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#### **Title**

Impairment to Maternal Health and Fetal Development Following Exposure to Air Pollutants

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#### **Authors**

Tran, Vivian Perez, Isabella Buxton, Jessica et al.

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Vivian Tran Isabella Perez Jessica Buxton Mikayla Bordador Niam Edralin

University of California, Berkeley
Undergraduate Laboratory at the University of California, Berkeley (ULAB)
Public Health Division
Health Sciences

#### **ABSTRACT**

Public health research has assessed the negative human health outcomes from continued exposure to air pollutants, in particular, fine particulate matter (PM<sub>2.5</sub>, PM<sub>10</sub>), nitrogen oxide (NO<sub>2</sub>), and ozone (O<sub>3</sub>). Recent studies have honed in on expectant mothers and their developing fetuses as a large, at-risk population for these exposures. Ambient air pollutant exposure is linked with negative physical, mental, and behavioral health outcomes in both child and mother. Expectant mothers subjected to contaminants (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, O<sub>3</sub>) over an extended period of time have an increased risk of their child being born prematurely with low birth weight and size, neurological delays, impaired motor and cognitive function, and development of lung related diseases such as cancer and asthma. In their early stages of life, children whose mothers were exposed to air pollutants during pregnancy also had detrimental mental and behavioral health outcomes. These negative health effects were not just limited to their children: expectant mothers also took this burden upon themselves. Pregnant mothers had elevated levels of blood cortisol and chronic stress, which ultimately impacts their child's development in the womb due to oxidative stress and inflammation of crucial organs including the placenta. Researchers have found that mothers with pre-existing health conditions such as diabetes and asthma faced an even greater risk of air pollutant-related health complications. Expectant mothers also faced harmful mental health outcomes during their pregnancy and postpartum period. Additionally, researchers conducted geographical comparisons of residential areas with less air pollutant estimates versus regions with higher levels. Their findings showed that high ambient air pollutant levels were concentrated in predominantly low-income and minority communities and subsequently how these populations are the most vulnerable to its negative health outcomes. Public health research

regarding maternal and child health has advanced rapidly in recent years, bringing to light about the issues of socioeconomic disparities and environmental racism surrounding air pollution exposure.

#### INTRODUCTION

In the late 1760s through mid-1800s, the Industrial Revolution brought forth a whirlwind of technological innovation and new inventions to improve the speed of manufacturing. Business and jobs were booming during this era, but these successes came with long-lasting environmental strains. Coal, steel, and raw materials were being processed in factories which produced large amounts of pollutants into the atmosphere as byproducts that would then be reintroduced into the air through precipitation and ash. Sustained exposure to these toxins over years of working in and living near these processing factories brought forth a multitude of health problems. There was a direct linkage between exposures to air pollutants and reduced quality of life; these effects were subsequently more prominent in low-income, minority dominated communities as they composed a majority of the labor force in the factories. Although the manufacturing industry has declined significantly in recent years due to technological advancements, the presence of air pollutants has persisted as a growing concern for global human health.

Currently, researchers are trying to better understand the effects of exposure to various air pollutants, specifically fine particulate matter (PM<sub>2.5</sub>, PM<sub>10</sub>), nitrogen oxide (NO<sub>2</sub>), and ozone (O<sub>3</sub>). Means of measuring these air pollutants have been adapted from the national Land Use Regression (LUR) model formulated by the National Air Pollution Surveillance (NAPS) database, satellite estimates given road lengths and postal codes, as well as industrial land usage

areas<sup>1</sup>. A large at-risk population of air pollutants are expectant mothers and their developing fetuses. Prenatal exposure to air pollutants such as PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2.</sub>, and O<sub>3</sub> have been correlated with a plethora of negative physical and mental health outcomes in both the growing fetus and the mother<sup>2</sup>. These air pollutants were associated with lowered birth weight and size, neurological developmental delays, behavioral issues in infanthood, increased risk for childhood cancers, impaired motor skill development, and chronic stress in the mothers during pregnancy and postpartum<sup>3</sup>. Blood cortisol levels were also studied to understand maternal stress responses to living in residential environments with above moderate levels of air pollutant exposure<sup>4</sup>. Expectant mothers with comorbidities and previous health conditions such as asthma and heart disease were also assessed in these air pollutant studies to analyze the range of associated health effects upon the mother and child<sup>5</sup>.

Our literature review aims to detail the detrimental effects of air pollutant exposure to expectant mothers and their fetuses. To narrow down modes of air pollution measurement, we specifically are focusing on research studies that utilize geographical location studies to

<sup>&</sup>lt;sup>1</sup> Eric Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes: Differences by Maternal Comorbidities," *Environmental Research* 148 (July 1, 2016): 457–66, https://doi.org/10.1016/i.envres.2016.04.026.

<sup>&</sup>lt;sup>2</sup> Perry E. Sheffield et al., "Association between Particulate Air Pollution Exposure during Pregnancy and Postpartum Maternal Psychological Functioning," *PLOS ONE* 13, no. 4 (April 18, 2018): e0195267, https://doi.org/10.1371/journal.pone.0195267; Zhongzheng Niu et al., "Association Between Ambient Air Pollution and Birth Weight by Maternal Individual- and Neighborhood-Level Stressors," *JAMA Network Open* 5, no. 10 (October 25, 2022): e2238174, https://doi.org/10.1001/jamanetworkopen.2022.38174.

<sup>3</sup> "Maternal Exposure to Air Pollution during Pregnancy and Child's Cognitive, Language, and Motor Function: ECLIPSES Study - ScienceDirect," accessed April 24, 2023, https://www.sciencedirect.com/science/article/pii/S0013935122008283; Éric Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers: A Population-Based Study in Ontario, Canada," *Environment International* 100 (March 1, 2017): 139–47, https://doi.org/10.1016/j.envint.2017.01.004.

<sup>&</sup>lt;sup>4</sup> Ramezanali Khamirchi et al., "Maternal Exposure to Air Pollution during Pregnancy and Cortisol Level in Cord Blood," *Science of The Total Environment* 713 (April 15, 2020): 136622, https://doi.org/10.1016/j.scitotenv.2020.136622; "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth: A Prospective Cohort Study," *Environmental Research* 212 (September 1, 2022): 113250, https://doi.org/10.1016/j.envres.2022.113250.

<sup>&</sup>lt;sup>5</sup> Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes."

understand the approximate levels of particulate matter, NO<sub>2</sub>, and O<sub>3</sub> around the residential areas that study participants live in. We also will be analyzing maternal stress and overall mental health through primary studies on blood cortisol levels and psychological tests following sustained contact with air pollutants. Expectant mothers' pre-existing medical conditions will additionally be explored alongside the pressures of continued air pollution exposure. The child's developmental process post-birth will also be assessed through various means such as birth weight, motor functioning, behavior, and cognitive functioning. Following our assessment of the effects of air pollutants, we will be comparing varying populations of expectant mothers and their children via air pollutant estimates from postal codes of residential areas.

In our literature review, we will address the various mechanisms in which mother and child are affected by air pollution during fetal development and post-birth. We also will explore racial and socio-economic inequities that contribute to the cycle of stunted fetal development following exposure to contaminants such as PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and O<sub>3</sub>. Ultimately, we hope to create a call to action for the development of additional environmental health policies to reduce exposures to air pollutants, primarily in residential areas, to aid in improving overall maternal and fetal health outcomes.

#### DATA AND METHODS

Recent public health efforts have been centered on the understanding how expectant mothers and their developing fetuses are impacted by exposure to ambient air pollutants, specifically PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and O<sub>3</sub>. In prior research studies, prolonged exposure to the mentioned air pollutants have been linked with negative physical and mental health outcomes in

adults and children<sup>6</sup>. In our literature review, we will be exploring the varied impacts of continued PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and O<sub>3</sub> exposure specifically within populations of expectant mothers and their children.

In the Journal of Environmental Research study titled "Ambient Air Pollution and Adverse Birth Outcomes: Differences by Maternal Comorbidities," researchers quantified particulate matter and pollutant levels for analysis through various measuring methodologies and previous government-collected atmospheric pollutant data. In this study specifically, records regarding pollutant levels and exposure on expectant mothers and their children were collected within the province of Ontario, Canada. To obtain accurate estimates of particulate matter levels in Ontario, Lavigne et al. divided the city into equal 1 km x 1 km sections and conducted satellite-derived estimates of particulate matter in those areas<sup>7</sup>. The researchers also gathered data on ambient levels of NO<sub>2</sub> in Ontario through the utilization of Land Use Regression (LUR) models, which are algorithms modeled after the Canadian National Air Pollution Surveillance model that are used to interpret pollutant concentrations in highly populated areas through a culmination of previous annual pollutant records and satellite imagery<sup>8</sup>. Researchers derived a linear model based on the Canadian and Hemispheric Regional Ozone System to determine hourly concentrations of O<sub>3</sub> in Ontario. Once levels of each pollutant were able to quantitatively be measured, Lavigne et al. began exploring the correlation between maternal exposure to varied levels of particulate matter, NO<sub>2</sub>, and O<sub>3</sub> and the health outcomes in both mother and child. Physical, emotional, and behavioral health factors were assessed across the expectant mothers

<sup>&</sup>lt;sup>6</sup> Yifeng Dai et al., "Early-Life Exposure to Widespread Environmental Toxicants and Maternal-Fetal Health Risk: A Focus on Metabolomic Biomarkers," *The Science of the Total Environment* 739 (October 15, 2020): 139626, https://doi.org/10.1016/j.scitotenv.2020.139626.

<sup>&</sup>lt;sup>7</sup> Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers."

<sup>&</sup>lt;sup>8</sup> Lavigne et al.

enrolled in the study as well as the child's health post-birth. Results showed that specific birth effects resulting from repeated exposure to air pollutants (particulate matter, NO<sub>2</sub>, and O<sub>3</sub>) included preterm births, abnormally small size given gestational age, and low birth weights<sup>9</sup>. The following three tables show the data that was collected in regard to the mothers' exposure to these air pollutants, the birth effects that were observed, and adjusted data taking the mother's medical and personal backgrounds into consideration; the prevalence of comorbidities amongst the expectant mothers were also addressed<sup>10</sup>. Health data was gathered through medical check-ups of expectant mothers and their children every 5 years.

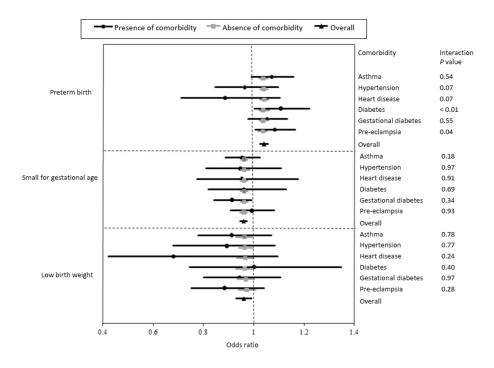


Fig 1: The range of effects following  $PM_{2.5}$  exposure on fetal development (accounting for the presence and lack of maternal comorbidities)<sup>11</sup>.

<sup>&</sup>lt;sup>9</sup> Lavigne et al.

<sup>&</sup>lt;sup>10</sup> Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes."

<sup>&</sup>lt;sup>11</sup> Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers."

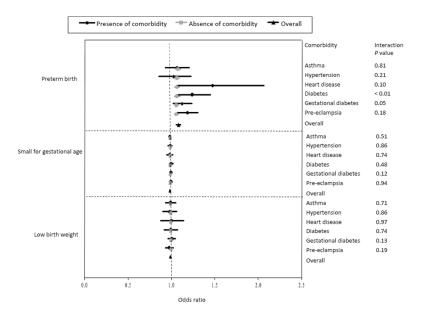


Fig 2: The range of effects following NO<sub>2</sub> exposure on fetal development (accounting for the presence and lack of maternal comorbidities)<sup>12</sup>.

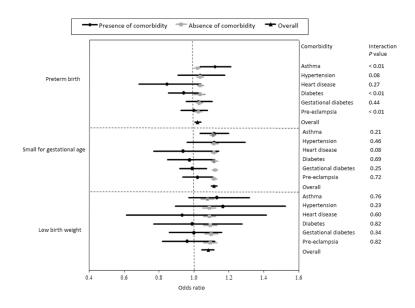


Fig 2: The range of effects following  $O_3$  exposure on fetal development (accounting for the presence and lack of maternal comorbidities)<sup>13</sup>.

<sup>&</sup>lt;sup>12</sup> Lavigne et al.

<sup>&</sup>lt;sup>13</sup> Lavigne et al.

Additional research was also conducted by Lei et al. within the province of Hefei, China to better understand the correlation between maternal blood biomarkers and nutrients following air pollutant exposure<sup>14</sup>. The study participants were screened to ensure comorbidities were minimized and to confine the topological study area to a specific region within China to minimize the effects of confounding variables<sup>15</sup>. Blood samples were retrieved from the mothers before delivery and from the umbilical cord post-birth. Fetal ultrasounds were also performed during each trimester of pregnancy to monitor the growth of the child and to perform birth outcome medical records including quantitative measures such as size and weight<sup>16</sup>. The ambient pollutant levels were collected using regional monitoring stations in the area by the Hefei City Ecology and Environmental Bureau and the values were adjusted for each expectant mother based on their distance from their respective monitoring stations<sup>17</sup>.

The table below shows the correlation between the ambient pollutant exposure to the ultrasound results of fetal growth.

<sup>&</sup>lt;sup>14</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

<sup>&</sup>lt;sup>15</sup> Dai et al., "Early-Life Exposure to Widespread Environmental Toxicants and Maternal-Fetal Health Risk": "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

<sup>&</sup>lt;sup>16</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

<sup>&</sup>lt;sup>17</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

Table 2
Associations between air pollutant exposure and ultrasound measures of fetal growth during pregnancy.

Pollutants	The second trimester $[\beta^a]$	95% <i>CI</i> )]		The third trimester $[\beta^0(95\%CI)]$				
	BPD	BPD AC FL BP		BPD	AC	FL		
The first trimes	ter							
$PM_{2.5}$ (µg/	-0.089 (-0.155,	-0.003 ( $-0.112$ ,	-0.076 ( $-0.158$ ,	-0.080 (-0.128,	-0.107 (-0.154,	-0.099 (-0.154,		
$m^3$ )	-0.024)	0.107)	0.006)	-0.031)	-0.060)	-0.044)		
$PM_{10} (\mu g/m^3)$	-0.028 (-0.091, 0.036)	0.072 (-0.034, 0.179)	-0.003 ( $-0.083$ ,	-0.066 (-0.113,	-0.089 (-0.135,	-0.090 (-0.144,		
			0.077)	-0.019)	-0.043)	-0.037)		
$SO_2 (\mu g/m^3)$	-0.022(-0.089, 0.045)	0.093(-0.022, 0.209)	0.019 (-0.066, 0.104)	-0.070 (-0.120,	-0.061 (-0.109,	-0.065 (-0.121,		
- 10				-0.021)	-0.013)	-0.009)		
$CO (mg/m^3)$	-0.054(-0.110, 0.002)	0.030 (-0.064, 0.125)	-0.028 (-0.099,	-0.081 (-0.122,	-0.077 (-0.117,	-0.076 (-0.123,		
			0.042)	-0.039)	-0.037)	-0.029)		
The second trin	nester							
$PM_{2.5}$ (µg/	_	_	_	-0.060 (-0.104,	0.006(-0.036, 0.049)	0.010 (-0.039, 0.060)		
$m^3$ )				-0.016)				
$PM_{10} (\mu g/m^3)$	-	-	-	-0.065 (-0.107,	-0.006(-0.047, 0.036)	-0.018 ( $-0.066$ , $0.031$ )		
				-0.022)				
$SO_2 (\mu g/m^3)$	_	_	_	-0.054 (-0.102,	0.002(-0.044, 0.049)	-0.011 ( $-0.065$ , $0.044$ )		
				-0.006)				
$CO (mg/m^3)$	_	_	_	-0.034(-0.073, 0.005)	0.032(-0.006, 0.070)	0.022 (-0.023, 0.067)		

Abbreviations: BPD, bi-parietal diameter; AC, abdominal circumference; FL, femur length.

Fig 3: Table depicting the correlation between varying air pollutants and fetal developmental outcomes.<sup>18</sup>

 Table 2

 Associations between air pollutant exposure and ultrasound measures of fetal growth during pregnancy.

Pollutants	The second trimester $[\beta^a]$	95% <i>CI</i> )]		The third trimester $[\beta^{\circ}(95)]$	3"(95%CI)]				The third trimester [ $\beta^0$ (95% <i>CI</i> )]		
	BPD	AC	FL	BPD	AC	FL					
The first trimest	ter										
$PM_{2.5} (\mu g/$	-0.089 (-0.155,	-0.003 ( $-0.112$ ,	-0.076 ( $-0.158$ ,	-0.080 (-0.128,	-0.107 (-0.154,	-0.099 (-0.154,					
$m^3$ )	-0.024)	0.107)	0.006)	-0.031)	-0.060)	-0.044)					
$PM_{10} (\mu g/m^3)$	-0.028 (-0.091, 0.036)	0.072 (-0.034, 0.179)	-0.003 (-0.083, 0.077)	-0.066 (-0.113, -0.019)	-0.089 (-0.135, -0.043)	-0.090 (-0.144, -0.037)					
$SO_2 (\mu g/m^3)$	-0.022 (-0.089, 0.045)	0.093 (-0.022, 0.209)	0.019 (-0.066, 0.104)	-0.070 (-0.120, -0.021)	-0.061 (-0.109, -0.013)	-0.065 (-0.121, -0.009)					
CO (mg/m <sup>3</sup> )	-0.054 (-0.110, 0.002)	0.030 (-0.064, 0.125)	-0.028 (-0.099, 0.042)	-0.081 (-0.122, -0.039)	-0.077 (-0.117, -0.037)	-0.076 (-0.123, -0.029)					
The second trim	nester										
PM <sub>2.5</sub> (μg/ m <sup>3</sup> )	-	-	-	-0.060 (-0.104, -0.016)	0.006 (-0.036, 0.049)	0.010 (-0.039, 0.060)					
$PM_{10}$ (µg/m <sup>3</sup> )	-	-	-	-0.065 (-0.107, -0.022)	-0.006 (-0.047, 0.036)	-0.018 (-0.066, 0.031)					
$SO_2 (\mu g/m^3)$	-	-	-	-0.054 (-0.102, -0.006)	0.002 (-0.044, 0.049)	-0.011 (-0.065, 0.044)					
$CO (mg/m^3)$	-	-	-	-0.034 (-0.073, 0.005)	0.032 (-0.006, 0.070)	0.022 (-0.023, 0.067)					

Abbreviations: BPD, bi-parietal diameter; AC, abdominal circumference; FL, femur length.

Fig 4: Table depicting the correlation between air pollutant exposure and blood biomarkers over the course of pregnancy (first two trimesters).<sup>19</sup>

<sup>&</sup>lt;sup>a</sup> Models were adjusted for maternal age, educational level, pre-pregnancy BMI, gestational weight gain, household income, physical activity, parity, calcium supplement, milk intake, gestational diabetes mellitus, gestational hypertension, depression and anemia during pregnancy. Change in BPD, AC, and FL per IQR increase of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, and CO exposure in the first and second trimesters.

<sup>&</sup>lt;sup>a</sup> Models were adjusted for maternal age, educational level, pre-pregnancy BMI, gestational weight gain, household income, physical activity, parity, calcium supplement, milk intake, gestational diabetes mellitus, gestational hypertension, depression and anemia during pregnancy. Change in BPD, AC, and FL per IQR increase of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, and CO exposure in the first and second trimesters.

<sup>&</sup>lt;sup>18</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

<sup>&</sup>lt;sup>19</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

Pollutants	The secon		er	The third trimester $[\beta^a]$ (95%C)									
	BPD	AC	FL	BPD	AC	FL							
The first tr	The first trimester												
$PM_{2.5}$ (µg/m³)	-0.089 (-0.155, -0.024)	-0.003 (-0.112, 0.107)	-0.076 (-0.158, 0.006)	-0.080 (-0.128, -0.031)	-0.107 (-0.154, -0.060)	-0.099 (-0.154, -0.044)							
$\begin{array}{c} PM_{10} \\ (\mu g/m^3) \end{array}$	-0.028 (-0.091, 0.036)	0.072 (-0.034, 0.179)	-0.003 (-0.083, 0.077)	-0.066 (-0.113, -0.019)	-0.089 (-0.135, -0.043)	-0.090 (-0.144, -0.037)							
$SO_2 \ (\mu g/m^3)$	-0.022 (-0.089, 0.045)	0.093 (-0.022, 0.209)	0.019 (-0.066, 0.104)	-0.070 (-0.120, -0.021)	-0.061 (-0.109, -0.013)	-0.065 (-0.121, -0.009)							
CO (mg/m³)	-0.054 (-0.110, 0.002)	0.030 (-0.064, 0.125)	-0.028 (-0.099, 0.042)	-0.081 (-0.122, -0.039)	-0.077 (-0.117, -0.037)	-0.076 (-0.123, -0.029)							
The second	l trimester												
$\begin{array}{c} PM_{2.5} \\ (\mu g/m^3) \end{array}$	-	-	-	-0.060 (-0.104, -0.016)	0.006 (-0.036, 0.049)	0.010 (-0.039, 0.060)							
$\begin{array}{c} PM_{10} \\ (\mu g/m^3) \end{array}$	-	-	-	-0.065 (-0.107, -0.022)	-0.006 (-0.047, 0.036)	-0.018 (-0.066, 0.031)							
$SO_2 \ (\mu g/m^3)$	-	-	-	-0.054 (-0.102, -0.006)	0.002 (-0.044, 0.049)	-0.011 (-0.065, 0.044)							
CO (mg/m³)	-	-	-	-0.034 (-0.073, 0.005)	0.032 (-0.006, 0.070)	0.022 (-0.023, 0.067)							

Abbreviations: BPD, bi-parietal diameter; AC, abdominal circumference; FL, femur length.

Fig 5: Table depicting the correlation between air pollutant exposure and blood biomarkers over the course of pregnancy (last two trimesters).<sup>20</sup>

The results showed that exposure to these air pollutants was associated with higher blood cortisol levels in the umbilical cord (which were more relevant in the first trimester of the

Models were adjusted for maternal age, educational level, pre-pregnancy BMI, gestational weight gain, household income, physical activity, parity, calcium supplement, milk intake, gestational diabetes mellitus, gestational hypertension, depression and anemia during pregnancy. Change in BPD, AC, and FL per IQR increase of PM2.5, PM10, SO2, and CO exposure in the first and second trimesters.

<sup>&</sup>lt;sup>20</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

pregnancy) that aid in causing impairment of overall fetal growth.<sup>21</sup> Further studies have also corroborated these results.

The previously mentioned particulates are not only harmful to both the mother and child, but specifically to fetuses because of their small size and ability to cross most biological barriers, including the fetus-maternal barrier<sup>22</sup>. With similar studies focusing on the effects of specific concentrations deemed dangerous or influential on the health of both the baby and mother, there is a pattern with concluding results revealing that PM<sub>2.5</sub> has a direct correlation with reduced infant weight and an increased likelihood of experiencing pregnancy-induced hypertension and preeclampsia<sup>23</sup>. Similar to the study conducted with a focus on maternal and cord blood profiles, a study done by Dai et al. found that exposure to air pollutants could result in disturbances to the mother's inflammatory responses and oxidative stress which can be not only detrimental to the mother but also to the child in terms of preterm birth, low birth weight, and stunted growth<sup>24</sup>.

Upon further review of additional literature, the aforementioned harmful effects are reiterated while other corollaries are detailed. For example, a study led by Lavigne et al. discussed how exposure to ambient air pollution during pregnancy increases the risk of childhood cancers<sup>25</sup>. The study included a cohort of pregnant women who gave birth to singleton

<sup>&</sup>lt;sup>21</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth"; Dai et al., "Early-Life Exposure to Widespread Environmental Toxicants and Maternal-Fetal Health Risk."

<sup>&</sup>lt;sup>22</sup> Veras, Mariana, et al. "Safe in the Womb? Effects of Air Pollution to the Unborn Child and Neonates." *Jornal De Pediatria*, U.S. National Library of Medicine, Mar. 2022, https://pubmed.ncbi.nlm.nih.gov/34740534/.

<sup>&</sup>lt;sup>23</sup> Khamirchi et al., "Maternal Exposure to Air Pollution during Pregnancy and Cortisol Level in Cord Blood."

<sup>&</sup>lt;sup>24</sup> Dai, Yifeng, et al. "Early-Life Exposure to Widespread Environmental Toxicants and Maternal-Fetal Health Risk: A Focus on Metabolomic Biomarkers." *The Science of the Total Environment*, U.S. National Library of Medicine, 3 June 2020, https://pubmed.ncbi.nlm.nih.gov/32535459/.

<sup>&</sup>lt;sup>25</sup> Lavigne, Éric, et al. "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers: A Population-Based Study in Ontario, Canada." 30 Jan. 2017, https://www.sciencedirect.com/science/article/pii/S0160412017300466

infants in Ontario, Canada between April 1, 1988 and March 31, 2012. In this population-based study, satellite-derived estimates of PM<sub>2.5</sub> in a 1 km x 1 km area were used during pregnancy and during the first year of a child's life<sup>26</sup>. Lavigne et al. determined average particulate matter levels through trimester-specific periods of exposure to better represent the entire pregnancy term<sup>27</sup>. A LUR model which estimated the prenatal exposure to ambient NO<sub>2</sub> was utilized, allowing for the denotation of fine-scale variations in vehicle emissions and was used for each year of the study<sup>28</sup>. However, because the LUR model only provided annual values, the researchers of this study temporally adjusted the LUR NO<sub>2</sub> model, allowing for them to be more accurately mapped based on gestational periods; this results in more precise results of NO<sub>2</sub> levels based on trimester<sup>29</sup>. This study also accounted for covariates such as smoking during pregnancy, urban/rural place of residence, and socioeconomic status (SES). To ensure SES did not influence the outcome of this statistical trial, researchers divided participants into five groups based on socioeconomic status quintiles<sup>30</sup>.

<sup>&</sup>lt;sup>26</sup> Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers."

<sup>&</sup>lt;sup>27</sup> Lavigne et al.

<sup>&</sup>lt;sup>28</sup> Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes"; Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers."

<sup>&</sup>lt;sup>29</sup> Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers."

<sup>&</sup>lt;sup>30</sup> Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes"; Niu et al., "Association Between Ambient Air Pollution and Birth Weight by Maternal Individual- and Neighborhood-Level Stressors."

Table 1	
Demographic and	socioeconomic characteristics of study participants <sup>a</sup>

Characteristics	Total cohort	ALL	AML	NHL	Epen-dymoma	Astro-cytoma	Medullo-blastoma	PNET	Neuro-blastoma	Retino-blastoma	Wilms tumor	Hepato-blastoma	Rhabdomyo-sarcoma	Germ cell tumor
n	2,350,898	849	92	112	52	208	63	26	162	142	211	84	13	30
Maternal age (mean)	29.4	29.7	30.0	29.1	29.1	29.3	31.0	28.5	29.8	29.4	29.3	30.2	30.7	28.5
Infant sex (%)														
Male	51.3	54.1	53.3	67.9	48.1	51.9	65.1	65.4	58.6	50.7	43.6	58.3		
Female	48.7	45.9	46.7	32.1	51.9	48.1	34.9	34.6	41.4	49.3	56.4	41.7		
Parity														
0	56.0	55.7	55.4	54.5	55.4	54.3	55.6	52.4	55.6	63.4	57.8	52.4		53.3
1	32.7	33.0	33.7	29.5	33.7	34.6	33.3	36.9	34.0	28.9	33.7	36.9		26.7
≥2	11.3	11.3	10.9	16.1	10.9	11.1	11.1	10.7	10.5	7.8	8.5	10.7		20.0
Median family income														
Quintile 1	19.4	19.1	19.6	20.5	17.3	17.3	17.5	17.3	15.4	19.0	22.3	13.1		
Quintile 2	19.4	19.3	17.4	16.1	21.2	21.2	14.3	21.2	16.1	17.6	20.4	26.2		
Quintile 3	19.3	21.4	13.0	25.9	17.3	17.3	17.5	17.3	20.4	26.8	17.1	20.2		
Quintile 4	19.4	18.9	30.4	16.1	21.2	21.2	25.4	21.2	23.5	23.9	21.8	20.2		
Quintile 5	19.4	19.3	18.5	19.6	19.2	19.2	23.8	19.2	21.6	16.9	14.2	16.7		
Missing	2.8	2.4	1.1	1.8	3.9	3.9	1.6	3.9	3.1	2.8	4.3	3.6		
Percent of females completed														
postsecondary education (age 25+)														
Quintile 1	19.4	19.4	19.6			19.2		19.2	15.4	19.0	19.9	19.1		
Quintile 2	19.4	19.0	18.5	16.1	19.2	19.2		19.2	22.8	20.4	23.7	16.7		
Quintile 3	19.6	19.6	15.2			21.2	25.4	21.2	14.8	20.4	17.5	19.1		
Quintile 4	19.4	20.7	25.0	24.1	19.2	19.2	25.4	19.2	21.6	21.8	14.7	20.2		
Quintile 5	19.4	19.0	20.7	15.2	17.3	17.3	20.6	17.3	22.2	15.5	19.9	21.4		
Missing	2.8	2.4	1.1	1.8	3.9	3.9		3.9	3.1	2.8	4.3	3.6		
Percent visible minority														
Quintile 1	19.4	20.7	20.7	22.3	23.1	22.1	20.6	20.6	16.7	18.3	19.4	19.1		
Quintile 2	19.4	19.1	20.7	23.2	25.0	21.6	14.3	14.3	15.4	21.1	17.5	23.8		
Quintile 3	19.4		27.2			19.7	31.8	31.8	22.2	19.7	20.9	17.9		
Quintile 4	19.4	17.3	21.7	17.9	15.4	17.8	12.7	12.7	26.5	15.5	21.8	17.9		
Quintile 5	19.4	20.6	8.7	19.6	17.3	15.9	19.1	19.1	16.1	21.8	16.1	17.9		
Missing	2.9	2.4	1.1	1.8	3.9	2.9	1.6	1.6	3.1	3.5	4.3	3.6		

a In accordance with the Institute for Clinical Evaluative Sciences disclosure rules, case counts of less than five were suppressed for descriptive statistics, and all related frequency percentages are not reported. Statistical analyses employed all data.

Fig 6: Table depicting the correlation between various socioeconomic variables and NO<sub>2</sub> levels stratified by quintiles.

A Cox proportional hazards model was used to assess associations between exposure during pregnancy and cancer risk.<sup>31</sup> The results are "expressed as the hazard ratio (HR) and 95% confidence interval (CI) corresponding to an increase across the interquartile range (IQR) of NO<sub>2</sub> and PM<sub>2.5</sub>."<sup>32</sup> The findings of this study resulted in a heterogeneous association between childhood cancers and ambient air pollution exposure throughout pregnancy. The most common childhood cancers for this study population were Wilms tumors, astrocytomas, and neuroblastomas.<sup>33</sup> The study found there to be a significant positive association between PM<sub>2.5</sub> and astrocytoma which is shown in the following table.

<sup>&</sup>lt;sup>31</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

<sup>&</sup>lt;sup>32</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth"; Khamirchi et al., "Maternal Exposure to Air Pollution during Pregnancy and Cortisol Level in Cord Blood."

<sup>&</sup>lt;sup>33</sup> Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers."

Table 4
Adjusted<sup>a</sup> hazard ratios and 95% confidence intervals for the associations between 1 IQR increase in trimester-specific and child's first year of life exposure to NO<sub>2</sub> and PM<sub>2.5</sub> and cancer risk.

Cancer site	1st trimester		2nd trimeste	r	3rd trimester		Child's 1st year		
	Obs. cases	HR (95% CI)	Obs. cases	HR (95% CI)	Obs. cases	HR (95% CI)	Obs. cases	HR (95% CI)	
Temporally adju	sted LUR NO <sub>2</sub> (pp	ob)							
ALL	302	1.20 (1.02-1.41)	289	1.11 (0.91-1.36)	287	0.95 (0.77-1.17)	300	0.98 (0.80-1.21)	
Astrocytoma	64	1.11 (0.72-1.72)	63	1.28 (0.83-1.97)	63	1.55 (1.02-2.37)	61	1.31 (0.93-1.84)	
Wilms tumor	78	1.01 (0.70-1.50)	79	1.08 (0.74-1.59)	76	0.93 (0.63-1.39)	77	0.93 (0.63-1.39)	
$PM_{2.5} (\mu g/m^3)$									
ALL	385	0.93 (0.81-1.08)	403	0.99 (0.87-1.14)	407	1.11 (0.97-1.28)	410	0.91 (0.79-1.05)	
Astrocytoma	94	1.40 (1.05-1.86)	94	1.26 (0.95-1.67)	96	0.96 (0.71-1.28)	97	1.07 (0.79-1.28)	
Wilms tumor	93	1.06 (0.79-1.42)	93	1.07 (0.80-1.42)	97	1.14 (0.86-1.51)	98	0.98 (0.74-1.31)	

IQR, interquartile range.

Fig 7. Table depicting the association of cancer risk with trimester-specific and child's first year of life exposure to NO<sub>2</sub> and PM<sub>2.5</sub>.

This study confirms how ambient air pollution exposure during pregnancy negatively impacts the health of the fetus while also discussing how exposure to these air pollutants after birth can continue to harm the development of the child.<sup>34</sup> While we have discussed the physical effects of exposure in great length, it is important to note that the mental and behavioral health of the mother and developing fetus can also be harmed by exposure to these pollutants. A study conducted by Sheffield et al.<sup>35</sup> discusses the effects of exposure on maternal cognitive health by specifically examining a lower income, ethnically mixed sample of pregnant women. In this study, a woman's daily exposure to PM<sub>2.5</sub> throughout pregnancy is examined and estimated based on their location of residence during gestation. To analyze postpartum psychological functioning,

<sup>&</sup>lt;sup>a</sup> Models adjusted for maternal age at delivery, infant sex, parity, year of birth, maternal cigarette smoking during pregnancy using multiple imputation, census tract median family income, census tract proportion of population who are visible minority and census tract proportion of the adult female population aged 25-64 years old who completed postsecondary education.

<sup>&</sup>lt;sup>34</sup> Yu Ni et al., "Associations of Pre- and Postnatal Air Pollution Exposures with Child Behavioral Problems and Cognitive Performance: A U.S. Multi-Cohort Study," *Environmental Health Perspectives* 130, no. 6 (n.d.): 067008, https://doi.org/10.1289/EHP10248.

<sup>&</sup>lt;sup>35</sup> Sheffield PE, Speranza R, Chiu Y-HM, Hsu H-HL, Curtin PC, Renzetti S, et al. (2018) Association between particulate air pollution exposure during pregnancy and postpartum maternal psychological functioning. PLoS ONE 13 (4): e0195267. https://doi.org/10.1371/journal.pone.0195267.

each participant completed the 10-item Edinburgh Postnatal Depression Scale (EPDS) at 6 and 12 months postpartum in an in-person interview. For this test, women were asked to rate symptoms on a Likert scale ranging from never to very often (0 most favorable, 3 least favorable) in the past 7 days. Some of these symptoms included: "1: 'able to laugh', 2: 'looking forward', 3: 'self-blaming', 4: 'worrying', 5: 'scared', 6: 'things get on top of me'(overwhelmed), 7: 'difficulty sleeping', 8: 'feeling sad or miserable', 9: 'crying', and 10: 'thought of self-harming'."<sup>36</sup> The mothers included in this study were only women who delivered at ≥ 37 weeks. This is because prenatal air pollution exposure is linked to preterm birth which has been associated with postpartum depression. Thus, to ensure this pathway variable is not included in the study, mothers delivering preterm were excluded. Regarding socioeconomic disparities, most mothers in this study had less than a high school education. Additionally, it was determined that women who identified as Black or Hispanic were exposed to, on average, a higher amount of PM<sub>2.5</sub> throughout their entire pregnancy.<sup>37</sup>

<sup>&</sup>lt;sup>36</sup> Sheffield et al., "Association between Particulate Air Pollution Exposure during Pregnancy and Postpartum Maternal Psychological Functioning."

<sup>&</sup>lt;sup>37</sup> Niu et al., "Association Between Ambient Air Pollution and Birth Weight by Maternal Individual- and Neighborhood-Level Stressors"; Dai et al., "Early-Life Exposure to Widespread Environmental Toxicants and Maternal-Fetal Health Risk."

Table 1. ACCESS study participant characteristics.

		N (%)			
Characteristics		Total (N = 557)	White (n = 57)	Black (n = 163)	Hispanic (n = 305)
HS Education	>HS	203 (36%)	30 (53%)	79 (49%)	71 (23%)
	< = HS	354 (64%)	27 (47%)	84 (51%)	234 (77%)
Maternal Age (years; median, IQI	₹)	25.8 (22.3, 31.3)	24.7 (21.4, 31.3)	25.8 (21.6, 31.1)	26.0 (22.8, 31.8)
Season of Delivery	Winter	151(27%)	16 (28%)	43 (30%)	84 (27%)
	Spring	126(23%)	11 (19%)	36 (25%)	71 (23%)
	Summer	126(23%)	9 (16%)	31 (19%)	78 (26%)
	Fall	154(28%)	21 (37%)	53 (26%)	72 (24%)
Smoking during pregnancy	No	477 (86%)	32 (56%)	143 (88%)	275 (90%)
	Yes	80 (14%)	25 (44%)	20 (12%)	30 (10%)
Average PM2.5 throughout pregn IQR)	ancy (μg/m3; median,	16.5 (12.8, 19.8)	14.6 (11.7, 19.0)	16.2 (12.6, 19.5)	17.0 (12.8, 19.9)
Anhedonia subscale a (median, IC	(R)	0 (0, 2)	0 (0, 2)	0 (0,2)	1 (0,2)
Anxiety subscale b (median, IQR)		2 (0, 5)	2 (0,4)	2 (0,4)	2 (0,4)
Depression subscale <sup>c</sup> (median, IC	QR)	1 (0, 4)	2 (1,8)	3 (0, 6)	1 (0,3)
Total EPDS Score (median, IQR)		5 (1, 9)	6 (2, 11)	6 (2,10)	4 (1,8)

<sup>&</sup>lt;sup>a</sup> Anhedonia symptom subscale consists of items 1 and 2 (score range 0–6) all racial/ethnic groups.

Fig 8. Table depicting the association of cancer risk with trimester-specific and child's first year of life exposure to  $NO_2$  and  $PM_{2.5}$ .

Distributed lag models (DLMs) were used to reduce bias from resolved exposures and to estimate the time association between weekly estimated PM<sub>2.5</sub> levels during pregnancy. This method incorporates data from all points within one time frame and "assumes the association between the exposure and outcome at a given time point varies smoothly as a function of time."<sup>38</sup> A statistically significant sensitive time frame of exposure to PM<sub>2.5</sub> for increased anhedonia scores during mid-pregnancy (weeks 13-20) was determined from this study. The Edinburgh Postnatal Depression Scale (EPDS) was utilized as a quantitative assessment of postnatal mental health outcomes.

b Anxiety symptom subscale consists of items 3,4,5 for Blacks and whites (score range 0-9), and items 3,4,5,6 for Hispanics (range 0-12).

<sup>&</sup>lt;sup>c</sup> Depressive symptom subscale consists of items 7,8,9 for Hispanic (score range 0-9), and items 6,7,8,9 for Black and white (range 0-12).

<sup>&</sup>lt;sup>38</sup> Sheffield et al., "Association between Particulate Air Pollution Exposure during Pregnancy and Postpartum Maternal Psychological Functioning."

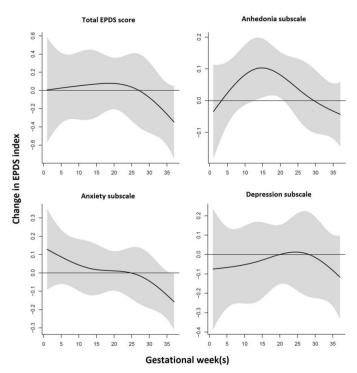


Fig 1. Association between weekly PM $_{2.5}$  exposure and EPDS scores (total score and anhedonia, anxiety and depressive symptom subscales). This figure demonstrates the association between weekly averaged PM $_{2.5}$  during pregnancy and postpartum EPDS total and subscale scores using a distributed lag model assuming weep-ecific effects, adjusting for race, education, age, prenatal smoking status and season of delivery. The y-axis shows the change in EPDS score in relation to a 10 µg/m3 increase in PM $_{2.5}$  level; the x-axis depicts gestational weeks of the pregnancy. The solid line shows the predicted change, and the gray area indicates the 95% confidence interval. A sensitive window is identified when the estimated pointwise 95% confidence interval does not include 0.

Fig 9. Graph showing association between weekly particulate matter exposures for total EPDS anhedonia, anxiety, and depression scores

Mothers are not the only ones impacted cognitively from exposure to ambient air pollutants. Their developing fetuses are also largely impacted and even deal with the harmful effects of exposure well into childhood. Because brain development begins in the third week post-conception, it is important to identify modifiable risk factors, such as air pollution, that negatively impact children. In this way, we can intervene to prevent brain development disturbances. Another done by Ni, Loftus, et al.<sup>39</sup> looks further into this. The Environmental

<sup>&</sup>lt;sup>39</sup>Yu Ni, Christine T. Loftus, Adam A. Szpiro, Michael T. Young, Marnie F. Hazlehurst, Laura E. Murphy, Frances A. Tylavsky, W. Alex Mason, Kaja Z. LeWinn, Sheela Sathyanarayana, Emily S. Barrett, Nicole R. Bush, and Catherine J. Karr. "Associations of Pre- and Postnatal Air Pollution Exposures with Child Behavioral Problems and Cognitive Performance: A U.S. Multi-Cohort Study." June 2022,

Influences on Child Health Outcomes (ECHO) combined three U.S. pregnancy cohorts: the Conditions Affecting Neurocognitive Development and Learning in Early Childhood (CANDLE), the Infant Development and Environment Study (TIDES), and the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS) to examine the association between pre- and postnatal air pollution exposure with child behavioral problems and cognitive performance.<sup>40</sup> The study included 1,967 CANDLE, TIDES, and GAPPS children who "completed behavioral and cognitive assessments at clinical visits at 4-6 y of age and had valid residential addresses in the pre- and/or postnatal windows reported by parents." Participant's addresses were used to estimate NO<sub>2</sub> and PM<sub>2.5</sub> exposures from a spatiotemporal model on a two week scale. Estimated pollution exposure was then averaged throughout each trimester, the entirety of the pregnancy, and two periods postnatal from childbirth to 2 y old and from 2 y old to 4 y old. The behavior of children was assessed using the Child Behavior Checklist (CBCL) and their cognitive performance was assessed using the Stanford-Binet Intelligence Scales (5th edition), the Wechsler Intelligence Scale for Children (5th edition), and the Wechsler Preschool and Primary Scale of Intelligence (4th edition). 41 The study regards these IQ batteries as "highly reliable and valid measures of intellectual and cognitive abilities in childhood." While no association was found between NO<sub>2</sub> exposure and IQ, higher NO<sub>2</sub> exposure throughout the entire pregnancy was found to be associated with more behavioral problems in children. 42 Conversely, children exposed to higher levels of PM<sub>2.5</sub> at age 0-2 y were shown to have more behavioral problems and

<sup>&</sup>lt;sup>40</sup> Sheffield et al., "Association between Particulate Air Pollution Exposure during Pregnancy and Postpartum Maternal Psychological Functioning"; Ni et al., "Associations of Pre- and Postnatal Air Pollution Exposures with Child Behavioral Problems and Cognitive Performance."

<sup>&</sup>lt;sup>41</sup> Ni et al., "Associations of Pre- and Postnatal Air Pollution Exposures with Child Behavioral Problems and Cognitive Performance."

<sup>&</sup>lt;sup>42</sup> Ni et al.

a lower IQ on average. This trend would be continued as children aged 2-4 y were found to have more behavioral problems and a lower IQ. It is important to discuss that there was also a difference in air pollution exposure and behavioral/cognitive development for the different sexes. 43 In this study, girls were found to have more behavioral problems than boys if they were exposed to high levels of PM<sub>2.5</sub> during the second trimester. Additionally, in both postnatal windows (0-2 y and 2-4 y) girls again experienced more behavioral issues as a result of higher exposure to PM<sub>2.5</sub>.<sup>44</sup>

Table 4. Associations of NO<sub>2</sub> and PM<sub>2.5</sub> in each pre- and postnatal window with child total problems score and IQ estimated from multivariable linear regressions in the overall analytic sample from the three U.S. pregnancy cohorts in the ECHO-PATHWAYS consortium (the CANDLE, TIDES, and GAPPS study).

		1	$NO_2^a$		$PM_{2.5}^{a}$				
	Tota	al problems score	7	IQ	То	tal problems score	IQ		
$Model^b$	$n^c$	β (95% CI)	$n^c$	β (95% CI)	$n^c$	β (95% CI)	$n^c$	β (95% CI)	
1st trimester									
Model 1	1,823	0.8 (0.32, 1.28)	1,776	-0.8(-1.17, -0.42)	1,823	1.07 (0.1, 2.04)	1,776	-0.67(-1.45, 0.11)	
Model 2	1,376	0.7 (0.13, 1.27)	1,423	0.28 (-0.1, 0.66)	1,376	1.32 (0.12, 2.52)	1,423	0.8 (-0.01, 1.62)	
Model 3	1,347	0.58 (-0.02, 1.17)	1,391	0.37 (-0.03, 0.77)	1,347	1.28 (0.08, 2.48)	1,391	0.89 (0.05, 1.73)	
2nd trimester									
Model 1	1,822	0.94 (0.4, 1.48)	1,775	-0.95 ( $-1.33$ , $-0.56$ )	1,822	0.58 (-0.36, 1.52)	1,775	-1.22(-1.9, -0.53)	
Model 2	1,376	0.92 (0.31, 1.53)	1,423	0.15 (-0.24, 0.54)	1,376	0.55(-0.6, 1.71)	1,423	-0.62(-1.36, 0.12)	
Model 3	1,347	0.94 (0.3, 1.59)	1,391	0.16 (-0.25, 0.57)	1,347	0.41(-0.83, 1.65)	1,391	-0.48(-1.27, 0.31)	
3rd trimester									
Model 1	1,811	0.34(-0.15, 0.82)	1,764	-1.31(-1.71, -0.91)	1,811	0.25(-0.64, 1.15)	1,764	-1.76(-2.42, -1.1)	
Model 2	1,368	0.27(-0.31, 0.84)	1,415	-0.25 (-0.64, 0.14)	1,368	-0.54(-1.48, 0.41)	1,415	-0.33(-0.98, 0.32)	
Model 3	1,339	0.3(-0.29, 0.9)	1,383	-0.27 ( $-0.67$ , $0.13$ )	1,339	-0.99(-2.05, 0.08)	1,383	-0.17 ( $-0.88$ , $0.54$ )	
Overall preg	nancy								
Model 1	1,821	1.22 (0.54, 1.9)	1,774	-1.59(-2.08, -1.1)	1,821	1.81 (0.25, 3.37)	1,774	-3.52(-4.72, -2.32)	
Model 2	1,376	1.24 (0.39, 2.08)	1,423	0.13 (-0.37, 0.63)	1,376	1.38 (-0.6, 3.35)	1,423	-0.26(-1.53, 1.01)	
Model 3	1,347	1.22 (0.34, 2.09)	1,391	0.17 (-0.35, 0.7)	1,347	1.03(-1.27, 3.34)	1,391	0.18(-1.25, 1.62)	
0-2 y									
Model 1	1,792	0.7(-0.03, 1.43)	1,741	-1.55 ( $-2.14$ , $-0.96$ )	1,792	2.09 (0.01, 4.16)	1,741	-6.03(-7.8, -4.25)	
Model 2	1,363	0.41(-0.53, 1.34)	1,407	0.37 (-0.21, 0.95)	1,363	2.55(-0.16, 5.27)	1,407	-1.47(-3.4, 0.46)	
Model 3	1,334	0.67(-0.28, 1.62)	1,375	0.25 (-0.35, 0.85)	1,334	1.62(-1.29, 4.53)	1,375	-0.8(-3, 1.41)	
2-4 y									
Model 1	1,783	0.63 (-0.07, 1.34)	1,741	-1.51 ( $-2.07$ , $-0.94$ )	1,691	3.45 (1.24, 5.67)	1,622	-8.31 (-10.33, -6.29)	
Model 2	1,347	0.32(-0.57, 1.21)	1,393	0.06 (-0.49, 0.61)	1,287	3.59 (0.35, 6.84)	1,311	-2.63(-5.08, -0.17)	
Model 3	1,318	0.44 (-0.46, 1.34)	1,361	0(-0.56, 0.57)	1,262	2.55(-0.82, 5.92)	1,284	-2.18(-5, 0.64)	

Fig 10. Table addressing association between NO2 and PM.5 exposure and resulting pre-natal and post-birth developmental outcomes

Model 5 1,318 0.44 (=0.46, 1.34) 1,361 0(=0.36), 0.57) 1,262 2.55 (=0.28, 3.92) 1,284 = 2.18 (=3, 0.04). More BMI, body mass index; CANDLE, Conditions Affecting Neurocognitive Development and Learning in Early Childhood; BGCL, Child Behavior Checklist; Cl, confidence interval; ECHO, Environmental Influences on Child Health Outcomes; GAPPS, Global Alliance to Prevent Prematurity and Stillbirth; IQ, intelligence quotient; TIDES, The Infant Development and Environment Study.

"Nog and PMs\_s in each window were rescaled to 2-unit increments."

"Multivariable linear regressions were performed. Model 1 (the minimal model) minimally controlled for child sex, child age at outcome assessments, and study site. An indicator of CBCL forms was additionally included in the analysis of Total Problems score. Model 2 (the primary model) was further adjusted for child race, maternal education, log-transformed region- and inflation-adjusted household income, household members, an interaction between household members and income, marrial status, maternal age at delivery, birth order, preprancy smoking, pregnancy alcohol consumption, maternal depression, maternal IQ, child secondhand smoking exposure, and Child Opportunity Index (the domains of educational and economic opportunity) in corresponding windows with PM<sub>2</sub>s and NO<sub>2</sub> exposures. Model 3 (the extended model) included additional adjustments for prepregnancy BMI, pregnancy supplement intakes, breastfeeding, and child year of birth.

"It is the analytic sample size for each model."

<sup>&</sup>lt;sup>43</sup> "Gender Differences in Fetal Growth of Newborns Exposed Prenatally to Airborne Fine Particulate Matter - ScienceDirect," accessed April 24, 2023, https://www.sciencedirect.com/science/article/pii/S001393510900019X.

<sup>44 &</sup>quot;Gender Differences in Fetal Growth of Newborns Exposed Prenatally to Airborne Fine Particulate Matter - ScienceDirect."

#### DATA ANALYSIS AND DISCUSSION

The literature review analyzed in this discussion section aims to explore the effects of ambient air pollution exposure on the health outcomes of expectant mothers and their children, specifically focusing on PM2.5, PM10, NO2, and O3. The studies analyzed were conducted in Canada and China, and the researchers utilized various measuring methodologies to quantify the levels of these air pollutants. The health outcomes assessed included physical, emotional, and behavioral factors in both the mother and child, and the prevalence of comorbidities among expectant mothers was also addressed.

The study by Lavigne et al. found that prolonged exposure to these air pollutants was linked to adverse birth outcomes, including preterm birth, abnormally small size given gestational age, and low birth weight.<sup>45</sup> These effects were observed in mothers with and without comorbidities. Lei et al. also found a correlation between exposure to air pollutants and fetal developmental outcomes, including impairment of fetal growth and higher blood cortisol levels in the umbilical cord.<sup>46</sup>

Additionally, studies have established a direct correlation between PM2.5 exposure and reduced infant weight, as well as an increased likelihood of experiencing pregnancy-induced hypertension and preeclampsia. Exposure to air pollutants was also found to disturb maternal inflammatory responses and oxidative stress, leading to preterm birth, low birth weight, and stunted growth in children.

The small size of particulates allows them to easily cross biological barriers, including the fetus-maternal barrier, making them particularly harmful to fetuses. The findings from these

<sup>&</sup>lt;sup>45</sup> Lavigne et al., "Maternal Exposure to Ambient Air Pollution and Risk of Early Childhood Cancers"; Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes."

<sup>&</sup>lt;sup>46</sup> "The Role of Cortisol in the Association between Prenatal Air Pollution and Fetal Growth."

studies highlight the need for continued efforts to reduce ambient air pollution and the importance of protecting expectant mothers and their children from exposure.

Overall, this literature review highlights the negative impacts of prolonged exposure to PM2.5, PM10, NO2, and O3 on the health outcomes of expectant mothers and their children, emphasizing the importance of addressing this issue through public health efforts to reduce air pollution.

#### **Impairment to Maternal Health:**

Air pollution has been found to have negative effects on maternal health. Exposure to air pollutants has been linked to respiratory illnesses such as asthma and chronic obstructive pulmonary disease (COPD).<sup>47</sup> Additionally, air pollutants were found to increase the risk of cardiovascular diseases, including hypertension and coronary artery disease. Maternal health is critical for the health of both the mother and the developing fetus, and impairment can have serious consequences.

#### **Post-Birth Effects on Mother:**

Exposure to air pollutants has been linked to postpartum effects on the mother, including an increased risk of postpartum depression and anxiety. Additionally, exposure to air pollutants was associated with an increased risk of complications during childbirth, including preterm labor, low birth weight, and stillbirth. These effects can be detrimental to the mother's mental and physical health and require attention from healthcare professionals.

<sup>&</sup>lt;sup>47</sup> Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes."

<sup>&</sup>lt;sup>48</sup> Sheffield et al., "Association between Particulate Air Pollution Exposure during Pregnancy and Postpartum Maternal Psychological Functioning."

#### **Psychological Effects on Child:**

Exposure to air pollutants during fetal development has been found to increase the risk of neurodevelopmental disorders such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). Furthermore, exposure to air pollutants was found to be associated with an increased risk of cognitive and behavioral problems in children.<sup>49</sup> These psychological effects can have long-term consequences and require attention from healthcare professionals and policymakers.

#### **Racial/Socioeconomic Disparities:**

Depending on the location of the mother, the effect of exposure to air pollutants would vary. There are racial and socioeconomic disparities in exposure to air pollution, with marginalized communities experiencing higher levels of pollution.<sup>50</sup> These disparities must be addressed through targeted environmental health policies that aim to reduce exposure to air pollutants in these communities.

#### **Environmental Health:**

Environmental health policies play a crucial role in reducing exposure to air pollutants, particularly in residential areas where vulnerable populations such as pregnant women and their fetuses are most at risk.<sup>51</sup> The above suggestions provide a starting point for policymakers to

<sup>&</sup>lt;sup>49</sup> Ni et al., "Associations of Pre- and Postnatal Air Pollution Exposures with Child Behavioral Problems and Cognitive Performance."

<sup>&</sup>lt;sup>50</sup> Niu et al., "Association Between Ambient Air Pollution and Birth Weight by Maternal Individual- and Neighborhood-Level Stressors."

<sup>&</sup>lt;sup>51</sup> Lavigne et al., "Ambient Air Pollution and Adverse Birth Outcomes."

develop effective policies that protect vulnerable populations from the harmful effects of air pollution.

Overall, the findings of the present study underscore the importance of addressing the issue of air pollution and its effects on maternal health and fetal development. By implementing effective environmental health policies, policymakers can work towards reducing exposure to air pollutants and promoting the health and well-being of mothers and their children.

#### **CONCLUSION**

Present studies have shown that exposure to air pollutants can have significant negative effects on maternal health and fetal development. Maternal exposure to air pollutants increases the risk of respiratory and cardiovascular diseases, postpartum depression and anxiety, as well as complications during childbirth. Fetal exposure to air pollutants increases the risk of neurodevelopmental disorders, cognitive and behavioral problems. Racial and socioeconomic disparities play a role in the effect of air pollutants on maternal and fetal health. The study recommends environmental health policies to improve air quality standards, increase monitoring and reporting, promote clean transportation, encourage energy-efficient homes, and implement indoor air quality regulations. Future research should explore the underlying biological mechanisms of these effects and address the limitations of this study, such as the single geographic area studied.

The findings of this study emphasize the need for immediate action to protect vulnerable populations from continued exposure to air pollutants. Low-income, underrepresented, and minority communities are at a higher risk of suffering from the negative effects of air pollution,

and it is our responsibility to address this issue through the implementation of effective environmental health policies.

We must prioritize the health and well-being of pregnant women and their fetuses by improving air quality standards, increasing monitoring and reporting of air quality data, promoting clean transportation, encouraging energy-efficient homes, and implementing indoor air quality regulations.

It is imperative that policymakers take action to address this issue and protect vulnerable populations from the harmful effects of air pollution. We must act now to ensure a healthy and sustainable future for all.

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