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Trimester Specific PM_{2.5} Exposure and Fetal Growth in Ohio, 2007-2010

Zana Percy¹, Emily DeFranco^{2,3}, Fan Xu¹, Eric S. Hall^{3,4}, Erin N. Haynes¹, David Jones⁵, Louis J. Muglia^{2,3,4,6}, and Aimin Chen^{1,*}

¹Division of Epidemiology, Department of Environmental Health, University of Cincinnati College of Medicine, Cincinnati, OH 45267

²Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Cincinnati College of Medicine, Cincinnati, OH 45267

³Perinatal Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229

⁴Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH 45229

⁵Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229

⁶Division of Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229

Abstract

Background: Exposure to particulate matter, particularly with aerodynamic diameter <2.5 μm (PM_{2.5}), may increase inflammation and oxidative stress in pregnant women and affect fetal growth. We examined trimester specific PM_{2.5} exposure levels and small for gestational age (SGA) using the statewide birth registry of Ohio from 2007 to 2010.

Methods: Exposure to PM_{2.5} in each trimester and for each gestational week was determined using data from 57 Environmental Protection Agency network monitoring stations across the state of Ohio. We restricted the data to 224,921 singleton live births, with a gestational age of 20–42 weeks, no genetic disorders or congenital abnormalities, and who had home addresses within a 10 km radius of any PM_{2.5} monitoring station. We estimated odds ratios of SGA using Generalized Linear Models (GLMs) and Distributed Lag Models (DLMs), and adjustment for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of the baby.

Results: Mean PM_{2.5} levels during the entire pregnancy were 13.03 $\mu\text{g}/\text{m}^3$ with a standard deviation of 1.57 $\mu\text{g}/\text{m}^3$. Covariates adjusted odds ratios and 95% confidence intervals of a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} levels with a 10 km buffer radius for SGA and trimesters modeled separately were 0.94 (0.88, 1.00) for the first trimester, 0.93 (0.86, 1.00) for the second trimester, 1.07 (1.00, 1.15) for the third trimester, and 0.92 (0.81, 1.06) for the entire pregnancy. When a 5

*Corresponding author contact information: Dr. Aimin Chen, Division of Epidemiology, Department of Environmental Health, University of Cincinnati College of Medicine, P.O. Box 670056, Cincinnati, OH 45267-0056, USA. Tel: 513-558-2129, Fax: 513-558-4397, aimin.chen@uc.edu.

km buffer radius was used, adjusted odds ratios and 95% confidence intervals for SGA were 0.97 (0.89, 1.05) for the first trimester, 0.96 (0.88, 1.05) for the second trimester, 1.09 (1.02, 1.17) for the third trimester, and 0.99 (0.85, 1.14) for the overall pregnancy, indicating sensitivity to buffer choice. DLMs showed gestational weeks 30-35 to be a particular window of vulnerability.

Conclusion: Increasing exposure to PM_{2.5} during the third trimester of pregnancy was associated with a small increase in risk of SGA in this population-based study. Selection of a buffer radius significantly impacted our results in the first trimester, but not in the third trimester.

Graphical Abstract

Keywords

PM_{2.5}; particulate matter; air pollution; fetal growth; SGA

1. Introduction

Air pollution is a widely accepted environmental and human health hazard that is composed of many different constituent solids, liquids, and gases. The particulate matter fraction of this mixture that measures <2.5 μm in aerodynamic diameter (PM_{2.5}) is usually generated from fossil fuel combustion from motor vehicles (Zhu et al., 2002). Once PM_{2.5} is inhaled and reaches the lungs, it induces local inflammatory changes that result in a systemic cytokine response causing oxidative stress and inflammation throughout the body (Brucker et al., 2013; Patel et al., 2013).

Recently, efforts have been made to reduce air pollution in the United States and other countries, resulting in decreasing levels of PM_{2.5} and other pollutants in the air (United States Environmental Protection Agency, 2017). Although levels are decreasing, they remain high enough that we continue to discover associations between relatively low exposure and human health. Exposure to air pollution has been linked to a host of health conditions including adverse pregnancy outcomes such as pre-eclampsia (Olsson et al., 2013; Wu et al., 2009), gestational hypertension (Van Den Hooven et al., 2011; Vinikoor-Imler et al., 2012), infant death (Defranco et al., 2015; Glinianaia et al., 2004), low birth weight (Dadvand et al., 2013), infant congenital malformations (Ren et al., 2017), preterm birth (Defranco et al., 2016), and infants born small-for-gestational-age (SGA) (Hyder et al., 2014; Parker et al.,

2005). A joint consensus statement by the International Societies of Pediatric Endocrinology and the Growth Hormone Research Society discusses the negative outcomes which babies born SGA face over their lifespans including decreased growth, cognitive impairment, endocrine abnormalities, insulin resistance, and cardiovascular disease (Clayton et al., 2007).

Although several studies have shown associations between prenatal exposure to $PM_{2.5}$ and increased risk for SGA, a recent meta-analysis (Zhu et al., 2015) highlights the need for more studies that specifically examine trimester specific effects of this association, as several only report results for the whole pregnancy. We used a geo-spatially defined birth cohort study located in Ohio to examine the relationship between prenatal $PM_{2.5}$ exposure and SGA births with particular attention to trimester specific exposures at concentrations experienced in many other parts of the country as well. We also utilized distributed lag models (DLMs) to determine specific windows of vulnerability over the course of the pregnancy.

2. Materials and Methods

In this geo-spatial, population based birth cohort study, we utilized a dataset consisting of live births in the state of Ohio from January 1, 2007 through December 31, 2010 provided by the Ohio Department of Health. This study was approved by the Ohio Department of Health and Human Subjects Institutional Review Board and was exempt from review by the University of Cincinnati Institutional Review Board. The exposure of interest was $PM_{2.5}$, measured daily throughout pregnancy, and the outcome of interest was SGA births. We defined SGA as $<10^{th}$ percentile of United States 2009-2010 sex- and gestational-age-specific fetal growth curves (Talge et al., 2014). Gestational age was gathered from the birth record, and we used best obstetric estimate based on last menstrual period and ultrasound parameters.

2.1 Study Population

We used state birth record data to evaluate numbers of SGA and non-SGA babies born in Ohio during the time period of interest. Subjects were included in our analysis if they were 1) singleton live births, 2) gestational age 20-42 weeks, 3) without genetic disorders or congenital abnormalities, 4) resided within a 10 kilometer radius from a monitoring station, and 5) had $PM_{2.5}$ level data for all three trimesters. Subjects were excluded if they had missing data for exposure or outcome variables.

2.2 $PM_{2.5}$ Exposure

To assess $PM_{2.5}$ exposure in the state of Ohio, we analyzed United States Environmental Protection Agency (EPA) data from 57 air quality monitoring stations in Ohio to develop a map of $PM_{2.5}$ exposure throughout the state (United States Environmental Protection Agency, 2018). Using ArcGIS 10.1 (ESRI, Redlands CA, USA), we geocoded maternal address at the time of birth and calculated the mother's residential distance to the nearest EPA monitoring station with methods previously described (Hall et al., 2014). In this

analysis we included births at gestational ages 20 through 42 weeks with a maternal address within 10 km of a monitoring station (n=224,921) (Defranco et al., 2016).

2.3 Statistical Analysis

Subject exposure to PM_{2.5} was calculated as a mean by gestational week, by trimester, and for the entire pregnancy based on daily monitoring data from the EPA station closest to the subject's residential address. We also rounded PM_{2.5} exposure means to the nearest whole number and calculated the proportion of SGA births at each exposure level.

To examine the relationship between PM_{2.5} exposure and SGA with consideration of clustering within a monitoring station, we used Generalized Estimating Equations (GEE) in the Generalized Linear Model with logit link, and adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use during pregnancy, prenatal care initiation, birth year, season of birth, and sex of the baby (Fiaz et al., 2012). We chose covariates based on significant differences in bivariate analysis, biologic plausibility, and parsimony in the statistical model.

Four different statistical models were used to examine the relationship between PM_{2.5} exposure and SGA. First, we determined the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) at each exposure level (integer, $\mu\text{g}/\text{m}^3$) by trimester and for the entire pregnancy in relation to SGA proportions. Only PM_{2.5} levels with at least 100 total births were included in the analysis to minimize the influence of unstable SGA percentage at both ends of the exposure range. Second, we modeled continuous PM_{2.5} exposure levels for each trimester and for the entire pregnancy to calculate a linear trend of dose-response. We used separate models for each trimester as well as a joint model for all three trimesters to take into account potential bias from separate models (Wilson et al., 2017). Third, we used binary PM_{2.5} exposure levels to calculate the association of high ($\geq 15 \mu\text{g}/\text{m}^3$) versus low ($<15 \mu\text{g}/\text{m}^3$) exposure. This cut-off was chosen because $15 \mu\text{g}/\text{m}^3$ was the EPA annual standard during the period of study. Additionally, we dichotomized the PM_{2.5} exposure levels to high ($\geq 12 \mu\text{g}/\text{m}^3$) versus low ($<12 \mu\text{g}/\text{m}^3$) exposure to consider the current EPA annual standard. Fourth, we used DLMs to examine weekly mean exposure to PM_{2.5} levels from gestational weeks 0-35 to identify potential windows of susceptibility that may be finer than trimester, because the latter is arbitrary for starting point and length of windows. The DLM constrains the association of weekly specific exposure with outcome to be smooth across gestational weeks, and can consider either linear or non-linear associations (Gasparrini, 2014). We considered three dose-response patterns between PM_{2.5} exposure and SGA proportion: linear, B-spline, and natural cubic spline, and modeled the gestational week and response relation as B-spline (Hsu et al., 2015; Sheffield et al., 2018; Wu et al., 2018). The degrees of freedom of the splines and the dose-response patterns were determined using smaller Akaike Information Criterion (Gasparrini, 2011; Sheffield et al., 2018). The DLMs were adjusted for the above-mentioned covariates. Statistical analyses were performed using SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA), and the DLMs were implemented using the dlrm package Version 2.3.6 in R 3.5.1 (Vienna, Australia). Tests with a probability value of <0.05 were considered statistically significant.

3. Results

There were 597,000 live births in Ohio from 2007-2010 captured for analysis. Of those, we excluded births in which: the gestational age was <20 weeks, >42 weeks, or missing; genetic disorders or congenital anomalies were present; the birth weight was <350 grams; there was a multifetal gestation; the mother lived >10 kilometers from a monitor station; or exposure data was not available for all trimesters, leaving a total of 224,921 births for the final analysis. Of these births, 24,299 were SGA (10.8%) (Figure 1).

Demographic, social, and socioeconomic characteristics of the cohort are presented in Table 1. Briefly, 67.4% of mothers were less than 30 years old at the time of birth, 61.8% were white, 54.5% had completed some post-secondary education, 44.5% had private health insurance, and 19.1% used tobacco during their pregnancy. SGA percentages were higher in mothers with a younger age, who are black, with less than high school education, having prepregnancy body mass index (BMI) <18.5 kg/m², receiving Medicaid, who smoked during pregnancy, and who had late or no prenatal care initiation. An analysis on mothers excluded because they lived >10 km from a monitoring station (mostly rural) showed that this group had slightly lower PM_{2.5} exposure, less SGA proportion, less teen pregnancy, higher white percentage, higher education, less Medicaid, and more prenatal care in the first trimester (data not shown).

Table 2 shows that the range of exposure to PM_{2.5} was 8.28-18.57 µg/m³ for the whole pregnancy, the average PM_{2.5} concentration was 13.03±1.57 (mean ± SD), and the median PM_{2.5} concentration was 13.04 µg/m³. The trimester specific exposure range was wider than that for the whole pregnancy, at 6.22-24.15 µg/m³, and the third trimester had the largest range of exposures for the cohort. The SGA percentages by each integer of PM_{2.5} concentration with a given trimester or entire pregnancy were shown in Supplemental Table S1. The correlation coefficient of exposures was 0.21 between the first and second trimesters, 0.31 between the first and the third trimesters, and 0.25 between the second and the third trimesters.

Figure 2 shows the aORs and 95% CIs of rounded mean PM_{2.5} concentrations during each trimester and for the whole pregnancy with reference set at 10 µg/m³. At high exposure levels there were negative associations in the first and second trimesters, but positive associations in the third trimester. The dose response curve for the whole pregnancy was generally flat.

When PM_{2.5} exposure was modeled continuously, there was a reduced risk in the first trimester in separate and joint models, and a higher risk in the third trimester in both model types (Table 3). We noted the same pattern when PM_{2.5} exposure was categorized as a binary using 15 µg/m³ as a cut-point, but there were no associations when 12 µg/m³ was used as the cut-point (Table 4).

In the DLMS, the linear pattern between PM_{2.5} exposure and the SGA proportion had the lowest Akaike Information Criterion and was used to describe the association. Figure 3 shows the ORs for an increase of 10 µg/m³ PM_{2.5}, with a “J” shape across gestational

weeks. The results indicate decreased risk of SGA for exposure between gestational weeks 5-15, and increased risk of SGA for exposure after week 30.

Additionally, we performed sensitivity analyses restricting to 1) pregnant women living within a 5km radius to the closest PM_{2.5} monitoring station, and 2) nulliparous women to remove the impact of previous pregnancy history. The association was modeled with continuous exposure, binary exposure, and DLMs. The analysis restricting to nulliparous women was similar to the results in Tables 3 and 4 (Supplemental Tables S2 and S3, and Supplemental Figure S1), but the analysis with buffer radius set to <5 km did not find any associations between PM_{2.5} and SGA during the first trimester (Tables 5 and 6, and Figure 4).

4. Discussion

4.1 General Findings

In this study of PM_{2.5} concentration and Ohio births between 2007 and 2010, we found that first trimester exposure to increasing levels of PM_{2.5} was associated with a slightly decreased risk of SGA in infants, and third trimester exposure was associated with a slightly increased risk. DLMs indicate that gestational weeks 30-35 in particular are a potential window of vulnerability to PM_{2.5} exposure for SGA. Both the first and third trimester associations held when exposure was modeled continuously, dichotomized, and with DLMs. However, an analysis restricting the buffer radius to <5km from the nearest EPA monitoring station showed that only the third trimester positive association remained significant.

4.2 Strengths and Limitations

An obvious limitation of our study is the use of EPA monitoring station data to assess individual exposure to PM_{2.5} during pregnancy. We restricted our primary analysis to mothers that lived within 10 km of a monitoring station, but this does not account for dynamic exposure during time spent away from the home or from indoor air pollution. Additionally, the 10 km buffer radius around stations is an imprecise estimate of daily exposure and actual personal exposure during the study period may have varied to an unknown degree. We also were unable to assess whether women moved during their pregnancies, however a 2014 review showed that pregnant women in the United States have approximately 24% residential mobility, but the moves tend to be <10km apart, which would reduce exposure misclassification (Bell and Belanger, 2012). Ideally, we would have obtained personal monitoring data to more accurately assess exposure, but that would not be feasible for a study of this size. Also, EPA monitoring stations are not distributed evenly throughout the state, creating inherent sample bias in our methodology because we excluded births in areas without nearby monitoring stations, most of which are in rural areas. Similar to the findings of others, the population that we were able to include in this analysis was significantly different from those excluded because of distance to the nearest monitoring station (Bell and Ebisu, 2012). These conditions with regard to the monitoring data may bias our study toward the null.

The exposure range measured in this study did not include PM_{2.5} levels <5 or >21 µg/m³, and therefore these results cannot be extrapolated to very pristine or very urban environments. However, according to the EPA regional PM_{2.5} data trends, average yearly levels of PM_{2.5} in the majority of the United States do fall within the range described in this study (United States Environmental Protection Agency, 2017). Although it is difficult to generalize our results to other regions and states because of population differences, this study describes pollution levels more similar to what the average US resident may experience as opposed to other studies that describe only very high levels of exposure (Coker et al., 2015; Sram et al., 2013; Vinikoor-Imler et al., 2012).

Another limitation of our study inherent to using birth records is the limited data available for covariate adjustment. We may have unmeasured confounding left in the model that could be biasing our estimates either toward or away from the null. We also were unable to account for other aspects of air pollution in our model such as CO, NO₂, or SO₂ due to the differing placement and smaller numbers of those EPA monitoring stations. However, the PM_{2.5} exposure data that we did have access to is more complete, and both weight and gestational age are expected to have been recorded with high validity.

The geo-spatial cohort design of our study is a significant strength as it allows us to examine a large sample size with temporal data in a single population. To our knowledge, this cohort also has the most recent birth records dates of any other large studies of PM_{2.5} and SGA with the exception of Smith et al., who studied a cohort from 2006-2010 (Smith et al., 2017). It is important to continue to study more recent cohorts of individuals with regard to air pollution exposure because both the composition and quantity of pollution changes over time (United States Environmental Protection Agency, 2017), potentially leading to differing health consequences.

4.3 Interpretation

Our sensitivity analysis examining associations between PM_{2.5} exposure and SGA infants born <5 km from the nearest EPA monitoring station differed significantly from our primary analysis, which used a 10 km buffer radius, in that it did not find a lower risk from exposure in the first trimester. Generally, individual exposure estimates from stationary monitors are thought to be more accurate when smaller buffer radii are drawn, and larger radii are more prone to exposure misclassification. Even though the 5 km buffer radius analysis had a smaller sample size (n=112,627), we do not believe that inadequate power is the reason we do not see an association during the first trimester. Our other sensitivity analysis that used a 10 km buffer and restricted to nulliparous women had an even smaller sample size (n=91,555) and still found the spurious association in the first trimester. Another potential explanation for the finding of lower risk in the first trimester is due to our inclusion of only live births. It is possible that the fetuses most predisposed to adverse effects from PM_{2.5} were lost in early pregnancy or stillborn, leaving the remaining cohort biased. Additionally, the third trimester is a more biologically plausible window of vulnerability because that is when the most rapid fetal growth occurs (Alexander et al., 1996; Grantz et al., 2018).

There is some inconsistency in the literature around PM_{2.5} exposure and SGA, particularly with regard to whole pregnancy and trimester specific effects. A recent paper by Stieb et al.

utilized birth record data from the large Canadian national registry and found an increased risk for SGA (OR= 1.04, 95% CI= 1.01-1.07) with a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ over the whole pregnancy, but no significant results by trimester (Stieb et al., 2015). Mannes et al. only found second trimester exposure to be significantly associated with SGA (OR= 1.34, 95% CI= 1.10-1.63) (Mannes et al., 2005). However, Rich et al. found $\text{PM}_{2.5}$ exposure during both the first (OR=1.11, 95% CI=1.01-1.23) and third (OR=1.11, 95% CI= 1.01-1.21) trimesters to be significantly associated with SGA (Rich et al., 2009). A recent study by DeFranco et al. also examined a similar cohort of Ohio births and found that exposure to high levels of $\text{PM}_{2.5}$ in the third trimester was associated with a 42% increased risk for stillbirth (Defranco et al., 2015). This could indicate that the exposure levels found in this study are sufficient to disrupt multiple fetal processes in the third trimester.

The discrepancy of trimester specific estimates of risk related to $\text{PM}_{2.5}$ concentrations could be from the exposure variation within trimesters, the composition and sources of $\text{PM}_{2.5}$ exposure, and population characteristics. Our use of DLMs allowed us to model $\text{PM}_{2.5}$ exposure on a weekly basis during pregnancy and discover that gestational weeks 30-35 are a particular window of vulnerability. Additionally, we showed that dichotomizing exposure at a cut-off of 15 $\mu\text{g}/\text{m}^3$, but not 12 $\mu\text{g}/\text{m}^3$ revealed trimester specific differences in SGA odds.

The present study contributes to the body of knowledge in this area with weekly and trimester specific assessments of births in Ohio, a population not previously studied in this way. Our study population consisted of 30.13% black women, which is much higher than the US average of 13.4% (United States Census Bureau, 2017), and could account for some of the differences between our findings and other authors'. This difference in population characteristics may also explain why we had slightly more SGA babies in our cohort when we would expect based on the definition of SGA as babies in <10th percentile of US 2009-2010 sex- and gestational-age-specific fetal growth curves. National data shows black women are almost twice as likely to deliver a SGA baby than white women (United States Census Bureau, 2017).

The mechanisms underlying exposure to $\text{PM}_{2.5}$ and impaired fetal growth are still unclear. Previously hypothesized mechanisms include coagulability changes, inflammation and oxidative stress, and direct effects on the autonomic nervous system (Glinianaia et al., 2004). Another compelling hypothesis is that $\text{PM}_{2.5}$ promotes placental dysfunction via vascular changes that results in decreased fetal growth (Liu et al., 2016; Veras et al., 2008). Since $\text{PM}_{2.5}$ has also been associated with an increased risk of preterm birth (Defranco et al., 2016), additional impact with impaired fetal growth put highly exposed babies at an even greater risk for early delivery and small size, which have short- and long-term risks on child physical, pulmonary, cardiovascular, and neuropsychological development.

Although we only found a 5-10% increased risk of SGA from increased $\text{PM}_{2.5}$ exposure in the third trimester, particulate air pollution is a ubiquitous exposure in US women, and continuing to improve air quality is still a worthwhile public health measure. While we studied SGA as the outcome of this investigation, the adverse impact of particulate matter exposure goes beyond fetal growth. Since the association we found was for the third

trimester of pregnancy, when fetal weight is steadily increasing, there is a potential to intervene and reduce exposure to PM_{2.5} in the pregnant women.

5. Conclusions

The findings reported in this study indicate that pregnant women exposed to increasing PM_{2.5} levels in their third trimester are at a modestly increased risk for delivering SGA babies, with a particular window of vulnerability between 30 and 35 weeks gestation. We also found that the selection of buffer radius significantly impacted our results in the first trimester, but not the third trimester of pregnancy. Although this study was conducted exclusively on women in Ohio, the exposure ranges we describe are experienced by many urban areas across the country, and this work contributes to a growing literature describing the deleterious impact of PM_{2.5} on human health. Additional research including personal monitoring data on a more diverse group of women would strengthen the science in this field, however we should also focus on continuing to decrease individuals' exposure to particulate air pollution.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

PM_{2.5}	particulate matter <2.5 µm in aerodynamic diameter
SGA	small-for-gestational-age
EPA	United States Environmental Protection Agency
aOR	adjusted odds ratio
CI	confidence interval
GEE	generalized estimating equation
DLM	distributed lag model

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Highlights:

- Exposure to PM_{2.5} during pregnancy has been associated with impaired fetal growth, but trimester-specific effects are still unclear.
- This study examines the association between PM_{2.5} and SGA in a Ohio geo-spatial cohort from 2007-2010 with n= 224,921.
- Exposure to increasing levels of PM_{2.5} during the third trimester of pregnancy, particularly gestational weeks 30-35, was associated with a 5-10% increased risk for SGA.
- This study was the first of its kind to examine Ohio births and also uses the more recent birth record data to examine PM_{2.5} exposure and SGA.

Figure 1:
Flow diagram of the study population.

Figure 2:

Adjusted ORs and 95% CIs of mean PM_{2.5} concentrations during each trimester and during the entire pregnancy for SGA infants, with reference at 10 µg/m³. Adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of baby.

Figure 3.

Adjusted ORs and 95% CIs of PM_{2.5} levels for SGA infants in distributed lag models. A) by gestational week; B) at gestational week 32. Adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of baby.

Figure 4.

Adjusted ORs and 95% CIs of PM_{2.5} levels for SGA infants in women living <5 km from the nearest EPA monitoring station in distributed lag models. A) by gestational week; B) at gestational week 32. Adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of baby.

Table 1:

Study Population Characteristics and SGA percentages.

	Non-SGA, n (row %)	SGA, n (row %)	Total, n (column %)
Births	200,622 (89.20)	24,299 (10.80)	224,921 (100)
Demographic Factors			
Maternal Age *, years			
<20	23,383 (84.36)	4,335 (15.64)	27,718 (12.32)
20-24	52,118 (87.22)	7,640 (12.78)	59,758 (26.57)
25-29	57,756 (90.23)	6,256 (9.77)	64,012 (28.46)
30-34	43,884 (91.82)	3,912 (8.18)	47,796 (21.25)
35-39	19,480 (91.87)	1,723 (8.13)	21,203 (9.43)
40	4,001 (90.23)	433 (9.77)	4,434 (1.97)
Maternal Race *			
Non-Hispanic White	126,109 (91.66)	11,467 (8.34)	137,576 (61.75)
Non-Hispanic Black	56,502 (84.16)	10,635 (15.84)	67,137 (30.13)
Other Non-Hispanic	5,681 (86.43)	892 (13.57)	6,573 (2.95)
Hispanic	10,425 (90.49)	1,095 (9.51)	11,520 (5.17)
Maternal Education *			
Less than high school	38,319 (84.34)	7,117 (15.66)	45,436 (20.4)
High school graduate	48,946 (87.64)	6,902 (12.36)	55,848 (25.07)
Some post-secondary education	111,484 (91.78)	9,981 (8.22)	121,465 (54.53)
Child Sex *			
Male	101,934 (89.04)	12,544 (10.96)	114,478 (50.9)
Female	98,688 (89.36)	11,755 (10.64)	110,443 (49.1)
Social Behaviors and Socioeconomic Factors			
Parity *			
0	79,822 (87.18)	11,733 (12.82)	91,555 (41.51)
1	61,371 (91.10)	5,999 (8.90)	67,370 (30.54)
2	55,584 (90.18)	6,053 (9.82)	61,637 (27.95)
Pre-pregnancy Body Mass Index *			
<18.5	7,914 (81.39)	1,810 (18.61)	9,724 (4.59)
18.5-24.9	90,613 (88.59)	11,668 (11.41)	102,281 (48.24)
25-29.9	45,695 (90.33)	4,894 (9.67)	50,589 (23.86)
30	44,968 (91.00)	4,448 (9.00)	49,416 (23.31)
Health Insurance Type *			
Medicaid	83,786 (86.11)	13,517 (13.89)	97,303 (43.26)
Private Insurance	92,416 (92.44)	7,553 (7.56)	99,969 (44.45)
Other	24,420 (88.32)	3,229 (11.68)	27,649 (12.29)
Maternal Tobacco Use During Pregnancy *			
Yes	35,670 (83.22)	7,190 (16.78)	42,860 (19.06)

	Non-SGA, n (row %)	SGA, n (row %)	Total, n (column %)
No	164,952 (90.60)	17,109 (9.40)	182,061 (80.94)
Prenatal Care Initiation *			
First Trimester	100,691 (90.48)	10,592 (9.52)	111,283 (67.24)
Second Trimester	35,102 (87.53)	4,999 (12.47)	40,101 (24.23)
Third Trimester	7,449 (86.57)	1,156 (13.43)	8,605 (5.2)
Never	4,703 (85.29)	811 (14.71)	5,514 (3.33)
Season of Birth *			
Spring	50,716 (89.58)	5,898 (10.42)	56,614 (25.17)
Summer	51,770 (89.25)	6,238 (10.75)	58,008 (25.79)
Fall	49,115 (88.75)	6,224 (11.25)	55,339 (24.6)
winter	49,021 (89.19)	5,939 (10.81)	54,960 (24.44)

* Significant difference in SGA percentage (p<0.05)

Table 2:

Mean PM_{2.5} (µg/m³) concentrations during the entire pregnancy in each of the study years, Ohio 2007-2010.

Year	n	Mean±SD	Median	Range
2007	60,559	13.72±1.30	13.79	9.65-18.57
2008	57,677	13.87±1.48	13.95	9.80-18.20
2009	54,964	11.95±1.22	11.81	8.33-15.65
2010	51,721	12.42±1.33	12.36	8.28-16.92
Total	224,921	13.03±1.57	13.04	8.28-18.57

Table 3: Adjusted ORs and 95% CIs of continuous PM_{2.5} concentrations for SGA infants.

Model	Trimester	aOR per 10 µg/m ³ PM _{2.5}	95% CI	p
Separate	First	0.94	0.88-1.00	0.051
	Second	0.93	0.86-1.00	0.130
	Third	1.07	1.00-1.15	0.046
	Entire pregnancy	0.92	0.81-1.06	0.243
Joint	First	0.92	0.86-0.99	0.027
	Second	0.93	0.85-1.02	0.111
	Third	1.08	1.01-1.16	0.021

Adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of baby.

Table 4: Adjusted ORs and 95% CIs of dichotomous PM_{2.5} concentrations for SGA infants.

Cut-off of PM _{2.5} (µg/m ³)	Trimester	Low exposure		High exposure		Modeled separately		Modeled jointly	
		n	% SGA	n	% SGA	aOR	95% CI	aOR	95% CI
15	First	175,649	10.82	49,272	10.73	0.96	0.92-0.99	0.96	0.92-0.99
	Second	185,883	10.78	39,038	10.93	0.97	0.94-1.01	0.97	0.93-1.01
	Third	181,665	10.65	43,256	11.44	1.04	1.00-1.09	1.04	1.00-1.09
	Entire pregnancy	200,259	10.76	24,662	11.16	1.00	0.96-1.04		
12	First	74,283	10.71	150,638	10.85	0.99	0.97-1.02	0.99	0.96-1.01
	Second	76,331	10.70	148,590	10.85	0.99	0.96-1.03	0.99	0.96-1.03
	Third	82,293	10.54	142,628	10.95	1.02	0.99-1.05	1.02	0.99-1.05
	Entire pregnancy	63,232	10.61	161,689	10.88	0.97	0.93-1.00		

Adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of baby.

Table 5:

Adjusted ORs and 95% CIs of continuous PM_{2.5} concentrations for SGA infants in women living <5 km from the nearest EPA monitoring station (N=112,627, SGA=13,963, 12.40%).

Model	Trimester	aOR per 10µg/m ³ PM _{2.5}	95% CI	p
Separate	First	0.97	0.89-1.05	0.459
	Second	0.96	0.88-1.05	0.327
	Third	1.09	1.02-1.17	0.013
	Entire pregnancy	0.99	0.85-1.14	0.849
Joint	First	0.95	0.87-1.04	0.271
	Second	0.95	0.87-1.04	0.291
	Third	1.10	1.02-1.18	0.009

Adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of baby.

Table 6:

Adjusted ORs and 95% CIs of dichotomous PM_{2.5} concentrations for SGA infants in women living <5 km from the nearest EPA monitoring station.

Cut-off of PM _{2.5} (µg/m ³)	Trimester	Low exposure		High exposure		Modeled separately		Modeled jointly	
		n	% SGA	n	% SGA	aOR	95% CI	aOR	95% CI
15	First	87,021	12.40	25,606	12.39	0.98	0.94-1.03	0.98	0.94-1.03
	Second	92,048	12.39	20,579	12.42	0.97	0.93-1.02	0.97	0.92-1.02
	Third	89,917	12.25	22,710	12.99	1.05	1.00-1.09	1.05	1.01-1.09
	Entire pregnancy	99,332	12.34	13,295	12.85	1.04	0.98-1.10		
12	First	36,153	12.36	76,474	12.41	1.00	0.97-1.04	0.99	0.96-1.03
	Second	36,825	12.46	75,802	12.37	0.99	0.95-1.02	0.99	0.95-1.03
	Third	40,032	12.15	72,595	12.53	1.04	0.99-1.08	1.04	0.99-1.08
	Entire pregnancy	29,926	12.43	82,701	12.39	0.97	0.94-1.01		

Adjusted for maternal age, race, education, parity, body mass index, insurance type, tobacco use, prenatal care initiation, birth year, season of birth, and sex of baby.