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**The Effect of Maternal Hypertension and Maternal Mental Illness on Adverse Neonatal Outcomes: A Mediation and Moderation Analysis in a U.S. Cohort of 9 Million Pregnancies**

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## ABSTRACT

### Background

While Hypertensive Disorders of Pregnancy (HDP) coexist with maternal anxiety and depression, it is unclear how these conditions affect neonatal outcomes. We evaluated the prevalence as well as associations and potential mechanisms between HDP, maternal anxiety and depression, preterm birth (PTB), and small for gestational age (SGA).

### Methods

We conducted a retrospective population-based study using the Healthcare Cost and Utilization Project (HCUP) database from 2004 to 2014. Preterm birth (<37 weeks), SGA (<10<sup>th</sup> percentile for gestational age and sex), HDP, and mental disorders (anxiety and depression) were extracted using the International Classification of Diseases, Ninth Revision (ICD-9). Mediation and moderation models were constructed separately to evaluate potential mechanisms between maternal anxiety and depression, HDP, and adverse neonatal outcomes. Multivariate logistic regressions were used to determine their associations.

### Results

Of 9,097,355 pregnant women, the prevalence of HDP was 6.9%, anxiety 0.91%, depression 0.36%, preterm birth 7.2%, and SGA 2.1%. Anxiety increased the probability of having HDP (OR=1.242, 95% CI 1.235–1.250), and HDP mediated the association between anxiety and preterm birth (mediation effect=0.048, p-value<0.001). Depression significantly moderated the effect of HDP on preterm birth (moderation effect=-0.126, p-value=0.027). HDP also mediated the association between anxiety and SGA (mediation effect=0.042, p-value<0.001), but depression did not moderate the association between HDP and SGA (p-value=0.29).

### Conclusion

Our study suggests that women with anxiety are more likely to have HDP, and HDP mediates the associations between anxiety and adverse neonatal outcomes. Depression moderates associations between HDP and preterm birth but not between HDP and SGA.

**Keywords:** preterm birth, small for gestational age, anxiety, depression, hypertensive disorders of pregnancy

**Abstract:** 246 words

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## INTRODUCTION

Globally, 2.4 million neonates and children died within the first month of life in 2019 (World Health Organization, 2020). Adverse neonatal outcomes during pregnancy, namely preterm birth, infant with low birth weight or small for gestation age (SGA), intrapartum-related complications, infections, and birth defects are the driving forces for neonatal deaths (World Health Organization, 2020). The estimated preterm birth rate is 7.8% in Canada and 8.4% in the United States (Ferré et al., 2016; Statistics Canada, 2021). In high-income countries preterm birth rates average around 9.3% (Chawanpaiboon et al., 2019). Infants with SGA in Canada and the United States were estimated to be 8.9% and 8.3% respectively (Martin et al., 2021; Statistics Canada, 2021).

Maternal mental disorders and hypertensive disorders of pregnancy (HDP, including gestational hypertension, preeclampsia, and eclampsia) have each been shown to be independently associated with the development of both preterm birth and SGA (Ding et al., 2014; Mengistu & Kuma, 2020). Research has delved into the associations between depression, anxiety and the risk of developing HDP through prospective longitudinal studies where factors contributing to the former may play a role (combined depression and anxiety, BMI) (Jackson et al., 2016). Exploring mediating factors between these variables during a very sensitive period of development (pregnancy) is critical, due to the heightened risk on well-being of mother and baby. Prior mediation and moderation models studies have shown biological determinants as well as physiological immaturity are associated with neonatal mortality with outcomes, namely preterm birth (Brown et al., 2014). However, the interplay between maternal hypertension and anxiety on neonatal outcomes has not been well studied. Our previous publication reported increasing trends of mental disorders including anxiety and depression among hospitalized pregnant women in the

United States. We also demonstrated consistent associations between HDP and anxiety, but not between HDP and depression (Raina et al., 2021). For this reason, we aimed to create models to evaluate HDP as the mediator of the associations between anxiety and adverse neonatal outcomes in a large population dataset. Separately, we evaluated models where depression moderated the associations between HDP and adverse neonatal outcomes.

## **MATERIALS AND METHODS**

### **Study samples**

We evaluated all hospital discharge records in the Healthcare Cost and Utilization (HCUP) – Nationwide Inpatient Sample (NIS) dataset from 2004-2014 using the pregnancy codes based on the International Classification of Diseases, Ninth Revision (ICD-9) codes for pregnancy (validated codes: 634x-679x, V22x, V23x, V27/x; or procedure codes: 72x-75x). The HCUP-NIS database is a 20% stratified sample of all discharges from hospitals in the United States with the exclusion of certain facilities, such as long-term care homes and rehabilitation centers. It contains data from an estimated 7 million per year inpatient hospital stays from over 1,000 community hospitals (HCUP, 2021). Information provided through the database is geographically unrestricted. Data obtained for this study is exclusively publicly accessible and anonymous; hence this study requires no Institutional Review Board approval.

### **Adverse neonatal outcomes, HDP, maternal mental disorders, and potential confounders**

We incorporated ICD-9 codes for gestational hypertension (642.3x), preeclampsia (642.4x, 642.5x), and eclampsia (642.6x), preterm birth (644.2x), and SGA (76x). We also extracted anxiety disorder (300.0x, 300.2x, 300.3x, 309.8x) and depression (296.2x, 296.3x, 300.4x, 311x). Covariates relevant to this study including those related to maternal demographics with or

without preterm birth and SGA were extracted from the dataset. Baseline characteristics included age, race, and insurance plan type. Potential cofounders included both maternal and pregnant comorbidities such as smoking during pregnancy, substance abuse, obesity, thyroid disease, underlying chronic hypertension, pregestational diabetes mellitus, gestational diabetes mellitus, and multiple gestations. Parity and advanced maternal age pregnancy (maternal age >35 years) were also considered.

### **Statistical methods**

Initial analysis consisted of determining the annual rates for the adverse neonatal outcomes in the presence or absence of either anxiety and/or HDP. Sociodemographic and clinical characteristics of the pregnant women as well as the adverse neonatal outcomes were stratified by the presence or absence of anxiety and/or HDP (i.e., no HDP, no anxiety; no HDP, had anxiety; had HDP, no anxiety; had HDP and anxiety) and compared using Chi-square test. The same applies to depression and/or HDP. Statistical significance was set at  $p < 0.05$ .

To examine potential associations between HDP and mental disorders on adverse neonatal outcomes, we used mediation and moderated models separately using a series of logistic regression. A mediation model was constructed to observe a potential relationship between anxiety and preterm birth or SGA using HDP as the mediator. The moderation model was constructed to determine if depression affects the association between HDP on preterm birth or SGA. We reported odds ratios (ORs) and 95 % confidence intervals (CIs) adjusted for sociodemographic characteristics and comorbidities (covariates: age, race, income, insurance type, hospital setting, smoking in pregnancy, substance use, obesity, thyroid disease, chronic hypertension, pregestational diabetes mellitus, gestational diabetes mellitus, and advanced maternal age (primigravida and multigravida)). To test the mediation model, the analysis was

done through R4.0.1 version with RStudio (R Core Team, 2021). Statistical significance was set at  $p < 0.05$ . R was also used to test the mediation model, using the lavaan package, creating a path analysis and computing the A\*B effect and testing the significance of that effect with a Wald test.

## RESULTS

Of 9,097,355 pregnant women evaluated, 628,140 (6.9%) had HDP, 82,629 (0.91%) had anxiety; 33,016 (0.36%) had depression; 653,895 (7.2%) had preterm birth; and 198,070 (2.1%) had SGA. Among women with any HDP, 95,507 had preterm birth and 30,070 had SGA (Fig. S1). Rates of preterm birth among pregnant women in the absence of anxiety, regardless of the presence of HDP, showed a decreasing trend during the study period (Fig. 1a). On the contrary, the rates of SGA among women without anxiety, showed increasing trend regardless the presence of HDP (Fig. 1b). Similar pattern was seen for the rates of preterm birth and SGA in the absence of depression, regardless of the presence of HDP during the same time period (Figure 2a and 2b, respectively).

Table 1 shows that in comparison to those without anxiety, women who experienced anxiety presented with more comorbidities such as smoking during pregnancy, obesity, thyroid disease, pregestational DM and depression. Similar distributions were found in depressed women than those without (Table 2).

Table S1 presents baseline characteristics of pregnant women stratified by the presence or absence of adverse neonatal outcomes (i.e., preterm birth and SGA). In comparison to those with uneventful deliveries, women who experienced preterm delivery and SGA were younger, Caucasians, and had low-income profiles and had more comorbidities such as smoking during

pregnancy, substance abuse, chronic hypertension, anxiety, preeclampsia, and elderly primigravida.

### **Mediation and moderation model for the association between Anxiety and Preterm Birth**

#### ***Anxiety on PTB Mediated by HDP; HDP on PTB Moderated by Depression***

Figure 3a shows that women with anxiety were more likely of having HDP (OR: 1.242, 95% CI: 1.226-1.257) and PTB (OR=1.098, 95% CI: 1.084-1.113). The effect of anxiety on preterm birth was significantly mediated by HDP (mediation effect=0.048, p-value<0.001). Women with HDP were at greater likelihood of having PTB (OR=1.249, 95% CI: 1.247-1.252). Depression significantly moderated the associations between HDP and preterm birth (moderation effect=-0.126, p-value=0.027). Figure 3a also demonstrates that women with both HDP and depression had the highest predicted probability of having PTB (13.7%), while those without these two conditions had the lowest probability (5.0%). Among women without depression, those with HDP were 2.355 (95% CI: 2.345 – 2.365) more likely to have PTB than those without HDP, while among women with depression were 2.076 (95% CI: 1.961 – 2.197) times more likely. Among women without HDP, those with depression were 1.444 (95% CI: 1.413 – 1.476) times more likely to have PTB than those without depression, while among women with HDP, those with depression were 1.273 (95% CI: 1.208 – 1.342) times more likely.

### **Mediation and moderation model for the association between Anxiety and SGA**

#### ***Anxiety on SGA Mediated by HDP; HDP on SGA Moderated by Depression***

Figure 3b displays the same association between anxiety and risk of HDP (OR: 1.242, 95% CI: 1.235-1.250). Anxiety increased the probability of SGA (OR: 1.100, 95% CI 1.081-1.120). HDP also mediated the association between anxiety and SGA (mediation effect=0.042, p-value<0.001).

Women with HDP had greater odds of having SGA (OR=1.216, 95% CI 1.212-1.220). However, depression did not moderate the association between HDP and SGA (p-value=0.29).

## COMMENT

### Principle Findings and Results in the Context of What is Known

Our study showed decreasing trends of preterm birth in pregnant women with no anxiety or HDP. *Ferré et al* (Ferré et al., 2016) also found that the rate for spontaneous preterm birth decreased from 10.41% to 9.54% from 2007 to 2014. In agreement with another study (Sarkar et al., 2017), we found that women with preterm birth or SGA were less likely to be older or with higher income levels. Furthermore, when we stratified age less than 25 years, women who experienced SGA/preterm birth were had a higher percentage among those with HDP than without.

Our moderated model suggested the presence of depression plays a role in the development of PTB. The probability of PTB in patients with HDP compared to those without is dependent on the presence or absence of depression. The negative moderation effect represents a lower probability of PTB due to combination of HDP and depression compared to having HDP or depression independently. Li et al conducted a population prospective cohort showing that pregnant women with depression were at risk for preterm delivery. The severity of the depression also dictated the risk of preterm delivery (Li et al., 2009). It suggests that depression management might reduce the risk of preterm birth. This may explain the negative moderation effect of depression we found on the association between HDP and preterm birth. Another study has shown an increased risk of SGA in pregnant women with depressive symptoms (Babu et al., 2018).

The results of our mediation and moderation models showed that women with anxiety are at an increased likelihood of having HDP. A prospective cohort study from Alberta, Canada suggested that anxiety and depression may contribute to increased risk of SGA associated with HDP (Horsley et al., 2019). The origins of psychosocial stress and anxiety in women can be a factor in downstream neonatal complications. *Hoffman et al* (Hoffman et al., 2016) used cortisol levels measured through maternal hair follicles as an index of stress. Higher stress levels as indicated in increased cortisol levels were found in the second trimester of pregnancy and in those with preterm birth. It has been advocated those pregnant women with stimulation of cortisol through cortisol-releasing hormones may complicate the endocrine function of the placenta which further complicates chronic hypertension and hypertensive states (Warren et al., 1995). In addition, alterations in the maternal vascular system have been shown to alter stress patterns in pregnancy. Evidence has shown that uterine artery blood flow increased in the last trimester, enhancing maternal distress and anxiety through measurable parameters, such as K10 test (Vythilingum et al., 2010). As seen in our study, the effect of anxiety on preterm birth or SGA was significantly mediated by HDP. HDP, such as preeclampsia, have been shown to augment cortisol metabolism through various enzymes (Kosicka et al., 2018). Similar studies have found that the enzyme involved in cortisol metabolism, the placental  $11\beta$ -hydroxysteroid dehydrogenase type 2, has decreased activity in a preeclampsia state, leading to cortisol elevation, and subsequent association with prematurity and low birth weight (Aufdenblatten et al., 2009).

Growth pathologies or prematurity can also be attributed to abnormal blood flow in the uteroplacental circulation. This can lead to insufficient blood supply to the fetus leading to early delivery, or pathological growth (Hüneke & Ude, 2002). McCubbin et al reported that a

substantial maternal diastolic blood pressure response to stress resulted in infants with low birth weights (McCubbin et al., 1996). This explains the role HDP plays during stress and the effect on a growing fetus.

### **Strengths and Limitations**

The strength of our study was the use of a large population-based database. This allowed for extensive analysis of maternal psychopathologies with neonatal outcomes in the course of a decade. A large dataset over an extended period of time is vital to establish trends and determine associations. However, HCUP-NIS is a medico-administrative database, and hence lacks of clinical details. By using this database, it is not possible to ascertain if the diagnosis of interest was made during hospitalization or if the patient had been diagnosed previously. In addition, the validity of the diagnostic codes in HCUP-NIS might contribute to lower rates as seen in other types of administrative databases. This can explain the lower-than-expected preterm birth and SGA rates compared to the national average in developed countries such as the Canada and the United States. HCUP displays data in a cross-sectional manner, thereby providing no link between years to observe temporal trends. In terms of diagnosis, maternal hypertensive disorders like HDP, are diagnosed beyond 20 weeks gestation while anxiety has no specific timing diagnostic parameters in pregnancy. Therefore, based on the data structure, we assumed most anxiety disorders were diagnosed before HDP, but we acknowledge that this has limitations. In addition, it does not provide any information on pharmacological history or any treatments used during the hospital stay. *Avalos et al* examined the role anti-depressants play in the development of preeclampsia. The timing of anti-depressant medication use was determined to be an important factor in the development of preeclampsia. There was a significant increase in the risk of preeclampsia, especially if medications were taken during the second trimester of pregnancy.

In addition, a significant relationship arose between the duration of the antidepressant use and preeclampsia (Avalos et al., 2015).

### **Research/Clinical Implications and Recommendations**

Our findings support the need of early screening of maternal mental disorders such as anxiety and depression and prompt management of pregnancy hypertensive disorders to reduce the risk of developing neonatal complications. Screening of maternal mental disorders should be done early in the first trimester of the pregnancy if it is to be used prospectively to prevent HDP and mental health disorders in the postpartum period. In addition, while many clinicians and researchers have lumped in anxiety and depression, the results of our study suggest that these disorders should be screened for and treated separately with extensive follow-ups. Mental health professionals and obstetricians play an important role in identifying and treating both psychological and hypertensive disorders. Early mental health surveillance is vital through the use of counselling, and screening tools which can be conducted in a resourceful manner. Simple scales such as Pregnancy-Related Anxiety Questionnaire (PRAQ), and Generalized Anxiety Disorder-7 (GAD-7), are efficient as brief screening measures for anxiety in pregnant women and to establish a mental picture of an individual prior to pursuing additional investigations. Having these screening tests provides a quick assessment of an individual's mental health which can be done quickly and in the office setting by any practitioner. However, there is a need to implement better and more routine screening measures during the prenatal period to improve the general well-being of women. The implementation of both systematic screening guidelines and mental health consultation on site has been shown to be an effective way to pinpoint women with higher risk without incorporating further burden on the medical care providers (Johnson et al., 2021). A recent systematic review by Verbeke et al. also showed that mental health intervention

during and after pregnancy was cost-effective (Verbeke et al., 2022). In addition, hypertensive disorders in the mother can have significant associations with the development of mental and behavioural problems in the offspring. *Robinson et al* conducted a metanalysis which showed significant associations between both these the disorders and the outcomes (Robinson et al., 2021). Evidence in this field provides implications for future research and development into effects of maternal conditions on the mental development of the offspring into childhood.

### **Conclusions**

Our study demonstrates potential mechanisms and associations between mental disorders, HDP and adverse neonatal outcomes in pregnant women. HDP mediates the associations between anxiety and preterm birth while depression moderates the effect of HDP on preterm birth. HDP also mediates the association between anxiety and SGA, but depression does not moderate the association between HDP and SGA. Based on our findings, we recommend clinicians screen pregnant women for anxiety and depression in the first trimester of pregnancy as early as possible. This would allow for timely surveillance, management, and treatment to avoid adverse downstream detrimental neonatal complications and possible subsequent mental and development problems in childhood.

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## **FIGURE LEGENDS**

### Figure 1a

Title: Prevalence of hospitalized pregnant women with preterm birth (PTB) with and without hypertensive disorders of pregnancy (HDP) and/or anxiety in the United States from the year 2004 to 2014

### Figure 1b

Title: Prevalence of hospitalized pregnant women with small for gestational age (SGA) with and without hypertensive disorders of pregnancy (HDP) and/or anxiety in the United States from the year 2004 to 2014

### Figure 2a

Title: Prevalence of hospitalized pregnant women with preterm birth (PTB) with and without hypertensive disorders of pregnancy (HDP) and/or depression in the United States from the year 2004 to 2014

### Figure 2b

Title: Prevalence of hospitalized pregnant women with small for gestational age (SGA) with and without hypertensive disorders of pregnancy (HDP) and/or depression in the United States from the year 2004 to 2014

Figure 3a. Mediation and moderation models for preterm birth (PTB) using HDP as the mediator and depression as the moderator. HDP: Hypertensive Disorders of Pregnancy; PTB: Preterm Birth. The numbers represent odds ratio (OR); \*:  $p < 0.05$ .

Figure 3b. Mediation and moderation models for small for gestational age (SGA) using HDP as the mediator and depression as the moderator. HDP: Hypertensive Disorders of Pregnancy; SGA: small for gestational age. The numbers represent odds ratio (OR); \*:  $p < 0.05$ .

**Table 1. Characteristics of Pregnant Women with and without Anxiety and Hypertensive Disorders of Pregnancy derived from Healthcare Costs and Utilization Project Nationwide Inpatient Sample data (2004-2014)**

	No HDP, no anxiety N=8,395,028	No HDP, had anxiety, N=73,620	Had HDP, no anxiety N=619,131	Had HDP and anxiety N=9,009	<i>p</i> -value
<b>Age (years)</b>					
<25	37.9	30.1	41.0	30.1	<0.001
25-34	47.5	51.9	44.0	51.4	
≥35	14.7	18.0	15.0	18.5	
<b>Race</b>					
White	51.9	77.8	53.9	78.1	<0.001
Black	13.5	7.6	17.7	8.2	
Hispanic	23.6	9.7	20.3	9.1	
Asian or Pacific Islander	5.3	1.6	3.1	1.4	
Native American	0.8	0.6	0.9	0.6	
Other					
<b>Income Quartiles</b>					
1 <sup>st</sup> Quartile (lowest income)	27.1	22.7	29.9	23.1	
2 <sup>nd</sup> Quartile	25.4	25.6	25.9	26.2	
3 <sup>rd</sup> Quartile	24.9	27.1	24.6	27.1	
4 <sup>th</sup> Quartile (highest income)	22.6	24.6	19.6	23.7	
<b>Plan Type</b>					
Medicare	0.6	2.5	0.7	2.4	<0.001
Medicaid	42.7	40.3	24.1	35.8	
Private	50.5	52.5	51.7	57.3	
Self-pay	3.2	1.5	2.6	1.3	
No charge	0.2	0.1	0.2	0.1	
Other	2.7	3.1	2.8	3.2	
<b>Co-morbidities</b>					
Smoking during pregnancy	4.8	17.2	4.3	13.0	<0.001
Substance use	1.3	7.2	1.3	5.6	<0.001
Obesity	3.2	8.9	8.1	15.2	<0.001
Thyroid disease	2.4	5.8	3.1	7.0	<0.001
Chronic hypertension	1.9	5.1	0.8	1.5	<0.001
Pregestational diabetes mellitus	0.8	1.5	2.0	2.7	<0.001
Depression	0.3	3.3	0.5	3.0	<0.001
<b>Pregnancy condition</b>					
Gestational hypertension	n/a	n/a	48.0	47.1	<0.001

Preeclampsia	n/a	n/a	52.1	53.3	<0.001
Gestational diabetes mellitus	5.5	7.2	8.8	10.1	<0.001
Elderly multigravida	9.4	12.2	8.5	11.4	<0.001
Elderly primigravida	1.6	2.4	2.6	3.9	<0.001
Multiple gestations	1.3	1.9	3.7	4.8	<0.001
<b>Outcomes</b>					
Preterm birth	6.6	9.3	15.2	17.3	<0.001
SGA	2.0	3.2	4.8	6.5	<0.001

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**Table 2. Characteristics of Pregnant Women with and without Depression and Hypertensive Disorders of Pregnancy derived from Healthcare Costs and Utilization Project Nationwide Inpatient Sample data (2004-2014)**

	No HDP, no depression N=8,438,718	No HDP, had depression, N=29,930	Had HDP, no depression N=625,054	Had HDP and depression N=3,086	<i>p</i> -value
<b>Age (years)</b>					
<25	37.8	31.5	40.9	31.7	<0.001
25-34	47.5	50.1	44.1	48.3	
≥35	14.7	18.4	15.1	20.0	
<b>Race</b>					
White	52.1	73.7	51.1	75.0	<0.001
Black	13.4	9.2	17.6	9.5	
Hispanic	23.5	12.2	20.2	10.7	
Asian or Pacific Islander	5.3	1.6	3.1	1.4	
Native American	0.8	0.6	0.9	0.8	
Other	4.9	2.8	4.2	2.5	
<b>Income Quartiles</b>					
1 <sup>st</sup> Quartile (lowest income)	27.1	23.7	29.8	22.5	<0.001
2 <sup>nd</sup> Quartile	25.4	26.5	25.9	27.3	
3 <sup>rd</sup> Quartile	24.9	27.0	24.7	28.0	
4 <sup>th</sup> Quartile (highest income)	22.6	22.8	19.6	22.2	
<b>Plan Type</b>					
Medicare	0.6	2.5	0.7	2.7	<0.001
Medicaid	42.7	43.9	42.0	38.5	
Private	50.6	48.8	51.8	54.8	
Self-pay	3.2	1.7	2.5	1.6	
No charge	0.2	0.1	0.2	0.0	
Other	2.7	2.9	2.8	2.4	
<b>Co-morbidities</b>					
Smoking during pregnancy	4.9	18.4	4.4	13.8	<0.001
Substance use	1.4	8.5	1.4	6.4	<0.001
Obesity	3.2	8.7	8.2	15.2	<0.001
Thyroid disease	2.4	5.6	3.1	6.7	<0.001
Chronic hypertension	1.9	4.8	0.8	1.0	<0.001
Pregestational diabetes mellitus	0.8	1.9	2.0	3.6	<0.001
Anxiety	0.8	8.2	1.4	8.7	<0.001
<b>Pregnancy condition</b>					

Gestational hypertension	n/a	n/a	48.0	45.7	<0.001
Preeclampsia	n/a	n/a	52.1	55.1	<0.001
Gestational diabetes mellitus	5.5	7.0	8.8	10.9	<0.001
Elderly multigravida	9.4	12.5	8.6	12.4	<0.001
Elderly primigravida	1.6	2.2	2.6	4.1	<0.001
Multiple gestations	1.3	1.8	3.7	4.3	<0.001
<b>Outcomes</b>					
Preterm birth	6.6	10.6	15.2	19.4	<0.001
SGA	2.0	3.0	4.8	6.1	<0.001

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## **AUTHOR STATEMENT**

### **CONTRIBUTION TO AUTHORSHIP**

ES, TM, TVN designed the project. JR and AB took part in the acquisition and management of HCUP data. JR and GE performed the analysis under the supervision of ES and with assistance of CC. JR and ES drafted the manuscript. MB, DK, TM, TVN, TT, ND, FY, CC critically reviewed the manuscript.

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None

**CONFLICT OF INTERESTS**

The authors report no conflict of interest

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**HIGHLIGHTS:**

- We used the HCUP-NIS database containing 9 million records of hospitalized pregnant women in the United States between 2004 and 2014 to analyze the prevalence as well as associations and potential mechanisms between maternal mental disorders (anxiety and depression), hypertensive disorders of pregnancy (HDP), and adverse neonatal outcomes (preterm birth and small for gestational age (SGA)).
- Mediation and moderation modeling were used to separately evaluate potential mechanisms between maternal mental disorders, HDP, and adverse neonatal outcomes.
- We found that associations between anxiety and adverse neonatal outcomes (preterm birth and SGA) were mediated by HDP. Depression was shown to moderate the association between HDP and preterm birth but not between HDP and SGA.
- Early screening in pregnant women for anxiety and depression is strongly recommended for clinicians and mental health professionals to reduce downstream complications in the newborn.

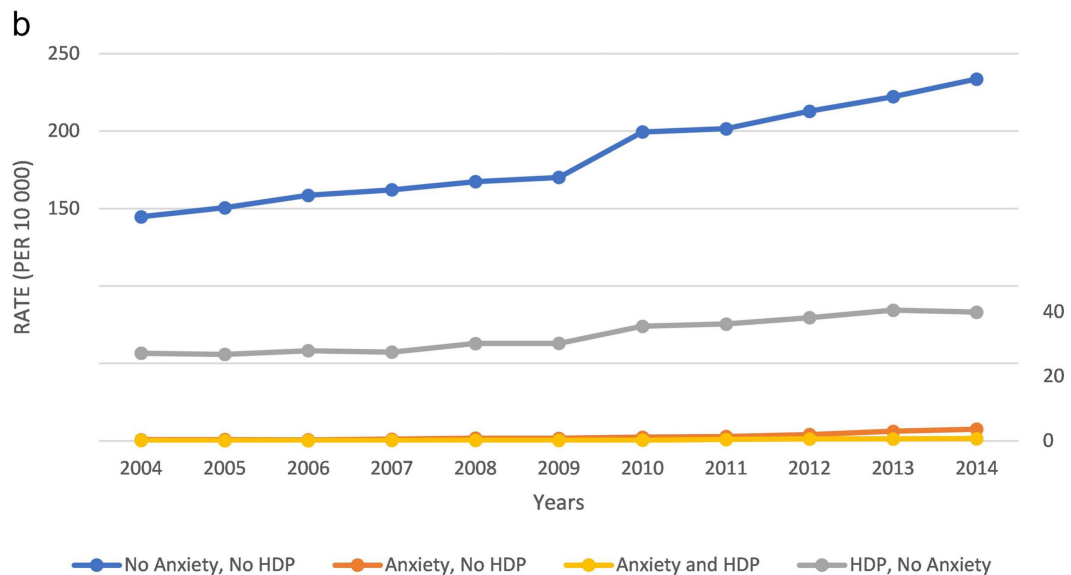
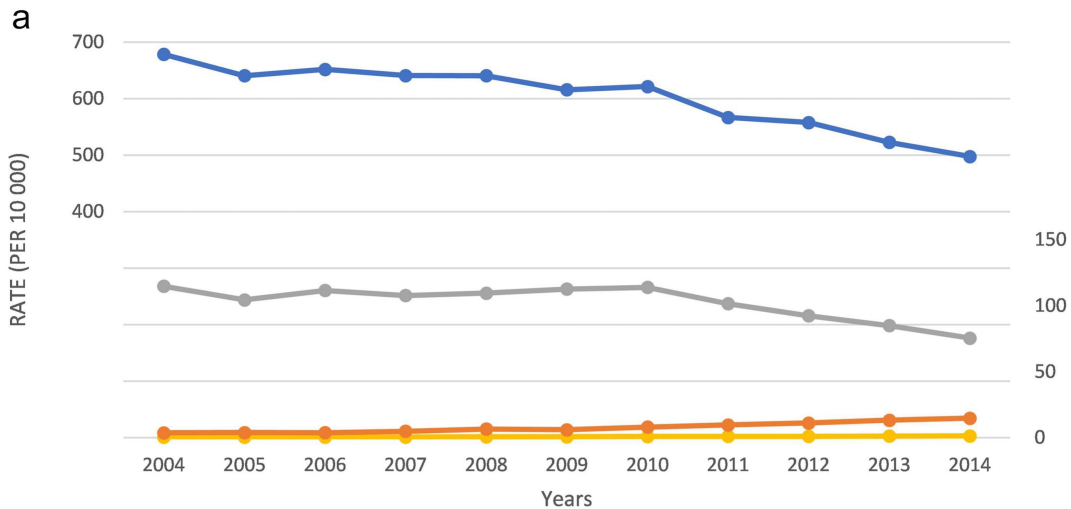


Figure 1

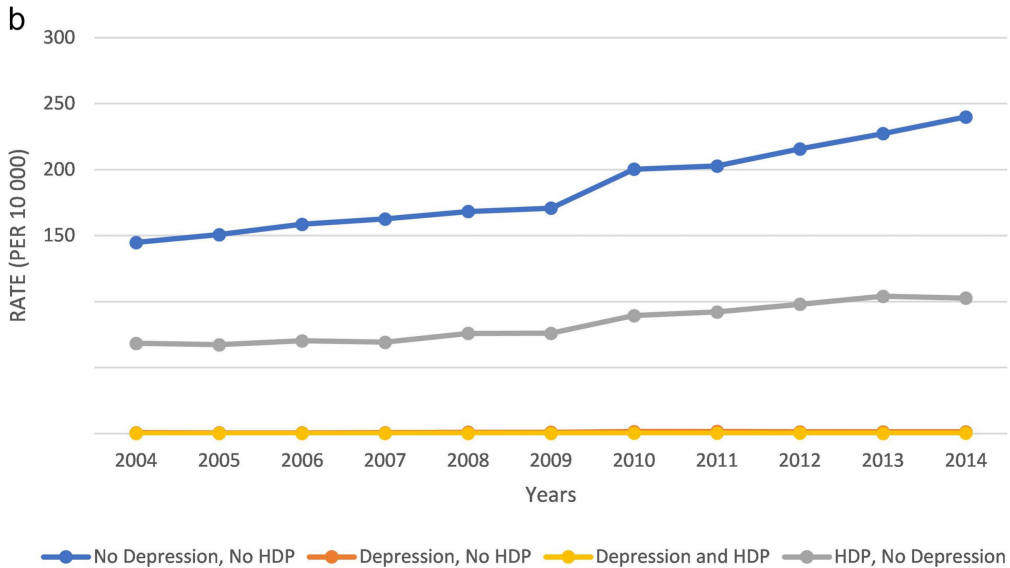
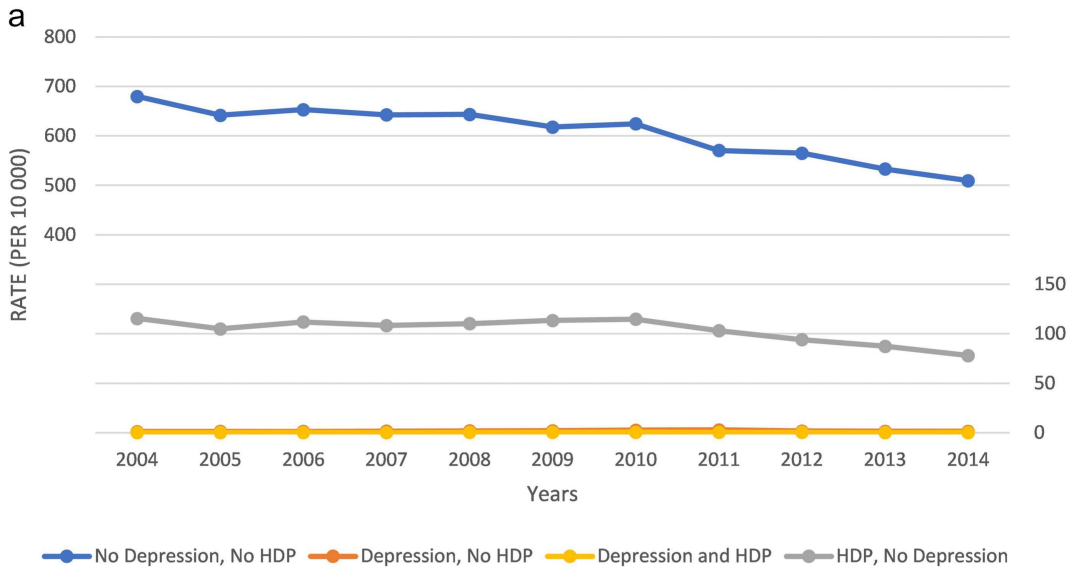
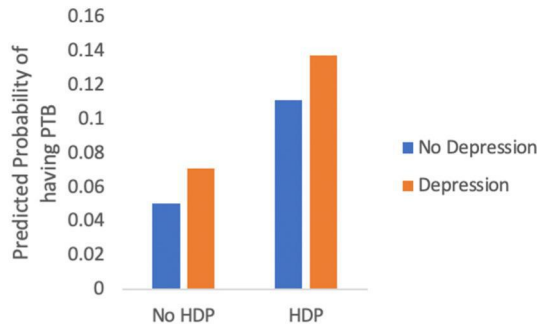
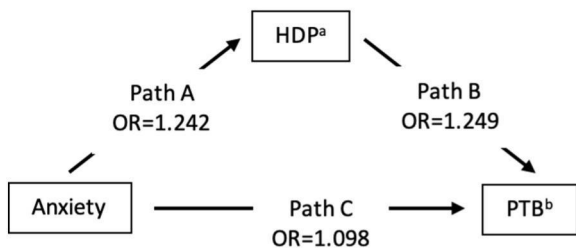


Figure 2

a



b

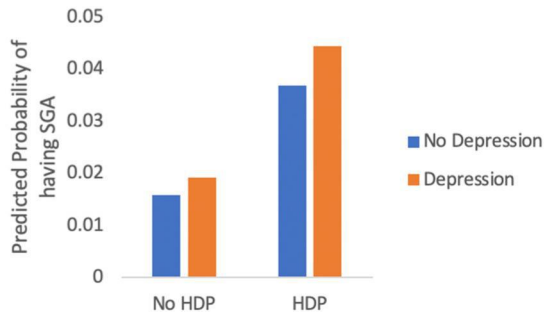
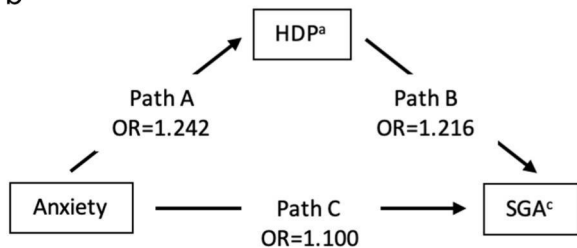


Figure 3