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# The effects of air pollution on adverse birth outcomes

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ABSTRACT

*Background:* Air pollution has been shown to have adverse effects on many health outcomes including cardiorespiratory diseases and cancer. However, evidence on the effects of prenatal exposure is still limited. The purpose of this retrospective cohort study is to evaluate the effects of prenatal exposure to air pollutants including particulate matter with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) and ozone ($O_3$) on the risk of adverse birth outcomes (ABOs) including term low birth weight (LBW), preterm delivery (PTD) and very PTD (VPTD).
*Methods:* singleton births from 2004 to 2005 in Florida were included in the study ($N$=423,719). Trimester-specific exposures to $O_3$ and $PM_{2.5}$ at maternal residence at delivery were estimated using the National Environmental Public Health Tracking Network data, which were interpolated using Hierarchical Bayesian models.
*Results:* After adjustment for potential confounders such as demographics, medical and lifestyle factors $PM_{2.5}$ exposures in all trimesters were found to be significantly and positively associated with the risk of all ABOs. Second-trimester exposure had the strongest effects. For an interquartile range (IQR) increase in $PM_{2.5}$ during the second trimester, the risk of term LBW, PTD and VPTD increased by 3% [95% confidence interval (CI): 1–6%)], 12% (11–14%) and 22% (18–25%), respectively. $O_3$ was also found to be positively associated with PTD and VPTD with the strongest effects over the whole pregnancy period [3% (1–5%) for PTD and 13% (7–19%) for VPTD for each IQR increase]. However, $O_3$ was observed to have protective effects on term LBW. Results were consistent for multi-pollutant models.
*Conclusion:* $PM_{2.5}$ has consistent adverse effects on ABOs whereas $O_3$ has inconsistent effects. These findings warrant further investigation.



## 1. Background

Adverse birth outcomes including preterm delivery (PTD), very preterm delivery (VPTD) and low birth weight (LBW) are associated with higher risk of subsequent morbidity and higher health care expenditure. Specifically, infants with these outcomes are more likely to have subsequent respiratory complications including both respiratory failures shortly after birth, and childhood asthma (Escobar et al., 2006; Sonnenschein-van der Voort et al., 2014). In addition, they are associated with a higher risk of neurobehavioral problems (Aarnoudse-Moens et al., 2009). According to a nationally representative cross-sectional analysis using the Nationwide Inpatient Sample database from the Healthcare Cost and Utilization Project, hospitalization cost for infants with PTD or LBW in 2001 was 5.8 billion dollars, which represents almost 50% of the costs of all infant hospitalization in the United States (Russell et al., 2007). This analysis also reported that on average, infants with PTD or LBW have longer hospital stays with a mean length of stay of 12.9 days and a cost of approximately $15,100 compared to an uncomplicated birth with an average of 1.9 days in the hospital and a cost of $600 (Russell et al., 2007). Due to the serious impact of these two adverse birth outcomes, efforts towards their prevention remain a critical part of Healthy People 2020 (2013).

In recent years, there has been a growing interest in focusing on environmental determinants of adverse birth outcomes including air pollution. Air pollutants that have commonly been studied in relation to adverse birth outcomes are particulate matter with

*Abbreviations:* LBW, Low birth weight; PTD, Preterm delivery; VPTD, Very preterm delivery; $PM_{2.5}$, Particulate matter with aerodynamics diameter less than 2.5 micrometer; O3, ozone; μg/m3, microgram per cubic meter; ppb, parts per billion; AQS, EPA's Air Quality System; CMAQ, Models-3/Community Multi-scale Air Quality Model; HBM, Hierarchical Bayesian Prediction Model

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aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) and ozone ($O_3$). However, studies have yielded inconsistent results. For example, some studies have found that $PM_{2.5}$ is positively associated with the risk of PTD (Geer et al., 2012; Hyder et al., 2014; Pereira et al., 2014). Others have found no difference (Fleischer et al., 2014; Rudra et al., 2011; Shah et al., 2011). Similar contradictory results have been found for $O_3$ (Shah et al., 2011; Stieb et al., 2012; Vinikoor-Imler et al., 2013). Due to these inconsistent findings, further investigation of the relationship between these air pollutants and birth outcomes is warranted. Moreover, previous studies mostly relied on air pollution data from fixed monitor sites for exposure assessment, which likely lack spatial coverage as fixed monitors only provide the information about air pollution at the sites where the monitors are located. Thus, there are no air pollution data available at locations without monitors. In previous studies, some houses were located very far from sparsely located air monitors; therefore, relying solely on the closest monitor value may not accurately represent individual air pollution exposure. The interpolated air pollution data from statistical modeling can address this weakness by additionally taking into account meteorological patterns, emission and photochemical properties of pollutants. Therefore, the purpose of this retrospective cohort study is to use a more sophisticated exposure assessment based on Hierarchical Bayesian Modeling to determine the association between prenatal exposure to $PM_{2.5}$ and $O_3$ and the risk of adverse birth outcomes (ABOs) including term low birth weight (LBW), preterm delivery (PTD), and very preterm delivery (VPTD).

## 2. Material and methods

### 2.1. Participants

Study participants included all singleton live births born in Florida from January 01, 2004 to December 31, 2005 identified from Florida Vital Statistics (FVS) ($N$=445,028). After excluding births that had addresses outside of Florida ($n$=4672), missing address (423), unable to geocode (e.g. only PO Box available) ($n$=563), missing gestational age ($n$=937), multiple births ($n$=13,686), those with birth weight out of range (i.e. less than 500 and more than 5000 g) ($n$=903), and those with gestational age out of range (i.e. less than 140 days and more than 320 days) ($n$=125), 423,719 births remained for analyses.

### 2.2. Exposure assessment

Air pollution data was obtained from the US Environmental Protection Agency's (USEPA) Hierarchical Bayesian Prediction Model (HBM) output. The HBM combines $PM_{2.5}$ and $O_3$ data from the EPA's Air Quality System (AQS) and the gridded output from the Models-3/Community Multi-scale Air Quality Model (CMAQ), which is based on the National Emission Inventory and meteorological and geographical factors. The methodology for the HBM model is described elsewhere (McMillan et al., 2010). The HBM model output includes $12 \times 12\ km^2$ gridded estimates of $PM_{2.5}$ (daily average) and $O_3$ (daily 8-h maximum) surfaces. For the purpose of this study, we extracted data for the state of Florida during the period 2003–2005.

To obtain exposure, we geocoded each mother's residential address at delivery and overlaid this layer with the HBM output layer. Individual exposure during pregnancy was then estimated using daily concentrations in the grid in which the residential address falls. We determined pregnancy period and each trimester period by using gestational age given in the data by FVS. On Florida birth certificates, gestational age in weeks is typically determined by ultrasound measurements. When ultrasound is not available, fundal height—determined by clinical examination—or menstrual history is used to estimate gestational age. Exposures were calculated as daily concentrations averaged over each trimester. First, second and third trimesters were defined as the first 13 weeks of gestation, week 14 through 26 and week 27 through birth, respectively.

### 2.3. Outcome assessment

The outcomes of interest were term LBW, PTD and VPTD, all of which are assessed using FVS. Term LBW is defined as a birth that occurred on or after the 37th week of gestation with weight less than 2500 g. PTD is defined as a birth that occurred before 37 weeks of gestation. VPTD is defined as a birth that occurred before 32 weeks of gestation.

### 2.4. Covariates

Covariates from this study come from FVS. They included infant's gender (female or male), maternal age in years (continuous), gestational age in weeks (continuous), maternal education ( < high school, high school graduate and/or some college, college graduate, graduate school), maternal race (White, Black, Hispanic, Asian/Pacific Islander, and Others), marital status (married or unmarried), prenatal care (yes or no), pregnancy tobacco use (yes < 10/day, yes > 10/day, quit and no), pregnancy alcohol drink (yes or no), maternal risk factors (yes or no), maternal infection (yes or no), maternal complications (yes or no), season of conception, urbanicity and year of birth. Season of conception was defined as warm (May through October) or cold (November to April). The presence of maternal risk factors was defined as whether or not the mother had previous ABOs, gestational/chronic diabetes or hypertension, or pre-eclampsia. Maternal infection was defined as whether the mother was diagnosed with an infection at the time of delivery or was treated during pregnancy for an infection. Maternal complications were defined as whether mother needed transfusion, had third or fourth degree perineal laceration, ruptured uterus, unplanned hysterectomy, admission to ICU or unplanned surgery. Since income was not available on the birth certificate, we obtained census block group level median household income information from the 2000 Census for each birth and categorized into quartiles. We also considered unemployment rate at the county level with two levels, high or low, defined as above or below the median.

### 2.5. Statistical analysis

*T*-tests and chi-square tests were performed to compare continuous and categorical characteristics for participants with and without ABOs. Univariate and multivariate logistic regression models were used to investigate the effects of $PM_{2.5}$ and $O_3$ on the risk of LBW, PTD, and VPTD. In the univariable models, we obtained the unadjusted effects of air pollutants. In the adjusted models, we selected confounders that have been found or reported to be associated with both the exposure and the outcomes to estimate the effects of air pollutants. Finally, multi-pollutant models were applied to estimate the effects after adjusting for their potential effects on each other. For all analyses, we compared births with a defined outcome with "healthy" births without any of the outcomes in this study. Data analyses were performed using SAS 9.3 (SAS Institute, Cary, NC). Statistical significance was set at $p < 0.05$.

### 2.6. Sensitivity analysis

We also performed a capture area analysis by which we included only births within 5 mile of air $O_3$ and $PM_{2.5}$ monitor stations. We estimated individual exposure for each trimester using average daily concentrations from the nearest monitor.

## 3. Results

Table 1 summarizes the characteristics of study participants by ABO status. Compared to the Controls (20.7%), the percentages of mothers with less than high school education were significantly higher among term LBW (27.8%), PTD(23.7%) and VPTD mothers (25.2%), respectively. In addition, among the ABO groups, the percentages of mothers who were Black, lived in census block with income in the lowest quartile, unmarried, had no prenatal care, smoked or used alcohol during pregnancy, and had maternal risk factors (e.g. had previous ABOs, gestational/chronic diabetes or hypertension, or pre-eclampsia,) were significantly higher than Controls. In addition, a higher percentage of term LBW infants were female (59.9% vs. 48.7%). However, the percentages of males were higher for PTD and VPTD. Unemployment status was not associated with any ABOs.

Table 2 displays summary statistics for the distribution of prenatal exposure to $PM_{2.5}$ and $O_3$ by trimester and the whole pregnancy period. The mean daily average concentrations of $PM_{2.5}$ during the first, second and third trimesters were 9.7, 9.9 and 10.2 $\mu g/m^3$, respectively. In addition, the mean daily average concentrations of $O_3$ were 37.2, 37.6, and 37.4 ppb for the first, second and third trimesters, respectively. There were significant but weak correlations between $PM_{2.5}$ and $O_3$ exposures during pregnancy periods with Pearson correlation coefficients ranging