: To Determine the Association between PPD and Prenatal Behaviors: The next step in this next aim is to look at how prenatal factors impact postpartum depression (Table 6). The Factors that are considered include medications taken, smoking during pregnancy, and drinking during pregnancy. Drinking at least once a week (OR=14.0, p-value=<0.0001) and Drinking most days during the pregnancy (OR=27.0, p-value=0.0008) increased the odds that women would experience PPD. While taking tranquilizers, antidepressants, and sleeping pills (p-value=0.0319) and smoking during pregnancy (p=0.0069) was more likely to indicate that women were suffering from MDD.

Table 6: The Relationship Between Prenatal Behaviors and PPD

	O.R. PPD	PPD P-value	MDD P-value
Meds during pregnancy	1.33 (0.639-2.75)	0.4495	0.8739
Tranquilizers, antidepressants, sleeping pills	2.27 (0.455-11.2)	.3176	**0.0319**
Smoked during pregnancy	.6600 (0.260-1.68)	0.3822	**0.0069**
Smoked more than 10 days	0.2080 (0.019-2.24)	0.1957	0.2028
Drank during pregnancy	4.57 (0.933-22.43)	0.0609	0.3634
Drank at least once per week	**14.0 (3.90-50.5)**	**<0.0001**	**0.0494**
Drank Most Days	**27.0 (3.90-187)**	**0.0008**	0.6748

Table 6: This table describes the association between drinking and PPD. Covariates included MDD. Smoking was associated with MDD and Drinking at least once per week was associated with PPD.

Aim 1C: Relationship between Familial Psychopathology and PPD: Having other diagnoses of mental illness puts a woman at higher risk for other mental health disorders, including postpartum depression (Ghaedrahmate et al. 2017; Lanchester, et al. 2010). An analysis was done to see the relationship between mental diagnosis and having postpartum depression. Major Depressive Disorder (MDD), Panic Disorder (PD), Antisocial Personality Disorder (ASPD) and Alcohol Abuse Disorders (AAD) were all considered associated. However, when considering all mental health disorders and their interplay in the regression, only MDD (ADJ. O.R.=2.77; p-value=<0.0001) and PD (ADJ. O.R.=3.14; p-value=0.0407) had a significant association with PPD (Table 7). Paternal psychopathology and its relationship with PPD was also done, with no significant results found (Supplemental Table 2)

Table 7: Association between Maternal Psychopathology and PPD

Mothers DATA	O.R. for PPD	P-Value	Adjusted O.R. for PPD	Adjusted P-Value
All	**15.1179 (4.5096-50.6811)**	**<0.0001**	**XXX**	**XXX**
MDD	**7.6611 (3.25-18.0356)**	**<0.0001**	**2.7694 (2.4533-14.8342)**	**<0.0001**
PD	**4.1831 (1.5850-11.0398)**	**0.0039**	**3.1378 (1.0496-9.3809)**	**0.0407**
GAD	1.8871 (0.7843-4.5405)	0.1563	XXX	XXX
ASP	3.7662 (1.0043-14.1226)	0.0493	2.5081 (0.5655-11.1235)	0.2263
Alcohol Abuse	3.9222 (1.4921-10.3099)	0.0056	2.1457 (0.7598-6.0590)	0.1495

Table 7: This table shows the association between PPD and maternal psychopathology. Once all covariates were accounted for, the data showed that MDD and panic disorder (PD) was associated with PPD.

Aim 1D: Impact of Social and Economic Factors on PPD: Several studies have demonstrated the relationship between low SES and higher incidence of PPD (Huang, et al. 2015; Khan, Wilson, & Wise; 2005 Miyake, et al. 2015). In analysis of SES and its effect on PPD there were no correlations between SES and PPD (Table 8). However, mothers with lower education had a higher chance of having MDD (OR=0.6461, p-value=0.0164).

Marriage discord and satisfaction also plays a role in PPD. Our data confirms this finding. Mothers who report a greater sense of happiness in their marriage have lower rates of

PPD (OR=0.5169, p-value=0.0066). Furthermore, mothers who have a more positive outlook on their marriages are less likely to have PPD (OR=1.3808, p-value=0.0445).

Table 8: The Association between PPD, MDD, SES, and Marriage

	PPD OR	P Value	MDD OR	P-value
Mothers Education	1.6248 (0.7136-3.6994)	0.2476	**0.6461 (0.4522-0.9231)**	**0.0164**
Fathers Education	0.3453 (0.1078-1.1055)	0.0733	0.6825 (0.2287-2.0368)	0.4934
Family Income	0.7898 (0.0883-6.0684)	0.7724	0.4423 (0.1613-1.2132)	0.1131
Happiness about Marriage	**0.5169 (0.3212-0.8319)**	**0.0066**	0.8953 (0.7535-1.0639)	0.2090
Positive Future about the Marriage	**1.3808 (1.0080-1.8916)**	**0.0445**	1.0339 (0.9282-1517)	0.5442

Table 8: This table shows that PPD is not associated with SES. However, PPD is associated with marital satisfaction measures. Mother's education was associated with a depressed mood. The less educated a mother was, the more likely they were to have MDD.

Aim 2: To determine the association between Postpartum Depression and Child Psychopathology: Controlling for Lifetime History of Major Depression.

The second aim in the analysis was to determine the association between PPD and childs internalizing and externalizing behavior. For internalizing behaviors, depression, anxiety and separation anxiety was analyzed together for their association with PPD while controlling for MDD and then separately for each internalizing behavior**.** No correlation was seen between postpartum depression and child internalizing behavior (Table 9). However, MDD did have an association with internalizing, particularly anxiety. There was, also, an association between sex

and all internalizing behavior. Female children had a higher chance of having an internalizing behavior (data not shown). However, this sex difference failed to stratify.

Table 9: Relationship between PPD and Childrens' Internalizing Behaviors

	Odds Ratio of Behavior (95% confidence interval)	P-value for PPD	Odds Ratio of Behavior (95% confidence interval)	P-value for MDD	P-value for Sex
All Internalizing	1.80 (0.889-3.64)	0.1028	**1.82 (1.29-2.56)**	**0.0006**	**0.0499**
Depression	2.98 (0.866-10.2)	0.0834	2.41 (0.966-6.02)	0.0592	0.7749
Anxiety	1.78 (0.889-3.58)	0.1033	**1.91 (1.32-2.76)**	**0.0006**	0.0590
Separation Anxiety	2.05 (0.586-7.18)	0.2611	1.47 (0.529-2.98)	0.2793	0.1651

Table 9: This table shows the OR increase for depression, anxiety and separation anxiety as it relates to PPD and MDD. PPD, MDD and sex were held as co-variates for each analysis. PPD did not increase the OR of having and internalizing behavior. MDD correlated with internalizing behavior, specifically anxiety (OR=1.91, p=0.0006).

The next step of this analysis looked at the relationship between PPD and externalizing behaviors (Table 10). These behaviors included attention deficit disorder (ADHD), conduct disorder (CD) and Oppositional Defiance Disorder (ODD). Both PPD and MDD had a signfigant relationship with externalizing behaviors. However, when broken down by behavior, PPD was only related to ADHD in children (O.R.=4.43, p-value=0.0002) and CD in children (O.R.=3.38, p-value=0.0392). MDD, however, was correlated with ODD (OR=2.18 ,p-value=0.0288).

Table 10: Relationship between PPD and Childrens' Externalizing Behaviors

	Odds Ratio of Behavior (95% confidence interval)	P-value for PPD	Odds Ratio of Behavior (95% confidence interval)	P-value for MDD	P-value for Sex
Any Externalizing	**3.24 (1.59-6.61)**	**0.0012**	**1.20 (1.04-2.79)**	**0.0355**	0.9637
ADHD	**4.43 (2.03-9.69)**	**0.0002**	1.48 (0.800-2.79)	0.2132	0.0506
Conduct Disorder	**3.38 (1.06-10.8)**	**0.0392**	1.63 (0.639-4.17)	0.3056	0.4256
Oppositional Defiant Disorder	1.93 (0.898-4.16)	0.0919	**2.18 (1.08-4.37)**	**0.0288**	0.1352

Table 10: This table shows the OR increase for ADHD, CD, and ODD as it relates to PPD and MDD. PPD, MDD and sex were held as co-variates for each analysis. PPD increased the odds of ADHD (O.R.=4.43, p-value=0.0002) and CD (O.R.=3.38, p-value=0.0392). MDD correlated with (OR= ,p-value=0.0288).

ADHD and CD are known to correlate with one another, with ADHD being the driving force behind conduct disorder (Pliszka, 1998). Therefore, another analysis was done to determine whether ADHD or CD were related to each other in this dataset or if they were independent. In this new regression analysis, ADHD remained significant (O.R.=4.14, p-value=0.0134) while CD was no longer significant (p-value=0.0854). Suggesting that ADHD is the true correlate here and not CD.

Table 11: Adjusted OR for the Relationship between PPD, ADHD, and CD

	Adjusted Odds Ratio (95% confidence interval)	Adjusted P-value for PPD	P-Value for ADHD	P-value for CD
ADHD	**4.14 (1.92-9.93)**	**0.0003**	-	**0.0134**
Conduct Disorder	2.87 (0.863-9.58)	0.0854	**0.0142**	-

Table 11 This table shows the OR increase for ADHD and CD ODD as it relates to PPD. Co-variates for this analysis inclueded MDD [p-value insignificant and not shown], ADHD, CD, and sex [p-value insignificant and not shown]. PPD increased the odds of ADHD (O.R.=4.14, p-value=0.0003), but not CD.

In Summary, PPD seems to be correlated with ADHD and CD. However, CD and ADHD are both correlated with each other. Once controlled for in the regression, a true correlation was found between ADHD and PPD.

Aim 3: To determine the relationship between PPD risk factors and ADHD

Aim 3A: To determine the association between ADHD and Select Birth Outcomes: Next was to see how birth variables that were associated with depression may also be associated with ADHD (Table 10). If these variables were associated with both depression and ADHD/CD, then these may play an important explanatory role in the mechanism between PPD and ADHD or CD. The variables that were associated with PPD, crying (O.R. = 2.37, p-value=0.0038) and staying with other family members (O.R.=4.05, p-value=<0.0001), were also associated with ADHD. Unresponsive to sight and sound, the baby being difficult to love, and the baby being apart from the father was associated with MDD and ADHD. Breech birth and encephalitis had no association with ADHD or CD.

Table 12: Association Between Selected Birth Outcomes, ADHD and CD

	Odds Ratio of ADHD (95% confidence interval)	**P-value for ADHD**	**P-value for CD**	**P-value for Sex**
Breech Birth	0.9103 (0.3904-2.1224)	0.8277	0.7087	0.0790
Unresponsive to sight and sound	**3.4827 (1.2814-9.4658)**	**0.0144**	0.1424	0.4819
Fretting	**2.3668 (1.3203-4.2430)**	**0.0038**	**0.0047**	0.0535
Difficult to love	**3.8931 (1.3254-11.4350)**	**0.0134**	-	0.5543
Had Encephalitis/meningitis	3.9676 (0.8077-19.4893)	0.0897	-	0.0827
Staying with other family	**4.0563 (2.1016-7.8291)**	**<0.0001**	0.4781	0.1080
Being apart from father	**3.8931**	**0.0134**	-	0.5542

Table 12: Table ten shows the increased odds of having ADHD given a particular birth outcome. Only outcomes that were significant for PPD or MDD were analyzed. Covariates included CD and sex. Fretting and staying with other family members was related to PPD and ADHD. Baby being unresponsive to sight and sound, being difficult to love , and being apart from their father was associated with MDD and ADHD.

Aim 3B: To determine the association between ADHD and Prenatal Behaviors: The next step was to see how prenatal behaviors related to ADHD. Drinking during pregnancy was the only factor that correlated with ADHD (OR=3.29, p-value=0.446). Furthermore, women had to

drink at least once a week or more to be associated with both PPD (OR=14.0, p-value=<0.0001) and ADHD (OR=2.71, p-value=0.0302).

Table 13: The Relationship Between Prenatal Behaviors and ADHD

	O.R ADHD	P-value
Meds during pregnancy	0.851 (0.467-1.55)	0.5972
Tranq., anti-dep, sleeping pills	2.77 (0.670-11.4)	0.1596
Smoked during pregnancy	1.16 (0.577-2.32)	0.6804
Smoked more than 10 days	0.839 (0.272-2.59)	0.7598
Drank during pregnancy	**3.29 (1.03-10.55)**	**0.0446**
Drank at least once per week	**2.71 (1.15-14.9)**	**0.0302**
Drank Most Days	**6.67 (1.43-31.1)**	**0.0158**

Table 13: This table shows the association between Prenatal behaviors and ADHD. ADHD is only associated with drinking during pregnancy.

Aim 3C: Relationship between Familial Psychopathology and ADHD: Next, the associations between maternal mental health and ADHD and conduct disorder were considered. In the bivariate regression analysis, MDD, PD, ASP and alcoholism and PPD were all related to an increased incidence of PPD. However, when multivariate regression was done, only alcoholism (ADJ O.R.=3.86; p-value=0.0058) and postpartum depression (ADJ. O.R.=3.03; p-value-0.0011) had a unique impact on ADHD. Fathers psychopathology was also considered its association with mother's rating of adhd, however no association was found (Supplemental Table 3).

Table 14: The Association Between Maternal Mental Health and Child ADHD and CD

Mother DATA	O.R. for ADHD	ADHD P-Value	Adjusted O.R. for ADHD	Adjusted ADHD P-Value	Adjusted P-Value for CD
All	**1.9964 (1.0911-3.6527)**	**0.0249**	XXX	XXX	XXX
MDD	1.8559 (1.0315-3.3394)	0.0391	1.1893 (0.6669-2.1208)	0.5570	0.5755
PD	2.9120 (1.1462-7.3979)	0.0247	1.8354 (0.7535-4.4708)	0.1813	0.2511
GAD	1.5646 (0.7474-3.2754)	0.2350	XXX	XXX	XXXX
ASP	3.2871 (1.28-8.4238)	0.0132	1.6900 (0.7701-3.7090)	0.1907	0.6652
ALCXI	**4.2180 (1.9826-8.9738)**	**0.0002**	**3.8570 (1.7120-8.6896)**	**0.0058**	**0.6006**
PPD	**4.7504 (2.2347-10.0983)**	**<0.0001**	**3.0305 (1.3790-6.6601)**	**0.0011**	**0.0839**

Table 14: This table shows the association between ADHD and Mother's psychopathology. Alcoholism and PPD are both related to increased reports of ADHD in children.

Aim 3D: Impact of Social and Economic Factors on ADHD: Finally, the association between SES and ADHD and conduct disorder was explored. Lower maternal education was associated with higher rates of ADHD (OR=0.5730, p-value=0.0387) and CD (OR=0.3197, p=0.0018). Lower education of the father was associated with higher amounts of ADHD (OR=0.2987, p-value=0.0172), but not CD. Finally, lower income was associated with higher rates of ADHD (OR=0.0743, p-value=0.0033) and CD (OR=0.0995, p-value=0.0248). Marital

satisfaction was not associated with ADHD. However, women who reported higher ratings of happiness within their marriage had children with lower rates of conduct disorder (OR=0.4945, p-value=0.0107).

Table 15: The Association between Social and Environmental Factors and ADHD

	ADHD OR	P Value	OR CD	P-value
Mothers Education	**0.5730 (0.3380-0.9716)**	**0.0387**	**0.3197 (0.1561-0.6546)**	**0.0018**
Fathers Education	**0.2987 (0.1105-0.8076)**	**0.0173**	0.9555 (0.3701-2.4666)	0.9250
Family Income	**0.0743 (0.0132-0.4199)**	**0.0033**	**0.0995 (0.0133-0.7461)**	**0.0248**
Happiness about Marriage	0.9877 (0.6806-1.4335)	0.9482	**0.4945 (0.2880-0.8490)**	**0.0107**
Positive Future about the Marriage	1.0658 (0.7672-1.4807)	0.7040	0.8894 (0.7047-1.227)	0.3241

Table 15: This table shows the association between social and environmental factors and ADHD. ADHD was associated with SES but not marital satisfaction.

Aim 4: Twin Analysis

The final aims of this paper is to show a twin analysis for the significant birth variables and ADHD. First set of analysis, the correlation for birth variables that correlated with both PPD and ADHD was done (Supplemental Table 4, Table 16; variables that also correlated with MDD were included). As expected, staying with other family members and being away from the father had nearly identical tetrachoric correlations since both twins would be kept together in these scenarios. In the cases of the babies being unresponsive to sight and sound and being difficult to love suggest environmental influence since the DZ correlation is greater than ½ the MZ

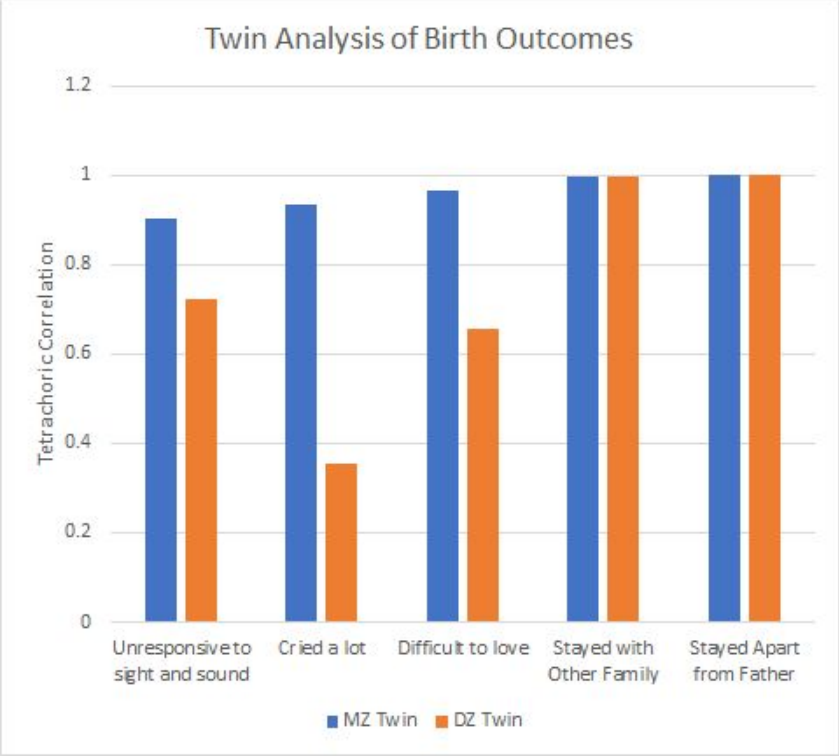
correlation. Fretting, however, suggested a strong genetic impact, seeing as the DZ twin correlation less than one-half the MZ correlation (MZ=0.9339, DZ=0.3535).

Table 16: The Twin Correlations for Selected Birth Variables

	MZ Twin Tetrachoric Correlations	DZ Twin Tetrachoric Correlations
Unresponsive to sight and sound	0.9019	0.7228
Fretting	0.9339	0.3535
Difficult to Love	0.9669	0.6576
Staying with Other Family	0.9949	0.9961
Being Apart From Father	1.000	1.000

Table 16: Table 11 gives the tetrachoric Correlations for MZ and DZ twins for selected Birth variables

Figure B: Graph of Twin Correlations for Selected Birth Variables



The next step was to analyze the GxE interaction of PPD on fretting was genetic or environmental by stratifying the correlations by mothers' depressive symptoms. Because twins are kept together, a stratification staying with other family members was not done.

Table 17: GxE Fretting with PPD

	Sample Correlation	95% Confidence Limits	
MZ	0.74812	0.72064	0.77299
DZ	0.19797	0.13591	0.25829
MZ No PPD	0.75698	0.71542	0.79262
DZ No PPD	0.16813	0.07433	0.25861
MZ with PPD	0.91287	0.7994	0.9605
DZ with PPD	-0.1931	-0.5201	0.18995

For fretting, genetic variance for fretting was slightly increased under the influence of PPD. Therefore, PPD is impacting the genes that increase crying in babies.

Next is to complete a twin analysis on ADHD. Instead of diagnosis of ADHD, symptomatology between the two twins was used. In the analysis MZ correlation between ADHD is 0.34073 and the DZ correlation was -0.03343 (Table 18). While negative twin correlations are unusual, higher discordance among DZ twins may occur due to a comparison effect.

Next, ADHD was stratified by maternal psychopathologies that were considered significant (from section 3C) to determine the GxE interaction. First was the GxE interaction between PPD and ADHD was analysed (Table 18; Figure D). PPD increased the genetic

heritability of ADHD from 75% to 95% (calculation no shows). This suggests that PPD increases the genetic expression of ADHD.

The GxE interaction between ADHD and alcoholism (AAD) was analysed next. (Table 19). Once stratified, there was no significant correlation within twin pairs. This suggests that the study lacks the power to estimate twin correlations.

Table 18: ADHD stratified by PPD

	Sample Correlation	95% Confidence Limits	
MZ	0.34073	0.29619	0.38362
DZ	-0.0334	-0.0865	0.01981
MZ No PPD	0.36308	0.30238	0.42049
DZ No PPD	-0.0399	-0.1127	0.0334
MZ with PPD	0.4693	0.19509	0.66949
DZ with PPD	-0.1205	-0.3902	0.17068

Table 19: ADHD stratified by Alcoholism (AAD)

	Sample Correlation	95% Confidence Limits	
MZ	0.34073	0.29619	0.38362
DZ	-0.0334	-0.0865	0.01981
MZ No AAD	0.37226	0.30342	0.43677
DZ No AAD	-0.0447	-0.1266	0.03788
MZ with AAD	0.10491	-0.233	0.41777
DZ with AAD	-0.1033	-0.435	0.25609

Chapter 4: Discussion

Aim 1: To determine the association between PPD and: 2A) Birth Outcomes, 2B) Prenatal Behaviors, 2C) Maternal Mental Health 2D) SES

This study was a four part analysis of the interplay between postpartum depression (PPD) and Child Psychopathology. In part one, the association between PPD and risk factors for PPD was assessed. The risk factors included: 1) birth variables, 2) prenatal behaviors, 3) maternal psychopathology, and 4) social and economic factors.

1A: When studying the interaction between birth variables and postpartum depression, it was expected that complicated births, such as having a cesarean section, early gestational age or a breech birth would increase the incidence of PPD. However, this data shows that this is not the case, departing from previous studies. This may be due to the twin effect. Mothers of twins may be more mentally prepared about how their births will occur and do not have as much discordance between their birth plans and the actuality of their birth as do parents of singletons. It has been suggested that the anxiety from their planned birth and their actual birth experience is the cause of the increase in PPD, and has nothing to do with having a c-section (DiMatteo, 1996). This would also explain why a correlation between other variables such as hospitalizations, birth weights and gestational age of the babies did not correlate with PPD. Mothers of twins will expect to have more complications and be prepared on how to handle them (Rissanen et al., 2019).

There was a positive association between fretting and postpartum depression, confirming the work of previous studies (Dagher & Shenassa 2012, Quist et al., 2019). A possible

explanation for this is that PPD mothers spend less time interacting with their children, which causes an increase in fretting to get the attention of the mother.

Staying with other family members for more than a week is another variable that is associated with PPD. A possible reason for its association with PPD is that mothers with PPD are more likely to rely on family support to get through the postnatal period. An alternative hypothesis is that the mother is unable to bond with her children during this time and that increases her depressed mood.

Having a child that was difficult to love had to do with MDD more so than PPD. Because depressed mothers tend to view their environments negatively, this may explain the association between moms perceiving their children as difficult to love.

It should be noted that none of the p-values for the birth values fell under adjusted p-value given the bonferroni correction (< 0.001). Therefore, an alternate case can be made that staying with other family members, fretting, and having a child that is difficult to love are not correlated with PPD or MDD. Instead, this was a misleading finding. Overall, while these variables are interesting, more in depth research will be needed to see how they interplay with PPD.

1B: The next part of the analysis looked at the interplay between postpartum depression and prenatal variables. In our analysis, smoking was more related to a diagnosis of MDD than it was at predicting PPD. This is a departure from previous research on the behavior (Dagher & Shenassa, 2012). This differentiation may be due to the fact that previous studies that looked at this association did not control for the effects of MDD which is associated with smoking behavior (Paperwalla, Levin, Weiner, & Saravay 2004). Alcohol consumption, however, was

associated with PPD. Finding was in line with previous research findings (Kahn, Wilson, & Wise, 2005).

1C: Maternal mental health is also a high risk factor for PPD, beyond just MDD, and the next part of the analysis focused on this. It was expected that general anxiety disorder (GAD) would have the next highest correlation with PPD because anxiety and depression are pathologies that are known to run together (Gorman, 1996). Unexpectedly, GAD did not play a role in PPD, though Panic Disorder (PD), which is a type anxiety disorder, did have a small effect.

1D: The final part of the first aims was to look at the association between PPD and social and economic factors. Socioeconomic measures used in this section were mother and father's education, as well as, family income. None of these were associated with PPD. This finding was unexpected. The lack of finding may be due to the linear regression used. Other studies have suggested that their relationship is nonlinear and the increase in PPD is only found in the lowest income groups. An alternative explanation is that this data set over sampled those from middle and upper income families and cannot accurately portray the relationship between PPD and SES.

Marital satisfaction was also examined and found to have an association with PPD. The more happy women were about their marriage and about the future of their marriage, the less likely they were to have PPD. This negative correlation may be due to the fact that a supportive environment helps decrease stress levels therefore decreasing the likelihood of PPD. It could also be that women who are not depressed are more likely to have happier marriages, view marriages in a positive light, or choose partners that are more supportive.

Aim 2: To determine the association between Postpartum Depression and Child Psychopathology: Controlling for Lifetime History of Major Depression.

The next aim in the paper was to see how PPD was related to child psychopathology. It was hypothesized that PPD would be associated with internalizing and externalizing behaviors when controlling for MDD. However, this is not what the data showed. Instead, internalizing behaviors were more likely to be correlated with MDD than PPD, suggesting that the timing of the depression during the first year of life is not important.

PPD, however, did have unique associations with externalizing behaviors. Specifically ADHD and CD, which confirms previous studies findings (Korhonen, Luoma, Salmelin, & Tamminen, 2012,). However, ADHD was the main driving factor after the additional analysis was completed.

Aim 3: To determine the relationship between PPD risk factors and ADHD

3A: The third aim of this paper, looked at how risk factors related to PPD were associated with ADHD. The reason that ADHD was focused on was because ADHD in children was found to have a significant correlation with PPD (aim 2). In part 3A of this aim, the birth variables that correlated with PPD (identified in 1A), were studied to see if they also correlated with ADHD. Both fretting and staying with other family members had a positive correlation with both ADHD and PPD. This suggests a few possible ideas. The first is that fretting, PPD, and ADHD share a common genetic and environmental etiology. An alternative interpretation is that PPD mothers have an increased chance of giving their children a rating both ADHD and fretting because they often view their environment negatively (Rush et al.,1979). Therefore, the rating may be a function of depressed mood and not an accurate portrayal of the child's behavior.

3B: In part three of this aim, the association between prenatal behaviors (identified in 1B) and ADHD was explored. Mothers who drank during pregnancy were more likely to have children with ADHD. There are several possible interpretations of this finding. One possibility is that alcoholism genes are associated with those of ADHD and those common genes are being passed on to the children. Further analysis on this possibility was done in later aims. An alternative hypothesis is that drinking during pregnancy could alter neural development of children which increases ADHD. A third possibility is that mothers with alcohol abuse may have harsher parenting styles that increase ADHD diagnosis (Conners-Burrow, et al. 2012).

3C: The third part of this aim looked at maternal mental health's effect on ADHD diagnosis. The data reconfirms that PPD and alcoholism both increase children's ADHD. This confirms the findings made in the previous section (3B) that maternal consumption of alcohol plays an important role in child psychopathology. However, MDD and panic disorder (PD) which increase PPD (identified in 1C), were not predictive of children's ADHD over and above PPD. It was also hypothesized that paternal psychopathology would play a role in ADHD diagnosis. However, this study was unable to confirm previous research findings.

3D: The last part of this aims to look at the correlation between social and economic factors and ADHD. ADHD diagnosis was more likely in families of low education and low income. Marital satisfaction was also explored, though it was not associated with ADHD.

Aim 4: Twin Analysis

The first set of twin analysis was to determine the heritability of relevant birth variables that had shared associations with PPD and ADHD (identified in 3A). These included fretting and

staying with other family members. First we determine that gretting was determined to be genetic in origin while staying with other family members was environmental. Fretting showed a high twin correlation suggesting either high reliability underlying the genes or mother's bias in rating their MZ children more similarly. Furthermore, twin correlations for ADHD revealed that it was also mostly driven by genetic factors, confirming previous studies (Knopik et al., 2005).

Next, a GxE analysis was done between PPD and its relationship with fretting and ADHD. The GxE interaction tests whether there are genetic differences in sensitivity to PPD. A GxE would result in increased heritability (genetic variance) in under condition of PPD. We observe increases in genetic variance for both fretting and ADHD reflected in changes in the MZ and DZ correlations.

Limitations and Future Directions

The first limitation in this paper was this paper is low rates of PPD, certain birth outcomes and child psychopathology and low rate of PPD in the sample. PPD is much lower than what is described in the population suggesting a protective effect of having twins. Alternatively, low rates of PPD may also be due to underreporting due to being unfamiliar with PPD (kahn et al., 2002). Awareness during the time of postpartum depression when the data was collected was low in comparison to current public knowledge and cause an underestimation in the reports of PPD. (Davé et al., 2010, Do, Hu, Otto, & Rohrbeck, 2013; Savitz et al., 2011, Silverman 2017). The same is true for many of the child psychopathologies (like depression). This may cause associations between child psychopathologies and PPD to go undetected. Future studied on connections between PPD and birth variables will need larger sample sizes containing the etiology being studied.

Another potential issue with this study is the survey method of data collection. Because the PPD was reported at least 8 years after giving birth, methods are prone to recall bias, experimenter bias, and most importantly lack clinical specificity, which may lead to further misclassification and poor estimation (Silverman, 2017). Furthermore, mothers' depression measures had to come within the first month of birth which is a time that perinatal depression is still at play and PPD has yet to peak which may add to under-reporting of PPD and misclassification of perinatal depression as postpartum depression

Another major limitation of this study was using the maternal rating of ADHD in children rather than a diagnosis or a rating from objective scores. Furthermore, diagnosis of ADHD usually requires 2 raters instead of only one. Depressed individuals have a negative view of their environment and may not accurately portray the child's behavior. Future studies on the effects of PPD on ADHD should make sure that unbiased reporters are being used and that there are multiple reporters.

Areas that were unable to be explored in regards to predicting PPD and ADHD in children include health complications of the mom, such as gestational diabetes, maternal age, ACE scores, and domestic violence issues. All of these are areas that have shown association with maternal mental health and may mediate the bridge between PPD and fretting or PPD and ADHD. Future studies should consider these avenues of research.

An additional limitation is that data set over samples middle and high SES families and consist of an entirely caucasion data set. Given the low diversity of the data set, future studies will need to be done to clarify the interaction between SES and postpartum and if race/ethnicity influence correlations.

Finally, this study could not determine if the impact that PPD and alcoholism had on ADHD was environmental or genetic. Future studies should continue to investigate the interplay of these variables through by studying the children of twins. These study designs allow phenotypic traits comparing the children to their parents and their parent's co-twin. If children correlate more with their parents than other family members, an environmental impact can be inferred. If they correlate equally with parents and their twin siblings, a genetic impact is inferred. Future Studies should include this study design.

Overall, comfort should be found in the lack of finding between PPD and child psychopathology. Though mothers should continue to be supported through this transitioning time.

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Supplemental Figures and Tables

Supplemental Table 1: Table of Birth Outcomes, Their Prevalence and Their Association with PPD

	Prevalence	Odds Ratio of Behavior (95% confidence interval)	P-value for PPD	P-value for MDD	P-value for Sex
Low Birth Weight <2500	487 (45.60%)	0.8996 (0.4679-1.7296)	0.7510	0.9774	0.6276
Low Birth Weight <1700	81 (7.58%)	0.6145 (1.388-2.7202)	0.5212	0.6025	0.3547
Normal Birth	464 (42.03%)	0.8996 (0.4679-1.7296)	0.7510	0.9774	0.6276
Breech Birth	131 (11.84%)	1.0784 (0.3557-3.2688)	0.8939	0.0315	0.0748
C-section	381 (34.45%)	0.6175 (0.3027-1.2596)	0.1850	0.7133	0.2218
Forceps	97 (8.77%)	0.9785 (0.5009-1.9116)	0.9493	0.9098	0.2170
Other Abn. Birth	92 (8.32%)	1.87 (0.7510-4.6846)	0.1781	0.8089	0.5524
Resuc	114 (10.50%)	2.1599 (0.9184-5.0800)	0.0776	0.5894	0.0841
Delay	27 (2.5%)	2.0006 (0.4229-9.4644)	0.3818	0.3816	0.4628
Incubator	187 (44.11%)	0.9785 (0.5009-1.9116)	0.9493	0.9098	0.2170

Had convulsions at birth	8 (0.73%)	3.2063 (0.4052-25.3688)	0.2696	0.3076	0.7252
Had a congenital abnormality	36 (3.26%)	1.5862 (0.3452-7.2894)	0.5532	0.1108	0.6346
Kept in hospital after mother went home	314 (28.39%)	1.0764 (0.5126-2.2605)	0.8458	0.2299	0.1771
Weak at Birth	148 (13.55%)	1.9607 (0.9291-4.1374)	0.0772	0.939	0.4289
Unresponsive to sight or Sound	47 (4.26%)	2.8111 (0.9856-8.0180)	0.0533	0.0108	0.6512
Fretting	278 (25.25%)	2.2486 (1.2029-4.2034)	0.0111	0.2934	0.0512
Difficult to Comfort	160 (14.48%)	1.2666 (0.6058-2.6482)	0.5299	0.2312	0.3645
Difficult to Love	19 (1.72%)s	0.8648 (0.1839-4.0677)	0.8541	0.0008	0.7553
Had Encephalitis/meningitis	11 (1.00%)	0.7958 (0.959-6.6067)	0.8325	0.0193	0.1387
Not Walking by 14 months	162 (16.7%)	1.5204 (0.6840-3.3796)	0.3040	0.3435	0.2042
No saying phrases by 24 months	473 (43.0%)	2.1838 (0.8459-5.6374)	0.1065	0.5626	0.0718

Stayed in hospital after birth	311 (28.17%)	0.6271 (0.3045-1.2915)	0.2055	0.9856	<0.0001
Had 2 or more hospital visits	158 (14.3%)	0.6373 (0.3354-1.2108)	0.1688	0.6548	<0.0001
Takes medication	262 (23.71%)	2.0085 (1.0284-3.9228)	0.0412	0.4857	0.0949
Speaking before 14 months	261 (23.66%)	0.8708 (0.3949-1.9202)	0.7318	0.5517	0.0436
Reading before 24 months	274 (24.84%)	1.2997 (0.6221-2.7156)	0.4856	0.0821	0.0784
Took remedial courses	155 (14.03%)	1,0757 (0.4219-2.7427)	0.8785	0.5077	0.2441
Held back	201 (18.24%)	0.8147 (0.3192-2.0794)	0.6682	0.4998	0.3333
Stayed with other family members for at least 1 week	92 (8.32%)	2.9295 (1.1685-7.3447)	0.0219	0.4702	0.2004
Entered foster care	6 (0.54%)	45.4830 (4.0216-514.3965)	0.0020	-	-
Apart from mother	19 (1.72%)	1.5772 (0.7694-3.2330)	0.2134	0.0594	0.0122
Apart from father	207 (18.72%)	.7145 (0.2818-1.8120)	0.4790	0.0002	0.3511

IQ <89	282 (9.97%)	0.2601 (0.0642-1.0538)	0.0592	0.3107	0.5070
IQ <79	214 (7.57%)	.3793 (0.0926-1.5539)	0.1778	0.2385	0.3198
Gestational Age <36 weeks	386 (35.15%)	1.1998 (0.5346-2.6924)	0.6587	0.2786	0.0415

ST1: This table shows the association between all birth outcomes and PPD. Covariates included MDD and Sex.

Supplemental Table 2: Fathers Psychopathology and Their Correlation with PPD

Fathers DATA	O.R. for PPD	P-Value
All	1.1052 (0.4928-2.4789)	0.8082
MDD	1.3909 (0.6191-3.1248)	0.4243
PD	xxx	xxx
GAD	1.9033 (0.5249-6.9018)	0.3275
ASP	1.3210 (0.2932-5.595)	0.7170
ALCXI	1.1540 (0.4175-3.1899)	0.7825

ST2: Describes father's psychopathology and its association with Mothers PPD. Covariates included MDD. No associations were found.

Supplemental Table 3: Association between father's psychopathology, ADHD and CD

DAD DATA	Adjusted O.R. for ADHD	P-Value	Adjusted O.R. for CD	P-Value
All	1.7562 (0.9052-3.4072)	0.0958	1.2539 (0.4553-3.4531)	0.6615
MDD	1.5651 (0.7759-3.1570)	0.2109	0.8405 (0.2827-2.4988)	0.7546
PD	1.01 (0.1677-6.1580)	0.9860	XXX	XXX
GAD	0.4213 (0.0582-3.0479)	0.3919	1.4398 (0.1956-10.5965)	0.7204
ASP	1.9558 (0.7579-5.0470)	0.1655	2.2273 (0.4785-10.3664)	0.3074
ALCXI	1.1286 (0.4958-2.5690)	0.7731	2.5198 (.8880-7.1502)	0.0824

ST3: Describes father's psychopathology and its association with children's ADHD. Covariates included children's CDs. No associations were found between father psychopathology and ADHD or CD.

Supplemental Table 4: Lists of associations found for PPD, MDD and ADHD

Variables Associated with PPD	Variables Associated with MDD	Variables associated with ADHD
● **Fretting** ● **Staying with Other family Members** ● **Drinking Alcohol during Pregnancy** ● Major Depressive Disorder ● Panic Disorder ● Happiness with the Marriage ● Positive Thoughts about Future of Marriage ● Attention Deficit Hyperactivity Disorder ● Conduct Disorder	● Breech Birth ● Unresponsive to Sight and Sound ● Difficult to Love ● Had Encephalitis/meningitis ● Being Apart from Father ● Taking tranquilizers, Antidepressants or sleeping pills ● Smoking ● Mother's Education ● Anxiety ● Oppositional Defiant Disorder	● Unresponsive to Sight and Sound ● Difficult to Love ● **Fretting** ● **Staying with Other family Members** ● Being Apart from Father ● **Drinking Alcohol during Pregnancy** ● Alcoholism ● Postpartum Depression ● Mother's Education ● Father's Education ● Income

ST4: List all the associations found in this research paper. Bolded items are items that were common between PPD and ADHD.

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