Distribution Agreement

Signature:

______________________________ _______________

Ying Lin Date

Ambient Air Pollution and Birth Weight Quantiles in Atlanta

By

Ying Lin
Master of Science in Public Health
Biostatistics

Howard H Chang, Ph.D.

Committee Chair

Matthew J Strickland, Ph.D.

Committee Member

Ambient Air Pollution and Birth Weight Quantiles in Atlanta

By

Ying Lin
B.A.
Xiamen University
2014

Thesis Committee Chair: Howard Chang, Ph.D.

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science in Public Health
in Biostatistics
2016

Abstract

Ambient Air Pollution and Birth Weight Quantiles in Atlanta

By

Ying Lin

BACKGROUND: Previous studies suggest associations between air pollution exposures during pregnancy and reduced mean birth weight.

OBJECTIVE: To investigate air pollution exposure and changes in birth weight quantiles, as well as whether the associations vary across quantiles.

METHODS: Birth certificates of singleton births ≥ 27 weeks of gestation in the five-county Atlanta metropolitan area were obtained from the Office of Health Indicators for Planning, Georgia Department of Public Health. This study included births with estimated dates of conception between 1 January 2002 and 28 February 2006 (N=189,900 births). Daily pollutant concentrations at 12 km resolution were estimated for 12 ambient air pollutants by combining monitoring measurements and simulations from chemical transport models. We used daily 1-hour maximum, 24-hour average, or maximum 8-hour average for different pollutants following previous studies in Atlanta. We used quantile regression to estimate associations between birth weights quantiles (5th, 25th, 50th, 75th and 95th) and average pollutant concentrations during the first, second, third trimester and over the entire pregnancy. Analyses were also stratified by preterm and full-term births.

RESULTS: Among all births, we observed consistent associations between reduced birth weight quantiles and carbon monoxide (CO), elemental carbon (EC), nitrogen dioxide (NO_2), nitrogen oxide (NO_x), organic carbon (OC), sulfur dioxide (SO_2), and fine particulate matter ($PM_{2.5}$). Generally, we also observed stronger negative associations during the first and second trimesters compared to the third trimester among these pollutants. Pollutants CO, EC, NO_2 and NO_x showed stronger negative associations at increasing quantile levels. These associations were similar for full-term births. Among preterm births, CO, EC, NO_2, NO_x and OC exposures during the first and second trimesters had the most consistent negative associations with birth weight quantiles. Moreover, the decrease in birth weight quantiles among preterm births were larger compared to full-term births.

CONCLUSION: Ambient air pollutants, particularly those associated with traffic, were negatively associated with birth weight quantiles. There is evidence that their associations vary from across trimesters and across different quantiles.

Ambient Air Pollution and Birth Weight Quantiles in Atlanta

By

Ying Lin
B.A.
Xiamen University
2014

Thesis Committee Chair: Howard Chang, Ph.D.

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science in Public Health
in Biostatistics
2016

Acknowledgements

I am extremely grateful for my amazing thesis advisor, Dr. Howard Chang, whose encouragement, guidance, and support made this thesis possible.

I am also thankful for Matthew Strickland for taking time to read my thesis.

Finally, I would like to thank my parents for their love and support throughout my education.

Table of Contents

INTRODUCTION

Low birth weight (LBW) is defined as a live birth having birth weight less than 2,500 g (5 pounds 8 ounces) regardless of gestational age [1]. LBW is associated with perinatal mortality and morbidity, inhibited growth and cognitive development, and chronic diseases later in life [2]. LBW is present in 60 to 80 percent of infant deaths in developing countries [3]. Infant mortality due to LBW is usually directly casual, stemming from other medical complications [4]. At the population level, the proportion of LBW newborns is an indicator of multifaceted public-health problems that include long-term maternal malnutrition, poor maternal health and poor health care during pregnancy. On an individual basis, LBW is an important predictor of newborn health and is associated with higher risk of infant and childhood mortality.

LBW is either caused by preterm birth (commonly defined as gestational age less than 37 weeks), slow prenatal growth rate, or the combination of both. In general, maternal risk factors that may contribute to low birth weight include young age, multiple pregnancies, previous LBW infants, poor nutrition, heart disease or hypertension, drug addiction, alcohol abuse, and insufficient prenatal care. Environmental risk factors include smoking, lead exposure, and outdoor air pollutants [5].

Many studies have been conducted to investigate associations between air pollution and birth weights – see meta-analysis conducted by Stieb et al. (2012) [6], Dadvand et al. (2013) [7], Amegah et al. (2014) [8] and Sun et al. (2016) [9]. Studies were conducted in different regions with different pollutants involved. For example, exposure to household air pollution, specifically fine particulate matter ($PM_{2.5}$), may adversely affect birth weight, according to study in an urban Tanzania cohort [10]. Short-term decreases in air pollution, specifically $PM_{2.5}$, CO, SO_2 and NO_2, late in pregnancy in Beijing during the 2008 Summer Olympics were associated with higher birth weight [11].

Various statistical methods have been applied to examine associations between air pollution and reduced birth weight. Standard approaches involve modeling continuous birth weight using linear regression [12] or LBW as a binary variable using logistic regression [13]. Studies that analyzed continuous birth weight have often found very small shifts in mean birth weight associated with air pollution exposure. For example, in the meta-analysis by Stieb et al. (2012) [6], a -11 g change in BW per 5 $\mu g/m^3$ increase in third trimester $PM_{2.5}$ exposure. More recently, a meta-analysis was performed to estimate the associations of maternal exposure to $PM_{2.5}$ and its chemical constituents with birth weight and to explore the sources of heterogeneity in regard to the findings of these associations. This meta-analysis found a clear association between $PM_{2.5}$ exposure during pregnancy and decreased birth weights, and late pregnancy might be the critical window for these adverse effects. Some specific chemical constituents of $PM_{2.5}$ might have more severe harmful effects on fetal weight. Important sources of the heterogeneity between studies include different exposure assessment methods, study designs and study settings [9].

Quantile regressions have been applied in other birth weight analyses, however, to our knowledge, this approach has not been applied to ambient air pollution. Quantile regression is a type of regression analysis commonly used in statistics and econometrics. Whereas the standard regression method results in estimates that approximate the conditional mean of the response variable given the predictor variables, quantile regression aims at estimating either the conditional median or other quantiles of the response variable. Quantile regression is desirable when conditional quantile functions are of interest. One advantage of quantile regression, relative to the standard mean regression, is that the quantile regression estimates are more robust against outliers in the response measurements. However, the main attraction of quantile regression goes beyond that. Specifically, different measures of central tendency and statistical dispersion can both be useful to obtain a more comprehensive analysis of the relationship between variables [14].

In this study, we investigated associations between 12 air pollutants and birth weight in 5-county metropolitan Atlanta. We present trimester-specific and overall-pregnancy average exposure associations for each pollutant at different quantiles. By using quantile regression we aim to examine whether air pollution exposure during pregnancy is associated with changes in birth weight quantiles, and whether the magnitude of the change differs across quantiles.

METHODS

Data and Outcome Assessment

Birth records were obtained from the Office of Health Indicators for Planning, Georgia Department of Public Health. We included singleton pregnancies with gestational lengths of 27-42 weeks and an estimated date of conception from January

1st, 2002 to February 28th, 2006. We only included birth records within the five-county Atlanta area (Clayton, Cobb, DeKalb, Fulton, and Gwinnett counties). Additional exclusion criteria include: (1) maternal residential address at delivery was unsuccessfully geocoded to the 2000 Census block group, (2) birth weight was less than 400 grams, (3) mother's age was less than 15 years or greater than 44 years, (4) one or more identified congenital anomaly was present, and (5) preterm births that had a procedure code for induction of labor. The final dataset contained 189,900 pregnancies.

Ambient Air Pollutant Concentrations

Ambient air pollutant concentrations were estimated by fusing 12-km by 12-km outputs from the U.S. EPA's Community Multi-scale Air Quality Model (CMAQ) with ambient air pollutant concentration measurements from Air Quality System stationary monitors [15]. We considered the following 12 pollutants: 1-hour maximum carbon monoxide (CO), nitrogen dioxide ($\mathrm{NO_2}$), nitrogen oxide ($\mathrm{NO_x}$), and sulfur dioxide ($\mathrm{SO_2}$), 8-hour maximum ozone ($\mathrm{O_3}$), 24-hour average particulate matter less than 10 and 2.5 microns in diameter ($\mathrm{PM_{10}, PM_{2.5}}$), and the $\mathrm{PM_{2.5}}$ components sulfate ($\mathrm{SO_4}$), nitrate ($\mathrm{NO_3}$), ammonium ($\mathrm{NH_4}$), elemental carbon (EC), and organic carbon (OC) were calculated for each grid cell [16].

Statistical Models

We estimated the change in birth weight quantiles (5^{th}, 25^{th}, 50^{th}, 75^{th} and 95^{th}) associated with average pollutant concentrations during the first trimester (weeks 1-13), second trimester (weeks 14-26), third trimester (weeks 28-birth) and over the entire pregnancy.

Let Y be a real-valued random variable with cumulative distribution function $\mathrm{F_Y(y) = P(Y \le y)}$. The τ^{th}quantile of Y is given by

$$\mathrm{Q_Y(\tau) = {F_Y}^{-1}(\tau) = \inf\{y\colon F_Y(y) \ge \tau\}}$$

where $\tau \in [0,1]$.

Define a loss function as $\mathrm{\rho_\tau(y) = |y\ (\tau - II_{(y<0)})|}$, where II is an indicator function. A specific quantile value can be found by minimizing the expected loss of Y-u with respect to u [11]:

$$\min_u \mathrm{E(\rho_\tau(Y-u)) = \min_u (\tau-1)\int_{-\infty}^{u}(y-u)dF_Y(y) + \tau\int_{u}^{\infty}(y-u)dF_Y(y).}$$

This can be shown by setting the derivative of the expected loss function to 0 and letting $\mathrm{q_\tau}$ be the solution of

$$\mathrm{0 = (1-\tau)\int_{-\infty}^{q_\tau} d\,F_Y(y) - \tau\int_{q_\tau}^{\infty} d\,F_Y(y).}$$

This equation reduces to

$$\mathrm{0\ = F_Y(q_\tau) - \tau,}$$

and then to

$$F_Y(q_\tau) = \tau.$$

Hence q_τ is τ^{th} quantile of the random variable Y.

Suppose the τ^{th} conditional quantile function is $Q_{Y|X}(\tau) = X\beta_\tau$. Given the distribution function of Y, β_τ can be obtained by solving

$$\beta_\tau = \mathrm{argmin}_{\beta\in R^k} E(\rho_\tau(Y - X\beta)).$$

Solving the sample analog gives the estimator of β.

$$\widehat{\beta_\tau} = \mathrm{argmin}_{\beta\in R^k} \sum_{i=1}^{n} (\, \rho_\tau(Y_i - X\beta)).$$

We considered the following potential confounders: block-group poverty levels (% population below poverty line as a continuous variable) of the maternal residence at delivery, conception year (2002/2003/2004/ 2005/2006), conception season (June to August/September to November/December to February/March to May), maternal age group (<19/20-24/25-29/30-34/35-39/>40), sex of the infant (female vs. male), maternal education (less than 9th grade/9th-12th grade/high school or general education diploma/some college or higher), maternal race (White/Black/Asian/Hispanic), reported alcohol use during pregnancy (yes vs. no), reported tobacco use during pregnancy (yes vs. no), indicators of completed gestational weeks, county of residence at delivery (Clayton/Cobb/DeKalb/Fulton/Gwinnett), and marriage status (married vs. unmarried).

We conducted quantile regression for each pollutant and each exposure window separately, fully adjusted by all the confounders. We also stratified the birth records by full-term births (gestational weeks greater than or equal to 37 weeks) and preterm births (gestational weeks less than 37 weeks). Quantile regression coefficients were scaled with an interquartile range (IQR) increase in the average concentration of air pollution during different exposure windows. We used the interquartile range to better reflect the range of exposure experienced in the observed data.

RESULTS

The study cohort consisted of 189,900 singleton births across the 5 Atlanta counties, 175,447 (92.4%) of whom were full-term and 14,453 (7.6%) of whom were preterm. Table 1 shows maternal characteristics of the study population, also stratified by full-term and preterm births. Compared to mothers of full term births, mothers of preterm births were more likely living in an area of higher poverty levels, be younger, have lower education attainment, be of African American race, live in Clayton, DeKalb and Fulton counties, and be unmarried.

Table 2 presents birth weight of full term and preterm singleton births in five-county Atlanta at different quantiles. Compared with full term births, preterm births were more likely to have lower birth weights in each quantile.

Table 3 presents descriptive statistics of the assigned pollutant exposures over pregnancy windows. The mean and IQR of a particular pollutant were similar across exposure windows. This is likely due to the small seasonal trends in conception dates in our cohort.

Table 4 presents change in birth weight and 95% confidence intervals (CI) per IQR change in pollutant concentrations for all births in five-county Atlanta during various exposure windows and at different quantiles. Estimates are also shown in Figure 1. There were consistent and similar negative associations between IQR changes in CO, EC, NO_2, NO_x, OC, SO_2 and birth weight; there were also weaker negative associations between $PM_{2.5}$ concentrations and birth weight. Among pollutants with consistent negative associations with birth weight, the negative associations were stronger in magnitude during the first and second trimester than the third trimester except for EC. For CO, EC, NO_2, NO_x, the associations were stronger at the 50th and 75th quantiles. Similar associations, but weaker, also apply to SO_2 and $PM_{2.5}$. For OC, its negative associations were similar across quantiles.

Figure 2 shows change in birth weight and 95% CI per IQR change in pollutant concentrations among full-term births only. These results are very similar compared to those in Figure 1 because 94% of the total births were full-term.

Figure 3 shows change in birth weight and 95% CI per IQR change in pollutant among preterm births only. We found that OC showed the strongest consistent negative associations with birth weight quantiles. Several other pollutants (e.g. CO, EC, NO2, NOx, PM10, PM2.5, SO2) also showed significant negative associations at certain quantile levels. The confidence intervals for these estimates are much wider compared to Figures 1 and 2 due to the reduced sample size. However, there is evidence that the decreases in birth weight associated with air pollution were larger among preterm births than full-term births. For example, first-trimester OC exposure was associated with a -20 g (95% CI: -29g, -11g) in the 50th quantile among preterm births, whereas the corresponding estimate among full-term births was -10g (95% CI: -15g, -6g).

DISCUSSION

In this study, we investigated associations between 12 ambient air pollutants and birth weight quantiles in the 5-county Atlanta area. For total births and full-term births, we observed consistent negative associations between pollutants, especially those associated with traffic, and birth weight. A previous study in Beijing reported that increases in $PM_{2.5}$, CO, SO_2 and NO_2 concentrations were associated with decreases in birth weight [11]. Another investigation into relationships between ambient levels of air pollution and birth weight in full-term infants in Atlanta also found that pollutants NO_2, SO_2 and $PM_{2.5}$ were significantly associated with small reductions in birth weight [17]. A historical cohort study from Tehran hospitals showed a significant association between exposure to CO and LBW particularly during the second trimester [18]. Another study evaluating the association between LBW and maternal exposure during pregnancy to traffic related pollutants in São Paulo, Brazil found an unexpected decreased risk of LBW associated with traffic related air pollution [19].

While we observed some associations in the 3rd trimester, the most consistent associations across pollutants and quantiles were for exposures during the first and second trimester. We observed stronger negative associations during the first and second trimesters than third trimester among many pollutants. However, in terms of other studies, maternal exposure to NO_2 was found to be negatively associated with birth weight in the third trimester in a study conducted in Beijing [20]. Ambient levels of NO_2, SO_2 and $PM_{2.5}$ during the third trimester were significantly associated with small reductions in birth weight [17].

Our study has several strengths. First, quantile regression has not been used in large environmental epidemiologic studies for air pollution and reduced birth weight. Second, most previous studies only conducted investigation among full-term births; our study also included preterm births and found evidence of larger impacts among this group.

This study has several limitations. First, exposure measurement error exists when assigning air pollution levels to individual pregnancies and the fused air pollutant estimates contain uncertainties. However, by restricting our analysis to the 5-county area where at least one monitor is present for each pollutant, we attempted to reduce this source of exposure measurement error. Maternal residential mobility is also a concern, as residence at the time of delivery was used to assign pollutant levels throughout pregnancy. However, a recent study has shown that consideration for maternal residential mobility in exposure assignment does not result in substantive differences in risk estimates [21]. Exposure measurement error may also arise from uncertainty in gestational age estimates. For example, we estimated conception dates based on reported last menstrual period and gestational age, and error in conception date will influence the daily pollutant concentrations used to calculate average exposure across the trimester windows and overall pregnancy. Gestational weeks were also used as a confounder in the health model and to define preterm births. Second, effect modification was not assessed in this study, which may offer important insights via identifying potential vulnerable populations to air pollution exposure.

REFERENCES

[1] "Disorders of Newborn Related to Short Gestation and Low Birth Weight, Not Elsewhere Classified P07-." Accessed April 02, 2016. http://www.icd10data.com/ICD10CM/Codes/P00-P96/P05-P08/P07-.

[2] Stevens-Simon, Catherine, and Miriam Orleans. "Low-Birthweight Prevention Programs: The Enigma of Failure." Birth 26, no. 3 (1999): 184-91.

[3] Andrews, K. M., D. B. Brouillette, and R. T. Brouillette. "Mortality, Infant." Encyclopedia of Infant and Early Childhood Development, 2008, 343-59. Accessed February 18, 2008.

[4] Norton, M. "New Evidence on Birth Spacing: Promising Findings for Improving Newborn, Infant, Child, and Maternal Health." International Journal of Gynecology & Obstetrics 89 (2005).

[5] "Labor and Delivery - Low Birth Weight." Accessed October 22, 2008. Umm.edu.

[6] Stieb, David M., Li Chen, Maysoon Eshoul, and Stan Judek. "Ambient Air Pollution, Birth Weight and Preterm Birth: A Systematic Review and Meta-analysis." Environmental Research 117 (2012): 100-11.

[7] Dadvand, Payam, Jennifer Parker, Michelle L. Bell, Matteo Bonzini, Michael Brauer, Lyndsey A. Darrow, Ulrike Gehring, Svetlana V. Glinianaia, Nelson Gouveia, Eun-Hee Ha, Jong Han Leem, Edith H. Van Den Hooven, Bin Jalaludin, Bill M. Jesdale, Johanna Lepeule, Rachel Morello-Frosch, Geoffrey G. Morgan, Angela Cecilia Pesatori, Frank H. Pierik, Tanja Pless-Mulloli, David Q. Rich, Sheela Sathyanarayana, Juhee Seo, Rémy Slama, Matthew Strickland, Lillian Tamburic, Daniel Wartenberg, Mark J. Nieuwenhuijsen, and Tracey J. Woodruff. "Maternal Exposure to Particulate Air Pollution and Term Birth Weight: A Multi-Country Evaluation of Effect and Heterogeneity." Environ. Health Perspect. Environmental Health Perspectives 121, no. 3 (2013): 267-373.

[8] Amegah, Adeladza K., Reginald Quansah, and Jouni J. K. Jaakkola. "Household Air Pollution from Solid Fuel Use and Risk of Adverse Pregnancy Outcomes: A Systematic Review and Meta-Analysis of the Empirical Evidence." PLoS ONE 9, no. 12 (2014).

[9] Sun, Xiaoli, Xiping Luo, Chunmei Zhao, Bo Zhang, Jun Tao, Zuyao Yang, Wenjun Ma, and Tao Liu. "The Associations between Birth Weight and Exposure to Fine Particulate Matter (PM2.5) and Its Chemical Constituents during Pregnancy: A Meta-analysis." Environmental Pollution 211 (2016): 38-47.

[10] Wylie, Blair J., Yahya Kishashu, Emmanuel Matechi, Zheng Zhou, Brent Coull, Ajibola Ibraheem Abioye, Kathie L. Dionisio, Ferdinand Mugusi, Zul Premji, Wafaie Fawzi, Russ Hauser, and Majid Ezzati. "Maternal Exposure to Carbon Monoxide and Fine Particulate Matter during Pregnancy in an Urban Tanzanian Cohort." Indoor Air, 2016.

[11] Rich, David Q., Kaibo Liu, Jinliang Zhang, Sally W. Thurston, Timothy P. Stevens, Ying Pan, Cathleen Kane, Barry Weinberger, Pamela Ohman-Strickland, Tracey J. Woodruff, Xiaoli Duan, Vanessa Assibey-Mensah, and Junfeng Zhang. "Differences in Birth Weight Associated with the 2008 Beijing Olympic Air Pollution Reduction: Results from a Natural Experiment." Environ Health Perspect Environmental Health Perspectives, 2015.

[12] Merklinger-Gruchala, Anna, and Maria Kapiszewska. "Association between PM10 Air Pollution and Birth Weight after Full-term Pregnancy in Krakow City 1995–2009 – Trimester Specificity." Annals of Agricultural and Environmental Medicine Ann Agric Environ Med 22, no. 2 (2015): 265-70.

[13] Santos, Veridiana De Paula, Andréa Paula Peneluppi De Medeiros, Thaiza Agostini Córdoba De Lima, and Luiz Fernando Costa Nascimento. "The Effect of Air Pollutants on Birth Weight in Medium-sized Towns in the State of São Paulo* *Study Conducted at the Department of Medicine of Universidade De Taubaté, Taubaté, SP, Brazil." Revista Paulista De Pediatria (English Edition) 32, no. 4 (2014): 306-12.

[14] Koenker, Roger. Quantile Regression. Cambridge: Cambridge University Press, 2005.

[15] Friberg, Mariel D., Xinxin Zhai, Heather A. Holmes, Howard H. Chang, Matthew J. Strickland, Stefanie Ebelt Sarnat, Paige E. Tolbert, Armistead G. Russell, and James A. Mulholland. "Method for Fusing Observational Data and Chemical Transport Model Simulations To Estimate Spatiotemporally Resolved Ambient Air Pollution." Environmental Science & Technology Environ. Sci. Technol., 2016.

[16] Hao, Hua, Howard H. Chang, Heather A. Holmes, James A. Mulholland, Mitch Klein, Lyndsey A. Darrow, and Matthew J. Strickland. "Air Pollution and Preterm Birth in the U.S. State of Georgia (2002–2006): Associations with Concentrations of 11 Ambient Air Pollutants Estimated by Combining Community Multiscale Air Quality Model (CMAQ) Simulations with Stationary Monitor Measurements." EHP Environmental Health Perspectives, 2015.

[17] Darrow, Lyndsey, Mitch Klein, Adolfo Correa, W. Dana Flanders, Lance Waller, Michele Marcus, Matthew Strickland, and Paige Tolbert. "Ambient Air Pollution and Birth Weight in Full-Term Infants in Atlanta, 1994-2004." Epidemiology 20 (2009).

[18] Araban, M., SS Tavafian, S. Motesaddi, H. Alavimajd, and FA Shokravi. "Air Pollution and Low Birth Weight: A Historical Cohort Study from Tehran." East Mediterr Health J, 556-60, 18, no. 6 (2012). Accessed June 2012.

[19] Habermann, Mateus, and Nelson Gouveia. "Socioeconomic Position and Low Birth Weight among Mothers Exposed to Traffic-Related Air Pollution." PLoS ONE 9, no. 11 (2014).

[20] Huang, Cheng, Catherine Nichols, Yang Liu, Yunping Zhang, Xiaohong Liu, Suhong Gao, Zhiwen Li, and Aiguo Ren. "Ambient Air Pollution and Adverse Birth Outcomes: A Natural Experiment Study." Popul Health Metrics Population Health

Metrics 13, no. 1 (2015).

[21] Pereira, Gavin, Michael B. Bracken, and Michelle L. Bell. "Particulate Air Pollution, Fetal Growth and Gestational Length: The Influence of Residential Mobility in Pregnancy." Environmental Research 147 (2016): 269-74.

Table 1: Maternal characteristics of total, full term and preterm singleton births in five-county Atlanta with an estimated date of conception during 1 January 2002 through 28 February 2006.

Maternal Characteristic	Total Birth (N=189,900) Number (%)	Full Term Birth (N=175,447) Number (%)	Preterm Birth (N=14,453) Number (%)
Poverty levels, mean (SD), % population below poverty line	0.11 (0.11)	0.11(0.11)	0.13 (0.13)
Conception year			
2002	43,566 (22.9%)	40,274 (23.0%)	3,292 (22.8%)
2003	44,358 (23.4%)	41,154 (23.5%)	3,204 (22.2%)
2004	45,585 (24.0%)	42,252 (24.1%)	3,333 (23.1%)
2005	48,216 (25.4%)	44,338 (25.3%)	3,878 (26.8%)
2006	8,175 (4.3%)	7,429 (4.2%)	746 (5.2%)
Conception season			
S1-Jun-Aug	45,097 (23.7%)	41,782 (23.8%)	3,315 (22.9%)
S2-Sept-Nov	46,119 (24.3%)	42,592 (24.3%)	3,527 (24.4%)
S3-Dec-Feb	53,862 (28.4%)	49,771 (28.4%)	4,091 (28.3%)
S4-Mar-May	44,822 (23.6%)	41,302 (23.5%)	3,520 (24.4%)
Maternal age group (years)			
<19	16,089 (8.5%)	14,589 (8.3%)	1,500 (10.4%)
20-24	42,831 (22.6%)	39,293 (22.4%)	3,538 (24.5%)
25-29	50,532 (26.6%)	46,929 (26.7%)	3,603 (24.9%)
30-34	50,216 (26.4%)	46,824 (26.7%)	3,392 (23.5%)
35-39	25,336 (13.3%)	23,346 (13.3%)	1,990 (13.8%)
>40	4,896 (2.6%)	4,466 (2.5%)	430 (3.0%)
Sex			
Female	93,137 (49.0%)	86,334 (49.2%)	6,803 (47.1%)
Male	96,763 (51.0%)	89,113 (50.8%)	7,650 (52.9%)
Education			
Less than 9th grade	16,585 (8.7%)	15,311 (8.7%)	1,274 (8.8%)
9-12th grade	23,913 (12.6%)	21,622 (12.3%)	2,291 (15.9%)
High school or General Education Diploma	47,815 (25.2%)	43,662 (24.9%)	4,153 (28.7%)
Some college or higher	93,254 (49.1%)	87,108 (49.6%)	6,146 (42.5%)
Missing	8,333 (4.4%)	7,744 (4.4%)	589 (4.1%)
Race			
White	64,128 (33.8%)	60,400 (34.4%)	3,728 (25.8%)
Black	70,965 (37.4%)	63,895 (36.4%)	7,070 (48.9%)
Asian	11,804 (6.2%)	11,100 (6.3%)	704 (4.9%)

Hispanic	43,003 (22.6%)	40,052 (22.8%)	2,951 (20.4%)
Reported alcohol use			
Yes	1,288 (0.7%)	173,930 (99.1%)	14,270 (98.7%)
No	188,200 (99.1%)	1,162 (0.7%)	126 (0.9%)
Missing	412 (0.2%)	355 (0.2%)	57 (0.4%)
Reported tobacco use			
Yes	4,903 (2.6%)	170,758 (97.3%)	13,833 (95.7%)
No	184,591 (97.2%)	4,342 (2.5%)	561 (3.9%)
Missing	406 (0.2%)	347 (0.2%)	59 (0.4%)
Gestational weeks			
33	1,165 (0.6%)		1,165 (8.1%)
34	2,152 (1.1%)		2,152 (14.9%)
35	3,756 (2.0%)		3,756 (26.0%)
36	7,380 (3.9%)		7,380 (51.1%)
37	19,613 (10.3%)	19,613 (11.2%)	
38	43,728 (23.0%)	43,728 (24.9%)	
39	53,743 (28.3%)	53,743 (30.6%)	
40	39,609 (20.9%)	39,609 (22.6%)	
41	14,747 (7.8%)	14,747 (8.4%)	
42	4,007 (2.1%)	4,007 (2.3%)	
County			
Clayton	17,142 (9.0%)	15,664 (8.9%)	1,478 (10.2%)
Cobb	38,956 (20.5%)	36524 (20.8%)	2,432 (16.8%)
DeKalb	40,584 (21.4%)	37,259 (21.2%)	3,325 (23.0%)
Fulton	44,578 (23.5%)	40,593 (23.1%)	3,985 (27.6%)
Gwinnett	48,640 (25.6%)	45,407 (25.9%)	3,233 (22.4%)
Married			
Yes	115,935 (61.05%)	108,477 (61.83%)	7,458 (51.60%)
No	73,943 (38.94%)	66,949 (38.16%)	6,994 (48.39%)
Missing	22 (0.01%)	21 (0.01%)	1 (0.01%)

Table 2. Mean birth weight of total, full term and preterm singleton births in five-county Atlanta in different quantiles (Unit: grams).

Birthweight Quantile	Total Birth	Full Term Birth	Preterm Birth
5%	2236.64	2422.135	1614.518
25%	2803.192	2878.011	2157.389
50%	3154.998	3195.966	2557.773
75%	3453.485	3481.34	2898.958
95%	3811.046	3837.87	3309.874

Table 3. Descriptive statistics of the assigned pollutant values in the five-county cohort.

Pollutant (unit)	Trimester	Mean (SD)	IQR
CO (ppm)	T1	0.83 (0.22)	0.29
	T2	0.81 (0.21)	0.28
	T3	0.81 (0.22)	0.29
	Total	0.82 (0.18)	0.24
EC (μg/m^3)	T1	1.27 (0.28)	0.37
	T2	1.26 (0.28)	0.38
	T3	1.27 (0.29)	0.39
	Total	1.26 (0.21)	0.26
NH_4 (μg/m^3)	T1	1.49 (0.41)	0.72
	T2	1.53 (0.41)	0.75
	T3	1.56 (0.46)	0.83
	Total	1.52 (0.17)	0.28
NO_2 (ppb)	T1	26.53 (6.20)	8.46
	T2	26.31 (6.16)	8.36
	T3	26.19 (6.27)	8.61
	Total	26.35 (5.44)	7.06
NO_3 (μg/m^3)	T1	0.71 (0.37)	0.63
	T2	0.68 (0.37)	0.62
	T3	0.67 (0.39)	0.66
	Total	0.69 (0.17)	0.25
NO_x (ppb)	T1	0.06 (0.02)	0.03
	T2	0.06 (0.02)	0.03
	T3	0.06 (0.03)	0.03
	Total	0.06 (0.02)	0.02
OC (μg/m^3)	T1	3.09 (0.35)	0.51
	T2	3.10 (0.35)	0.52
	T3	3.09 (0.38)	0.56
	Total	3.10 (0.25)	0.30
O_3 (ppb)	T1	0.04 (0.01)	0.02
	T2	0.04 (0.01)	0.02
	T3	0.04 (0.01)	0.02
	Total	0.04 (0.01)	0.01
PM_{10} (μg/m^3)	T1	22.03 (4.41)	7.04
	T2	22.73 (4.64)	7.59
	T3	23.16 (5.29)	8.62
	Total	22.61 (2.16)	3.37
PM_{25} (μg/m^3)	T1	15.85 (2.88)	4.75
	T2	16.21 (2.95)	4.96
	T3	16.40 (3.28)	5.47
	Total	16.14 (1.29)	2.01
SO_2 (ppb)	T1	11.20 (3.10)	4.09
	T2	11.11 (3.00)	3.99
	T3	11.24 (3.11)	4.14
	Total	11.18 (2.39)	3.22
SO_4 (μg/m^3)	T1	4.72 (1.77)	3.43
	T2	4.86 (1.78)	3.50

	T3	4.92 (1.90)	3.65
	Total	4.83 (0.74)	1.29

Table 4. Change in birth weight and 95% confidence intervals (CI) per IQR change in pollutant for total births in five-county Atlanta

		5%			25%			50%			75%			95%		
Pollutant	Trimester	Estimate	Lower 95% CI	Upper 95% CI	Estimate	Lower 95% CI	Upper 95% CI	Estimate	Lower 95% CI	Upper 95% CI	Estimate	Lower 95% CI	Upper 95% CI	Estimate	Lower 95% CI	Upper 95% CI
CO	T1	-5.3	-12.8	2.3	-11.1	-15.9	-6.3	-14.9	-19.5	-10.3	-15.9	-21.3	-10.5	-9.1	-18.9	0.7
	T2	-6.7	-14.5	1.1	-8.9	-13.6	-4.1	-7.5	-12.1	-2.9	-11.2	-16.6	-5.8	-14.8	-24.6	-4.9
	T3	-3.0	-10.6	4.5	-5.0	-9.7	-0.2	-5.4	-9.9	-0.8	-7.8	-13.0	-2.5	-6.3	-15.9	3.4
	Total	-5.6	-13.0	1.8	-9.1	-13.6	-4.5	-10.0	-14.4	-5.6	-12.9	-18.0	-7.8	-10.7	-19.8	-1.6
EC	T1	-8.3	-16.0	-0.5	-13.0	-17.7	-8.3	-13.9	-18.4	-9.3	-17.7	-23.0	-12.4	-12.9	-22.7	-3.1
	T2	-2.3	-10.0	5.3	-8.4	-13.3	-3.6	-8.7	-13.3	-4.2	-12.8	-18.1	-7.5	-17.2	-26.9	-7.5
	T3	-7.9	-15.4	-0.3	-7.6	-12.4	-2.8	-8.2	-12.7	-3.7	-11.7	-17.0	-6.3	-10.2	-19.7	-0.7
	Total	-6.2	-12.6	0.2	-9.8	-13.8	-5.8	-10.1	-13.9	-6.4	-14.2	-18.7	-9.8	-13.1	-21.2	-5.0
NH_4	T1	1.8	-13.3	16.8	-2.7	-12.0	6.5	0.6	-8.4	9.6	0.3	-10.1	10.8	-9.4	-27.9	9.1
	T2	2.8	-12.0	17.7	-0.3	-10.0	9.4	-5.2	-14.5	4.0	-4.5	-15.4	6.4	-4.8	-24.7	15.0
	T3	-2.6	-15.9	10.7	-2.7	-11.5	6.1	-7.0	-15.4	1.3	-8.0	-17.8	1.9	-5.0	-22.7	12.6
	Total	1.6	-11.0	14.1	-4.5	-12.7	3.6	-8.5	-16.1	-0.9	-9.1	-18.2	0.1	-13.9	-30.4	2.5
NO_2	T1	-10.1	-17.8	-2.4	-13.5	-18.3	-8.6	-16.4	-20.9	-11.9	-19.9	-25.2	-14.5	-15.3	-25.0	-5.6
	T2	-8.9	-16.3	-1.5	-10.1	-14.9	-5.3	-12.3	-16.8	-7.9	-17.0	-22.2	-11.8	-14.9	-24.1	-5.7
	T3	-8.3	-15.8	-0.8	-8.2	-13.1	-3.4	-9.1	-13.5	-4.6	-13.5	-18.9	-8.2	-10.5	-19.9	-1.0
	Total	-9.6	-16.6	-2.7	-10.7	-15.1	-6.4	-12.6	-16.6	-8.5	-17.0	-21.8	-12.1	-13.1	-21.6	-4.6
NO_3	T1	-0.9	-14.4	12.6	-3.7	-12.2	4.8	-8.8	-16.9	-0.8	-0.9	-10.6	8.8	1.9	-15.4	19.3

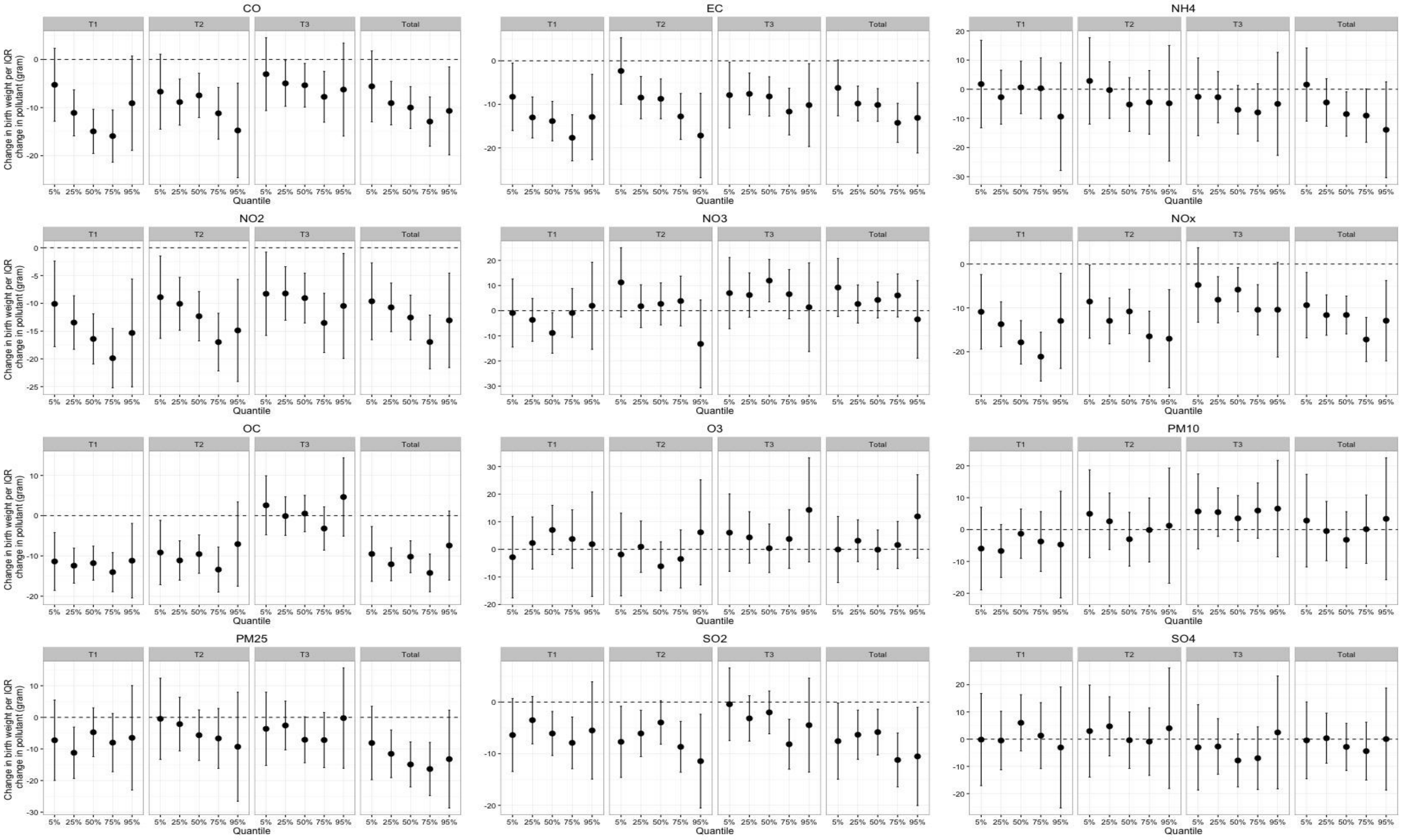
	T2	11.3	-2.5	25.0	1.8	-6.7	10.3	2.7	-5.7	11.1	3.8	-6.1	13.8	-13.2	-30.7	4.3
	T3	7.0	-7.2	21.1	6.2	-2.6	15.0	12.0	3.5	20.4	6.6	-3.2	16.4	1.4	-16.3	19.0
	Total	9.2	-2.3	20.8	2.7	-4.9	10.2	4.3	-2.9	11.4	6.1	-2.5	14.6	-3.4	-18.9	12.0
NO_x	T1	-10.9	-19.4	-2.4	-13.7	-18.8	-8.6	-17.9	-22.8	-12.9	-21.1	-26.7	-15.5	-13.0	-23.8	-2.1
	T2	-8.6	-16.9	-0.2	-13.0	-18.2	-7.7	-10.8	-15.9	-5.8	-16.5	-22.2	-10.8	-17.0	-28.2	-5.8
	T3	-4.8	-13.3	3.7	-8.1	-13.4	-2.9	-5.8	-10.9	-0.8	-10.4	-16.2	-4.7	-10.4	-21.2	0.4
	Total	-9.4	-16.8	-1.9	-11.6	-16.2	-7.0	-11.6	-15.9	-7.3	-17.2	-22.2	-12.2	-12.9	-22.1	-3.8
OC	T1	-11.4	-18.6	-4.2	-12.4	-16.8	-8.1	-11.8	-16.0	-7.6	-14.0	-18.9	-9.2	-11.2	-20.4	-1.9
	T2	-9.2	-17.2	-1.2	-11.1	-16.0	-6.2	-9.5	-14.3	-4.8	-13.4	-19.0	-7.8	-7.1	-17.5	3.4
	T3	2.6	-4.8	9.9	-0.1	-4.9	4.7	0.5	-4.0	5.0	-3.2	-8.6	2.2	4.6	-5.1	14.4
	Total	-9.5	-16.3	-2.7	-12.1	-16.2	-8.0	-10.2	-14.2	-6.2	-14.2	-18.9	-9.5	-7.4	-16.0	1.2
O_3	T1	-2.9	-17.6	11.9	2.3	-7.2	11.7	7.0	-1.9	15.9	3.7	-6.9	14.3	1.9	-17.1	20.8
	T2	-1.9	-16.9	13.1	1.0	-8.4	10.3	-6.1	-15.0	2.7	-3.5	-14.0	7.0	6.2	-12.9	25.2
	T3	6.0	-8.0	20.1	4.3	-5.0	13.6	0.4	-8.4	9.2	3.8	-6.9	14.4	14.3	-4.6	33.1
	Total	-0.1	-12.0	11.9	3.1	-4.5	10.7	-0.1	-7.3	7.0	1.6	-6.9	10.1	11.9	-3.2	27.0
PM_{10}	T1	-6.0	-18.9	7.0	-6.7	-15.0	1.6	-1.3	-9.0	6.5	-3.7	-13.1	5.6	-4.7	-21.4	12.0
	T2	5.0	-8.8	18.7	2.6	-6.3	11.5	-3.0	-11.5	5.4	-0.1	-10.2	9.9	1.2	-16.9	19.3
	T3	5.7	-6.1	17.5	5.5	-2.1	13.1	3.5	-3.6	10.7	6.0	-2.7	14.6	6.6	-8.6	21.7
	Total	2.8	-11.7	17.3	-0.5	-9.8	8.8	-3.2	-12.0	5.6	0.1	-10.6	10.9	3.4	-15.7	22.5
PM_{25}	T1	-7.2	-20.0	5.5	-11.2	-19.4	-3.1	-4.7	-12.4	3.0	-8.0	-17.2	1.2	-6.5	-23.0	10.1
	T2	-0.5	-13.3	12.4	-10.6	-10.6	6.3	-5.7	-13.6	2.3	-6.7	-16.2	2.8	-9.3	-26.6	7.9
	T3	-3.6	-15.2	8.0	-2.6	-10.3	5.1	-7.1	-14.4	0.2	-7.2	-15.9	1.5	-0.2	-16.1	15.6
	Total	-8.1	-19.7	3.5	-11.5	-19.1	-4.0	-14.9	-22.0	-7.8	-16.3	-24.8	-7.9	-13.2	-28.7	2.3
SO_2	T1	-6.4	-13.5	0.7	-3.5	-8.1	1.1	-6.1	-10.4	-1.8	-7.9	-12.9	-2.9	-5.5	-14.9	3.9

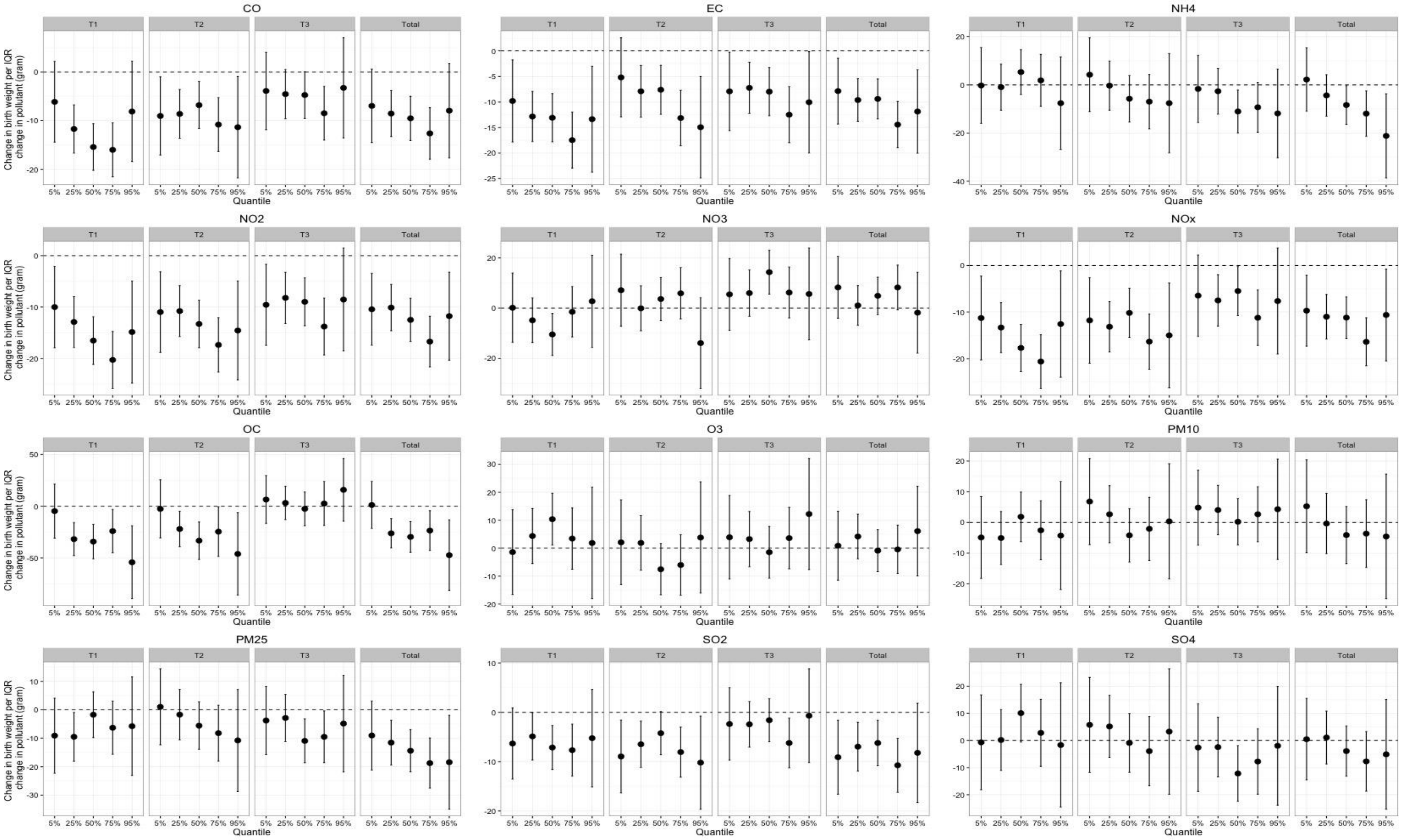
	T2	-7.7	-14.6	-0.8	-6.1	-10.6	-1.6	-4.0	-8.2	0.3	-8.7	-13.6	-3.7	-11.4	-20.5	-2.4
	T3	-0.4	-7.5	6.6	-3.2	-7.6	1.2	-2.0	-6.1	2.1	-8.2	-13.0	-3.3	-4.5	-13.6	4.6
	Total	-7.6	-14.9	-0.2	-6.3	-11.1	-1.6	-5.8	-10.2	-1.4	-11.2	-16.4	-6.0	-10.5	-20.0	-1.0
SO_4	T1	-0.2	-17.1	16.8	-0.5	-11.2	10.2	6.0	-4.3	16.3	1.3	-10.8	13.4	-3.1	-25.3	19.2
	T2	3.0	-13.9	19.9	4.7	-6.2	15.6	-0.4	-10.7	10.0	-0.9	-13.3	11.5	4.0	-18.1	26.1
	T3	-3.0	-18.7	12.7	-2.7	-12.9	7.5	-7.8	-17.5	1.9	-7.0	-18.5	4.5	2.5	-18.2	23.2
	Total	-0.4	-14.5	13.7	0.4	-8.8	9.6	-2.8	-11.5	5.8	-4.4	-15.0	6.2	0.0	-18.7	18.8

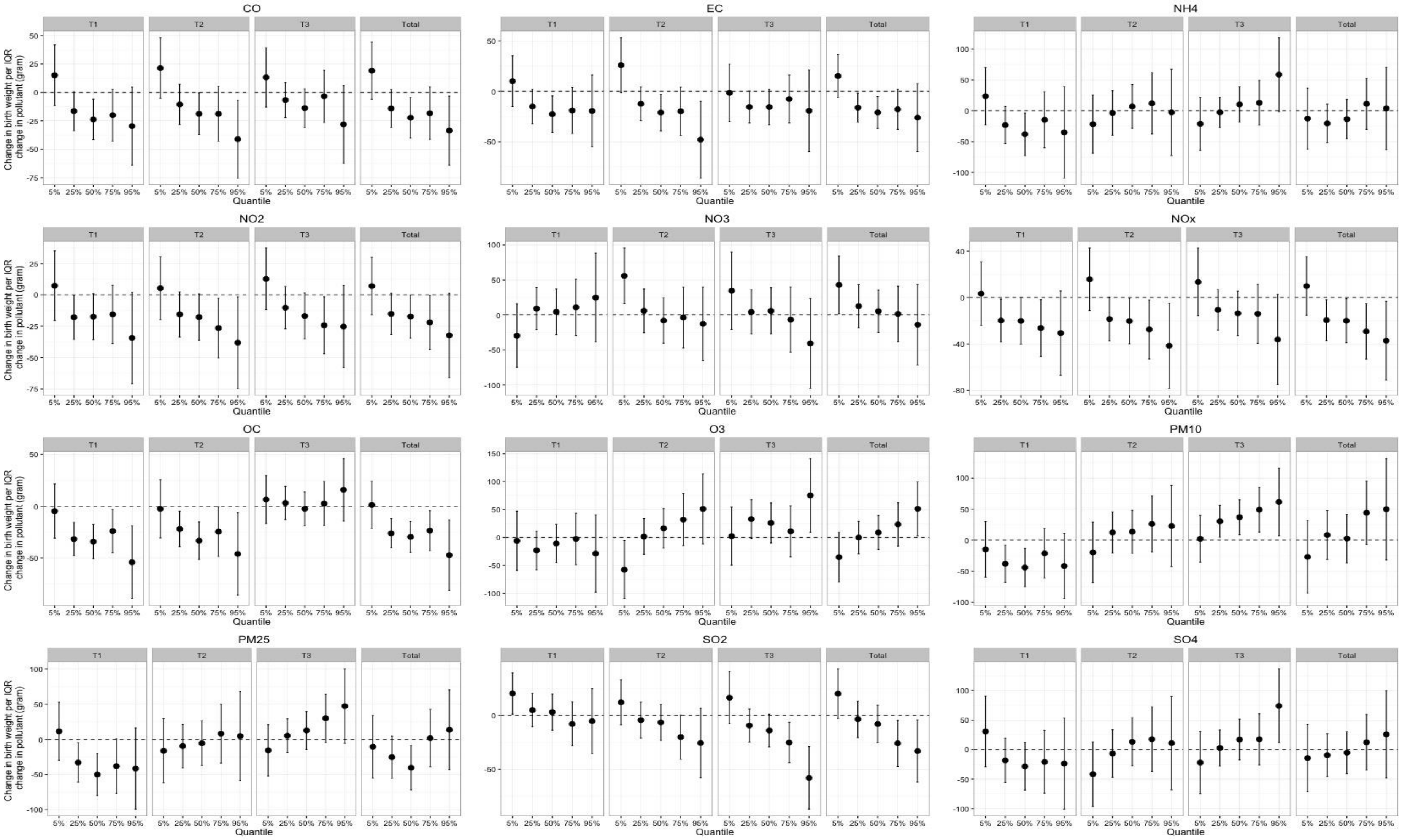
Figure 1: Trimester-specific change in birth weight per interquartile (IQR) change in pollutant for total births in the concentrations of 12 pollutants. Interquartile ranges of each pollutant can be found in Table 3.

Figure 2: Trimester-specific change in birth weight per interquartile (IQR) change in pollutant for full-term births in the concentrations of 12 pollutants. Interquartile ranges of each pollutant can be found in Table S1.

Figure 3: Trimester-specific change in birth weight per interquartile (IQR) change in pollutant for preterm births in the concentrations of 12 pollutants. Interquartile ranges of each pollutant can be found in Table S2.


CO
EC
NH4
NO2
NO3
NOx
OC
O3
PM10
PM25
SO2
SO4
T1
T2
T3
Total
Change in birth weight per IQR change in pollutant (gram)
Quantile
5%
25%
50%
75%
95%


CO
EC
NH4
NO2
NO3
NOx
OC
O3
PM10
PM25
SO2
SO4
T1
T2
T3
Total
Change in birth weight per IQR change in pollutant (gram)
Quantile
5%
25%
50%
75%
95%


CO
EC
NH4
NO2
NO3
NOx
OC
O3
PM10
PM25
SO2
SO4
T1
T2
T3
Total
Change in birth weight per IQR change in pollutant (gram)
Quantile
5%
25%
50%
75%
95%
50
25
0
-25
-50
-75
100
-100
150
40
-40
-80

Supplemental Material, Table S1: Descriptive statistics of the assigned pollutant values in the five-county cohort for full-term births.

Pollutant	Trimester	Mean	SD	IQR
CO	T1	0.83	0.22	0.29
	T2	0.81	0.21	0.29
	T3	0.81	0.22	0.29
	Total	0.82	0.18	0.24
EC	T1	1.27	0.28	0.37
	T2	1.26	0.28	0.38
	T3	1.27	0.29	0.38
	Total	1.26	0.20	0.25
NH_4	T1	1.49	0.41	0.72
	T2	1.53	0.41	0.75
	T3	1.56	0.46	0.83
	Total	1.52	0.17	0.28
NO_2	T1	26.47	6.18	8.44
	T2	26.25	6.13	8.33
	T3	26.13	6.23	8.58
	Total	26.29	5.41	7.03
NO_3	T1	0.71	0.37	0.63
	T2	0.68	0.37	0.62
	T3	0.67	0.39	0.66
	Total	0.69	0.17	0.24
NO_x	T1	0.06	0.02	0.03
	T2	0.06	0.02	0.03
	T3	0.06	0.03	0.03
	Total	0.06	0.02	0.02
OC	T1	3.09	0.35	0.51
	T2	3.10	0.35	0.52
	T3	3.09	0.37	0.56
	Total	3.10	0.25	0.30
O_3	T1	0.04	0.01	0.02
	T2	0.04	0.01	0.02
	T3	0.04	0.01	0.02
	Total	0.04	0.01	0.01
PM_{10}	T1	22.03	4.41	7.05
	T2	22.72	4.64	7.57
	T3	23.16	5.26	8.62
	Total	22.61	2.13	3.32
$PM_{2.5}$	T1	15.85	2.88	4.75
	T2	16.20	2.95	4.95
	T3	16.39	3.26	5.47
	Total	16.13	1.26	1.97
SO_2	T1	11.18	3.10	4.09
	T2	11.10	2.99	3.98
	T3	11.23	3.09	4.12
	Total	11.17	2.38	3.21
SO_4	T1	4.72	1.78	3.43
	T2	4.86	1.78	3.50
	T3	4.92	1.89	3.65

	Total	4.83	0.72	1.27

Supplemental Material, Table S2: Descriptive statistics of the assigned pollutant values in the five-county cohort for preterm births.

Pollutant	Trimester	Mean	SD	IQR
CO	T1	0.84	0.22	0.28
	T2	0.82	0.22	0.29
	T3	0.82	0.22	0.29
	Total	0.83	0.18	0.25
EC	T1	1.28	0.28	0.38
	T2	1.27	0.29	0.39
	T3	1.28	0.31	0.41
	Total	1.28	0.22	0.28
NH_4	T1	1.49	0.41	0.71
	T2	1.54	0.41	0.75
	T3	1.57	0.50	0.86
	Total	1.53	0.21	0.35
NO_2	T1	27.25	6.32	8.76
	T2	27.04	6.40	8.83
	T3	26.96	6.61	9.05
	Total	27.11	5.74	7.57
NO_3	T1	0.71	0.37	0.62
	T2	0.67	0.37	0.62
	T3	0.67	0.41	0.68
	Total	0.69	0.20	0.31
NO_x	T1	0.06	0.03	0.03
	T2	0.06	0.03	0.03
	T3	0.06	0.03	0.04
	Total	0.06	0.02	0.03
OC	T1	3.09	0.36	0.52
	T2	3.11	0.36	0.52
	T3	3.11	0.43	0.63
	Total	3.10	0.26	0.32
O_3	T1	0.04	0.01	0.02
	T2	0.04	0.01	0.02
	T3	0.04	0.01	0.02
	Total	0.04	0.01	0.01
PM_{10}	T1	21.97	4.37	6.94
	T2	22.82	4.72	7.81
	T3	23.27	5.61	8.72
	Total	22.59	2.53	4.23
$PM_{2.5}$	T1	15.85	2.89	4.67
	T2	16.30	3.00	5.05
	T3	16.51	3.54	5.48
	Total	16.17	1.55	2.56
SO_2	T1	11.37	3.15	4.16
	T2	11.26	3.07	4.08
	T3	11.38	3.38	4.46
	Total	11.33	2.49	3.34
SO_4	T1	4.72	1.76	3.41
	T2	4.90	1.78	3.50
	T3	4.96	2.02	3.71

	Total	4.84	0.90	1.64