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UNIVERSITY OF CALIFORNIA,
IRVINE

The Association Between Air Pollution Exposure and the Risk of Postpartum Depression
and Gestational Diabetes Mellitus During the COVID-19 Pandemic

THESIS

submitted in partial satisfaction of the requirements
for the degree of

MASTER OF SCIENCE

in Biomedical and Translational Science

by

Kathryne Scarlett Headon

Thesis Committee:
Professor Jun Wu, Co-Chair
Professor Sherrie Kaplan, Co-Chair
Assistant Professor, Robert Wilson (UD)

2024

DEDICATION

To

Dr. Christina Lynn Staudhammer

For being the person who was always in my corner, supported me throughout my academic journey, pushed me to become the best student possible, encouraged me to pursue my dreams, and for being an amazing aunt.

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ABSTRACT OF THE THESIS

The Association Between Air Pollution Exposure and the Risk of Postpartum Depression and Gestational Diabetes Mellitus During the COVID-19 Pandemic

by

Kathryne Scarlett Headon

Master of Science in Biomedical and Translational Sciences

University of California, Irvine, 2024

Professor Jun Wu, Chair

Air pollution exposure has been known to increase the risk of several adverse birth outcomes, including postpartum depression (PPD) and gestational diabetes mellitus (GDM). In March 2020, the COVID-19 pandemic caused the state of California to shut down to prevent the spread of the virus. This led to changes in air pollution concentrations. Understanding how these changes influenced the association between air pollution and both PPD and GDM will provide further information into the health impacts seen during the COVID-19 pandemic period. Therefore, we sought to investigate the association between air pollution exposure and the risk of PPD and GDM. We also incorporated the impacts of experiencing the pandemic during and after pregnancy to assess whether these associations changed. Patient records from Kaiser Permanente Southern California (KPSC) electronic health records (EHRs) provided health data, socioeconomic status (SES) data, and residential address histories. Pollution data for monthly averages of particulate matter with an aerodynamic diameter $\leq 2.5 \mu\text{g}/\text{m}^3$ (PM_{2.5}), particulate matter with an aerodynamic diameter $\leq 10 \mu\text{g}/\text{m}^3$ (PM₁₀), nitrogen dioxide (NO₂), and 8-hour ozone (O₃) was spatiotemporally linked to participant residential addresses. A discrete time approach

with pooled logistic regression was used for PPD models, while Cox proportional hazard models were used for GDM analyses. Subgroup analyses were performed with Cox proportional hazard models, and to investigate whether experiencing the pandemic before conception, after birth, or during pregnancy altered the associations with air pollution. We found increased risks of PPD with exposure to O₃ during pregnancy and in the postpartum period; PM_{2.5} had significantly negative associations with PPD risk in the late pregnancy and postpartum periods. Hispanic, white, or multi-racial/other mothers, or mothers with higher incomes were more susceptible to PPD risk with ozone exposure. Positive associations between GDM risk and exposure to PM_{2.5}, PM₁₀, and O₃ were found; no significant associations were seen with NO₂ exposure, except for negative associations with second trimester exposure. Mothers with more than a college education had greater associations between GDM and exposure to all pollutants, including NO₂. For PPD analyses, mothers were grouped by COVID time: not impacted (gave birth before March 2019), postpartum (gave birth between March 2019-March 2020), pregnant (pregnant in March 2020), or conceived after (date of conception after March 2020). Experiencing the COVID-19 pandemic while pregnant or in the 12-month postpartum period was positively associated with exposure to PM₁₀ and O₃. For GDM analyses, COVID time groups included: not impacted (gave birth before March 2020), pregnant (pregnant in March 2020), or conceived after (date of conception after March 2020). GDM risk was positively associated with exposure to PM_{2.5} for mothers who were pregnant when the pandemic began. Overall, this study shows the associations between air pollution exposure and the risk of PPD and GDM have changed since the COVID-19 outbreak. The results were different from our group's previous studies, which found positive associations between PM exposure and PPD,

and positive associations between NO₂ exposure and GDM. These differences may be explained by decreases in ambient air pollution levels during the COVID-19 pandemic period, or by altered PM_{2.5} constituent levels. Future studies should continue to investigate the association between air pollution and maternal health during the pandemic period, especially the association with PM_{2.5} constituent levels.

CHAPTER 1: INTRODUCTION

Overview

Air pollution exposure has been associated with several adverse health outcomes (Hsu et al., 2017; Kanner et al., 2021; Niedzwiecki et al., 2020; O'lenick et al., 2017; Thomson et al., 2019), and is estimated to be responsible for 7 million premature deaths worldwide every year (World Health Organization, n.d.). The implementation of several regulatory policies has contributed to the decrease in air pollution levels seen in southern California over the past twenty years (Lurmann et al., 2015); but research is still finding that health is impacted by exposure to air pollution. Past research has found a relationship between air pollution exposure and adverse impacts on several biological systems such as the respiratory system, reproductive system, and cardiovascular system (H. Chen et al., 2022; Dominski et al., 2021; Manisalidis et al., 2020; Ming et al., 2022; Sexton et al., 2007), and recently, scientists have identified a potential association with mental health (Jia et al., 2018; H. Li et al., 2020; Nguyen et al., 2021; Qiu et al., 2022). With air pollution known to impact human health, there has been support for perinatal air pollution exposure research. Pregnancy and the postpartum period are vulnerable stages for women (Bastain et al., 2021; Lamichhane et al., 2021a, 2021b; Mughal et al., n.d.). Not only do women experience large hormonal changes, but they also require greater oxygen demands (LoMauro & Aliverti, 2015; Magon & Kumar, 2012; Soma-Pillay et al., 2016). This may increase their exposure to air pollution and put them at an even greater risk of the adverse impacts from exposure. Understanding the influence of perinatal air pollution exposure may increase awareness of different environmental exposures, which can improve the prevention of certain adverse birth outcomes. Postpartum depression (PPD) and gestational diabetes

mellitus (GDM) are two of the most common adverse birth outcomes, with a worldwide prevalence of 10-20% and 14%, respectively (Ashwal & Hod, 2015; Bauman et al., n.d.; Fisher et al., 2012; Mughal et al., n.d.; Plows et al., 2018). With no single cause known for either of these disorders, further research into their current risk factors is important. Therefore, this thesis seeks to examine the relationship between air pollution exposure and both PPD and GDM occurrence using a cohort of women from Southern California who gave birth between 2019 and 2021.

PPD and Air Pollution

Previous studies have provided support for the association between higher levels of air pollution throughout pregnancy and an increased risk of PPD (Ahlers & Weiss, 2021; Bastain et al., 2021; C. C. Duan et al., 2022; Niedzwiecki et al., 2020; Sheffield et al., 2018). Duan et al. published a study that assessed the relationship between different types of air pollutants and the risk of PPD at 6 weeks postpartum (C. C. Duan et al., 2022), while placing an emphasis on looking at different vulnerability windows (C. C. Duan et al., 2022). Their group found there was an increased risk of PPD with higher average exposures to particulate matter (PM) with an aerodynamic diameter $\leq 10 \text{ mg/m}^3$, carbon monoxide (CO), and nitrogen dioxide (NO₂) for the entire pregnancy (C. C. Duan et al., 2022). They also found increased risk of PPD for people with higher average exposures to SO₂ during the second trimester and higher exposures to PM_{2.5} and O₃ during the first trimester (C. C. Duan et al., 2022). Sheffield et.al assessed the relationship between PM_{2.5} during different periods of pregnancy and the risk of PPD at 6 and 12 months postpartum with an ethnically diverse population (Sheffield et al., 2018). They found there was an increased risk for PPD when there were higher average exposures to PM_{2.5} in mid-pregnancy; they also reported

that black women, who were exposed to higher levels of PM_{2.5} throughout their entire pregnancy were at an increased risk of developing PPD (Sheffield et al., 2018). This research group also published the Niedzwiecki et al. study in Mexico City, which assessed the relationship between PM_{2.5} exposure throughout pregnancy, and psychological functioning at 1 and 6 months postpartum (Niedzwiecki et al., 2020). They found an 83% increased risk of PPD when there were increased levels of PM_{2.5} exposure throughout pregnancy (Niedzwiecki et al., 2020). They also found a 158% increased risk of late-onset PPD when there were increased levels of PM_{2.5} exposure throughout pregnancy (Niedzwiecki et al., 2020).

Our research group also recently published a study that investigated the association between antepartum and postpartum air pollution exposure, and the risk of PPD (Sun et al., 2023). We used a cohort of women from Southern California who gave birth between 2008-2018 (Sun et al., 2023). We found that exposure to O₃, PM₁₀, and PM_{2.5} both during pregnancy and the postpartum period was associated with greater risks of PPD (Sun et al., 2023). Specifically, we found that O₃ exposure during the entire pregnancy and 6 months postpartum, as well as PM exposure later in the pregnancy and in the postpartum periods, were associated with PPD (Sun et al., 2023).

While these studies suggest that increased exposure to certain pollutants may increase one's risk of developing PPD, the findings have been inconsistent regarding vulnerability windows, and the pollutants that pose the greatest risk. The COVID-19 pandemic was also not considered in previous studies, so future studies should assess whether the pandemic has influenced the association between air pollution exposure and PPD development.

Overall, further assessment of the potential relationship between PPD and air pollution is warranted.

GDM and Air Pollution

Several studies have reported an association between air pollution exposure and GDM. Our research group has previously studied the association between air pollution and GDM using a cohort of women who gave birth between 2008-2018 at Kaiser Permanente Southern California (KPSC) facilities (Sun et al., 2022). Exposure periods were defined as preconception (3 months before conception), first trimester (gestational months 1-3), second trimester (gestational months 4-6), first two trimesters (gestational months 1-6), and entire pregnancy (conception to birth). We found that exposure to kriged PM_{2.5}, PM₁₀, and NO₂ increased the odds of GDM in every exposure period (Sun et al., 2022). O₃ exposure in all exposure periods decreased the odds of GDM, proposing a potential protective association (Sun et al., 2022).

Most studies have reported positive associations between PM exposure and GDM. First and second trimester PM_{2.5} and PM₁₀ exposure has most commonly been found to be associated with an increased risk of GDM (Choe et al., 2018, 2019; Gong et al., 2023; Hu et al., 2015; Jo et al., 2019; Lin et al., 2020; Miron-Celis et al., 2023; Niu et al., 2023; Rammah et al., 2020; Shen et al., 2017; Yan et al., 2023; Yao et al., 2020; B. Ye et al., 2020; Yu et al., 2020; M. Zhang et al., 2020). One study from Chiayi City, Taiwan even reported that second trimester PM_{2.5} exposure was associated with a nearly 50% increased risk of GDM (Yan et al., 2023). Another period of vulnerability to PM exposure may be the period before conception (Jo et al., 2019; Niu et al., 2023; Rammah et al., 2020; Shen et al., 2017; Yao et al., 2020; Zhang et al., 2020). Only one study found a negative association between first

trimester PM_{2.5} exposure and GDM (Zhang & Zhao, 2021), and a few studies did not find any significant associations during the first trimester (Hu et al., 2021), the second trimester (Hu et al., 2021; Kang et al., 2020), or the first two trimesters (Hu et al., 2021). No significant associations were found in two studies from China regarding PM₁₀ exposure and GDM (Hu et al., 2021; Zhang & Zhao, 2021). Overall, these results indicate that early pregnancy exposure to PM may increase the risk of developing GDM.

Overall, the results for NO₂ and NO_x exposure have been mixed. Increased NO₂ and NO_x exposure during the preconception period (Jo et al., 2019; Niu et al., 2023; Robledo et al., 2015), first trimester (Choe et al., 2019; Niu et al., 2023; Pedersen et al., 2017; Robledo et al., 2015), and second trimester (Malmqvist et al., 2013; Zhang & Zhao, 2021), were all reported to increase the risk of GDM. However, negative associations were reported for exposure during the second trimester, and the first and second trimesters in a study from Foshan, China (Lin et al., 2020).

Several studies reported positive associations between GDM and O₃ exposure during the preconception period (Gong et al., 2023; Z. Li et al., 2022; Miron-Celis et al., 2023; Yao et al., 2020), first trimester (Gong et al., 2023; Hu et al., 2015; Z. Li et al., 2022; Miron-Celis et al., 2023; Yao et al., 2020), second trimester (Gong et al., 2023; Hu et al., 2015; Miron-Celis et al., 2023; Zhang & Zhao, 2021), entire pregnancy (Hu et al., 2015), and even early third trimester (Miron-Celis et al., 2023). These results contrast with findings from other studies, where O₃ exposure was found to have a protective association with GDM during the preconception period (Jo et al., 2019; Robledo et al., 2015), first trimester (Jo et al., 2019; Lin et al., 2020), and second trimester (Lin et al., 2020).

Environmental Exposures and the COVID-19 Pandemic

On March 11, 2020, the COVID-19 pandemic caused the world to shut down. This virus led to great concern regarding the safety and health of many individuals. To combat these concerns, many unessential businesses either shut down or converted to a virtual, work-from-home setting. With more individuals working from home, the lockdowns were estimated to decrease vehicle traffic and industrial activities, potentially explaining the decline in anthropogenic air pollution after the pandemic began (Berman & Ebisu, 2020; Jiang et al., 2021). Since air pollution has been known to influence disease and illness, such as PPD and GDM, the difference in concentrations of pollutants may impact the development of these illnesses differently. Therefore, a study that compares PPD and GDM risk due to air pollution exposure before and after the COVID-19 pandemic may provide insight regarding how environmental factors contribute to the development of these illnesses. This study may also increase our understanding of how the COVID-19 pandemic impacted pregnant women's vulnerability to air pollution exposure.

Rationale: Air Pollution as an Exposure Variable

Air pollution is known to impact multiple physiological systems in the human body (Manisalidis et al., 2020; Ming et al., 2022; Sexton et al., 2007; West et al., 2016; Zhang & Batterman, 2013). With air pollution levels changing over recent years (County of Los Angeles Public Health, n.d.; Lurmann et al., 2015; Rowan, 2019), further investigating its impact on health with a more recent cohort may be beneficial. Therefore, using a cohort from recent years, such as 2019-2021, may increase our understanding of the detrimental impacts from air pollution at the levels relevant to people's recent or current exposures. Through understanding the current adverse health effects, policymakers can have the

necessary information to create policies that will best improve the current air pollution crisis.

Overall objective: To evaluate the relationship between perinatal air pollution exposure and postpartum depression and gestational diabetes mellitus for women who gave birth between January 2019 and December 2021.

Specific Aim 1: Assess the association between air pollution exposure during pregnancy and the postpartum period (12 months after birth) and postpartum depression occurrence.

Hypothesis: Increased exposure to certain pollutants, such as PM_{2.5}, PM₁₀, and O₃ during the third trimester and the postpartum period will increase the risk of developing PPD.

Specific Aim 2: Assess the association between air pollution exposure during pregnancy and gestational diabetes mellitus occurrence.

Hypothesis: Increased exposure to certain pollutants, such as PM_{2.5}, PM₁₀, and NO₂ during the first and second trimesters will increase the risk of developing GDM.

Specific Aim 3: Assess whether there is a difference between air pollution's association with postpartum depression and gestational diabetes mellitus before, during, and after the COVID-19 pandemic.

Hypothesis: There will be a stronger association between PPD and GDM and air pollution exposure during pregnancy before the COVID-19 pandemic compared to during the COVID-19 pandemic due to pandemic lockdowns contributing to lower air pollution concentrations in southern California.

CHAPTER 2: BACKGROUND

What is PPD?

PPD is the perinatal form of major depressive disorder (Guintivano et al., 2018; Payne & Maguire, 2019). With a prevalence rate of 10-20% (Glynn et al., 2013; Guintivano et al., 2018; Mughal et al., n.d.; Niedzwiecki et al., 2020; Payne & Maguire, 2019), it's estimated that about 500,000 women in the US are diagnosed with PPD every year (Guintivano et al., 2018). Additionally, a study revealed a 7-fold increase in depressive disorders recorded during delivery hospitalizations in the United States from 2000 - 2015 (Haight et al., 2019).

There are three psychiatric outcomes that can occur after delivery: baby blues, PPD, and postpartum psychosis. Baby blues affects about 70-75% of new mothers (Cleveland Clinic, 2022; Sit & Wisner, 2009; Stewart & Vigod, 2016). Baby blues are brief crying spells, irritability, poor sleep, and emotional reactivity; symptom onset begins 1-2 days after delivery and usually resolves by 10-14 days postpartum (Cleveland Clinic, 2022; Mayo Clinic, 2022b; Miller, 2002; Mughal et al., n.d.; Sit & Wisner, 2009; Stewart & Vigod, 2016). Postpartum psychosis can also occur, which is the rapid onset of intense mood disturbance, confusion, strange or delusional beliefs, hallucinations, and disorganized thought (Cleveland Clinic, 2022; Mayo Clinic, 2022b; Sit & Wisner, 2009). Postpartum psychosis is the perinatal form of bipolar disorder, and women with bipolar disorder are at a high risk for an episode within the first month postpartum (Miller, 2002; Sit & Wisner, 2009; Stewart & Vigod, 2016). Postpartum psychosis is different from PPD and requires immediate medical attention due to the increased risk of suicide and infanticide (Cleveland Clinic, 2022; Mayo Clinic, 2022b; Mughal et al., n.d.; Stewart & Vigod, 2016). For the following study, we will concentrate on PPD specifically.

PPD can emerge in the form of different symptoms, including depressed mood, feelings of worthlessness, lack of appetite, insomnia or hypersomnia, impaired concentration, suicidal tendencies, and many more (Mayo Clinic, 2022b; Mughal et al., n.d.; Payne & Maguire, 2019). Symptom onset can begin during pregnancy, and up to 12 months postpartum (Cleveland Clinic, 2022; Mayo Clinic, 2022b; Payne & Maguire, 2019; Stewart & Vigod, 2016), although diagnosis usually occurs between 4 and 6 weeks postpartum (Sit & Wisner, 2009). PPD can also affect infants (Glynn et al., 2013; Mughal et al., n.d.; Niedzwiecki et al., 2020); studies have shown that children born to mothers with PPD are more at risk for developing cognitive issues, behavioral and emotional issues, delays in language development, sleeping and eating concerns, obesity, and many more (Cleveland Clinic, 2022; Glynn et al., 2013; Guintivano et al., 2018; Mayo Clinic, 2022b; Payne & Maguire, 2019). PPD also can impact mother-infant bonding, and there are higher rates of infanticide among children born to mothers with PPD (Glynn et al., 2013; Guintivano et al., 2018; Mughal et al., n.d.).

There are several potential risk factors that have been identified in the past, but currently, there is no single predictor of PPD (Glynn et al., 2013; Guintivano et al., 2018; Mayo Clinic, 2022b). These potential risk factors include past mental health disorders, adverse life events, and physiological factors. Studies have shown that past psychiatric disorders increase a woman's odds of developing PPD (Cleveland Clinic, 2022; Glynn et al., 2013; Guintivano et al., 2018; Mayo Clinic, 2022b; Mughal et al., n.d.; Payne & Maguire, 2019). Adverse life events have also been shown to be a risk factor (Mayo Clinic, 2022b; Mughal et al., n.d.; Payne & Maguire, 2019). Women who have had traumatic experiences either in childhood or adulthood are more at risk for PPD (Guintivano et al., 2018; Payne &

Maguire, 2019). Women who had adverse pregnancy outcomes are also more at risk; this includes women who had preterm and stillborn births (Cleveland Clinic, 2022; Guintivano et al., 2018). Physiological changes include different hormonal levels during pregnancy, differences in neurotransmitter availability, and immune system responses (Guintivano et al., 2018; Payne & Maguire, 2019). Normally, a woman's body changes drastically throughout pregnancy and the postpartum period; these changes include increases in pro-inflammatory cytokines, changes in hormone levels, and increases in respiratory requirements (Hendrick et al., n.d.; LoMauro & Aliverti, 2015; Palm et al., 2013; Racicot et al., 2014; Soma-Pillay et al., 2016). For example, one study reported that the pro-inflammatory cytokine, IL-6 increased with gestational age (Palm et al., 2013). Hormonal changes include rising stress hormone levels during pregnancy, which drop drastically following delivery; there are also increases in oxytocin and prolactin (Hendrick et al., n.d.; Soma-Pillay et al., 2016). Finally, respiratory requirements are altered during pregnancy with oxygen consumption and metabolic rate increasing by 20% and 15%, respectively (LoMauro & Aliverti, 2015; Soma-Pillay et al., 2016). These drastic changes are normal for pregnancy, but they can increase a woman's vulnerability to PPD.

PPD also impacts both mother and infant long-term. A recent review found that mothers with PPD are more likely to have lower mood scores one year postpartum compared to those without PPD (Slomian et al., 2019). It's also reported that depressed mothers have higher levels of both state and trait anxiety at 1 and 3.5 years postpartum (Slomian et al., 2019; Vliegen et al., 2013). If left untreated, mothers with PPD are at an increased risk of future episodes of major depression (Mayo Clinic, 2022b), and chronic depressive disorder (Corner & Miller, n.d.; Mughal et al., n.d.). For infants, there is an

increased incidence of infant night-time awakenings, and more problematic sleep patterns for infants with mothers with more depressive symptoms (Gress-Smith et al., 2012; Miller, 2002; Pinheiro et al., 2011; Slomian et al., 2019). There's overall strong support for a negative association between maternal PPD and cognitive development in children (Miller, 2002; Mughal et al., n.d.; Slomian et al., 2019). One study found that children born to mothers with persistent PPD had more internalizing problems, such as bodily complaints, worrying, and social withdrawal, at 6 years old (Tainaka et al., 2022). It's also reported that higher maternal depressive symptoms at 5 months postpartum is associated with less infant weight gain from 5 to 9 months (Gress-Smith et al., 2012).

According to the Diagnostic and Statistical Manual, postpartum depression, or major depression after delivery is two or more weeks of persistent 1) depressed mood, or 2) loss of interest in daily activities plus four of the following symptoms (appetite disturbance, sleep disturbance, psychomotor agitation or slowing, fatigue, feelings of worthlessness or inappropriate guilt, poor concentration, suicidal ideation) that onset after childbirth (Mughal et al., n.d.; Sit & Wisner, 2009; Stewart & Vigod, 2016). The optimal screening time for PPD is during the first postnatal obstetrical visit (Sit & Wisner, 2009). One of the most common diagnosis tools is the Edinburg Postnatal Depression Scale (EPDS) (Cleveland Clinic, 2022; Levis et al., 2020; Mughal et al., n.d.; Sit & Wisner, 2009). The EPDS is a self-report instrument that contains 10 items ranked from 0-3 that reflect one's experience over the past week (Cleveland Clinic, 2022; Levis et al., 2020; Sit & Wisner, 2009). An EPDS score of ≥ 13 or 10 is an acceptable indicator of PPD (Levis et al., 2020; Mughal et al., n.d.; Sit & Wisner, 2009). When women are diagnosed with PPD, prompt treatment is necessary,

with psychotherapy and/or antidepressant medication being the most common treatment plans (Cleveland Clinic, 2022; Mayo Clinic, 2022b; Mughal et al., n.d.; Sit & Wisner, 2009).

What is GDM?

Pregnant women are diagnosed with GDM when they develop diabetes for the first time during their pregnancy (Centers for Disease Control and Prevention, 2022; Chen et al., 2016; Mayo Clinic, 2022a; Mumtaz, 2000); GDM impacts about 18 million births every year (Plows et al., 2018). GDM usually results from a combination of beta-cell (β -cell) dysfunction and chronic insulin resistance (Plows et al., 2018; Quintanilla Rodriguez & Mahdy, 2023; Sharma et al., 2022). β -cells are cells in the pancreas that are responsible for storing and secreting insulin when blood glucose levels are high (Bartolomé, 2023; Cleveland Clinic, 2024; Dłudla et al., 2023; Khin et al., 2023; Marchetti et al., 2017; Plows et al., 2018; Sharma et al., 2022). β -cell dysfunction occurs when these cells cannot either adequately sense rising glucose levels, or when they no longer can release the proper amount of insulin (Cerf, 2013; Dłudla et al., 2023; Plows et al., 2018). Insulin is normally produced by the pancreas to allow cells to take in glucose from the blood and use it for energy (Centers for Disease Control and Prevention, 2022; Cleveland Clinic, 2024; Dłudla et al., 2023; Khin et al., 2023). Insulin resistance occurs when the cells don't properly respond to insulin (American Diabetes Association, 2024b; Cerf, 2013; Freeman et al., 2023; Sharma et al., 2022). Insulin resistance exacerbates β -cell dysfunction, since it results in hyperglycemia, or high blood glucose levels (American Diabetes Association, 2024b; Cernea & Dobreanu, 2013; Freeman et al., 2023; Khin et al., 2023). Hyperglycemia leads to β -cells overproducing insulin, which further contributes to insulin resistance and β -cell dysfunction (Cernea & Dobreanu, 2013; Dłudla et al., 2023; Sharma et al., 2022). Pregnant women are vulnerable to β -cell dysfunction and

insulin resistance due to hormones produced by the placenta. During pregnancy, the placenta produces several hormones, such as lactogen, estrogen, and cortisol, that block insulin's function and promotes insulin resistance (Cleveland Clinic, 2024; Johns Hopkins Medicine, 2023; Plows et al., 2018; Quintanilla Rodriguez & Mahdy, 2023; Sharma et al., 2022). Normally, the pancreas can overcome the adverse impacts from insulin resistance by producing more insulin, but during pregnancy, the pancreas may not overcome the effects from the placental hormones (Johns Hopkins Medicine, 2023).

Women who have GDM are also at a greater risk of experiencing high blood pressure during pregnancy, preeclampsia, and cesarian-section delivery (Centers for Disease Control and Prevention, 2022; Mayo Clinic, 2022a; Mumtaz, 2000). Women with GDM are at an increased risk of developing cardiovascular disease, and it's also estimated that about 50%-60% of women with GDM will develop Type 2 diabetes later in life, compared to the worldwide prevalence of 6.3% (Centers for Disease Control and Prevention, 2022; Mayo Clinic, 2022a; Plows et al., 2018). Infants born to mothers with GDM are at a greater risk for preterm birth, breathing difficulties, hypoglycemia, low blood pressure immediately after birth, childhood obesity, cardiovascular disease, and developing Type 2 diabetes later in life (American Diabetes Association, 2003; Centers for Disease Control and Prevention, 2022; Johns Hopkins Medicine, 2023; Mayo Clinic, 2022a; Mumtaz, 2000; Plows et al., 2018). Another common complication for infants, is macrosomia, or large infant birth weight (more than 9 pounds) (American Diabetes Association, 2003; Johns Hopkins Medicine, 2023; Mayo Clinic, 2022a; Mumtaz, 2000). The growing fetus receives all its nutrients directly from their mother's blood. If the mother's blood has high levels of glucose, the fetal pancreas senses this, and produces more insulin. The extra glucose is then converted to fat, which can lead to

excessively large fetal growth (Johns Hopkins Medicine, 2023; Mayo Clinic, 2022a; Mumtaz, 2000).

Almost all pregnant women have some insulin resistance in late pregnancy (Centers for Disease Control and Prevention, 2022). Although, some women are at a greater risk of GDM, including women who are overweight or obese, have a family history of diabetes, have prediabetes or glucose intolerance, are older than 25 years, who have previously given birth to a baby larger than 9 pounds, or are of African American, American Indian/Alaska Native, Asian, Hispanic, or Pacific Islander descent (Johns Hopkins Medicine, 2023; Lavery et al., 2017; Mayo Clinic, 2022a; Plows et al., 2018).

Usually, GDM does not have any visible symptoms (Centers for Disease Control and Prevention, 2022; Mayo Clinic, 2022a; Mumtaz, 2000). Therefore, it's diagnosed through tests performed at perinatal visits. Since GDM usually develops around 24 weeks gestation, testing is recommended between 24-28 weeks (Centers for Disease Control and Prevention, 2022; Johns Hopkins Medicine, 2023; Mumtaz, 2000; Quintanilla Rodriguez & Mahdy, 2023). A common GDM test is an oral glucose tolerance test (OGTT), which assesses fasting plasma glucose levels (American Diabetes Association, 2003; Mumtaz, 2000; Quintanilla Rodriguez & Mahdy, 2023).

The current GDM treatment plan includes checking blood sugar levels regularly, developing a healthy eating plan, engaging in moderately intense regular exercise, and regularly monitoring the baby's growth and development (Centers for Disease Control and Prevention, 2022; Johns Hopkins Medicine, 2023; Mayo Clinic, 2022a; Mumtaz, 2000; Quintanilla Rodriguez & Mahdy, 2023). If those treatments don't work, then GDM patients

may be prescribed insulin, metformin, or other diabetes medications (Centers for Disease Control and Prevention, 2022; Johns Hopkins Medicine, 2023; Mayo Clinic, 2022a; Mumtaz, 2000). After birth, maternal blood sugar levels usually return to normal (Centers for Disease Control and Prevention, 2022; Johns Hopkins Medicine, 2023; Mayo Clinic, 2022a).

GDM is especially concerning because its prevalence is increasing (CDC, 2023; Dabelea et al., 2005; Ferrara et al., 2004; Gregory & Ely, 2016; Lavery et al., 2017; Thorpe et al., 2005). In a nationally representative study in the United States, researchers reported a 78% relative increase in the GDM rate from 2006 to 2016 (Zhou et al., 2022). A study that assessed births in the United States, reported that the GDM rate from 1979-1980 was 0.3%; the GDM rate from 2008-2010 increased to 5.8% (Lavery et al., 2017). The CDC has also reported a 20% increase in gestational diabetes diagnoses from 6% in 2016 to 8.3% in 2021 (CDC, 2023). Another study reported that GDM rates increased 30% from 6% in 2016 to 7.8% in 2020 (Gregory & Ely, 2016). In New York City alone, there was a 46% increase in GDM diagnoses from 1990-2001 (Thorpe et al., 2005). These increasing trends support further investigation into the potential factors that influence GDM development.

What is Air Pollution?

Air pollution is defined as the contamination of either the indoor or outdoor environments by any chemical, physical, or biological agent that can modify the characteristics of the atmosphere (World Health Organization, n.d.). The Environmental Protection Agency (EPA) and the World Health Organization (WHO) have identified six criteria air pollutants – ozone (O₃), particulate matter (PM), carbon monoxide (CO), lead, sulfur dioxide (SO₂), and nitrogen dioxide (NO₂) (County of Los Angeles Public Health, n.d.; EPA, 2023c, 2015; Manisalidis et al., 2020). In 1999, the WHO developed the Air Quality

Guidelines (AQGs), which aim to serve as a “target” level of air pollution exposure (World Health Organization, 2021). Levels that exceed the concentrations recommended in the AQGs may be associated with important risks to population health (World Health Organization, 2021). These guidelines are presented in Table 1. In 2019, 99% of the world’s population was living in areas where the air pollution concentration was greater than the WHO’s AQGs (World Health Organization, n.d.). This is of great concern due to the growing evidence that air pollution may have adverse impacts on human health (Suglia et al., 2008; West et al., 2016; World Health Organization, 2021; Zhang & Batterman, 2013).

Pollutant	Average Time	2021 AQG
PM _{2.5} , µg/m ³	Annual	5
	24 - Hour	15
PM ₁₀ , µg/m ³	Annual	15
	24 - Hour	45
O ₃ , µg/m ³	Peak Season	60
	8 - Hour	100
NO ₂ , µg/m ³	Annual	10
	24 - Hour	25
SO ₂ , µg/m ³	24 - Hour	40
CO, mg/m ³	24 - Hour	4

Table 1: The WHO's 2021 Air Quality Guidelines. Source: World Health Organization, “What are the WHO Air Quality Guidelines?”, 2021. Accessed via <https://www.who.int/news-room/feature-stories/detail/what-are-the-who-air-quality-guidelines>.

Ozone

Ground-level ozone, which is one of the main constituents of smog (California Air Resources Board, 2023; WHO, 2023; World Health Organization, 2022), has been found to cause lung inflammation and can aggravate several lung diseases (County of Los Angeles Public Health, n.d.; EPA, 2023b; WHO, 2023). Ground-level ozone is produced by chemical reactions between pollutants, such as volatile organic compounds (VOCs) and nitrogen oxides (NO_x) produced by cars, power plants, and other sources (California Air Resources Board, 2023; EPA, 2023b, 2015; WHO, 2023). These reactions occur in the presence of

sunlight, so ozone levels often reach higher levels during summer months and hotter days (County of Los Angeles Public Health, n.d.; EPA, 2023b; WHO, 2023; World Health Organization, 2022). Ozone can also travel long distances by wind, which increases the number of those exposed (EPA, 2023b).

Particulate Matter

PM can come from a variety of sources such as construction sites, fires, automobiles, power plants, wood combustion, and chemical reactions from different chemicals produced from motor vehicles, such as sulfur oxides (SO_x), NO_x, or VOCs (California Air Resources Board, 2023; EPA, 2023d, 2015; WHO, 2023). The two most common types of PM are PM with an aerodynamic diameter $\leq 2.5 \mu\text{m}$ (PM_{2.5}) and $\leq 10 \mu\text{m}$ (PM₁₀) (EPA, 2023d; Manisalidis et al., 2020). PM₁₀, or coarse PM, is most often produced by mechanical processes or uncontrolled burning, while PM_{2.5}, or fine PM, is most often formed by combustion processes (EPA, 2015). PM pollution, especially smaller PM pollution, is of great concern since it's small enough to be inhaled, enter the lungs, and pass into the bloodstream (EPA, 2023d; Manisalidis et al., 2020). Once it reaches the bloodstream or the brain, it can cause adverse health effects (EPA, 2015; Manisalidis et al., 2020; WHO, 2023). From 2000-2022, there was a national decrease in PM_{2.5} by 42% (EPA: United States Environmental Protection Agency, 2023), but recent studies are still finding its association with adverse health effects.

Nitrogen Dioxide

NO₂ enters the atmosphere through fuel burning; it's commonly emitted from cars, trucks, and other vehicles (California Air Resources Board, 2023; County of Los Angeles Public Health, n.d.; EPA, 2023a, 2015; Manisalidis et al., 2020; World Health Organization,

2022). NO₂ causes respiratory irritation and contributes to the development and exacerbation of asthma (County of Los Angeles Public Health, n.d.; EPA, 2023a, 2015; Manisalidis et al., 2020), and the development of PM and ground-level ozone (EPA, 2023a).

Pollution in Southern California

Over the past 30 years, levels of outdoor air pollution have decreased in the state of California (County of Los Angeles Public Health, n.d.; Lurmann et al., 2015). One study reported that between 2012 to 2015, there was a general decrease in the frequency of ozone exceedance events, which are over 70 parts per billion (ppb) (Wu et al., 2023). Another study reported that PM_{2.5} and its constituents decreased by a factor of 2 between 1999 to 2012 (Nussbaumer & Cohen, 2021). These reductions may be due to the numerous regulatory policies and emissions reduction strategies that have been implemented by the state and federal government to improve California's air quality (Lurmann et al., 2015). Despite these efforts, many California communities remain highly polluted (Lung Association, n.d.; Lurmann et al., 2015). Research has shown that over 90% of Californians breath unhealthy air pollution levels (California Air Resources Board, 2024). Los Angeles County is still one of the most polluted counties in the United States (County of Los Angeles Public Health, n.d.; Lung Association, n.d.). One study investigated the average pollutant levels in several cities throughout the United States, including Los Angeles; they reported that Los Angeles experiences levels of ozone, PM_{2.5}, and carbon monoxide above the exceedance limits (Yaya et al., n.d.).

The Unequal Burden of PPD, GDM, and Air Pollution Exposure

Certain populations may be at an increased risk of exposure to air pollution. For example, in 2019, a study found that lower-income areas with larger Black and Hispanic

populations had higher than average concentrations of both PM_{2.5} and NO₂ compared to other communities (Bluhm et al., 2022). Another study from the United States reported that areas with higher-than-average white or Native American populations are exposed to lower levels of PM_{2.5} compared to areas with higher-than-average black, Hispanic, or Asian populations (Jbaily et al., 2022). This study also reported that low-income areas are exposed to higher levels of PM_{2.5} compared to high-income communities (Jbaily et al., 2022). In North America, it has been reported that low SES communities experience higher levels of criteria air pollutants compared to low SES neighborhoods (Hajat et al., 2015). In addition, a third study reported that black populations were exposed to the highest national average concentration of PM_{2.5}, Asian populations were exposed to the highest concentration of NO₂ and O₃, while Hispanic populations were exposed to the highest concentration of PM₁₀ (J. Liu, Clark, et al., 2021).

Previous studies have found that certain populations are more at risk for PPD and its symptoms. One population that is more at risk for PPD symptoms is younger women (Bauman et al., n.d.; Rich-Edwards et al., 2006); a study that analyzed data from the Pregnancy Risk Assessment Monitoring System reported that 40% of women 24 years of age or younger experience PPD symptoms compared to 22.7% of women 25 years or older (Bauman et al., n.d.). Regarding maternal race and ethnicity, conflicting results have been reported. Two studies have reported that Native American/Alaska Native women have the highest prevalence of PPD symptoms (Bauman et al., n.d.; Wei et al., 2008); although a third study reported that black women have the highest rates of PPD symptoms (Onyewuenyi et al., 2023). They also reported that black women experience an increased risk of PPD with increasing neighborhood disadvantage (Onyewuenyi et al., 2023). The lowest prevalence of

PPD symptoms was seen among Hispanic populations in one study from Robeson County, North Carolina (Wei et al., 2008). A different study that used patients from Kaiser Permanente Northern California did not find the same results; they found that Asian women had a 52.0% decreased risk of PPD compared to white women (Onyewuenyi et al., 2023). Finally, research has also shown that mothers with less than 12 years of education have an increased risk of PPD symptoms (Bauman et al., n.d.).

In the US, there is a difference in GDM prevalence among different ethnicities, age groups, and SES, although results have not been consistent. One study reported that white mothers have the lowest prevalence of GDM, and Asian Americans have the highest prevalence (L. Chen et al., 2016). A different study reported that white mothers had a higher GDM prevalence compared to black mothers in 2006; this same study though, reported that white women experienced the lowest increase in GDM prevalence between 2006-2016 (Zhou et al., 2022). Another study that used a nationally representative cohort supported Zhou et al.'s findings in 2006 and reported higher GDM risks among white mothers (Lavery et al., 2017). Older mothers may also be more at risk for GDM; one study showed that mothers 15-19 years of age had a GDM rate of 1.6% compared to mothers aged 40-44 who experienced a GDM rate of 14.3% (Lavery et al., 2017). Finally, mothers with a lower SES may be more at risk for GDM. Women below the poverty threshold experienced a greater increase in GDM prevalence between 2006-2016 compared to those with incomes greater than or equal to the poverty threshold (Zhou et al., 2022).

Air Pollution Levels Before and During the COVID-19 Pandemic

Beginning in March 2020, the COVID-19 shutdowns were estimated to decrease vehicle traffic and industrial activities, potentially decreasing pollution emissions (Jiang et al., 2021; Naeger & Murphy, 2020).

Globally, there was a decline in anthropogenic ambient air pollution after the COVID-19 pandemic began (Berman & Ebisu, 2020; Fu et al., 2020; Jiang et al., 2021). PM_{2.5} concentrations decreased (Berman & Ebisu, 2020), with a 15% reduction seen in southern California five weeks after the shutdown began (Jiang et al., 2021), and a 36.3% decrease compared to 2019 (Naeger & Murphy, 2020). In California, the lower-income communities experienced the greatest PM_{2.5} reductions during the pandemic shutdown (Bluhm et al., 2022). All PM_{2.5} constituents decreased in concentration during the COVID-19 lockdowns, with nitrate decreasing the most (Jiang et al., 2021). NO₂ concentrations decreased even more than PM_{2.5}, with one study estimating a 27% decrease in concentrations during the COVID-19 shutdowns compared to pre-shutdown concentrations (Jiang et al., 2021). When specifically assessing NO₂ levels in Los Angeles, studies have estimated a 29%-40% decrease in NO₂ concentrations (J. Liu, Lipsitt, et al., 2021; Naeger & Murphy, 2020). Another study reported similar findings, where compared to pollutant levels in 2017-2019, NO₂ concentrations were decreased by 25.5% in 2020 (Berman & Ebisu, 2020). NO₂ concentrations may have dropped more than PM_{2.5} because NO₂ mainly comes from vehicular traffic, which was reduced during the COVID-19 shutdowns (EPA, 2023a; Fu et al., 2020; J. Liu, Lipsitt, et al., 2021). PM_{2.5} is produced by both transportation and non-transportation sources, such as emissions from industries, so not all PM_{2.5} sources were impacted by the pandemic (Berman & Ebisu, 2020; EPA: United States Environmental Protection Agency, 2023). While most air pollutants decreased in concentration during the

shutdowns, O₃ concentrations actually increased (Fu et al., 2020; Jiang et al., 2021). This may be due to higher temperatures, which elevate ozone concentrations (EPA, 2023d; Fu et al., 2020; Jiang et al., 2021; Wu et al., 2023); in 2020, high temperatures occurred more frequently, and there were more persistent heatwave events that extended even into late September (K. Wu et al., 2023).

Occurrence of PPD and GDM Before and During the COVID-19 Pandemic

In a recent meta-analysis that investigated PPD occurrence during the COVID-19 pandemic, there was a 34% pooled prevalence of PPD across eight studies – much larger than the prevalence before the pandemic (Q. Chen et al., 2022). The COVID-19 pandemic may have increased PPD risk due to the social isolation felt by mothers, limited social support, limited access to healthcare professionals, and the fear of potential infection (Q. Chen et al., 2022; Meaney et al., 2022). One study reported that 25% of women experienced a loss of maternal autonomy during both delivery and breastfeeding (Tsuno et al., 2022); this is concerning, since less autonomy has been found to lower overall well-being (Deci & Ryan, 2000). This same study also reported that 20-30% of mothers had fewer opportunities to learn about breastfeeding and childcare from physicians, midwives, and nurses during their hospital stay following delivery; these women were two times more likely to develop PPD (Tsuno et al., 2022).

Studies have reported that GDM prevalence was significantly higher during the COVID-19 pandemic lockdown periods compared to previous time periods (La Verde et al., 2022; Mendez et al., 2023; Mirsky et al., 2022; Rhou et al., 2023; Zanardo et al., 2022). One study estimated a 38.9% increase in GDM prevalence compared to pre-pandemic times (Mirsky et al., 2022). Another study from Northeast Italy found that experiencing the COVID-19

lockdowns during the first trimester increased GDM risk by a factor of 2.29 (Zanardo et al., 2022). This increase in GDM prevalence may be partially due to the social isolation placed upon pregnant women during the pandemic (La Verde et al., 2022; Mendez et al., 2023; Rhou et al., 2023). One study reported that body mass index (BMI) at delivery and mean weight gained during pregnancy was significantly higher during the pandemic lockdown period compared to the pre-pandemic period (La Verde et al., 2022).

CHAPTER 3: METHODS

Study Population

Patient data was retrieved from electronic health records (EHRs) through Kaiser Permanente Southern California (KPSC) facilities. KPSC is a health maintenance organization that serves approximately 19% of the population in Southern California (W. Chen et al., 2019; Koebnick et al., 2012). Mothers who gave birth between January 1st, 2019 and December 31st, 2021 were included in the study. Women who were not KPSC members, who gave birth at either less than 20 weeks or more than 47 weeks gestation, who did not have a residential address, who had multiple births, or who had stillbirths were excluded. In addition, participants with missing GDM status due to missing lab test results (n=8,165) were excluded from all GDM analyses.

Outcome: PPD Assessment

PPD was assessed using the Edinburg Postnatal Depression Scale (EPDS) during postpartum visits (American College of Obstetricians and Gynecologists, 2018; Cox et al., 1987). Participants who earned a score of ≥ 10 on the EPDS were referred for a clinical interview for further assessment. Pharmacy use clinical codes were also supplemented to further improve PPD identification. Overall, PPD diagnosis was defined as a combination of the International Classification of Diseases, Ninth and 10th Revision diagnostic codes and prescription medication records from the date of delivery through 12 months postpartum.

Outcome: GDM Assessment

GDM was assessed during routine prenatal visits between 24 to 28 weeks of gestation. Two criteria were used to determine GDM diagnosis. The first method is the Carpenter-Coustan criteria, which is a 1-hour 50-gram glucose challenge test. If glucose

levels are greater than 200 mg/dL or if there are two abnormal values for 3-hour 100-gram oral glucose tolerance tests (cutoff values were fasting ≥ 95 , 1-hour ≥ 180 , 2-hours ≥ 155 , and 3-hours ≥ 140 mg/dL), GDM was diagnosed (Carpenter & Coustan, 1982). The second method was the International Association of Diabetes and Pregnancy Study Groups criteria, in which one abnormal value for a 2-hour 75-gram oral glucose tolerance test (cutoff values were fasting ≥ 92 , 1-hour ≥ 180 , and 2-hours ≥ 153 mg/dL) indicated GDM (Metzger, 2010).

Exposure Data and Assessment

Daily data for PM_{2.5}, PM₁₀, NO₂, and O₃ (8-hour windows: 10 AM – 6 PM) from 2018 to 2022 was retrieved from the US Environmental Protection Agency's (EPA) monitoring stations. Monthly averages for each pollutant were calculated from the daily averages, and empirical Bayesian kriging (EBK) was performed to spatially interpolate the data between monitoring stations. Kriging is a method used to predict the spatial correlation between monitoring sites (Krivoruchko, 2012). It uses a semivariogram, which is a function of the distance and direction between two points, to determine the weight each point contributes to an estimated, unmeasured point (Krivoruchko, 2012). Classical kriging alone assumes a single semivariogram is the true correlation of the observed data (Krivoruchko, 2012; Wu et al., 2016). With ambient air pollution research, classical kriging may be inapplicable in practice (Krivoruchko, 2012; Wu et al., 2016). EBK models account for potential uncertainty by estimating several semivariograms rather than one semivariogram (Krivoruchko, 2012). In addition, EBK models have less under and overestimation, which may increase the accuracy of the estimations (Wu et al., 2016). The EBK model is further described in the literature (Krivoruchko, 2012; Wu et al., 2016).

Residential addresses were regularly updated due to KPSC membership requirements. Maternal residential histories (address, start date, and end date) were obtained from KPSC EHRs and geocoded (Sun et al., 2022, 2023). Geocoding translates a physical address into a geographic address by using latitude and longitude (Wu et al., 2016). Monthly air pollution estimates were spatiotemporally linked to each participant based on their residential address pre-pregnancy, during pregnancy, and the postpartum period.

Time Periods

Different time periods were used to determine potential vulnerability windows. These time periods were calculated by averaging the exposure for each month in that period. Since PPD can be diagnosed up to one year postpartum, the time periods included in our PPD analyses were: entire pregnancy, 1st trimester (pregnancy months 1-3), 2nd trimester (pregnancy months 4-6), 3rd trimester (pregnancy months 7-delivery), 6-months postpartum, 12-months postpartum, conception through 12-months postpartum, conception through 6-months postpartum, 3rd trimester through 12-months postpartum, and 3rd trimester through 6-months postpartum. GDM is most commonly diagnosed in the second trimester; therefore, the time periods used in GDM analyses were: 3-months preconception, entire pregnancy, 1st trimester (pregnancy months 1-3), 2nd trimester (pregnancy months 4-6), the first two trimesters (pregnancy months 1-6), and the entire GDM time period (3-months preconception through the 2nd trimester). Date of conception was determined based on last menstrual period (LMP) date and early pregnancy ultrasonography. If disagreement was found between LMP and sonogram, the date generated from the latter was used.

Covariates

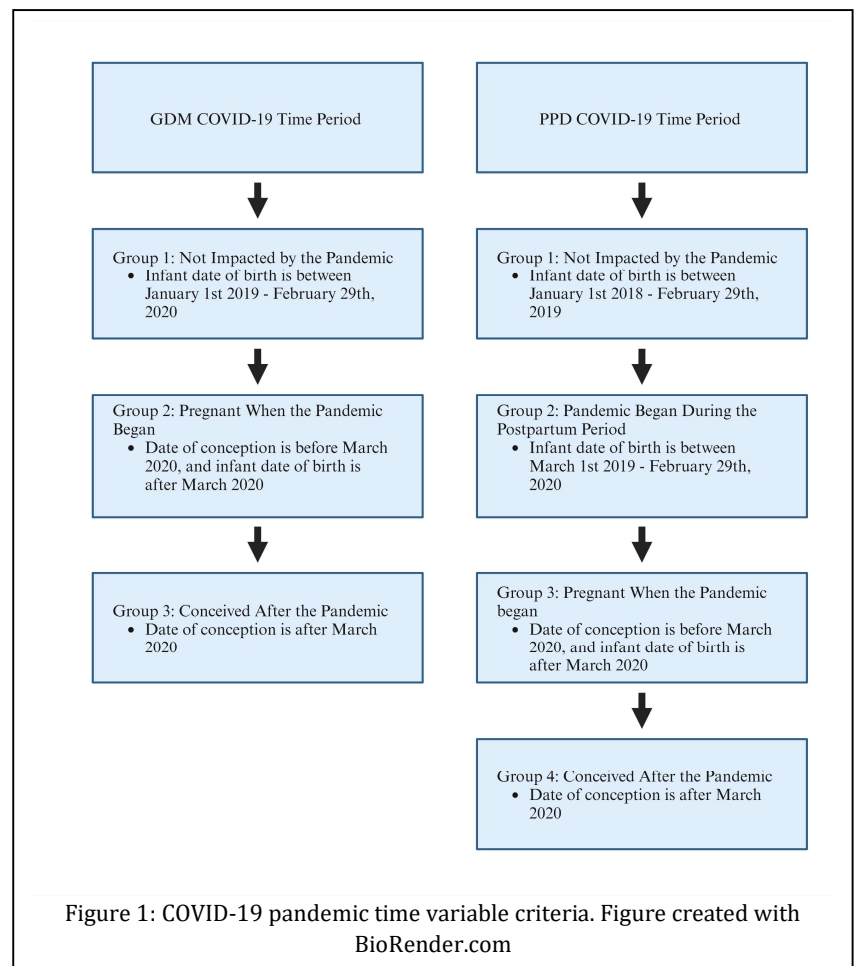
Covariates were selected a priori based on existing literature (Sun et al., 2022, 2023). The covariates were included in KPSC EHRs. KPSC EHRs contain detailed information for each patient and provided our team with both demographic and SES data. EHRs recorded each participant's median household income in infant year of birth and the year 2020, maternal race/ethnicity, maternal educational level, smoking status, and passive smoking status. For our study, participants' block-group level median household income was assigned to level 1 if their median household income was < \$43,644, level 2 if income was \$43,644 - \$55,833, level 3 if income was \$55,834-\$71,429, or level 4 if income was >\$71,429 (categorized as quartiles). Maternal race and ethnicity was recorded as: African American, Asian, Hispanic, Non-Hispanic White, or Multiple/Other. Maternal education was reported as: 8th grade or less, high school diploma or less, some college – no degree, college degree, or more than a college degree. Smoking status was based on status from 1-year preconception through 1 year postpartum; mothers were listed as either having never smoked, ever smoked, or smoked during pregnancy. The same time period was used to determine passive smoking, where women who lived with another person who smokes indicating passive smoking. Season of conception was determined based on LMP. If LMP was during the months May-October, season of conception was reported as warm. If LMP was during the months November-April, season of conception was reported as cool. Similarly, season of delivery based on infant date of birth was reported as warm (May-October), or cool (November-April). Numerical BMIs were converted to categories: Underweight (<18.5 kg/m²), Normal (18.5-24.9 kg/m²), Overweight (25.0-29.9 kg/m²),

Obese Class 1 (30.0-34.9 kg/m²), Obese Class 2 (35.0-39.9 kg/m²), and Obese Class 3 (≥40.0 kg/m²).

PPD covariates included maternal age, maternal race/ethnicity, maternal educational level, median household income in the year of birth, smoking status, passive smoking, and season of delivery. GDM covariates included maternal age, maternal race/ethnicity, maternal educational level, median household income in the year of birth, smoking status, passive smoking, pre-pregnancy BMI, and season of conception. For COVID-19 analyses, covariates remained the same for each outcome.

COVID-19 Time Periods

A variable was created to assess whether there were certain time periods, in which experiencing the COVID-19 pandemic increased the risk of developing PPD or GDM due to air pollution exposure. Time periods were based on when the COVID-19 pandemic began in March 2020 (World Health Organization, 2024). For the PPD analyses, there were four COVID-19 pandemic time periods: group 1 was not impacted by the pandemic during pregnancy or the postpartum period, group 2



experienced the pandemic while in the postpartum period, group 3 was pregnant when the pandemic began, and group 4 conceived after the pandemic began. For GDM, three time periods were created; group 1 was not impacted by the pandemic, group 2 was pregnant when the pandemic began, and group 3 conceived after the pandemic began. The criteria used to assign women to each COVID-time are presented in Figure 1.

Statistical Analysis

Descriptive statistics were calculated for each study group (total population, PPD group, No PPD group, GDM group, No GDM group). Chi-square tests were used to determine if there was a difference between PPD and non-PPD, and GDM and non-GDM groups for each categorical variable. Additionally, chi-square tests were used to determine whether there was a difference in PPD or GDM rates during different COVID-19 pandemic time periods. T-tests were used to determine if there was a difference between PPD and non-PPD, and GDM and non-GDM groups for each continuous variable. Pearson correlation coefficients were calculated to assess the correlation between exposure metrics.

For the PPD analysis, we used a discrete time approach with pooled logistic regressions to assess the associations between PPD risk and air pollution exposure. A discrete time approach is a more flexible model that allows for the estimation of time-varying associations. This approach was chosen instead of Cox proportional hazard models since we found that our data did not follow the Cox proportional hazards assumption. Per-interquartile range (IQR) increases for each air pollutant were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs), and county at delivery was fitted as a random effect.

Cox proportional hazard models were used to assess the relationship between GDM and air pollution exposure. Cox models are one of the most commonly used survival analysis models (Deo et al., 2021). They allow us to assess the influence of multiple continuous and categorical variables on survival, while also accounting for potential confounding variables (Deo et al., 2021). Time in the model was defined as the period between LMP and GDM diagnosis. If GDM was not diagnosed, time was defined as the period between the last menstrual period and date of infant birth. Hazard ratios (HRs) and 95% CIs were estimated based on per-IQR increase for each pollutant.

Cox proportional hazard models were also used in both PPD and GDM subgroup analyses. Subgroup analysis will separate data based on variable responses, lowering the sample size. Multilevel logistic regression models may be more accurate with large datasets, and therefore may not converge in subgroup analyses (Ali et al., 2019). Hazard ratios (HRs) and 95% CIs were determined based on per-IQR increase in pollutant. In the PPD Cox model, exposures during pregnancy through 12 months postpartum were used. Time was defined as the period between LMP and PPD diagnosis. If PPD was not diagnosed, the time was defined as the period between LMP and 12 months postpartum. The GDM Cox model for subgroup analyses was similar to the main GDM model. If GDM was not diagnosed, time was defined as the period between LMP and date of infant birth. Analyses were performed with pollution exposure from 3 months prior to conception through the 2nd trimester. HRs and 95% CIs were estimated based on per-IQR increases.

Subgroup analyses were also used to evaluate whether the COVID-19 pandemic influenced the risk of PPD or GDM from air pollution exposure. Participants were separated

based on COVID time group, and Cox proportional hazards models were used to estimate HRs and 95% CIs based on per-IQR increases in each pollutant. The covariates previously described were still included in the COVID-19 pandemic time analyses.

All analyses were conducted using SAS, version 9.4 statistical software (SAS Institute Inc). A P-value of < 0.05 was considered significant.

CHAPTER 4: RESULTS

Descriptive Statistics

We had 115,804 participants, with 21,652 PPD cases (18.70%) and 12,174 GDM cases (10.51%). Participants with PPD were more likely to be older and have higher annual household incomes. PPD participants were also more likely to be African American or non-Hispanic white, as well as have a history of smoking before or during pregnancy. Patients with GDM were more likely to be older, have a lower median household income, to have a cool season of conception, and to have an obese pre-pregnancy BMI. Interestingly, 42.21% of GDM participants had inadequate weight gain throughout their pregnancy compared to 25.22% of non-GDM participants. Both GDM and PPD participants were exposed to higher average O₃ levels, and slightly higher average PM₁₀ levels during the entire pregnancy. Pollution exposure averages are presented in Table 2 and the Appendix. Simple summary statistics for demographic and medical variables are presented in Tables 3 and 4, respectively.

Table 2: Air pollution exposure averages for the total population, PPD cases, and GDM cases. Pollution averages are in $\mu\text{g}/\text{m}^3$. SD = Standard Deviation, Min = Minimum, Max = Maximum, IQR = Interquartile Range.

Pregnancy Exposure Summary Statistics												
	Total Population				PPD Cases				GDM Cases			
	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR
PM _{2.5}	10.89 (1.78)	4.65	23.30	2.43	10.85 (1.79)	5.17	21.34	2.43	11.02 (1.78)	4.90	18.36	2.46
PM ₁₀	26.35 (4.65)	10.56	71.20	5.59	26.45 (4.69)	10.56	60.19	5.72	26.49 (4.73)	14.51	57.02	5.78
NO ₂	13.60 (3.18)	2.74	25.34	4.74	13.49 (3.23)	4.80	24.20	4.97	13.71 (3.10)	5.13	24.14	4.35
O ₃	45.90 (6.01)	22.14	74.03	8.77	46.15 (6.06)	22.14	70.17	8.94	46.02 (6.08)	25.44	71.16	8.85

Table 3: Summary statistics for sociodemographic characteristics. Statistics are divided into groups: total population, participants with PPD, participants without PPD, participants with GDM, and participants without GDM. P-values for chi-square and T-tests are presented for PPD and GDM analyses. Significant results are bolded. Significance was < 0.05. YOB =Year of Birth.

Sociodemographic Characteristic	No. (%)						Total Births (n = 115,804)
	PPD (n = 21,652)	Non-PPD (n = 94,152)	PPD Chi-Square and T-Test P-Values	GDM (n = 12,174)	Non-GDM (n = 96,450)	GDM Chi-Square and T-Test P-Values	
Maternal Age, mean (SD)	31.02 (5.29)	30.91 (5.32)	<0.0001	33.00 (4.96)	30.77 (5.24)	<0.0001	31.02 (5.29)
Maternal Race and Ethnicity			<0.0001			<0.0001	
African American	1,683 (7.77)	5,825 (6.19)		503 (4.14)	6,255 (6.51)		7,508 (6.48)
Asian	1,986 (9.17)	13,695 (14.55)		2,695 (22.20)	12,268 (12.76)		15,681 (13.54)
Hispanic	11,597 (53.57)	50,626 (53.78)		6,648 (54.77)	51,309 (53.39)		62,223 (53.74)
Non-Hispanic White	5,391 (24.90)	19,859 (21.09)		1,772 (14.60)	22,044 (22.94)		25,250 (21.81)
Multiple or Other	993 (4.59)	4,138 (4.40)		520 (4.28)	4,233 (4.40)		5,131 (4.43)
Unknown or Missing	2 (0.00)	9 (0.00)		2 (0.02)	8 (0.00)		11 (0.00)
Maternal Education			<0.0001			<0.0001	
8 th Grade or Less	19 (0.09)	253 (0.29)		49 (0.43)	199 (0.22)		272 (0.25)
9 th Grade Through High School	4,344 (21.29)	21,751 (24.52)		2,574 (22.54)	21,328 (23.50)		26,095 (23.91)
Some College, No Degree (<4 y)	4,604 (22.56)	17,979 (20.26)		2,307 (20.20)	18,577 (20.47)		22,583 (20.69)
College	7,519 (36.85)	32,932 (37.12)		4,380 (38.35)	33,887 (37.33)		40,451 (37.07)
More Than College	3,918 (19.20)	15,809 (17.82)		2,111 (18.48)	16,774 (18.48)		19,727 (18.08)
Missing	1,248 (5.76)	5,428 (5.77)		719 (5.91)	5,352 (5.55)		6,676 (5.76)
Median Household Income at Block Group Level - 2020			<0.0001			<0.0001	
<\$43,667	1,714 (7.92)	8,159 (8.68)		1,061 (8.75)	7,972 (8.30)		9,873 (8.54)
\$43,668 - \$55,930	3,021 (13.97)	13,740 (14.61)		1,857 (15.31)	13,627 (14.19)		16,761 (14.49)
\$55,931 - \$71,591	4,414 (20.40)	19,019 (20.23)		2,571 (21.20)	19,209 (20.01)		23,433 (20.26)
>\$71,592	12,483 (57.71)	53,110 (56.48)		6,628 (54.65)	55,191 (57.49)		65,593 (56.71)
Missing	20 (0.09)	124 (0.13)		11 (0.09)	118 (0.12)		762 (0.66)
Median Household Income at Block Group Level - YOB			0.0011			0.0001	
<\$43,667	1,875 (8.67)	8,788 (9.35)		1,133 (9.34)	8,646 (9.01)		10,663 (9.22)
\$43,668 - \$55,930	3,009 (13.91)	13,576 (14.44)		1,804 (14.87)	13,504 (14.07)		16,585 (14.34)
\$55,931 - \$71,591	4,420 (20.43)	19,103 (20.32)		2,564 (21.14)	19,297 (20.10)		23,523 (20.34)
>\$71,592	12,328 (56.99)	52,562 (55.90)		6,628 (54.65)	54,553 (56.83)		64,890 (56.10)
Missing	20 (0.09)	123 (0.13)		11 (0.09)	117 (0.12)		761 (0.66)
Smoking Status			<0.0001			0.0018	
Never	17,857 (82.48)	82,998 (88.15)		10,481 (86.33)	84,054 (87.45)		100,855 (87.09)
Ever	3,065 (14.16)	9,018 (9.58)		1,335 (11.00)	9,795 (10.19)		12,083 (10.43)
Smoked During Pregnancy	729 (3.37)	2,135 (2.27)		324 (2.67)	2,267 (2.36)		2,864 (2.47)
Missing	1 (0.00)	1 (0.00)		0 (0.00)	1 (0.00)		2 (0.00)
Passive Smoker			0.5086			0.0056	
Yes	286 (1.32)	1,191 (1.26)		121 (1.00)	1,244 (1.29)		1,477 (1.28)
No	21,366 (98.68)	92,960 (98.74)		12,019 (99.00)	94,872 (98.71)		114,326 (98.72)
Missing	0 (0.00)	1 (0.00)		0 (0.00)	1 (0.00)		619 (0.53)

Table 3 Continued: Summary statistics for sociodemographic characteristics. Statistics are divided into groups: total population, participants with PPD, participants without PPD, participants with GDM, and participants without GDM. P-values for chi-square and T-tests are presented for PPD and GDM analyses. Significant results are bolded. Significance was < 0.05. YOBB =Year of Birth.

Sociodemographic Characteristic	No. (%)						
	PPD (n = 21,652)	Non-PPD (n = 94,152)	PPD Chi-Square and T-Test P-Values	GDM (n = 12,174)	Non-GDM (n = 96,450)	GDM Chi-Square and T-Test P-Values	Total Births (n = 115,804)
Year of Infant Birth			<0.0001			<0.0001	
2019	7440 (34.36)	32,511 (34.53)		3,776 (31.10)	33,472 (34.82)		39,951 (34.50)
2020	6433 (29.71)	29,310 (31.13)		3,671 (30.24)	29,787 (30.99)		35,743 (30.87)
2021	7779 (35.93)	32,331 (34.34)		4,693 (38.66)	32,858 (34.19)		40,110 (34.64)
Season of Conception			0.1740			<0.0001	
Warm Season (May - October)	10,315 (47.64)	45,336 (48.15)		5,383 (44.34)	46,581 (48.46)		55,930 (48.04)
Cool Season (November - April)	11,337 (52.36)	48,816 (51.85)		6,757 (55.66)	49,536 (51.54)		60,492 (51.96)
Season of Delivery			0.8852			0.9252	
Warm Season (May - October)	11,607 (53.61)	50,421 (53.55)		6,532 (53.81)	51,673 (53.76)		62,028 (53.28)
Cool Season (November - April)	10,045 (46.39)	43,731 (46.45)		5,608 (46.19)	44,444 (46.24)		54,394 (46.72)
Insurance Type			0.5768			<0.0001	
Medicaid	3,031 (13.93)	1,3242 (14.08)		1,469 (12.11)	13,126 (13.67)		16,255 (14.05)
Other Insurance	18,613 (86.07)	80,816 (85.92)		10,657 (87.89)	82,901 (86.33)		99,429 (85.95)
Missing	26 (0.12)	94 (0.10)		14 (0.11)	90 (0.09)		120 (0.10)

Table 4: Summary statistics for medical characteristics. Statistics are divided into groups: total population, participants with PPD, participants without PPD, participants with GDM, and participants without GDM. P-values for chi-square and T-tests are presented for PPD and GDM analyses. Significant results are bolded. Significance was < 0.05. YOB =Year of Birth.

Medical Characteristic	No. (%)						
	PPD (n = 21,652)	Non-PPD (n = 94,152)	PPD Chi-Square and T-Test P-Values	GDM (n = 12,174)	Non-GDM (n = 96,450)	GDM Chi-Square and T-Test P-Values	Total Births (n = 115,804)
Pre-pregnancy Weight (lbs), mean (SD)	168.25 (42.50)	160.61 (40.06)	<0.0001	173.07 (43.86)	159.68 (39.24)	<0.0001	162.04 (40.63)
Pre-pregnancy BMI, mean (SD)	28.84 (6.76)	27.72 (6.45)	<0.0001	30.33 (6.95)	27.47 (6.28)	<0.0001	27.93 (6.52)
Pre-pregnancy BMI in Categories			<0.0001			<0.0001	
Underweight (<18.5)	256 (1.18)	1,780 (1.89)		102 (0.84)	1,802 (1.88)		2,036 (1.76)
Normal Weight (18.5-24.9)	6,942 (32.09)	36,044 (38.35)		2,894 (23.86)	37,961 (39.54)		42,986 (37.18)
Overweight (25.0 - 29.9)	6,432 (29.74)	27,433 (29.19)		3,401 (28.04)	28,555 (29.74)		33,865 (29.29)
Obese Class 1 (30.0-34.9)	4,241 (19.61)	16,205 (17.24)		2,870 (23.66)	16,002 (16.67)		20,446 (17.69)
Obese Class 2 (35.0-39.9)	2,281 (10.55)	7,783 (8.28)		1,712 (14.11)	7,356 (7.66)		10,064 (8.71)
Obese Class 3 (40.0+)	1,478 (6.83)	4,734 (5.04)		1,150 (9.48)	4,336 (4.52)		6,212 (5.37)
Missing	22 (0.10)	173 (0.18)		11 (0.09)	105 (0.11)		195 (0.17)
Gestational Weight Gain in IOM Categories			<0.0001			<0.0001	
Inadequate	5,765 (26.65)	26,293 (27.98)		5,120 (42.21)	24,211 (25.22)		32,058 (27.73)
Appropriate	6,375 (29.47)	29,982 (31.91)		3,692 (30.44)	30,634 (31.91)		36,357 (31.45)
Excess	9,489 (43.87)	37,692 (40.11)		3,317 (27.35)	41,161 (42.87)		47,181 (40.82)
Missing	23 (0.11)	185 (0.20)		11 (0.09)	111 (0.12)		208 (0.18)
COVID-19 Positive During 1st Trimester			<0.0001			0.3742	
No	21,385 (98.77)	93,282 (99.08)		12,030 (99.09)	95,165 (99.01)		114,667 (99.02)
Yes	267 (1.23)	870 (0.92)		110 (0.91)	952 (0.99)		1,137 (0.98)
COVID-19 Positive During 2nd Trimester			0.0001			0.0090	
No	21,300 (98.37)	92,935 (98.71)		11,945 (98.39)	94,852 (98.68)		114,235 (98.65)
Yes	352 (1.63)	1,217 (1.29)		195 (1.61)	1,265 (1.32)		1,569 (1.35)
COVID-19 Positive During 3rd Trimester			0.7254			0.7251	
No	21,181 (97.82)	92,140 (97.86)		11,875 (97.82)	94,066 (97.87)		113,321 (97.86)
Yes	471 (2.18)	2,012 (2.14)		265 (2.18)	2,051 (2.13)		2,483 (2.14)

Correlations Among Pollutants

The results from the correlation analysis among pollutants are presented in Table 5 and the Appendix. Negative associations were seen between NO₂ and ozone, and large positive correlations were seen between PM_{2.5} and PM₁₀.

Table 5: Pearson's correlation coefficients for pollutant exposures. Correlations presented are from the date of conception through 1-year postpartum.

	PM _{2.5}	PM ₁₀	NO ₂	O ₃
PM _{2.5}	1	0.45864	0.77343	-0.04146
PM ₁₀		1	0.29203	0.57338
NO ₂			1	-0.03371
O ₃				1

Associations Between Air Pollution and PPD

Using a discrete time approach, we found significantly positive associations between O₃ exposure and PPD risk in the following time periods: entire pregnancy (OR=1.043; 95% CI, 1.014-1.074), 2nd trimester (OR=1.024; 95% CI, 1.003-1.046), pregnancy through 12-months postpartum (OR=1.063; 95% CI, 1.029-1.098), pregnancy through 6-months postpartum (OR=1.042; 95% CI, 1.006-1.079), and 12-months postpartum (OR=1.022; 95% CI, 1.005-1.039). PM_{2.5} was found to be negatively associated with PPD risk, except in the 1st trimester (OR=1.008; 95% CI, 0.989-1.028). PM₁₀ exposure was positively associated with PPD during the entire pregnancy (OR=1.004; 95% CI, 0.982-1.026), 1st trimester (OR=1.009; 95% CI, 0.990-1.028), and the 2nd trimester (OR=1.013; 95% CI, 0.989-1.036), although these results were not significant. PM₁₀ exposure in the late pregnancy and postpartum periods were insignificant, but negatively associated with PPD risk. Discrete time results are presented in Table 6.

PPD Subgroup Analyses

Cox proportional hazard models showed different associations with pollution exposure among different groups. For race/ethnicity, white mothers were more susceptible to the effects from PM₁₀ (HR=1.063; 95% CI, 1.022-1.107) and ozone exposure (HR=1.090;

95% CI, 1.027-1.157). Hispanic (HR=1.103; 95% CI, 1.052-1.156) and multi-racial/other (HR=1.125; 95% CI, 1.018-1.244) mothers were more susceptible to the effects from O₃. Hazard ratios were large for mothers who had more than a college education, although only ozone (HR=1.112; 95% CI, 1.055-1.172) and PM₁₀ (1.091; 95% CI, 1.045-1.139) were significant. Interestingly, smoking during or before pregnancy lowered the hazard ratio for PPD and PM_{2.5}, PM₁₀, and NO₂ exposure. Similar results were seen for passive smoking. Results for PPD subgroup analyses are presented in Table 7.

Table 6: Results from the PPD discrete time approach model. Covariates included: mom age, mom race/ethnicity, mom educational level, income group in year of birth, smoking status, passive smoking, and season of delivery. Significant negative associations are presented in red, and significant positive associations are bolded. Significance level was <0.05. CI = Confidence Interval, OR = Odds Ratio.

	PM _{2.5}			PM ₁₀			NO ₂			O ₃		
	OR	95% CI	P-Value	OR	95% CI	P-Value	OR	95% CI	P-Value	OR	95% CI	P-Value
Entire Pregnancy	0.981	0.959 - 1.004	0.0993	1.004	0.982 - 1.026	0.7168	0.972	0.944 - 1.000	0.0517	1.043	1.014 - 1.074	0.0040
1st Trimester	1.008	0.989 - 1.028	0.4071	1.009	0.990 - 1.028	0.3740	0.976	0.943 - 1.011	0.1836	1.019	0.996 - 1.042	0.0993
2nd Trimester	0.987	0.967 - 1.008	0.2304	1.013	0.989 - 1.036	0.2867	0.985	0.961 - 1.009	0.2178	1.024	1.003 - 1.046	0.0256
3rd Trimester	0.980	0.963 - 0.998	0.0263	0.991	0.972 - 1.012	0.4015	0.973	0.940 - 1.007	0.1177	1.017	0.992 - 1.041	0.1814
12-Months Postpartum	0.984	0.968 - 0.999	0.0421	0.994	0.979 - 1.009	0.4419	0.988	0.968 - 1.009	0.2635	1.022	1.005 - 1.039	0.0121
6-Months Postpartum	0.980	0.962 - 0.998	0.0303	0.986	0.966 - 1.006	0.1595	0.996	0.971 - 1.023	0.7886	1.013	0.992 - 1.034	0.2295
Conception - 12-Months Postpartum	0.970	0.949 - 0.992	0.0070	0.995	0.974 - 1.016	0.6249	0.967	0.939 - 0.996	0.0240	1.063	1.029 - 1.098	0.0002
Conception - 6-Months Postpartum	0.960	0.937 - 0.983	0.0009	0.985	0.963 - 1.007	0.1856	0.980	0.949 - 1.012	0.2122	1.042	1.006 - 1.079	0.0221
3rd Trimester - 12-Months Postpartum	0.974	0.958 - 0.991	0.0030	0.989	0.973 - 1.005	0.1642	0.978	0.954 - 1.002	0.0702	1.030	1.007 - 1.053	0.0107
3rd Trimester - 6-Months Postpartum	0.969	0.949 - 0.988	0.0017	0.981	0.962 - 1.001	0.0592	0.988	0.958 - 1.018	0.4142	1.016	0.990 - 1.042	0.2302

Table 7: PPD subgroup analysis using Cox Proportional Hazard Models. Hazard ratios, 95% confidence intervals, and p-values are presented for each subgroup and each pollutant. Negative associations are presented in red, and positive associations are bolded. Significance was determined at the ≤ 0.05 level. HR = Hazard Ratio, CI = Confidence Interval.

	PM _{2.5}			PM ₁₀			NO ₂			O ₃		
	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value
Maternal Race/Ethnicity												
African American	0.991	0.922 - 1.064	0.7981	1.054	0.973 - 1.142	0.1959	1.021	0.953 - 1.094	0.5557	1.094	0.967 - 1.237	0.1552
Asian	0.971	0.906 - 1.040	0.4024	1.015	0.950 - 1.084	0.6655	0.932	0.872 - 0.995	0.0352	1.014	0.939 - 1.095	0.7226
Hispanic	0.959	0.931 - 0.986	0.0038	0.996	0.964 - 1.029	0.8103	0.954	0.924 - 0.984	0.0033	1.103	1.052 - 1.156	<0.0001
White	1.012	0.966 - 1.060	0.6150	1.063	1.022 - 1.107	0.0027	0.966	0.901 - 1.035	0.3277	1.090	1.027 - 1.157	0.0045
Multi/Other	0.956	0.867 - 1.054	0.3681	1.049	0.961 - 1.131	0.3204	0.973	0.872 - 1.087	0.6289	1.125	1.018 - 1.244	0.0212
Maternal Education												
High School or Less	0.962	0.918 - 1.009	0.1101	1.015	0.958 - 1.076	0.6073	0.938	0.886 - 0.992	0.0262	1.168	1.090 - 1.252	<0.0001
Some College	0.965	0.924 - 1.008	0.1101	1.011	0.969 - 1.056	0.6073	0.950	0.909 - 0.994	0.0262	1.133	1.072 - 1.198	<0.0001
College Degree	0.946	0.912 - 0.982	0.0037	1.009	0.974 - 1.045	0.6264	0.946	0.902 - 0.992	0.0233	1.041	0.991 - 1.093	0.1120
More Than College	1.041	0.987 - 1.098	0.1367	1.091	1.045 - 1.139	<0.0001	1.023	0.958 - 1.092	0.5043	1.112	1.055 - 1.172	<0.0001
Smoking Status												
Never Smoked	0.984	0.960 - 1.009	0.2063	1.032	1.006 - 1.059	0.0151	0.976	0.947 - 1.006	0.1199	1.083	1.044 - 1.124	<0.0001
Smoked	0.925	0.878 - 0.975	0.0037	0.983	0.938 - 1.031	0.4794	0.892	0.835 - 0.953	0.0008	1.115	1.055 - 1.179	0.0001
Passive Smoking												
No	0.971	0.949 - 0.994	0.0121	1.018	0.995 - 1.042	0.1296	0.958	0.932 - 0.985	0.0029	1.093	1.057 - 1.130	<0.0001
Yes	1.115	0.926 - 1.342	0.2526	1.165	0.986 - 1.377	0.0731	0.978	0.833 - 1.147	0.7809	1.233	0.990 - 1.536	0.0616
Income Group												
< \$43,667	0.947	0.885 - 1.015	0.1226	1.016	0.962 - 1.074	0.5667	0.965	0.908 - 1.025	0.2488	1.043	0.936 - 1.163	0.4451
\$43,668 - \$55,930	1.031	0.973 - 1.092	0.2984	1.065	1.022 - 1.111	0.0029	1.013	0.959 - 1.069	0.6444	1.108	1.042 - 1.178	0.0011
\$55,931 - \$71,591	0.962	0.917 - 1.008	0.1065	1.001	0.951 - 1.053	0.9673	0.951	0.904 - 1.001	0.0538	1.106	1.033 - 1.183	0.0038
≥ \$71,592	0.959	0.929 - 0.989	0.0083	1.012	0.981 - 1.044	0.4577	0.935	0.897 - 0.976	0.0019	1.085	1.042 - 1.130	<0.0001
Season of Delivery												
Cool	0.982	0.950 - 1.014	0.2599	1.041	1.008 - 1.075	0.0152	0.965	0.928 - 1.004	0.0784	1.092	1.042 - 1.144	0.0002
Warm	0.965	0.936 - 0.995	0.0214	1.005	0.974 - 1.037	0.7497	0.951	0.916 - 0.987	0.0088	1.096	1.049 - 1.145	<0.0001
Maternal Age Group												
Less Than 25 Years Old	0.982	0.924 - 1.043	0.5470	1.031	0.968 - 1.099	0.3365	0.928	0.870 - 0.990	0.0231	1.128	1.029 - 1.236	0.0099
25 - 30 Years Old	0.954	0.917 - 0.994	0.0242	1.018	0.977 - 1.061	0.3937	0.966	0.922 - 1.012	0.1397	1.095	1.031 - 1.163	0.0026
30 - 35 Years Old	0.971	0.935 - 1.009	0.1311	1.012	0.976 - 1.049	0.5335	0.954	0.911 - 0.998	0.0429	1.073	1.021 - 1.128	0.0030
≥ 36 Years Old	0.981	0.935 - 1.030	0.4363	1.040	0.996 - 1.085	0.0736	0.967	0.912 - 1.026	0.2666	1.089	1.026 - 1.155	0.0047

Associations between air pollution and GDM

Overall, significantly positive associations were seen with exposure to PM_{2.5}, PM₁₀, and O₃. Specifically, PM_{2.5} exposure was positively associated with GDM risk during all time periods, with significant results found for the entire pregnancy (HR=1.061; 95% CI, 1.033-1.090), 3-months preconception period (HR=1.040; 95% CI, 1.015-1.066), 1st trimester (HR=1.046; 95% CI, 1.016-1.076), 1st and 2nd trimesters (1.048; 95% CI, 1.019-1.078), and entire GDM period (HR=1.063; 95% CI, 1.035-1.092). For PM₁₀, significantly positive associations were seen during the entire pregnancy (HR=1.043; 95% CI, 1.017-1.069), 2nd trimester (HR=1.024; 95% CI, 1.000-1.049), 1st and 2nd trimesters (HR=1.032; 95% CI, 1.003-1.062), and entire GDM time period (HR=1.040; 95% CI, 1.013-1.067); all other time periods reported insignificantly positive associations with GDM risk. Ozone exposure in all time periods was positively associated with GDM risk; significant results were seen with exposure in the entire pregnancy (HR=1.058; 95% CI, 1.023-1.094), 2nd trimester (HR=1.039; 95% CI, 1.010-1.069), and entire GDM time period (HR=1.043; 95% CI, 1.007 – 1.080). NO₂ exposure during the 1st trimester was positively associated with GDM risk (HR=1.014; 95% CI, 0.984-1.046), although this association was not significant. All other regressions showed negative associations between NO₂ exposure and GDM risk. All results from the GDM regression analyses are presented in Tables 8-9.

GDM Subgroup Analysis

Subgroup analyses with Cox models showed that certain populations may be at a greater risk of the impacts from air pollution exposure on GDM. Asian and Hispanic mothers were more susceptible to the effects from PM_{2.5} and PM₁₀. We also found that white mothers are the most susceptible to O₃ exposure (HR=1.118; 95% CI, 1.030-1.213).

For maternal education, results showed that higher education increased the risk of GDM with exposure to PM_{2.5}, PM₁₀, NO₂, and O₃. Results also showed that higher annual income increased the risk for GDM when exposed to PM and ozone. Age had a small influence on GDM risk, with mothers over 30 years old being more susceptible to PM exposure. Mothers with a pre-pregnancy BMI considered underweight, normal weight, or overweight were more susceptible to the impacts from PM₁₀ exposure, and overweight mothers had a significantly increased risk of GDM from ozone. These results are presented in Table 10.

Table 8: Results from GDM and PM Cox Proportional Hazard models. Odds ratios, 95% confidence index, and p-values are presented in the table. Covariates included: mom age, mom race/ethnicity, mom educational level, pre-pregnancy BMI groups, season of conception, income level, smoking status, and passive smoking status. Significant positive associations are bolded, and significant negative associations are presented in red. The entire GDM time period refers to 3-months preconception through the second trimester. Significance level was <0.05. CI = Confidence Index.

	PM _{2.5}			PM ₁₀		
	Hazard Ratio	95% CI	P-Value	Hazard Ratio	95% CI	P-Value
Entire Pregnancy	1.061	1.033 - 1.098	<0.0001	1.043	1.017 - 1.069	0.0012
3-Months Preconception	1.040	1.015 - 1.066	0.0016	1.023	0.998 - 1.048	0.0726
1 st Trimester	1.046	1.016 - 1.076	0.0023	1.022	0.991 - 1.054	0.1716
2 nd Trimester	1.022	0.999 - 1.046	0.0618	1.024	1.000 - 1.049	0.0487
1 st and 2 nd Trimesters	1.048	1.019 - 1.078	0.0012	1.032	1.003 - 1.062	0.0289
Entire GDM Period	1.063	1.035 - 1.092	<0.0001	1.040	1.013 - 1.067	0.0028

Table 9: Results from GDM and NO₂ and O₃ Cox Proportional Hazard models. Odds ratios, 95% confidence index, and p-values are presented in the table. Covariates included: mom age, mom race/ethnicity, mom educational level, pre-pregnancy BMI groups, season of conception, income level, smoking status, and passive smoking status. Significant positive associations are bolded, and significant negative associations are presented in red. The entire GDM period refers to 3-months preconception through the second trimester. Significance level was <0.05. CI = Confidence Index.

	NO ₂			Ozone		
	Hazard Ratio	95% CI	P-Value	Hazard Ratio	95% CI	P-Value
Entire Pregnancy	0.985	0.949 - 1.022	0.4155	1.058	1.023 - 1.094	0.0012
3-Months Preconception	0.994	0.953 - 1.037	0.7696	1.009	0.982 - 1.038	0.5137
1 st Trimester	1.014	0.984 - 1.046	0.3593	1.008	0.983 - 1.034	0.5387
2 nd Trimester	0.958	0.918 - 1.000	0.0527	1.039	1.010 - 1.069	0.0076
1 st and 2 nd Trimesters	0.996	0.960 - 1.033	0.8250	1.024	0.999 - 1.049	0.0600
Entire GDM Period	0.993	0.959 - 1.029	0.7082	1.043	1.007 - 1.080	0.0179

Table 10: GDM subgroup analysis using Cox Hazards Proportional Models. Hazard ratios, 95% confidence intervals, and p-values are presented for each subgroup and each pollutant. Negative associations are presented in red, and positive associations are bolded. Significance was ≤ 0.05 . HR = Hazard Ratio, CI = Confidence Interval.

	PM _{2.5}			PM ₁₀			NO ₂			O ₃		
	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value
Maternal Race/Ethnicity												
African American	1.068	0.944 - 1.209	0.2976	1.052	0.951 - 1.164	0.3290	0.896	0.798 - 1.006	0.0632	0.980	0.839 - 1.146	0.8025
Asian	1.071	1.012 - 1.133	0.0169	1.051	1.002 - 1.104	0.0430	1.009	0.952 - 1.070	0.7615	1.037	0.982 - 1.094	0.1968
Hispanic	1.061	1.025 - 1.099	0.0009	1.047	1.011 - 1.085	0.0108	1.009	0.968 - 1.052	0.6669	1.038	0.985 - 1.093	0.1603
White	1.031	0.959 - 1.107	0.4080	1.009	0.947 - 1.076	0.7784	0.960	0.863 - 1.068	0.4525	1.118	1.030 - 1.213	0.0078
Multi/Other	1.055	0.929 - 1.199	0.4073	0.976	0.873 - 1.090	0.6606	0.986	0.848 - 1.146	0.8517	0.952	0.833 - 1.087	0.4673
Maternal Education												
High School or Less	1.056	1.000 - 1.116	0.0505	1.035	0.982 - 1.092	0.2000	1.021	0.958 - 1.088	0.5231	0.993	0.921 - 1.072	0.8624
Some College	1.040	0.983 - 1.101	0.1751	0.988	0.935 - 1.044	0.6697	0.946	0.885 - 1.012	0.1083	1.039	0.971 - 1.112	0.2677
College Degree	1.059	1.014 - 1.106	0.0094	1.038	1.000 - 1.077	0.0495	1.024	0.976 - 1.075	0.3351	1.052	1.006 - 1.081	0.2562
More Than College	1.133	1.065 - 1.205	<0.0001	1.102	1.045 - 1.162	0.0004	1.081	1.009 - 1.160	0.0275	1.090	1.025 - 1.160	0.0059
Smoking Status												
Never Smoked	1.070	1.040 - 1.101	<0.0001	1.046	1.018 - 1.075	0.0012	0.985	0.949 - 1.023	0.4439	1.054	1.015 - 1.093	0.0055
Smoked	1.036	0.964 - 1.114	0.3373	1.008	0.947 - 1.072	0.8054	1.075	0.989 - 1.169	0.0896	1.006	0.934 - 1.084	0.8710
Passive Smoking												
No	1.064	1.036 - 1.093	<0.0001	1.043	1.016 - 1.070	0.0013	0.994	0.959 - 1.030	0.7488	1.046	1.010 - 1.083	0.0128
Yes	0.926	0.714 - 1.202	0.5650	0.704	0.523 - 0.948	0.0207	0.869	0.659 - 1.146	0.3203	0.851	0.606 - 1.195	0.3520
Income Group												
< \$43,667	1.049	0.965 - 1.141	0.2624	1.011	0.944 - 1.084	0.7536	0.944	0.924 - 1.070	0.8712	1.004	0.915 - 1.101	0.9361
\$43,668 - \$55,930	1.030	0.965 - 1.100	0.3755	1.034	0.974 - 1.097	0.2725	0.964	0.895 - 1.038	0.3323	1.013	0.932 - 1.100	0.7656
\$55,931 - \$71,591	1.053	0.994 - 1.116	0.0808	1.042	0.985 - 1.102	0.1530	0.980	0.915 - 1.050	0.7833	1.072	0.991 - 1.161	0.0844
\geq \$71,592	1.079	1.040 - 1.119	<0.0001	1.047	1.012 - 1.083	0.0087	1.024	0.974 - 1.076	0.3609	1.062	1.018 - 1.107	0.0050
Season of Conception												
Cool	1.064	1.029 - 1.100	0.0002	1.054	1.019 - 1.091	0.0024	1.029	0.985 - 1.075	0.1930	1.020	0.975 - 1.068	0.3873
Warm	1.060	1.019 - 1.102	0.0037	1.027	0.994 - 1.061	0.1089	0.999	0.956 - 1.043	0.9563	1.063	1.017 - 1.111	0.0067
Maternal Age Group												
<25 Years Old	1.076	0.976 - 1.187	0.1405	1.035	0.948 - 1.129	0.4429	1.031	0.928 - 1.145	0.5715	1.036	0.921 - 1.165	0.5551
25 - 30 Years Old	1.016	0.963 - 1.072	0.5622	1.010	0.963 - 1.060	0.6733	0.972	0.916 - 1.030	0.3351	1.059	0.997 - 1.125	0.0626
30 - 35 Years Old	1.066	1.022 - 1.113	0.0032	1.039	1.000 - 1.079	0.0479	1.010	0.962 - 1.061	0.6927	1.022	0.990 - 1.085	0.1247
\geq 36 Years Old	1.100	1.050 - 1.152	<0.0001	1.065	1.021 - 1.110	0.0034	1.076	1.022 - 1.133	0.0052	1.055	0.991 - 1.100	0.1090
Pre-Pregnancy BMI												
Under or Normal Weight	1.073	1.017 - 1.133	0.0102	1.059	1.010 - 1.109	0.0165	1.020	0.960 - 1.084	0.5169	1.058	0.998 - 1.121	0.0587
Overweight	1.064	1.013 - 1.118	0.0136	1.053	1.008 - 1.100	0.0200	1.048	0.993 - 1.106	0.0887	1.065	1.008 - 1.126	0.0258
Obese Class 1, 2, or 3	1.065	1.024 - 1.107	0.0016	1.021	0.983 - 1.059	0.2848	0.981	0.936 - 1.028	0.4136	1.019	0.965 - 1.077	0.4908

COVID-19 Statistical Analyses

The results from the COVID pandemic time analyses are presented in Tables 11-16. For PPD, 6,956 were not affected by the

Table 11: Summary Statistics for PPD COVID Time Periods. Results are presented as n (%).

	PPD (n =21,652)	Non-PPD (n = 94,152)
Not Impacted	7,927 (27.98)	43,783 (33.03)
Pregnant When the Pandemic Began	7,398 (26.11)	32,372 (24.42)
Conceived After the Pandemic Began	4,610 (16.27)	21,397 (16.14)
Pandemic Began in the Postpartum Period	8,394 (29.63)	35,019 (26.42)

pandemic during pregnancy or the postpartum period, 39,778 experienced the pandemic within the first year postpartum, 26,010 were pregnant when the pandemic started, and 43,417 conceived after the pandemic began. Chi-square test results showed significant differences in PPD diagnosis between COVID time groups. Mothers who were pregnant when the pandemic began in March 2020 had significantly higher rates of PPD compared to mothers who conceived after the pandemic. Additionally, mothers in the postpartum period had significantly higher rates of PPD compared to all other time groups.

Experiencing the pandemic while pregnant (HR=1.037; 95% CI, 1.004-1.072) and within the first year postpartum (HR=1.051; 95% CI,1.000-1.104) significantly increased the risk of PPD with exposure to PM₁₀. O₃ exposure remained significantly positive for all four time periods. In addition, mothers who conceived after the pandemic began in March 2020 experienced significantly lower risks for PPD with exposure to PM_{2.5} (HR=0.945; 95% CI,

0.909-0.982) and NO₂ (HR=0.927; 95% CI, 0.889-0.966).

Table 12: Results of chi-square tests for PPD COVID times. Chi-square statistics and P-values are presented. Not impacted mothers were those who gave birth before March 2019. Pregnant mothers were pregnant in March 2020. Postpartum mothers gave birth between March 2019-March 2020. Mothers who conceived after were those with a date of conception after March 2020. Significance was <0.05.

	Chi-Square Statistic	P-Value
Not Impacted and Pregnant	28.22	0.6265
Not Impacted and Postpartum	4.42	0.0354
Not Impacted and Conceived After	0.8231	0.3643
Pregnant and Postpartum	8.06	0.0045
Pregnant and Conceived After	7.34	0.0067
Postpartum and Conceived After	27.76	<0.0001

For GDM, 43,086 participants gave birth before the pandemic, 24,461 were pregnant when the pandemic began, and 40,591 conceived after the pandemic started. Results show that mothers who gave birth before March 2020 had lower associations with GDM risk with exposure to PM. In addition, mothers who were pregnant when the pandemic occurred may have been more vulnerable to the effects from PM_{2.5} (HR=1.068; 95% CI, 1.003-1.137), while mothers who conceived after the pandemic did not have any significant associations between GDM and air pollution exposure.

Table 13: Summary statistics for GDM COVID time groups. Results are presented as n (%).

	GDM (n = 12,174)	Non-GDM (n = 96,450)
Not Impacted	4,439 (35.87)	38,737 (40.34)
Pregnant When the Pandemic Began	2,630 (21.69)	21,831 (22.74)
Conceived After the Pandemic Began	5,144 (42.43)	35,453 (36.92)

Table 14: Results of chi-square tests for GDM COVID times. Chi-square statistics and P-values are presented. Not impacted mothers were those who gave birth before March 2020. Pregnant mothers were pregnant in March 2020. Mothers who conceived after were those with a date of conception after March 2020. Significance was <0.05.

	Chi-Square Statistic	P-Value
Not Impacted and Pregnant	7.29	0.0069
Not Impacted and Conceived After	138.03	<0.0001
Pregnant and Conceived After	53.43	<0.0001

Table 15: Results from the PPD cox proportional hazards model for subgroup analyses. Odds ratios, 95% confidence index, and p-values are presented in the table. Covariates included: mom age, mom race/ethnicity, mom educational level, season of delivery, income level, smoking status, and passive smoking status. Significant positive associations are bolded, and significant negative associations are presented in red. COVID-19 Time Period describes the point in pregnancy when the pandemic began (March 2020); Not Impacted = gave birth before March 2019, Postpartum = gave birth between March 2019 – March 2020, Pregnant = pregnant in March 2020, Conceived After = date of conception is after March 2020. Subgroup analyses was performed with exposure during the entire pregnancy and 12-month postpartum period. Significance level was <0.05. HR = Hazard Ratio, CI = Confidence Index.

	PM _{2.5}			PM ₁₀			NO ₂			O ₃		
	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value
COVID-19 Time Period												
Not Impacted	0.979	0.892 – 1.075	0.6553	1.079	0.992 – 1.174	0.0774	1.027	0.918 – 1.149	0.6410	1.197	1.071 – 1.338	0.0015
Postpartum	0.981	0.944 – 1.019	0.3186	1.037	1.004 – 1.072	0.0302	0.959	0.916 – 1.004	0.0729	1.136	1.081 – 1.194	<0.0001
Pregnant	0.980	0.932 – 1.030	0.4285	1.051	1.000 – 1.104	0.0480	0.978	0.924 – 1.035	0.4361	1.076	1.007 – 1.149	0.0302
Conceived After	0.945	0.909 – 0.982	0.0040	0.979	0.937 – 1.022	0.3261	0.927	0.889 – 0.966	0.0004	1.077	1.017 – 1.140	0.0111

Table 16: Results from the GDM Cox proportional hazards model for subgroup analyses. Odds ratios, 95% confidence index, and p-values are presented in the table. Covariates included: mom age, mom race/ethnicity, mom educational level, season of delivery, income level, smoking status, and passive smoking status. Significantly positive associations are bolded, and significantly negative associations are presented in red. COVID-19 Time Period describes the point in pregnancy when the pandemic began (March 2020); Not Impacted = gave birth before March 2020, Pregnant = pregnant in March 2020, Conceived After = date of conception is after March 2020. Subgroup analyses was performed with exposure 3-months preconception through the 2nd trimester. Significance level was <0.05. HR = Hazard Ratio, CI = Confidence Index.

	PM _{2.5}			PM ₁₀			NO ₂			O ₃		
	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value	HR	95% CI	P-Value
COVID-19 Time Period												
Not Impacted	0.932	0.890 – 0.977	0.0036	0.952	0.909 – 0.997	0.0355	0.971	0.927 – 1.017	0.2099	1.013	0.968 – 1.060	0.5797
Pregnant	1.068	1.003 – 1.137	0.0397	1.000	0.955 – 1.046	0.9961	1.052	0.986 – 1.122	0.1252	1.005	0.940 – 1.076	0.8753
Conceived After	1.003	0.956 – 1.052	0.9033	0.999	0.954 – 1.046	0.9578	1.030	0.977 – 1.086	0.2684	0.961	0.901 – 1.025	0.2249

CHAPTER 5: DISCUSSION

Specific Aim 1

Based on our results, exposure to ozone during and after pregnancy may increase the risk of PPD. Our group's previous study found that ozone exposure had the largest association with PPD risk (Sun et al., 2023), which is similar to what our current study reported. We did not find significant associations between PM₁₀ and PPD risk, which is different from previous studies. One study from China reported increased risks of PPD with exposure to PM₁₀ during pregnancy, while our previous study reported increased risks with exposure in the late pregnancy and postpartum period (C. C. Duan et al., 2022; Sun et al., 2023). In a previous study, we found significantly positive associations between PPD and PM_{2.5} exposure in the late pregnancy and postpartum period (Sun et al., 2023). We did not find these same results in the current study and actually found significantly negative associations with exposure in the late pregnancy and postpartum periods. These results are different from several other previous studies, which found increased risks with PM_{2.5} exposure during pregnancy (Bastain et al., 2021; Niedzwiecki et al., 2020; Sheffield et al., 2018). A few studies have suggested that NO₂ exposure may increase the risk of PPD (Bastain et al., 2021; C. C. Duan et al., 2022), although our previous and current studies do not support this association (Sun et al., 2023).

Specific Aim 2

Our study found that the risk of GDM may increase with exposure to PM_{2.5} in the 1st trimester, first two trimesters, entire pregnancy, entire GDM period, and the 3-month preconception period. These results are supported by several studies, including our group's previous GDM and air pollution analysis (Hu et al., 2015; Jo et al., 2019; Kang et al., 2020;

Lin et al., 2020; Niu et al., 2023; Rammah et al., 2020; Sun et al., 2022; Ye et al., 2020; Zhang et al., 2020). Interestingly, multiple studies reported positive associations with PM_{2.5} exposure in the 2nd trimester (Hu et al., 2015; Lin et al., 2020; Rammah et al., 2020; Sun et al., 2022; Ye et al., 2020); while we found a positive association, our results were not significant, which is supported by three studies (Hu et al., 2021; Yan et al., 2023; Zhang & Zhao, 2021). Interestingly, three studies reported no associations with 1st trimester PM_{2.5} exposure, but significantly positive associations in the 2nd trimester (Choe et al., 2019; Gong et al., 2023; Yu et al., 2020).

Our results also indicate that PM₁₀ exposure throughout the entire pregnancy, 2nd trimester, first two trimesters, and entire GDM period may also increase the risk of GDM. Previous research somewhat supports these results. Preconception, 1st trimester, 2nd trimester, and first two trimesters PM₁₀ exposure have been reported to increase the risk of GDM (Jo et al., 2019; Lin et al., 2020; Niu et al., 2023; Sun et al., 2022; Yao et al., 2020); while we found positive associations with all time periods, only the 2nd trimester, first two trimesters, entire pregnancy, and entire GDM period were significant.

We did not find any previous studies that have found an association between GDM and O₃ exposure during the entire pregnancy and 2nd trimester. Several studies have reported positive associations between O₃ exposure and GDM, but during the 1st trimester, first two trimesters, and preconception period (Gong et al., 2023; Z. Li et al., 2022; Miron-Celis et al., 2023; Yao et al., 2020); there were also multiple articles that discussed protective effects from ozone exposure, including our previous study (Jo et al., 2019; Lin et al., 2020; Pan et al., 2017; Robledo et al., 2015; Sun et al., 2022).

The biggest difference between our previous GDM and air pollution study and the current study was NO₂ exposure, which previously had the largest positive association with GDM risk (Sun et al., 2022). Several other studies have also reported positive associations with 1st trimester and preconception exposure to NO₂ (Choe et al., 2019; Jo et al., 2019; Niu et al., 2023). While our study did find positive associations with 1st trimester NO₂ exposure, the results were not significant.

Specific Aim 3

Regarding COVID-19 and PPD, interesting results were found. Mothers who were either pregnant or in the postpartum period when the pandemic began in March 2020 were the most at risk for PPD from exposure to PM₁₀. Additionally, mothers who conceived after March 2020 experienced a significantly negative association with NO₂ and PM_{2.5} exposure. O₃ remained significantly positive, regardless of the COVID time period. For GDM risk due to air pollution exposure, the only significantly positive association seen was with PM_{2.5} exposure for mothers who were pregnant when the pandemic began. This was different for mothers who gave birth before March 2020, who experienced a significantly negative association with both PM_{2.5} and PM₁₀.

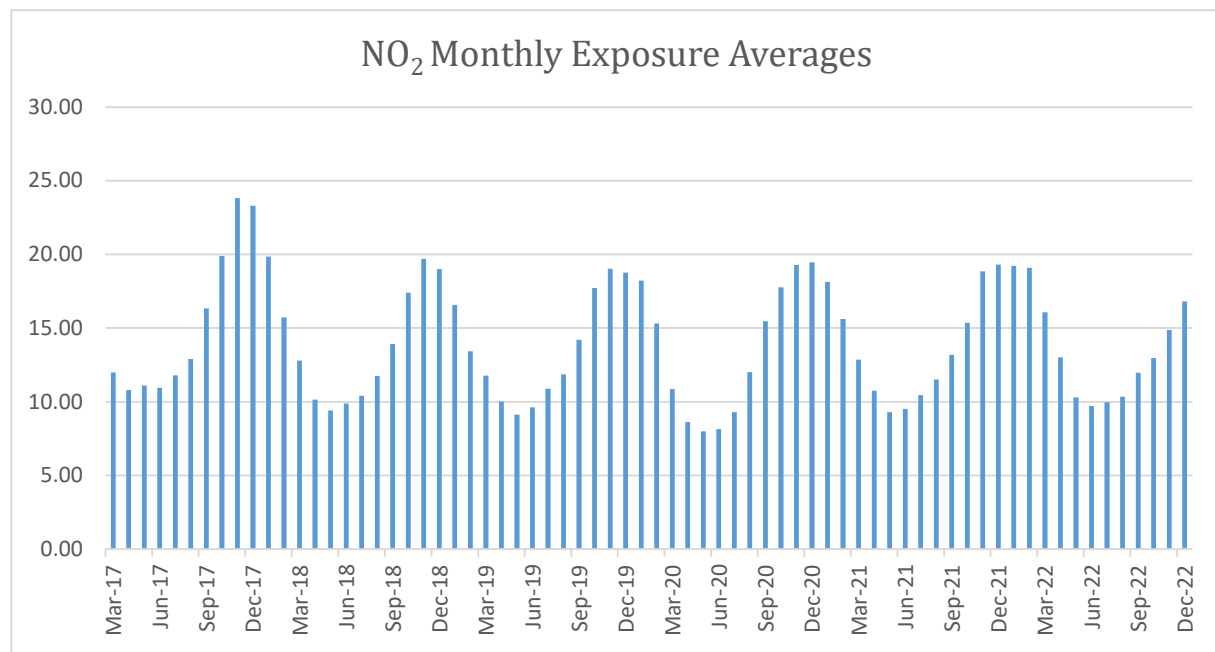
In our study, we found an overall PPD prevalence of 18.70% while our previous study from 2008-2018 found a prevalence of 7.54% (Sun et al., 2023). There have been studies that have suggested overall mental health deteriorated during the lockdown period (Marroquín et al., 2020; Pierce et al., 2020; Wu et al., 2021). In a study that used a nationwide online sample of US adults, being under a stay-at-home order and personal distancing behavior was associated with higher depression, generalized anxiety disorder symptoms, and acute stress (Marroquín et al., 2020). Another study reported that

depression, anxiety, distress, and insomnia increased after the COVID-19 outbreak (Wu et al., 2021). They found a 31.4% pooled prevalence of depression, compared to a 6.6% prevalence before the pandemic (Wu et al., 2021). Another study from the UK used scores from the General Health Questionnaire to measure mental distress; they found that in late April 2020, more than a quarter of the population earned a score that indicated mental distress (Pierce et al., 2020). During the pandemic, many women may have experienced stress due to isolation, fear of infection, and lack of social support; this may have put them at an even greater risk of developing PPD.

Studies have found that daily activities were altered during the pandemic lockdown periods (Mun & So, 2022; Sumalla-Cano et al., 2022), which may have been influenced by more time spent indoors. Two studies reported that almost 50% of individuals experienced a decrease in physical activity during the pandemic (Mun & So, 2022; Sumalla-Cano et al., 2022). Another study that used a population of students found that more than half of their population experienced decreased physical activity after the COVID-19 outbreak (Guo et al., 2021). Regarding diet, one study reported that 21.4% saw an increase in pastries/snack consumption, while 48.2% said their pastries/snack consumption stayed the same (Sumalla-Cano et al., 2022). In addition, 17% saw an increase in unhealthy diets in a study from South Korea (Mun & So, 2022). Eating a healthy diet and regular physical activity are suggested as potential ways to prevent GDM (Centers for Disease Control and Prevention, 2022; Mayo Clinic, 2022a). GDM risk may have been influenced by activity changes during the COVID-19 pandemic, such as decreasing physical activity in combination with unhealthy diets either remaining the same, or even increasing.

Several studies have shown that air pollution levels have decreased over time, especially during the COVID-19 pandemic lockdown period (Jiang et al., 2021; Lurmann et al., 2015; Naeger & Murphy, 2020). Our study did find lower pollution exposure levels compared to the previous study. These averages are presented in the Appendix. In the study from 2008-2018, average NO₂ levels during pregnancy were 15.86 µg/m³, compared to 13.78 µg/m³ in the current study. It has been reported that during the COVID-19 lockdown period, NO₂ levels decreased significantly, and may have been the pollutant that decreased the most (Berman & Ebisu, 2020; Elshorbany et al., 2021; Fu et al., 2020; Jiang et al., 2021; J. Liu, Lipsitt, et al., 2021; Naeger & Murphy, 2020). This decrease in NO₂ may have been due to the stay-at-home orders since fewer individuals needed to commute to work (Berman & Ebisu, 2020; Fu et al., 2020; J. Liu, Lipsitt, et al., 2021). Some studies estimate there was a 60% decrease in automobile usage in Los Angeles, and a 15% decrease in vehicle miles traveled (Elshorbany et al., 2021; Naeger & Murphy, 2020) Since NO₂ is produced mostly from fuel burning related to transportation (County of Los Angeles Public Health, n.d.; EPA, 2023a; Fu et al., 2020), the decrease in traffic volume during the lockdown period may explain why NO₂ exposures were lower. Further, this may partially explain why we did not see an association with GDM or PPD. Figure 2 shows NO₂ exposure levels for the participants in our study. There was a large decrease around March 2020, which is slightly lower than the decreases seen in previous years. In addition, the peak levels of NO₂ were higher before the pandemic compared to the peak levels after the pandemic began.

Figure 2: NO₂ exposure levels for participants who gave birth between 2019-2021. The X-axis is the month, and the Y-axis is the estimated exposure. Exposure estimates are based on preconception, pregnancy, and postpartum exposures. Pollutant data is presented in parts per million.

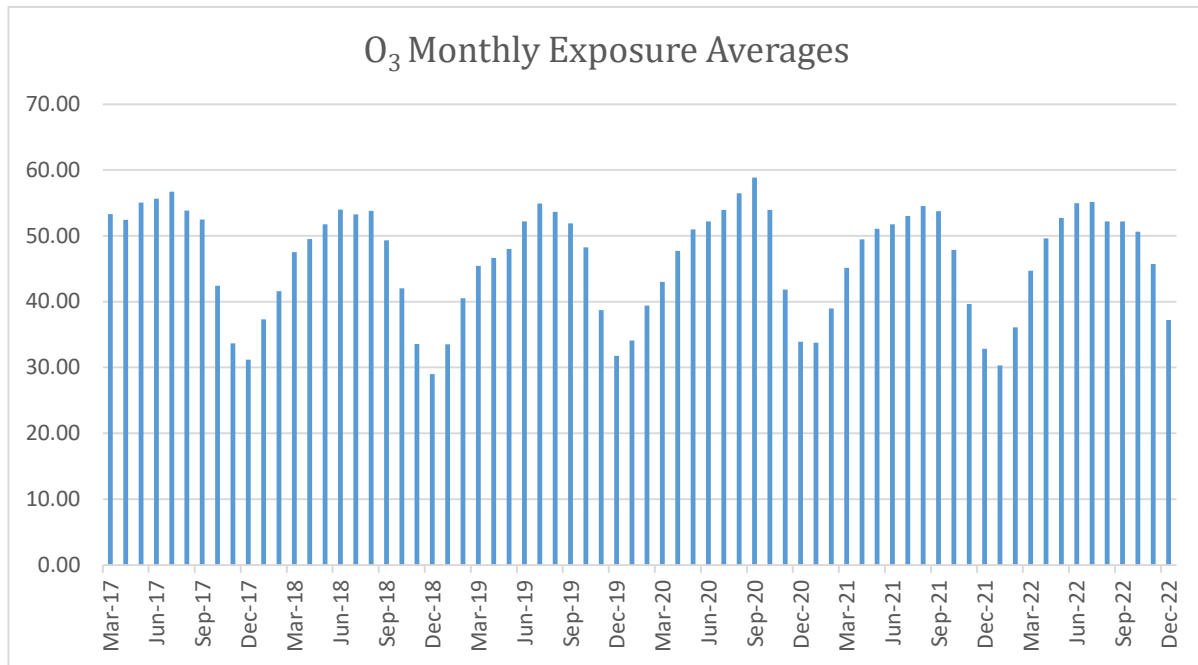


Ozone levels increased from the previous cohort; from 2008-2018, the average O₃ exposure during pregnancy was 43.64 µg/m³ compared to 45.90 µg/m³ from 2019-2021. This is supported by studies that report increases in O₃ concentration during the pandemic time (Fu et al., 2020; Jiang et al., 2021). Ozone levels may have increased due to rising temperatures (Fu et al., 2020; Jiang et al., 2021); the year 2020 was the second hottest on record globally (EPA, 2023e; National Aeronautics and Space Administration, 2021). This may offer a potential explanation as to why some associations with ozone were seen in the current study that were not previously reported. Figure 3 shows O₃ exposure levels over time across Southern California.

PM exposure did decrease compared to our previous study; PM_{2.5} exposure average for the entire pregnancy in the 2008-2018 cohort was 11.69 µg/m³ compared to 11.01 µg/m³ from 2019-2021. PM₁₀ exposure for the entire pregnancy in 2008-2018 was 28.53 µg/m³

compared to 26.60 $\mu\text{g}/\text{m}^3$ from 2019-2021. A potential explanation for the decrease in PM may be the decreased vehicular traffic, which is known to contribute to PM pollution (EPA, 2023c). Although the decrease in traffic may have lowered PM concentrations, other sources of PM emissions were not impacted by the pandemic shutdowns; these sources include food industries, agricultural sources, and biomass burning (Berman & Ebisu, 2020; Jiang et al., 2021). In addition, wildfires are known to contribute significantly to PM pollution (Aguilera et al., 2021; Jiao et al., 2024; Liu et al., 2016; Ye et al., 2021); in late July and August 2020, southern California experienced three large wildfires (Safford et al., 2022), which may explain the large spike in $\text{PM}_{2.5}$ and PM_{10} pollution seen in the late summer of 2020.

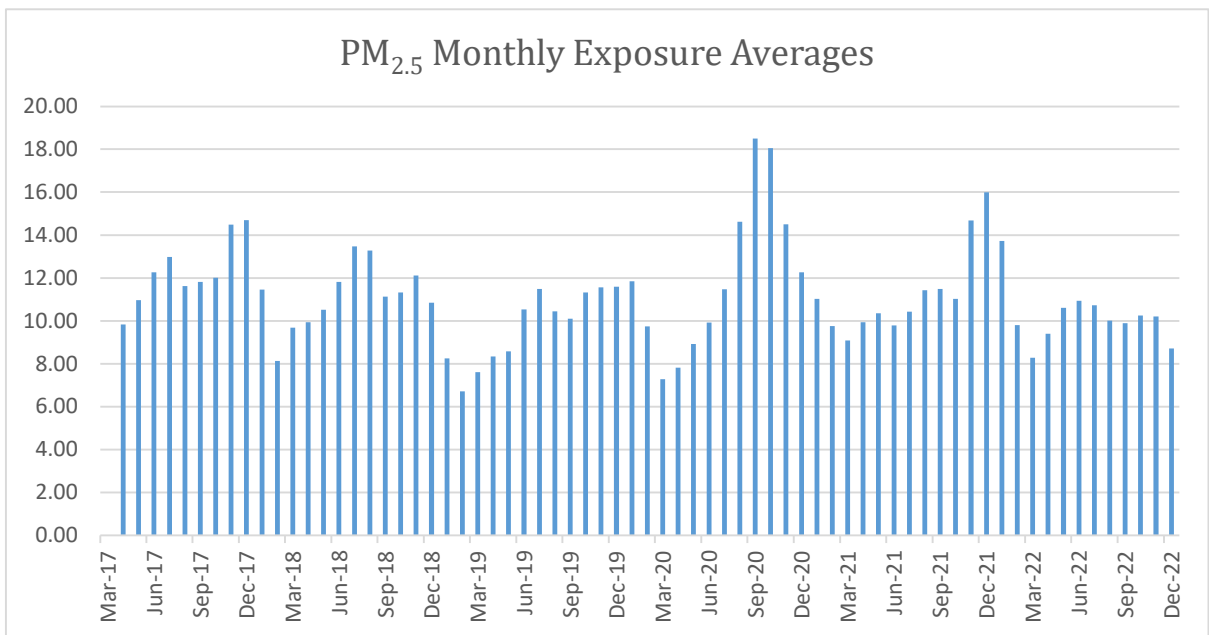
Figure 3: Ozone exposure levels for participants who gave birth between 2019-2021. The X-axis is the month, and the Y-axis is the estimated exposure. Exposure estimates are based on preconception, pregnancy, and postpartum exposures. Pollutant data is presented in parts per million.



Interestingly, our results indicated a protective association between PM exposure and PPD risk. PM constituents may explain this association. $\text{PM}_{2.5}$ contains several constituents,

including sulfate, nitrate, ammonium, organic carbon, organic matter, black carbon, and more (Bressi et al., 2013; Li et al., 2023; Yang et al., 2018). In our previous PPD and air pollution study, we found that PM_{2.5} black carbon and organic matter were the main constituents that increased the risk of PPD (Sun et al., 2023). Sources of black carbon and organic matter are primarily the incomplete combustion of various fossil fuels and biomass (Bressi et al., 2013; B. Li et al., 2023; H. Li et al., 2022). Specifically, it's estimated that fossil fuel combustion contributes to more than 90% of black carbon emissions (H. Li et al., 2022). Lower traffic emissions seen during the pandemic shutdowns strongly reduced black carbon concentrations (H. Li et al., 2022). One study from the Yangtze River Delta in Eastern China investigated the correlation between PM_{2.5} and black carbon concentrations (H. Li et al., 2022). In the pre-lockdown period, black carbon was significantly correlated with PM_{2.5} at 7 of 9 locations; during the lockdown periods, black carbon and PM_{2.5} were no

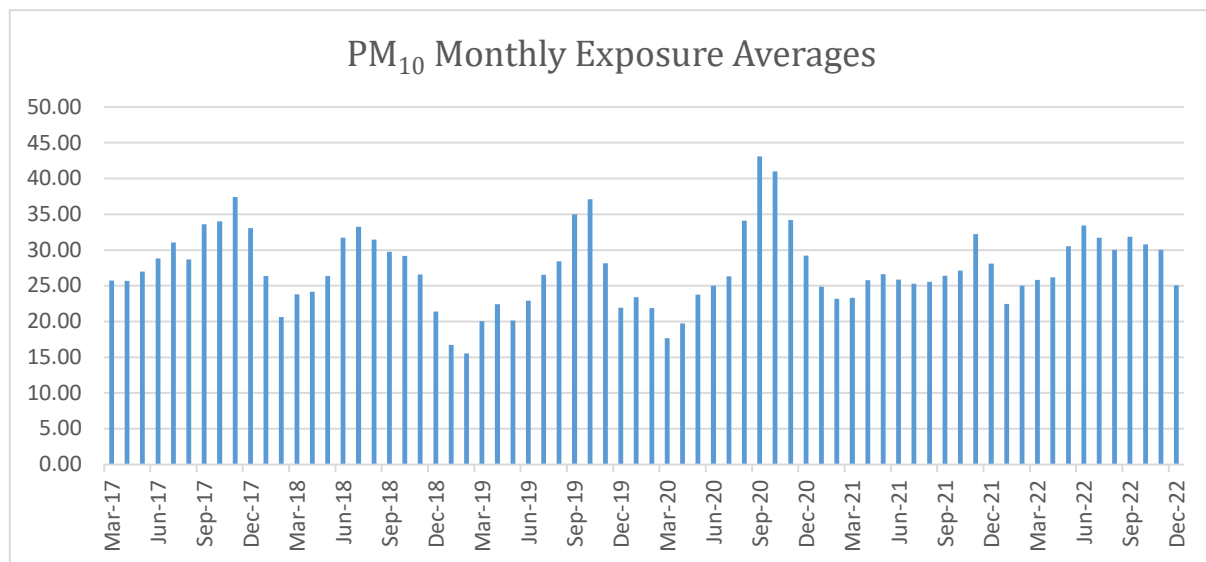
Figure 4: PM_{2.5} monthly exposure averages for the entire population. The average exposure in parts per million are presented in the Y-axis, and the month of exposure is presented in the X-axis.



longer significantly correlated (H. Li et al., 2022). The decrease in black carbon may explain the decreased odds ratio for PPD risk due to PM exposure.

Regarding GDM risk, our previous GDM and air pollution paper found increased risks of GDM from all PM_{2.5} constituents. Some PM constituents are produced from sources other than traffic sources. For example, agriculture is one of the biggest contributors to ammonia emissions, with one study estimating that agriculture contributed to over 80% of global ammonia concentrations (Bray et al., 2018; Van Damme et al., 2021; Wyer et al., 2022). It was estimated that during the pandemic, agricultural sources of pollutants did not change, while pollution from on-road traffic and aircrafts decreased by up to 70% (Jiang et al., 2021). If agricultural sources did not change their pollutant emissions during the pandemic, this may provide a potential explanation as to why we continued to see associations between PM and GDM. More research should be done to investigate these potential explanations for our findings. PM exposure averages over time in southern California are presented in Figures 4 and 5.

Figure 5: PM₁₀ monthly exposure averages for the entire population. The average exposure in parts per million are presented in the Y-axis, and the month of exposure is presented in the X-axis.



Biological Mechanisms

Air pollution exposure may increase the release of inflammatory cytokines and reactive oxygen species (ROS) (Lelieveld et al., 2021; Li et al., 2018; Liu et al., 2018; MohanKumar et al., 2008). ROS are reactive species that are oxygen-containing; they are also known as free radicals (Li & Trush, 2016). Common ROS includes peroxide ($\bullet\text{O}_2^{2-}$), hydrogen peroxide (H_2O_2), hydroxyl radical ($\bullet\text{OH}$), and superoxide ($\bullet\text{O}_2^-$) (Correia et al., 2023; Li & Trush, 2016). ROS are concerning, since they can lead to oxidative stress, which is a condition that can cause cell dysfunction, and cell death (Li & Trush, 2016). Oxidative stress has been associated with several pathological conditions (Li & Trush, 2016). $\text{PM}_{2.5}$ contains redox-active components, including copper, irons, and quinones; these components lead to the generation of ROS (Lakey et al., 2016; Lelieveld et al., 2021). NO_2 itself is a free radical that has been suggested to decrease antioxidant levels, which further promotes oxidative stress (Jarvis et al., 2010; Petit et al., 2017). While air pollution is known to increase inflammatory cytokine production, ROS production may also contribute to increased inflammatory cytokine levels (Correia et al., 2023; Mittal et al., 2014). In addition, inflammatory cytokines may activate signaling pathways that further produce ROS (Correia et al., 2023; Eguchi et al., 2021; D. Yang et al., n.d.).

PPD Mechanisms

ROS and inflammatory cytokine production may lead to the development of PPD through several pathways. ROS production and inflammatory cytokines have been known to dysregulate the hypothalamic-pituitary-adrenal-axis (HPA-axis), which is responsible for the body's stress response (Brianna Chu et al., n.d.; Correia et al., 2023; Dunlavey, 2018; Glynn et al., 2013; MohanKumar et al., 2008; Payne & Maguire, 2019). The dysregulation of

the HPA-axis results in altered cortisol release, which may contribute to a poor stress response (Glynn et al., 2013; Payne & Maguire, 2019; Thomson et al., 2019). Further, the release of glucocorticoids from the HPA-axis promotes mitochondrial oxidation to produce ATP; this process produces more ROS (Correia et al., 2023; Dinić et al., 2022; Eguchi et al., 2021; Mittal et al., 2014; Mukai et al., 2022; Newsholme et al., 2019).

Additionally, the blood-brain barrier (BBB) may also be a potential mechanism for PPD and air pollution. The BBB is responsible for regulating the transport of molecules in and out of the brain (Cleveland Clinic, 2023b; Daneman & Prat, 2015; Dotiwala et al., 2024); inflammatory cytokines and oxidative stress contribute to a weakened BBB, which may lead to increased permeability (Archie et al., 2021; Huang et al., 2021; Kadry et al., 2020; Mittal et al., 2014). The BBB may also be further weakened from neuroinflammation, which may disrupt the tight junctions responsible for maintaining the BBB's integrity (Cleveland Clinic, 2023b; Kadry et al., 2020; MohanKumar et al., 2008). The BBB is also vulnerable to PM exposure since it's been reported that PM may be small enough to cross the BBB (Calderón-Garcidueñas et al., 2008, 2015; You et al., 2022). PM can penetrate deep into the lungs and enter the bloodstream; from there, can cross the BBB and induce cytotoxicity and neuroinflammation, which can further damage the BBB (Calderón-Garcidueñas et al., 2008, 2015; EPA, 2023d; Manisalidis et al., 2020).

Finally, lower serotonin levels are often seen in patients with depression (Correia et al., 2023; Duan et al., 2018; Payne & Maguire, 2019). Serotonin is produced from tryptophan metabolism (Duan et al., 2018; Roth et al., 2021). Tryptophan metabolism may either take the serotonin pathway, or the kynurenine pathway (Duan et al., 2018; Roth et

al., 2021). When tryptophan metabolism produces kynurenine pathway products, serotonin is limited (Duan et al., 2018; Payne & Maguire, 2019). An increase in stress hormones, and an increase in inflammatory activity, may promote tryptophan to metabolize to kynurenine (Correia et al., 2023; Payne & Maguire, 2019; Roth et al., 2021). Normal pregnancy is associated with increased levels of stress hormones, and inflammatory cytokines (Palm et al., 2013; Racicot et al., 2014). When there are high levels of inflammatory cytokines, such as those seen after air pollution exposure, the degradation of tryptophan may be promoted, creating kynurenine instead of serotonin. These mechanisms are summarized in a graph in the Appendix.

GDM Mechanisms

It's proposed that GDM develops from a combination of pancreatic β -cell dysfunction and chronic insulin resistance (Plows et al., 2018; Quintanilla Rodriguez & Mahdy, 2023; Sharma et al., 2022). Both conditions have been associated with air pollution exposure (Alderete et al., 2017; Dang et al., 2018; Wolf et al., 2016). Most pregnant women experience some insulin resistance, since hormones produced by the placenta block insulin's function (Cleveland Clinic, 2023a; Sonagra, 2014). When insulin is not able to take in glucose, hyperglycemic conditions occur (American Diabetes Association, 2024a; Cleveland Clinic, 2023a). β -cells sense high blood glucose levels and produce more insulin (Kolb et al., 2020; Newsholme et al., 2019; Plows et al., 2018). This places a large burden on β -cells, leading to a decrease in cell mass, and β -cell dysfunction (Dinić et al., 2022; Dlundla et al., 2023; Newsholme et al., 2019; Plows et al., 2018). The hyperglycemic conditions seen from chronic insulin resistance and β -cell dysfunction promotes the production of

inflammatory cytokines and apoptotic mechanisms in β -cells (Cerf, 2013; Dinić et al., 2022; Maedler et al., 2002).

ROS produced from air pollution exposure may promote the production of inflammatory cytokines. One study reported that ROS increased the expression of the pro-inflammatory cytokine, IL- β in β -cells, which may then mediate pancreatic β -cell programmed cell death (Dinić et al., 2022). In addition, levels of ROS seen in the body further increase when insulin is released from β -cells since this stimulates ATP production in the mitochondria (Dludla et al., 2023; Eguchi et al., 2021; Mukai et al., 2022; Newsholme et al., 2019). ROS are byproducts of this process, which further increases the levels of ROS seen in the body (Dinić et al., 2022; Eguchi et al., 2021; Mittal et al., 2014; Mukai et al., 2022; Newsholme et al., 2019). Pancreatic β -cells also express fewer antioxidants, which places them more at risk for oxidative stress when exposed to ROS (Dludla et al., 2023; Eguchi et al., 2021; Mukai et al., 2022). Studies have shown that inflammatory cytokines and ROS may promote pancreatic β -cell death (Dinić et al., 2022; Stancic et al., 2022). A graph summarizing these mechanisms is presented in the Appendix.

Scientific Impact

This study contributes to the growing scientific literature investigating the association between air pollution exposure and adverse birth outcomes. Our study used a large pregnancy cohort in the southern California, USA, region to provide information on the pollutants that posed the greatest risk to maternal health during the COVID-19 pandemic period. Our results further support the association between PPD and exposure to ground-level O₃, while also showing that the relationship between PPD and PM_{2.5} decreased significantly during the COVID-19 pandemic period. In addition, our results continue to

support a relationship between PM_{2.5} exposure and GDM, while also reporting that the association between O₃ and GDM may have increased during the pandemic.

Climate change is projected to increase peak ozone levels and the number of days that ozone concentrations exceed the standard maximum daily 8-hour levels (Zhu et al., 2019). In the southern California air basin, it is estimated that peak wintertime PM_{2.5} concentrations and the number of days exceeding the National Ambient Air Quality Standards will increase (Zhu et al., 2019). It is important to continue researching the current impacts that air pollution has on human health. This may help policymakers develop new policies and create ways to decrease air pollution production and exposure.

Strengths and Limitations

This study has several strengths. First, we used a large pregnancy cohort with detailed information for each participant. Second, we had detailed residential information that allowed us to estimate ambient air pollution exposure throughout the entire study period based on the current residential address. By having this information, we were able to estimate PPD risk up to 1-year postpartum. Several limitations should be discussed. First, while our PPD diagnosis criteria allowed us to identify several PPD cases, some PPD patients may not have been included. One study reported that over 50% of depressive episodes among pregnant women in the US went undiagnosed (Ko et al., 2012); therefore, our results may underestimate the association between PPD and air pollution. Second, our exposure averages were estimations of ambient outdoor pollution exposure based on residential address. We did not include indoor air pollution exposure. One study that investigated indoor and outdoor air pollution changes in California before, during, and after the COVID-19 lockdowns reported that the contribution of indoor sources on PM_{2.5}

concentrations increased both during and after the lockdowns in residential locations (Mousavi & Wu, 2021). This study also reported that before the lockdowns, PM_{2.5} in dining/kitchen areas of residential locations was 20-44% lower than the concentrations outdoors; during the lockdowns, PM_{2.5} concentrations in dining/kitchen areas were comparable to the outdoor levels (Mousavi & Wu, 2021). Since our pollution data is based on outdoor ambient air pollution, our data may not reflect the total pollutant exposure that each participant experienced. Finally, we did not use individual monitors to estimate daily exposure based on activity patterns, which may have led to some exposure misclassification.

Future Directions

Several future studies may be beneficial to further assess the relationship between adverse birth outcomes and air pollution, especially during the COVID-19 pandemic lockdowns. First, a study that investigates the association by monitoring indoor air pollution exposure may be helpful to assess whether pollution exposure from residential sources has an association with PPD or GDM. Many individuals stayed home during the pandemic lockdowns, which changed their exposure to air pollution; understanding how indoor air pollution contributes to GDM or PPD risk may help us further understand the health impacts from the COVID-19 lockdowns. In addition, future studies may also investigate the association between GDM or PPD and PM_{2.5} constituents. Several studies have supported a relationship between these constituents, and an increased risk for either GDM or PPD (Robledo et al., 2015; Sun et al., 2023; Yu et al., 2020). A study that investigates the association between PM_{2.5} constituent exposure during the COVID-19 pandemic, and the risk of PPD or GDM could help us understand how fine particulate

matter influenced birth outcomes during the pandemic time. In addition, future studies may use a multi-pollutant model to investigate how multiple pollutants together influence the risk of PPD and GDM. This may further provide insight into associations seen during the COVID-19 pandemic period since pollutant concentrations changed.

Conclusion

In conclusion, PPD risk may have been influenced by exposure to ambient outdoor O₃ during and after pregnancy, while GDM risk may have been influenced by exposure to PM_{2.5}, PM₁₀, and O₃. These associations may have been influenced by the COVID-19 pandemic lockdowns due to several factors, including pollution decreases and increased exposure to indoor air pollution. Our study results are different from previous studies that have assessed these associations before the COVID-19 pandemic period. Future studies should continue to investigate the association between adverse birth outcomes and air pollution exposure to further provide information regarding these associations.

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Table 1A: ICD9/10 Diagnostic codes and medications used in postpartum depression diagnosis.

300.4	F32.9	Bupropion
309.0	F33.0	Celexa
311	F33.2	Citalopram
	F33.3	Cymbalta
	F33.41	Desvenlafaxine
	F33.9	Duloxetine
	F34.1	Effexor
	F43.21	Escitalopram
	F53.0	Fluoxetine
		Lexapro
		Paroxetine
		Paxil
		Pristiq
		Prozac
		Sertraline
		Venlafaxine
		Wellbutrin
		Zoloft

Table 2A: Trimester-specific pollutant exposure averages for the total population, PPD cases, and GDM cases. Summary statistics are presented for the 1st trimester, 2nd trimester, 3rd trimester, and both the 1st and 2nd trimesters. SD = Standard Deviation, Min = Minimum, Max = Maximum, IQR = Interquartile Range.

Trimester-Specific Exposure Summary Statistics												
	Total Population				PPD Cases				GDM Cases			
	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR
1st												
PM _{2.5}	10.98 (2.91)	3.56	33.52	3.75	10.97 (2.91)	3.57	30.88	3.74	10.99 (2.94)	4.09	21.54	3.80
PM ₁₀	26.64 (7.45)	9.42	118.66	9.31	26.74 (7.47)	9.67	90.89	9.35	26.41 (7.34)	10.98	69.22	9.28
NO ₂	13.84 (4.88)	2.70	30.51	7.47	13.73 (4.88)	3.58	28.38	7.37	14.02 (4.91)	3.44	28.51	7.72
O ₃	45.30 (9.98)	22.14	84.78	12.00	45.53 (10.12)	22.14	84.08	12.40	45.02 (9.91)	25.44	83.29	11.55
2nd												
PM _{2.5}	10.77 (2.84)	3.71	38.42	3.39	10.73 (2.82)	4.14	27.18	3.31	10.85 (2.84)	4.21	21.77	3.20
PM ₁₀	26.04 (7.29)	10.57	106.93	8.93	26.16 (7.34)	10.95	76.95	8.97	26.14 (7.32)	11.11	70.34	8.90
NO ₂	13.45 (4.79)	2.95	29.04	7.05	13.33 (4.76)	3.40	29.04	6.88	13.35 (4.72)	3.78	27.90	6.87
O ₃	45.88 (10.16)	22.14	84.93	12.33	46.19 (10.29)	22.14	84.93	12.74	46.39 (10.16)	23.19	84.93	12.29
3rd												
PM _{2.5}	10.92 (2.81)	3.84	31.85	3.17	10.87 (2.79)	4.20	31.85	3.12	11.18 (2.90)	4.09	31.85	3.21
PM ₁₀	26.38 (7.24)	10.24	104.28	9.20	26.44 (7.28)	11.14	104.28	9.25	26.83 (7.46)	11.04	104.28	9.54
NO ₂	13.54 (4.77)	2.52	28.88	7.12	13.43 (4.79)	3.13	27.60	7.13	13.76 (4.76)	3.46	28.16	7.32
O ₃	46.38 (10.00)	21.82	84.91	12.01	46.63 (10.20)	22.14	84.91	12.53	46.67 (10.03)	24.55	83.04	12.40
1st & 2nd												
PM _{2.5}	10.88 (2.31)	4.07	28.36	2.96	10.85 (2.30)	4.57	27.62	2.93	10.92 (2.30)	4.90	19.11	2.90
PM ₁₀	26.34 (5.98)	10.56	81.50	7.58	26.45 (6.02)	10.56	72.36	7.68	26.28 (5.98)	13.87	59.89	7.69
NO ₂	13.65 (4.03)	2.88	27.87	6.10	13.53 (4.04)	4.10	27.29	6.00	13.68 (3.99)	4.37	26.63	6.05
O ₃	45.59 (7.94)	22.14	77.51	9.49	45.86 (8.05)	22.14	76.05	9.73	45.71 (7.97)	25.44	77.51	9.61

Table 3A: Preconception pollutant exposure averages for the total population, PPD cases, and GDM cases. Summary statistics are presented for the time period 12 months before conception. SD = Standard Deviation, Min = Minimum, Max = Maximum, IQR = Interquartile Range.

Preconception Exposure Summary Statistics												
	Total Population				PPD Cases				GDM Cases			
	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR
3-Months												
PM _{2.5}	11.16 (2.72)	3.70	31.22	3.46	11.15 (2.76)	4.03	28.30	3.51	11.36 (2.81)	4.22	29.48	3.57
PM ₁₀	27.12 (7.02)	9.86	106.20	8.79	27.24 (7.07)	9.86	83.15	8.96	27.36 (7.18)	12.27	82.42	9.00
NO ₂	13.94 (4.68)	2.56	28.94	7.18	13.83 (4.70)	3.50	28.61	7.11	14.34 (4.71)	2.69	27.37	7.44
O ₃	45.85 (9.53)	22.14	81.52	11.77	46.12 (9.68)	22.14	80.15	12.25	45.48 (9.36)	25.44	79.23	11.83

Table 4A: Postpartum pollutant exposure averages for the total population, PPD cases, and GDM cases. Summary statistics are presented for either the 6 months following delivery or the 12 months following delivery. SD = Standard Deviation, Min = Minimum, Max = Maximum, IQR = Interquartile Range.

Postpartum Exposure Summary Statistics												
	Total Population				PPD Cases				GDM Cases			
	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR
6-Months												
PM _{2.5}	11.20 (2.29)	4.46	27.71	3.22	11.15 (2.28)	4.57	22.20	3.18	11.31 (2.29)	4.54	27.59	3.19
PM ₁₀	27.00 (5.67)	10.87	89.04	6.62	27.07 (5.69)	11.50	62.64	6.67	26.94 (5.50)	14.32	62.36	6.37
NO ₂	14.08 (4.15)	2.90	28.08	6.39	13.97 (4.18)	3.91	26.29	6.36	14.46 (5.50)	4.09	26.36	6.44
O ₃	45.90 (7.58)	22.14	77.68	9.12	46.15 (7.67)	22.14	76.75	9.39	45.42 (7.40)	25.44	77.00	8.84
12-Months												
PM _{2.5}	11.15 (1.56)	4.36	21.11	2.29	11.09 (1.57)	4.36	19.12	2.34	11.22 (1.53)	4.90	19.08	2.21
PM ₁₀	27.30 (4.11)	12.77	64.30	5.22	27.44 (4.14)	13.71	53.15	5.38	27.26 (4.03)	15.43	53.15	5.11
NO ₂	13.84 (3.05)	2.92	25.34	4.46	13.73 (3.11)	3.33	22.63	4.77	14.05 (2.97)	4.97	23.65	4.03
O ₃	46.34 (5.33)	22.14	73.03	8.91	46.62 (5.36)	22.14	60.87	9.10	46.25 (5.25)	25.44	61.11	8.76

Table 5A: Pollutant exposure averages for the total population, PPD cases, and GDM cases. Summary statistics are presented for the time period between the 3rd trimester through 12-months postpartum. SD = Standard Deviation, Min = Minimum, Max = Maximum, IQR = Interquartile Range.

3 rd Trimester Through 12-Months Postpartum Exposure Summary Statistics												
	Total Population				PPD Cases				GDM Cases			
	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR
PM _{2.5}	11.09 (1.56)	4.36	20.09	2.25	11.04 (1.57)	4.36	20.09	2.14	11.21 (1.54)	4.90	20.09	2.20
PM ₁₀	27.09 (4.19)	13.09	63.38	5.26	27.21 (4.23)	14.46	63.38	4.63	27.17 (4.18)	15.18	63.38	5.17
NO ₂	13.77 (3.12)	2.82	26.21	4.56	13.66 (3.18)	3.33	22.90	4.75	13.98 (3.04)	5.41	23.65	4.17
O ₃	45.35 (5.73)	22.14	67.62	8.77	46.62 (5.77)	22.14	64.94	8.81	46.35 (5.65)	25.44	65.10	8.72

Table 6A: Pollutant exposure averages for the total population, PPD cases, and GDM cases. Summary statistics are presented for the time period between 3-months preconception through the 2nd trimester. SD = Standard Deviation, Min = Minimum, Max = Maximum, IQR = Interquartile Range.

3-Months Preconception Through 2 nd Trimester Exposure Summary Statistics												
	Total Population				PPD Cases				GDM Cases			
	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR	Mean (SD)	Min	Max	IQR
PM _{2.5}	10.99 (1.76)	4.57	22.64	2.38	10.96 (1.77)	5.36	21.65	2.43	11.10 (1.75)	4.90	20.90	2.37
PM ₁₀	26.66 (4.46)	12.25	69.21	4.68	26.77 (4.49)	12.25	62.49	5.45	26.71 (4.50)	16.73	53.74	5.50
NO ₂	13.76 (3.12)	2.98	25.34	4.68	13.65 (3.18)	4.81	23.37	4.95	13.95 (3.05)	4.96	23.65	4.34
NO _x	22.29 (5.90)	3.75	49.68	9.07	22.05 (5.98)	6.54	47.08	9.44	22.61 (5.80)	7.72	47.72	8.68
O ₃	45.70 (5.75)	22.14	65.70	8.58	45.96 (5.79)	22.14	65.45	8.79	45.62 (5.70)	25.44	65.55	8.56

Table 6A: P-Values from the pollution T-Tests. Test results are presented for both PPD and GDM analyses. Significance was <0.05. Insignificant associations are presented in red.

	PM _{2.5}		PM ₁₀		NO ₂		Ozone	
	PPD	GDM	PPD	GDM	PPD	GDM	PPD	GDM
Pregnancy	0.0003	<0.0001	0.0013	0.0001	<0.0001	<0.0001	<0.0001	0.0003
3-Months Preconception	0.5989	<0.0001	0.0056	0.0001	<0.0001	<0.0001	<0.0001	<0.0001
1 st Trimester	0.4638	0.6932	0.0282	0.0003	0.0002	0.0001	0.0002	0.0027
2 nd Trimester	0.0061	0.0013	0.0072	0.0289	<0.0001	0.0119	<0.0001	<0.0001
3 rd Trimester	0.0027	<0.0001	0.1177	<0.0001	0.0001	<0.0001	<0.0001	0.0022
1 st and 2 nd Trimester	0.0321	0.0256	0.0026	0.3750	<0.0001	0.3969	<0.0001	0.0417
6-Months Postpartum	0.0001	<0.0001	0.0346	0.2358	<0.0001	<0.0001	<0.0001	<0.0001
12-Months Postpartum	<0.0001	<0.0001	<0.0001	0.5083	<0.0001	<0.0001	<0.0001	0.0373
Conception – 12-Months Postpartum	<0.0001	<0.0001	<0.0001	0.0798	<0.0001	<0.0001	<0.0001	0.4902
Conception – 6-Months Postpartum	<0.0001	<0.0001	0.0005	0.0319	<0.0001	<0.0001	<0.0001	0.1558
3-Months Preconception – 2 nd Trimester	0.0428	<0.0001	<0.0001	0.0743	<0.0001	<0.0001	<0.0001	0.1512
3 rd Trimester – 12-Months Postpartum	<0.0001	<0.0001	<0.0001	0.0067	<0.0001	<0.0001	<0.0001	0.8567
3 rd Trimester – 6-Months Postpartum	<0.0001	<0.0001	0.0119	0.0004	<0.0001	<0.0001	<0.0001	0.0002

Table 7A: Chi-square test results for PPD and GDM analyses. Chi-square statistics and p-values are presented. Insignificant associations are presented in red. Significance was determined at the <0.05 level.

	Entire Period			
	PPD		GDM	
	Chi-Square Statistic	P-Value	Chi-Square Statistic	P-Value
Maternal Race/Ethnicity				
African American and Asian	362.46	<0.0001	414.11	<0.0001
African American and Hispanic	62.03	<0.0001	99.88	<0.0001
African American and White	3.88	0.0488	0.0001	0.9941
African American and Multi/Other	17.14	<0.0001	42.15	<0.0001
Asian and Hispanic	310.38	<0.0001	455.42	<0.0001
Asian and White	493.91	<0.0001	1007.47	<0.0001
Asian and Multi/Other	140.99	<0.0001	132.14	<0.0001
Hispanic and White	84.46	<0.0001	296.83	<0.0001
Hispanic and Multi/Other	1.60	0.2066	1.22	0.2695
White and Multi/Other	10.25	0.0014	65.78	<0.0001
Maternal Education				
8th Grade or Less and High School or Less	18.20	<0.0001	20.486	<0.0001
High School or Less and Less Than College	112.88	<0.0001	0.89	0.3467
Less Than College and College	30.20	<0.0001	2.15	0.1429
College and More Than College	13.96	0.0002	0.90	0.3427
8th Grade or Less and Less Than College	29.92	<0.0001	18.78	<0.0001
8th Grade or Less and College	24.11	<0.0001	16.73	<0.0001
8th Grade or Less and More Than College	28.133	<0.0001	17.99	<0.0001
High School or Less and College	40.80	<0.0001	6.79	0.0092
High School or Less and More Than College	78.53	<0.0001	1.81	0.1783
Less Than College and More Than College	1.81	0.1784	0.17	0.6770
IOM Gestational Weight Gain				
Inadequate and Adequate	2.35	0.1254	595.34	<0.0001
Inadequate and Excess	55.65	<0.0001	1745.24	<0.0001
Adequate and Excess	88.67	<0.0001	260.07	<0.0001
Pre-Pregnancy BMI				
Underweight and Normal Weight	18.51	<0.0001	8.32	0.0039
Underweight and Overweight	52.21	<0.0001	54.13	<0.0001
Underweight and Obese Class 1	77.21	<0.0001	136.90	<0.0001
Underweight and Obese Class 2	104.07	<0.0001	208.51	<0.0001
Underweight and Obese Class 3	116.24	<0.0001	244.61	<0.0001
Normal Weight and Overweight	106.56	<0.0001	287.59	<0.0001
Normal Weight and Obese Class 1	201.28	<0.0001	977.16	<0.0001
Normal Weight and Obese Class 2	241.03	<0.0001	1232.94	<0.0001

Normal Weight and Obese Class 3	223.52	<0.0001	1169.64	<0.0001
Overweight and Obese Class 1	24.71	<0.0001	228.61	<0.0001
Overweight and Obese Class 2	65.79	<0.0001	439.26	<0.0001
Overweight and Obese Class 3	76.33	<0.0001	467.00	<0.0001
Obese Class 1 and Obese Class 2	14.83	0.0001	60.23	<0.0001
Obese Class 1 and Obese Class 3	26.31	<0.0001	102.15	<0.0001
Obese Class 2 and Obese Class 3	2.75	0.0972	9.39	0.0022
Smoking Status				
Never and Ever	419.54	<0.0001	8.26	0.0041
Never and During Pregnancy	113.67	<0.0001	5.13	0.0235
Ever and During Pregnancy	0.01	0.9228	0.51	0.4731
Year of Infant Birth				
2019 and 2020	4.92	0.0265	13.03	0.0003
2019 and 2021	7.74	0.0054	103.75	<0.0001
2020 and 2021	24.20	<0.0001	39.63	<0.0001
Income YOB				
1 and 2	1.38	0.2406	0.23	0.6332
1 and 3	7.10	0.0077	0.13	0.7152
1 and 4	12.00	0.0005	4.90	0.0268
2 and 3	2.70	0.1004	0.03	0.8689
2 and 4	6.33	0.0119	11.30	0.0008
3 and 4	0.49	0.4851	13.11	0.0003
COVID Pandemic Time				
Not Impacted and Pregnant When the Pandemic Began	172.60	<0.0001	7.29	0.0069
Not Impacted and Postpartum When the Pandemic Began	73.44	<0.0001		
Not Impacted and Conceived After the Pandemic Began	266.38	<0.0001	138.03	<0.0001
Pregnant and Postpartum When the Pandemic Began	8.09	0.00045		
Pregnant and Conceived After the Pandemic Began	7.26	0.0071	53.43	<0.0001
Postpartum and Conceived After the Pandemic Began	27.67	<0.0001		

Table 8A: Pearson's correlation coefficients for pollutant exposures throughout the first trimester. Correlations are based off the entire study population.

	PM _{2.5}	PM ₁₀	NO ₂	O ₃
PM _{2.5}	1	0.75265	0.52235	0.19265
PM ₁₀		1	0.29943	0.53680
NO ₂			1	-0.37827
O ₃				1

Table 9A: Pearson's correlation coefficients for pollutant exposures throughout the second trimester. Correlations are based off the entire study population.

	PM _{2.5}	PM ₁₀	NO ₂	O ₃
PM _{2.5}	1	0.75150	0.55709	0.17088
PM ₁₀		1	0.32860	0.52190
NO ₂			1	-0.34467
O ₃				1

Table 10A: Pearson's correlation coefficients for pollutant exposures throughout the third trimester. Correlations are based off the entire study population.

	PM _{2.5}	PM ₁₀	NO ₂	O ₃
PM _{2.5}	1	0.73184	0.58562	0.15635
PM ₁₀		1	0.36181	0.50006
NO ₂			1	-0.30979
O ₃				1

Table 11A: Pearson's correlation coefficients for pollutant exposures. Correlations presented are based on pollution exposures throughout the entire pregnancy.

	PM _{2.5}	PM ₁₀	NO ₂	O ₃
PM _{2.5}	1	0.62872	0.64670	0.05806
PM ₁₀		1	0.35163	0.55144
NO ₂			1	-0.08523
O ₃				1

Table 12A: Pearson's Correlation Coefficients for pollutant exposures throughout the 12-months postpartum. Correlations are based off the entire study population.

	PM _{2.5}	PM ₁₀	NO ₂	O ₃
PM _{2.5}	1	0.37554	0.74125	-0.03319
PM ₁₀		1	0.22196	0.55616
NO ₂			1	-0.01345
O ₃				1

Table 13A: Pearson's Correlation Coefficients for pollutant exposures throughout the first 6-months postpartum. Correlations are based off the entire study population.

	PM _{2.5}	PM ₁₀	NO ₂	O ₃
PM _{2.5}	1	0.65263	0.69070	0.02537
PM ₁₀		1	0.38179	0.44294
NO ₂			1	-0.27589
O ₃				1

Figure 1A: Graph summarizing the potential mechanisms influencing the risk of GDM from air pollution exposure. Figure was created with BioRender.com.

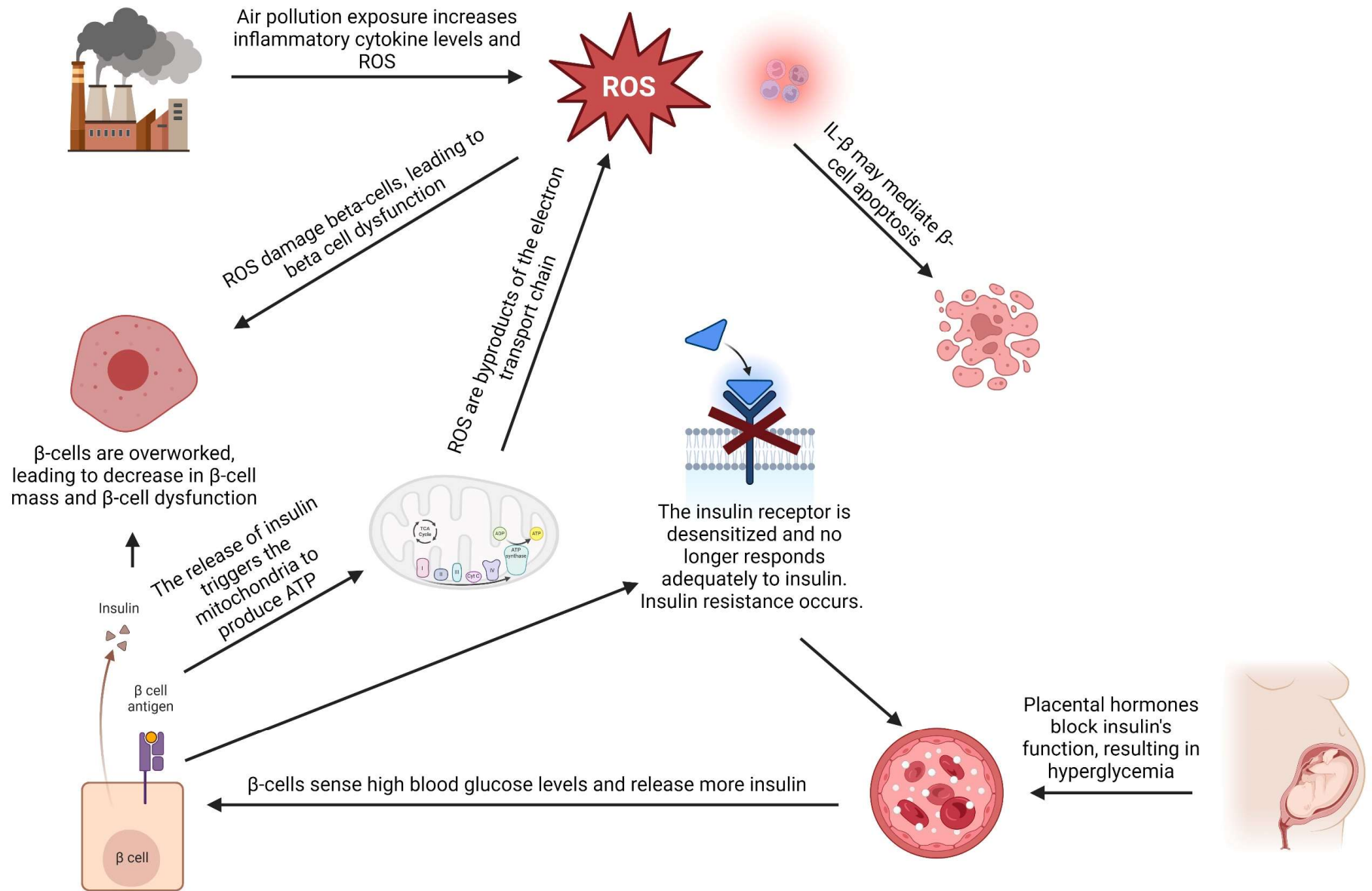


Figure 2A: Graph summarizing the potential mechanisms between PPD and air pollution exposure. Figure was created with BioRender.com.

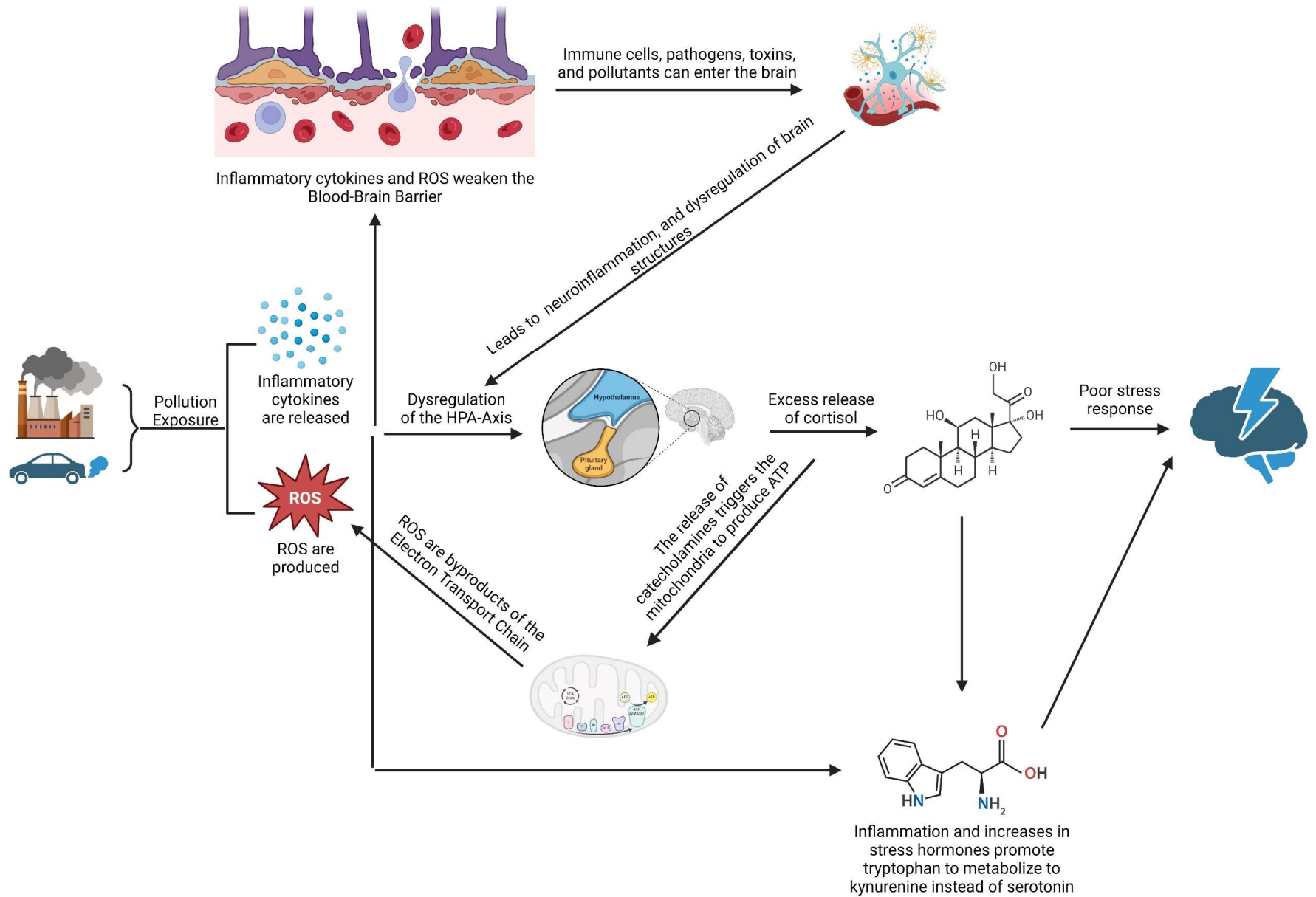


Table 14A: Comparisons between average pollution exposure levels from the previous study (2008-2018) and the current study (2019-2021).

	Mean (Standard Deviation)	
	2008-2018	2019-2021
PM _{2.5}	11.69 (2.25)	11.01 (1.57)
PM ₁₀	28.53 (5.17)	26.60 (4.06)
NO ₂	15.86 (3.82)	13.78 (3.09)
O ₃	43.64 (5.73)	45.90 (5.46)

Table 15A: Comparison between our group's previous air pollution and PPD study and the current air pollution and PPD study. Previous results are presented under "Previous Study" and results from this study are presented under "Current Study". Significantly positive associations are labeled as "+", significantly negative results are presented as "-" and non-significant results are presented as "□". Significance was ≤0.05.

	PM _{2.5}		PM ₁₀		NO ₂		O ₃	
	Previous Study	Current Study	Previous Study	Current Study	Previous Study	Current Study	Previous Study	Current Study
Entire Pregnancy	□	□	□	□	□	□	+	+
1 st Trimester	□	□	□	□	□	□	+	□
2 nd Trimester	□	□	□	□	□	□	□	+
3 rd Trimester	+	-	+	□	□	□	+	□
3 rd Trimester Through 6-Months Postpartum	+	-	+	□	□	□	+	□
Conception Through 6-Months Postpartum	+	-	+	□	□	□	+	+

Table 16A: Comparison between our group's previous air pollution and GDM study and the current air pollution and GDM study. Previous results are presented under "Previous Study" and results from this study are presented under "Current Study". Significantly positive associations are labeled as "+", significantly negative results are presented as "-" and non-significant results are presented as "□". Significance was ≤0.05.

	PM _{2.5}		PM ₁₀		NO ₂		O ₃	
	Previous Study	Current Study	Previous Study	Current Study	Previous Study	Current Study	Previous Study	Current Study
3-Months Preconception	+	+	+	□	+	□	-	□
1 st Trimester	+	+	+	□	+	□	-	□
2 nd Trimester	+	□	+	+	+	□	-	+
1 st and 2 nd Trimesters	+	+	+	+	+	□	-	□
Entire Pregnancy	+	+	+	+	+	□	-	+

