

### **Original Contribution**

# Ambient Fine Particulate Matter, Nitrogen Dioxide, and Term Birth Weight in New York, New York

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Building on a unique exposure assessment project in New York, New York, we examined the relationship of particulate matter with aerodynamic diameter less than 2.5  $\mu$ m and nitrogen dioxide with birth weight, restricting the population to term births to nonsmokers, along with other restrictions, to isolate the potential impact of air pollution on growth. We included 252,967 births in 2008–2010 identified in vital records, and we assigned exposure at the residential location by using validated models that accounted for spatial and temporal factors. Estimates of association were adjusted for individual and contextual sociodemographic characteristics and season, using linear mixed models to quantify the predicted change in birth weight in grams related to increasing pollution levels. Adjusted estimates for particulate matter with aerodynamic diameter less than 2.5  $\mu$ m indicated that for each 10- $\mu$ g/m<sup>3</sup> increase in exposure, birth weights declined by 18.4, 10.5, 29.7, and 48.4 g for exposures in the first, second, and third trimesters and for the total pregnancy, respectively. Adjusted estimates for nitrogen dioxide indicated that for each 10-ppb increase in exposure, birth weights declined by 14.2, 15.9, 18.0, and 18.0 g for exposures in the first, second, and third trimesters and for the total pregnancy, respectively. These results strongly support the association of urban air pollution exposure with reduced fetal growth.

air pollution; birth weight; nitrogen dioxide; particulate matter; pregnancy

Abbreviations: NYCCAS, New York City Community Air Survey; PM<sub>2.5</sub>, particulate matter with aerodynamic diameter less than 2.5 μm.

Over the past decade, the literature suggesting possible adverse effects of air pollution on pregnancy has grown considerably (1, 2). Air pollution may affect pathways involving oxidative stress and chronic inflammation, which are believed to influence the course and outcome of pregnancy (3). Studies have generated results that support possible adverse effects of particulate matter with aerodynamic diameter less than 2.5  $\mu$ m (PM<sub>2.5</sub>), particulate matter with aerodynamic diameter less than 10  $\mu$ m, nitrogen dioxide, and carbon monoxide on fetal growth, preterm birth, preeclampsia, birth defects, and infant mortality (3, 4). Although the volume and quality of studies have grown considerably, the evidence remains inconclusive.

Several sources of uncertainty limit confidence in the findings (3). Exposure assessment methods are often based on regulatory monitoring data, which lack the spatial resolution to capture intraurban differences in exposure at the neighborhood or individual level. Air pollution levels are often highest in the most socioeconomically deprived areas, and adjustment for confounding by socioeconomic deprivation is incomplete. Definition of health endpoints varies across studies, which hinders attempts at replication. Finally, data analysis is challenging, with multiple candidate time windows for adverse effects, pregnancy duration that spans seasons with varying exposures, and both temporal and spatial determinants of exposure with differing susceptibility to measurement error and confounding.

We report findings on exposures to  $PM_{2.5}$  and nitrogen dioxide and birth weight among term births from a study with uniquely detailed exposure assessment data from the New York City Community Air Survey (NYCCAS) (5). NYCCAS data, which provide far greater spatial resolution than was available in previous birth outcome studies, were linked to individual addresses for a large number of births in a setting where lower socioeconomic status is not associated with higher air pollution exposure, reducing the potential for confounding.

#### MATERIALS AND METHODS

#### Study population

Birth records of 348,585 livebirths to residents of New York, New York, in New York City hospitals during the years 2008–2010 (Figure 1) were available for analysis, excluding the estimated 4% of livebirths to New York residents that occurred at hospitals outside the city of New York. Our interest was in variation in normal fetal growth, so we included only singleton births free of congenital malformations to nonsmoking mothers with 37–42 completed weeks' gestation. We sought a cohort of conceptions in a defined time period that resulted in term livebirths, and therefore excluded births with an estimated date of conception more than 22 weeks before July 31, 2007, or less than 42 weeks after March 12, 2010, to avoid the fixed-cohort bias (6). We also excluded those missing residence information for assigning exposure, those with implausible birth weights (<500 or >5,000 g), and those with missing covariate information (Figure 1). This left 252,967 births for the analysis of air pollution and birth weight.



Figure 1. Population source and exclusions for the study of air pollution and birth weight, New York, New York, 2008–2010.

#### **Exposure assignment**

We used 2 sources of air pollution data to estimate exposures to PM<sub>2.5</sub> and nitrogen dioxide at each mother's address at the birth of her child, 1 to generate a spatial surface of exposure and the other to temporally adjust the spatial estimates to match gestational exposure time windows (7, 8). Briefly, as part of NYCCAS (5, 9), 2-week average concentrations at street level (10–12 feet above the ground; 1 foot = 30.5 cm) of several pollutants, including PM2.5 and nitrogen dioxide, were collected in each of the 4 seasons for the period December 2008 through December 2010. These measurements were used to generate annual averages at the monitoring locations (9). The annual average estimates for December 2008-December 2009 were used to fit spatial models for each pollutant as described below, and data from December 2009-December 2010 were used for validation of the spatiotemporal model.

The approach for development of the spatial component of the exposure models is described in detail elsewhere (9, 10). Briefly, geographic information systems were used to compute variables on emissions and land use within buffer regions around each monitoring location. Each of these variables was tested for inclusion in regression models predicting the annual average pollutant concentrations across the 790 km<sup>2</sup> of the city. The final regression models included the strongest predictor variables and were extended to account for residual spatial autocorrelation using kriging with external drift (11). These models were applied to estimate average pollutant concentrations within 300 m of each maternal address. The spatial exposure surface described above (based on annual average concentrations) was then temporally adjusted to match pregnancy time windows using a citywide time series computed from continuous regulatory monitors. In a validation, the  $R^2$  values for predictions of 2-week average concentrations of PM2.5 and nitrogen dioxide against actual concentrations measured during year 2 at the 150 NYCCAS distributed sites were 0.83 and 0.79, respectively.

#### Birth outcome and covariates

With the restrictions noted above, we considered births in the 37- to 42-week range and examined the impact of air pollution on a continuous measure of birth weight in grams. We considered and adjusted as needed for covariates known or suspected to be associated with birth weight, including maternal age, race/ethnicity (non-Hispanic white, black, Hispanic, Asian, other, or unknown), education (<9, 9–11, 12, 13–15, 16, or >16 years), parity (0, 1, 2, or  $\geq$ 3), gestational age at birth (37, 38, 39, 40, 41, or 42 weeks), and Medicaid status (no/yes), identifying women of low income who qualified for this program. Mothers who reported smoking were excluded from the analysis. We assigned maternal residence according to the 2,140 US Census tracts (mean = 118 births/ tract) and developed a social deprivation index for addressing potential confounding by neighborhood socioeconomic status. We adapted the approach of Messer et al. (12), using principal components analysis to derive a composite index, which included the following 7 contextual variables: percent with college degree, percent unemployment, percent management/professional occupation, percent residential crowding, percent below 200% of the federal poverty line, percent of households receiving public assistance, and percent nonwhite race. We adjusted for year of conception because pollution levels and birth weight varied by year, and we considered adjustment for season and for month of conception in sensitivity analyses.

#### Statistical analysis

Associations between PM<sub>2.5</sub>, nitrogen dioxide, and birth weight. We estimated the associations between  $PM_{2.5}$ , nitrogen dioxide, and birth weight by using linear mixed models with a random intercept for mother's census tract of residence. We considered exposure in the first trimester (weeks 1-12), second trimester (weeks 13-26), and third trimester (weeks 27 and onward) of pregnancy, as well as the average exposure over the entire pregnancy. For each exposure window and each pollutant (PM2.5 and nitrogen dioxide), we considered 3 models that included increasingly extensive sets of covariates, as follows: 1) unadjusted; 2) adjusted for all of the individual-level covariates described above, an indicator of socioeconomic status in the census tract, and a categorical variable for conception year ("routine adjustment model"); and 3) routine adjustment plus average temperature over the exposure window ("fully adjusted model").

Sensitivity analyses. First, because the pollutants' association with birth weight may come from either temporal or spatial components of exposure, we examined the distinct contribution of each component with birth weight. More specifically, we considered exposure derived from the citywide temporal variation alone (the average pollutant concentrations from regulatory monitors during the entire pregnancy and during specific trimesters for each study birth) and exposure derived from spatial variation only (the estimated annual average pollutant concentrations from the NYCCAS spatial model based on the 300-m buffer from maternal address). Second, we considered adjusting PM2.5 and nitrogen dioxide for one another, recognizing that measurement accuracy and temporal versus spatial contributions vary for the 2 pollutants ("2-pollutant model"). Third, we investigated whether the pollutant-birth weight association was nonlinear by fitting penalized spline models (13, 14) for each exposure window and each pollutant. In contrast to our previous sensitivity analysis to adjust for seasonality, which used spline models with fixed degrees of freedom, the penalized spline model used here allows the data to determine the degree of smoothing in order to flexibly estimate the air pollutant-birth weight exposure-response function.

#### RESULTS

#### **Descriptive statistics**

The study population is ethnically diverse, covers a wide range of maternal age and educational levels, and includes few births of less than 2,500 g after restriction to term deliveries (Table 1). The interquartilve range for  $PM_{2.5}$  exposure (Figure 2) ranged from 2.5 µg/m<sup>3</sup> for average exposure over

Characteristic	No.	%
Maternal age years		
<20	16 717	6.6
20-24	52 378	20.7
25_29	67 139	26.5
30-34	66 954	26.5
35_39	38 727	15.3
>40	11 052	13.5
≥40 Maternal ethnicity	11,052	4.4
Non-Hispanic white	70 00/	28.1
Black	54 201	20.1
Hispanic	85 117	21.4
Asian	37 261	14.7
Othor	5 070	2.0
	3,079	2.0
Meternal education years	315	0.1
	00 577	0.1
<9	20,577	0.1
9-11	44,250	17.5
12	60,378	23.9
13-15	55,233	21.8
	41,316	10.3
	31,213	12.3
Parity	117 007	40.0
0	74,000	46.6
	74,638	29.5
2	34,210	13.5
$\geq 3$	26,182	10.4
Season and year of conception	0.404	
Summer 2007 (July–August)	8,461	3.3
Fall 2007 (September–November)	24,615	9.7
Winter 2007/2008 (December–February)	25,211	10.0
Spring 2008 (March-May)	24,575	9.7
Summer 2008 (June–August)	24,002	9.5
Fall 2008 (September–November)	24,318	9.6
Winter 2008/2009 (December–February)	23,858	9.4
Spring 2009 (March–May)	23,697	9.4
Summer 2009 (June–August)	23,200	9.2
Fall 2009 (September–November)	23,791	9.4
Winter 2009/2010 (December–February)	23,973	9.5
Spring 2010 (March)	3,266	1.3
Birth weight, g		
<1,500	94	0.04
1,500–2,499	6,698	2.7
2,500–3,999	228,371	90.3
≥4,000	17,804	7.0
Medicaid		
No	98,789	39.1
Yes	154,178	61.0

 Table 1.
 Demographic Characteristics, Periods of Conception, and

 Birth Weights of the Study Population, New York, New York, 2008–2010

Table 1. Continued

Characteristic	No.	%		
Gestational age (clinical estimate), weeks				
37	20,496	8.1		
38	46,720	18.5		
39	87,358	34.5		
40	74,848	29.6		
41	21,798	8.6		
42	1,747	0.7		

the entire pregnancy to  $3.3 \,\mu\text{g/m}^3$  in the first trimester, whereas the interquartile range for nitrogen dioxide ranged from 6.2 ppb for average exposure over the entire pregnancy to 8.0 ppb in both the first and second trimesters. For each pollutant, PM<sub>2.5</sub> and nitrogen dioxide, higher exposure was correlated with slightly lower census tract–level social deprivation (Pearson's  $\rho$  was approximately –0.1 for each pollutant and each exposure window).

Because of seasonal patterns in air pollution in relationship to the duration of pregnancy, trimester-specific exposures are correlated to varying degrees (Table 2). The seasonality of



**Figure 2.** Change in birth weight in grams per interquartile range (IQR) of particulate matter with aerodynamic diameter less than  $2.5 \,\mu\text{m}$  (PM<sub>2.5</sub>) and nitrogen dioxide with 95% confidence intervals for each exposure time window based on models with the following different degrees of confounder adjustment: unadjusted (triangles), routine adjustment (circles), and fully adjusted (squares), New York, New York, 2008–2010. Corresponding numerical values are in Web Table 1, available at http://aje.oxfordjournals.org/.

Period of Exposure by Pollutant	Period of Exposure to PM <sub>2.5</sub>				Period of Exposure to Nitrogen Dioxide			
	First Trimester	Second Trimester	Third Trimester	All Pregnancy	First Trimester	Second Trimester	Third Trimester	All Pregnancy
PM <sub>2.5</sub>								
First trimester		0.27	0.75	0.84	0.63	0.39	0.61	0.63
Second trimester			0.27	0.66	0.58	0.59	0.40	0.60
Third trimester				0.85	0.62	0.62	0.53	0.69
All pregnancy					0.77	0.69	0.65	0.81
Nitrogen dioxide								
First trimester						0.69	0.46	0.81
Second trimester							0.67	0.92
Third trimester								0.84
All pregnancy								

**Table 2.** Correlation (Pearson's ρ) Between Exposures for PM<sub>2.5</sub> and Nitrogen Dioxide Within the Different Pregnancy Windows, New York, New York, 2008–2010

Abbreviation:  $PM_{2.5}$ , particulate matter with aerodynamic diameter less than 2.5  $\mu$ m.

 $PM_{2.5}$  is bimodal and peaks both in summer and winter (9), and adjacent pregnancy windows were less correlated than the first and third trimesters. In contrast, the seasonality of nitrogen dioxide is monomodal and peaks in winter (9), which leads to higher correlation between adjacent trimesters than between distant trimesters. The correlation (Pearson's  $\rho$ ) between  $PM_{2.5}$  and nitrogen dioxide exposure was 0.63 within the first trimester, 0.59 within the second trimester, 0.53 within the third trimester, and 0.81 for the entire pregnancy.

## Statistical model of the associations between PM<sub>2.5</sub>, nitrogen dioxide, and birth weight

When we considered the covariates alone (Table 3), increasing gestational age was strongly predictive of increased birth weight, and children of black and Asian mothers, younger mothers, less educated mothers, and those who were born in later study years and in more socioeconomically deprived census tracts tended to have lower birth weights. Outdoor temperature and Medicaid status were essentially unrelated to birth weight after adjustment for the other covariates.

Figure 2 shows the estimated association between exposures to PM<sub>2.5</sub> and nitrogen dioxide and birth weight per IQR (Web Table 1, available at http://aje.oxfordjournals. org/, provides the corresponding values). Results are expressed as grams of birth weight per 10-unit change in air pollutant exposure  $(10 \ \mu g/m^3$  for PM<sub>2.5</sub> or 10 ppb for nitrogen dioxide) (Figure 3), as well as per interquartile range change in air pollutant exposure. Before covariate adjustment, pollutant exposure and birth weight were essentially unrelated for nitrogen dioxide and had weakly positive coefficients for PM<sub>2.5</sub> across exposure windows. Adjustment had a substantial impact, primarily due to higher levels of exposure and higher birth weights among non-Hispanic whites, among older mothers, and in earlier calendar years. With or without adjustment for temperature, results indicated that higher PM<sub>2.5</sub> and nitrogen dioxide exposures in all pregnancy windows were associated with lower birth weights. Among the trimester-specific exposure windows, for PM<sub>2.5</sub>, the strongest associations occurred in the first and third trimesters; for nitrogen dioxide, there was a less notable difference in the estimated associations across exposure windows.

#### Sensitivity analyses

Figure 4 compares estimates of the association between pollutant exposure and birth weight, where exposure was assigned based solely on either temporal or spatial variation to estimates from our primary analysis (Figure 3) where exposure was assigned based on both sources of variation (Web Table 2). To aid in the interpretation of health-effect estimates associated with exposures with different degrees of variability, Web Figure 1 shows box plots of the spatial and temporal components for PM<sub>2.5</sub> and nitrogen dioxide. Whereas for nitrogen dioxide, the spatial component exhibited greater variability than the temporal component, for  $PM_{2.5}$  the temporal component was more variable. For PM<sub>2.5</sub>, the associations based on both sources of variation in exposure lie between the estimates based on only spatial or only temporal variation, suggesting that both sources of variability contribute to the PM<sub>2.5</sub> associations. On the other hand, for nitrogen dioxide, the estimates based on both temporal and spatial variation are nearly identical to the estimates based on spatial variation only, providing evidence that the association between nitrogen dioxide and birth weight is driven almost completely by the variation in exposure across mothers' residences and not over time.

When we adjusted the pollutants for one another (2-pollutant model), higher nitrogen dioxide remained independently associated with lower birth weight, whereas  $PM_{2.5}$  was no longer associated with birth weight (except for during the second trimester, in which higher exposure was associated with higher birth weight) (Figure 5).

In sensitivity analyses allowing for a potential nonlinear exposure-response relationship,  $PM_{2.5}$  exhibited no evidence of a nonlinear relationship with birth weight for any of the exposure windows (Web Figure 2). For average nitrogen dioxide exposure over the study period, birth weights decreased

Covariate	Birth Weight, g	95% Cl	
Ethnicity			
Black	-73.3	-79.1, -67.5	
Hispanic	0.7	-4.7, 6.1	
Asian	-105.6	–111.5, –99.7	
Other	-55.8	-67.7, -43.8	
Unknown	-52.7	-98.6, -6.8	
Age, years			
20–24	31.1	23.6, 38.6	
25–29	70.9	63.3, 78.6	
30–34	93.6	85.6, 101.7	
35–39	107.2	98.5, 115.9	
≥40	98.9	88.0, 109.8	
Education, years			
9–11	8.8	1.8, 15.8	
12	12.8	6.0, 19.6	
13–15	29.0	22.0, 36	
16	25.6	17.6, 33.6	
>16	23.7	15.0, 32.4	
Parity			
1	73.4	69.4, 77.3	
2	86.4	81.0, 91.8	
≥3	88.5	82.1, 94.9	
Has Medicaid			
Yes	3.3	-0.9, 7.6	
Gestational age, weeks			
38	198.1	191.3, 204.9	
39	348.0	341.7, 354.3	
40	456.2	449.8, 462.6	
41	590.8	582.8, 598.7	
42	655.2	634.9, 675.5	
Census tract SDI <sup>b</sup>	-3.8	-6.3, -1.3	
Conception year			
2008	-13.6	-19.2, -8.0	
2009	-20.5	-27.6, -13.4	
2010	-33.1	-43.7, -22.4	
Temperature per 10° F <sup>c</sup>	-0.1	-5.8, 5.5	

**Table 3.** Coefficients for Covariates From the Fully Adjusted Model for Total Pregnancy Period, New York, New York, 2008–2010<sup>a</sup>

Abbreviations: CI, confidence interval; SDI, social deprivation index.

<sup>a</sup> Reference categories are as follows: ethnicity, white; age, <20 years; education, <9 years; parity, 0; has Medicaid, no; and conception year, 2007.

<sup>b</sup> SDI was adapted from the approach of Messer et al. (12), using principal components analysis to derive a composite index, which included the following 7 contextual variables: percent with college degree, percent unemployment, percent management/professional occupation, percent residential crowding, percent below 200% of the federal poverty line, percent of households receiving public assistance, and percent nonwhite race.

<sup>c</sup> Average outdoor temperature over the exposure window.

with increasing levels of exposure until approximately 20 ppb, after which they leveled off and remained flat until approximately 35 ppb and then continued to decrease over the remaining range of the data (Web Figure 2). The form of the exposure-response function was similar for the other time windows of nitrogen dioxide exposure.

#### DISCUSSION

Our finding of a relationship between both  $PM_{2.5}$  and nitrogen dioxide in relation to birth weight is consistent with those of some other studies but somewhat greater in magnitude than has typically been reported (2). For comparison, the estimates based on absolute change (per 10 µg/m<sup>3</sup> for PM<sub>2.5</sub> or per 10 ppb for nitrogen dioxide) are most readily compared, because the exposure ranges across studies, and thus the effects of interquartile shifts, are not comparable. Our estimated birth weight effects of PM<sub>2.5</sub> of approximately 20 g for first-trimester exposure, 30 g for third-trimester exposure, and 40 g for total pregnancy exposure per 10 µg/m<sup>3</sup> are broadly in the range observed in some studies (15–20) and much greater than was found in other studies (21–25).

Our findings for nitrogen dioxide suggest a birth weight reduction of approximately 18 g per 10 ppb for exposure in the first or third trimester and for the total pregnancy. These estimates are broadly comparable to some studies (16, 24, 26– 28), much greater than those found in others (8, 29, 30), and markedly weaker than a large but imprecise estimate reported in Valencia, Spain (31).

Some of the differences in estimated effect sizes across studies could be due to the exposure assignment methods used and their spatial resolutions. For example, Kloog et al. (25) estimated  $PM_{2.5}$  exposure on the basis of aerosol optical depth at a 10-km spatial resolution. Our study incorporated information about local emission sources to estimate exposure within 300 m of the maternal address. Among the candidate explanations besides exposure assignment accuracy are particle composition and toxicity, contributions from spatial and temporal variations in pollution, exact definition of the birth weight measure, exclusions, covariates used in adjustment, varying susceptibility to socioeconomic confounding, and analytical methods. The most distinctive features of our study, which potentially resulted in somewhat stronger effects, are the enhanced exposure assessment (i.e., high spatial resolution) from NYCCAS and restriction of the study population to those individuals and outcome measures most purely indicative of growth, excluding births in which pathology caused a reduction in size (e.g., preterm births or congenital defects). On the other hand, the more modest and irregular association of air pollution and socioeconomic status and the exclusion of smokers may well reduce apparent effect size to the extent that incomplete adjustment has affected other studies. A systematic evidence review, which is beyond the scope of this paper, would be needed to draw inferences about which of the many variables related to study setting and design may be responsible for variable findings across studies.



**Figure 3.** Change in birth weight in grams A) per 10 μg/m<sup>3</sup> of particulate matter with aerodynamic diameter less than 2.5 μm, and B) per 10 ppb of nitrogen dioxide with 95% confidence intervals for each exposure time window based on models with the following 3 degrees of confounder adjustment: unadjusted (triangles), routine adjustment (circles), and fully adjusted (squares), New York, New York, 2008–2010. Corresponding numerical values are in Web Table 1, available at http://aje.oxfordjournals.org/.

A major concern for studies of pregnancy is the distinctive contributions of spatial and temporal variations in exposure. A recent multicountry meta-analysis found that studies using temporal assignment found stronger inverse associations of particulate matter and birth weight (32). However, given that the quality of exposure assignment based on these 2 determinants likely differs, and the susceptibility to confounding clearly differs, the observed patterns are not easily interpreted. Comparable effect sizes for the 2 sources for PM2.5 might suggest a causal effect (assuming that mass concentration is the biologically relevant measure of exposure), in that it is highly unlikely that both indices would be confounded by other factors. The isolation of nitrogen dioxide associations to spatial, not temporal, variation may support either a true effect that reflects the more accurate indicators of spatial variation or confounding of 1 or both of the measures. This spatial/temporal distinction is embedded in our attempts to examine mutually adjusted results and makes the predominance of nitrogen dioxide over PM<sub>2.5</sub> of uncertain significance.

fect on a range of health outcomes including birth weight may be modified by its chemical composition, which is related to sources. For example, Bell et al. (23) found that the concentrations of zinc, elemental carbon, silicon, aluminum, vanadium, and nickel were associated with lower birth weight in selected Massachusetts and Connecticut communities, and numerous studies suggest effect modification of cardiovascular and other outcomes by PM<sub>2.5</sub> composition (33). Nitrogen dioxide, which is less influenced by regional sources and has greater spatial variation within New York than does PM<sub>2.5</sub> (5), may be a surrogate for local combustion sources, such as traffic or residual oil combustion, that contribute to spatial variation in PM<sub>2.5</sub> mass (10) and composition within the city. In future studies, we plan to apply PM2.5 chemical speciation data from NYCCAS to develop exposure metrics and assess the association of spatial source and PM2.5 composition differences on birth outcomes. Other pollutants of concern (e.g.,

In this study, we examined only the association with  $PM_{2.5}$ 

mass concentration, whereas the toxicity of PM2.5 and its ef-



**Figure 4.** Change in birth weight in grams A) per 10 μg/m<sup>3</sup> of particulate matter with aerodynamic diameter less than 2.5 μm, and B) per 10 ppb of nitrogen dioxide with 95% confidence intervals for each exposure time window based on the fully adjusted model for the following 3 exposure metrics: temporal variation only (squares), spatial variation only (triangles), and combined temporal and spatial variation (circles), New York, New York, 2008–2010. Corresponding numerical values are in Web Table 1, available at http://aje.oxfordjournals.org/, (combined temporal and spatial variation) and Web Table 2 (temporal variation only and spatial variation only).

carbon monoxide, which was not measured in NYCCAS) were not addressed, and we did not incorporate information on particle constituents in this analysis, but plan to do so later.

As in other studies of this nature, our exposure estimates were limited to the location of the maternal residence, not considering variability due to work and other activities and the nature of housing as it affects indoor/outdoor gradients (which may be especially problematic in New York given the variable height of apartment buildings). Potential confounders that we were not able to address include noise and environmental tobacco smoke. In addition, we know from unpublished analyses of New York City Pregnancy Risk Assessment Monitoring System data that smoking during pregnancy is underreported on birth certificates in New York, as has been previously reported for multiple states (34). Additional limitations include the inability to account for repeat births to the same mother, slightly understating the variance of effect estimates, and the lack of residential history information other than the birth address. There are many potential influences on fetal growth, with only some pathways vulnerable to the adverse effects of air pollution, and we were not able to refine the outcome to isolate those most plausibly affected by eliminating those with known complications affecting fetal growth.

In this large and rapidly expanding research avenue, our results add support to the possible impact of common air pollutants, specifically  $PM_{2.5}$  and nitrogen dioxide, on fetal growth. Although the magnitude of estimated change in birth weight is clinically inconsequential for a given infant, there may be health consequences to a shift in the population birth weight distribution with regard to both near-term health outcomes (e.g., hospital stay, survival) and long-term consequences (e.g., neurodevelopment, cardiovascular risk markers). Additional analyses are needed to determine whether the predicted impacts of a small shift in birth weight on morbidity are identifiable, which are feasible for outcomes such as neonatal intensive care unit admissions and respiratory distress.



**Figure 5.** Change in birth weight in grams A) per  $10 \ \mu g/m^3$  of particulate matter with aerodynamic diameter less than 2.5  $\mu$ m, and B) per 10 ppb of nitrogen dioxide with 95% confidence intervals for each exposure time window based on the 2-pollutant model, New York, New York, 2008–2010. Corresponding numerical values are in Web Table 3, available at http://aje.oxfordjournals.org/.

Careful examination of specific indicators of fetal and infant health is needed, along with refined pollution assessment that considers temporal and spatial contributors, chemical speciation of particulates, and evaluation of pollutant sources. Although the signal relating air pollution to reproductive health is difficult to discern, there is ample encouragement to take the next steps to refine our understanding of its presence and meaning.

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