Environmental Research 142 (2015) 624–632

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Area-level socioeconomic deprivation, nitrogen dioxide exposure, and term birth weight in New York City

Jessie L.C. Shmool [a,*], Jennifer F. Bobb [b], Kazuhiko Ito [c], Beth Elston [d], David A. Savitz [d,e], Zev Ross [f], Thomas D. Matte [c], Sarah Johnson [c], Francesca Dominici [b], Jane E. Clougherty [a]

[a] *Department of Environmental and Occupational Health, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA*
[b] *Department of Biostatistics, Harvard School of Public Health, Boston, MA, USA*
[c] *Bureau of Environmental Surveillance and Policy, New York City Department of Health and Mental Hygiene, New York City, NY, USA*
[d] *Department of Epidemiology, Brown University, Providence, RI, USA*
[e] *Department of Obstetrics and Gynecology, Brown University, Providence, RI, USA*
[f] *ZevRoss Spatial Analysis, Ithaca, NY, USA*

ARTICLE INFO

Article history:
Received 12 May 2015
Received in revised form
12 August 2015
Accepted 17 August 2015

Keywords:
Nitrogen dioxide
Socioeconomic deprivation
Term birth weight

ABSTRACT

Numerous studies have linked air pollution with adverse birth outcomes, but relatively few have examined differential associations across the socioeconomic gradient. To evaluate interaction effects of gestational nitrogen dioxide (NO_2) and area-level socioeconomic deprivation on fetal growth, we used: (1) highly spatially-resolved air pollution data from the New York City Community Air Survey (NYCCAS); and (2) spatially-stratified principle component analysis of census variables previously associated with birth outcomes to define area-level deprivation. New York City (NYC) hospital birth records for years 2008–2010 were restricted to full-term, singleton births to non-smoking mothers ($n=243{,}853$). We used generalized additive mixed models to examine the potentially non-linear interaction of nitrogen dioxide (NO_2) and deprivation categories on birth weight (and estimated linear associations, for comparison), adjusting for individual-level socio-demographic characteristics and sensitivity testing adjustment for co-pollutant exposures. Estimated NO_2 exposures were highest, and most varying, among mothers residing in the most-affluent census tracts, and lowest among mothers residing in mid-range deprivation tracts. In non-linear models, we found an inverse association between NO_2 and birth weight in the least-deprived and most-deprived areas (p-values < 0.001 and 0.05, respectively) but no association in the mid-range of deprivation ($p=0.8$). Likewise, in linear models, a 10 ppb increase in NO_2 was associated with a decrease in birth weight among mothers in the least-deprived and most-deprived areas of -16.2 g (95% CI: -21.9 to -10.5) and -11.0 g (95% CI: -22.8 to 0.9), respectively, and a non-significant change in the mid-range areas [$\beta=0.5$ g (95% CI: -7.7 to 8.7)]. Linear slopes in the most- and least-deprived quartiles differed from the mid-range (reference group) (p-values < 0.001 and 0.09, respectively). The complex patterning in air pollution exposure and deprivation in NYC, however, precludes simple interpretation of interactive effects on birth weight, and highlights the importance of considering differential distributions of air pollution concentrations, and potential differences in susceptibility, across deprivation levels.

1. Introduction

There is considerable attention on the role of prenatal air pollution exposure on adverse birth outcomes (Shah and Balkhair, 2011; Stieb et al., 2012). Despite a growing understanding of the biological mechanisms underlying this association, including systemic oxidative stress (Kannan et al., 2006; Burton and Jauniaux, 2011) and inflammation (Munoz-Suano et al., 2011), epidemiological evidence remains inconclusive. This mixed evidence may be attributable to differing exposure assignment methods and

Abbreviations: ACS, US Census American Community Survey; BMI, body mass index; FPL, Federal Poverty Level; IQR, Inter-Quartile Range; LISA, Local Indicators of Spatial Association; NO_2, Nitrogen Dioxide; NYCCAS, New York City Community Air Survey; PCA, principle component analysis; $PM_{2.5}$, fine particulate matter with aerodynamic diameter < 2.5 μm; SD, standard deviation; SDI, socioeconomic deprivation index; SEP, socioeconomic position; SPARCS, New York State Department of Health Statewide Planning and Research Cooperative System; US, United States

* Corresponence to: Department of Environmental and Occupational Health, University of Pittsburgh Graduate School of Public Health, 100 Technology Dr., Ste. 350, Pittsburgh, PA, USA. Fax: +1 412 624 9361.
E-mail address: jlcshmool@pitt.edu (J.L.C. Shmool).

http://dx.doi.org/10.1016/j.envres.2015.08.019

measurement error (Dadvand et al., 2013), or to varying co-pollutant exposures and adjustment methods (Woodruff et al., 2009). Alternatively, inconsistencies may arise from incomplete adjustment for confounding, or from differential exposure–response relationships across populations. Of particular concern is sufficiently accounting for socioeconomic deprivation, which may be spatially correlated with air pollution (Clark et al., 2014; Tian et al., 2013), and thus may confound measures of association, or may operate synergistically through common biological pathways [e.g., chronic stress-induced inflammation, or dysregulation of immune and endocrine systems (Clougherty and Kubzansky, 2009; Schwartz et al., 2011)].

The need to integrate socioeconomic context and environmental pollution exposures into health research has long been recognized (IOM, 1999; Gee and Payne-Sturges, 2004; Morello-Frosch and Shenassa, 2006), and there is growing attention to the role of multiple exposures and heightened physiologic susceptibility [i.e., allostatic load (McEwen and Seeman, 1999)] in driving health disparities (Nweke et al., 2011; Sexton and Linder, 2011). There is substantial evidence for adverse impacts of area-level deprivation on pregnancy outcomes, even after accounting for individual socioeconomic position (SEP) (Picket and Pearl, 2001; O'Campo et al., 2008; Blumenshine et al.,2010). However, only a few studies have examined differential associations between exposure to air pollution (or traffic-related proxy variables) and fetal growth outcomes across the socioeconomic gradient. Among these studies, results range from no interaction with fine particulate matter (particles with aerodynamic diameter $<2.5\ \mu m^3$, $PM_{2.5}$) or ozone (Gray et al., 2014), to heightened associations with carbon monoxide (CO) and nitrogen dioxide (NO_2) (Morello-Frosch et al., 2010) or distance-weighted traffic density in low-SEP areas (Wilhelm and Ritz, 2003), to heightened associations with residential proximity to highway in high-SEP areas (Généreux et al., 2008). These mixed results may arise from real differences in exposure and/or susceptibility across populations, or from methodological differences (e.g., socioeconomic measures, or pollution exposure assignment). Disentangling the complex relationships between social and environmental exposures requires large and diverse samples, detailed exposure and outcome information, and innovative analytic strategies to address spatial confounding (Ness et al., 2013).

This is the first study, to our knowledge, to consider potential non-linear associations and effect modification between NO_2 and area-level deprivation on term birth weight. Specifically, we used vital records and hospital data covering in New York City (NYC) births 2008–2010 to examine: (1) mutually-adjusted NO_2 and area-level deprivation associations with birth weight and (2) differential associations between NO_2 and birth weight by deprivation levels, adjusted for individual-level SEP and co-occurring $PM_{2.5}$. We focus on fetal growth among term births, which has important lifecourse and population health implications (Barker et al., 2002). To quantify area-level deprivation, we developed a composite index of area-level deprivation, which reflects the spatial heterogeneity of socioeconomic factors across NYC. We build on a study of air pollution and birth outcomes in NYC which was designed to minimize spatial and temporal uncertainty in air pollution exposure estimates in a densely populated city (Ross et al., 2013; Savitz et al., 2014). We previously reported significant associations between fine-scale NO_2 and $PM_{2.5}$ and term birth weight, and observed that variance in exposure estimates were primarily spatial for NO_2 vs. temporal for $PM_{2.5}$ (Savitz et al., 2014). Because our deprivation index does not vary temporally over the study period, we focus here on spatial variation in NO_2 exposures over the entire pregnancy.

2. Methods

2.1. Study population

Vital records for 348,585 live births to mothers residing within the five boroughs of NYC during 2008–2010 were merged with patient-level data from the New York State Department of Health Statewide Planning and Research Cooperative System (SPARCS), covering all licensed NYC healthcare facilities. We restricted the study population to full-term (37–42 weeks gestation), singleton births with no congenital anomalies, born to (self-reported) non-smoking mothers with complete residential address and covariate data, leaving 243,853 births. Exclusion criteria for implausible clinical values and fixed cohort bias (Strand et al., 2011) in this population are detailed elsewhere (Savitz et al., 2014).

2.2. Term birth weight outcome and covariates

We examined changes in term birth weight as a continuous variable. We adjusted for individual-level covariates previously associated with fetal growth, including: maternal age, pre-pregnancy body mass index (BMI), receipt of prenatal care (yes/no), number of previous lives births, and gestational age (in weeks). We included three measures of maternal SEP, including: Medicaid status (yes/no), years of education (<9, 9–11, 12, 13–15, 16, or >16), and race/ethnicity (White, Black, Hispanic, or Asian) cross-classified by United States (US)- or foreign-born status. To account for temporal trends in pollution we adjusted for year and season of conception, as in our prior analysis of this data (Savitz et al., 2014).

2.3. Composite index of area-level socioeconomic deprivation

We adapted Messer et al.'s(2006) area-level deprivation index originally developed to reflect between-city differences in prevalence in, and combinations of, SEP indicators using spatially-stratified principle component analysis (PCA). This effort to capture distinct SEP typologies using cities as spatial regimes, or strata, represented an important methodological innovation, as traditional application of data reduction techniques can obscure heterogeneity in spatial patterns in SEP (Pickett and Pearl, 2001). Here, we adapted this approach to describe intra-urban SEP heterogeneity across NYC census tracts, and propose a geostatistical technique for identifying optimal spatial strata for PCA. Based on Messer et al.'s (2006) literature review of census SEP variables previously associated with birth outcomes, we selected 20 indicators covering multiple domains of deprivation – educational attainment, employment, occupation, housing, poverty, and racial/ethnic composition – from the American Communities Survey (ACS) 2005–2009 five-year estimates, to best match years of air pollution and outcome data (Supplemental Table 1). We used census tracts as our unit of analysis to maximize comparability with other studies of area-level SEP and birth outcomes (Krieger et al., 2003; Janevic et al., 2010), excluding tracts with total residential population fewer than 20 persons ($n=62$ of 2216).

To identify spatial strata which maximized autocorrelation in each tract-level SEP indicator, and minimized correlations between strata, we used Local Indicators of Spatial Association (LISA) statistics to quantify between-tract clustering (Anselin, 1995). More information on the LISA statistic, and our process for identifying boroughs ($n=5$) as the optimal spatial strata, can be found in supplemental materials (Supplemental Fig. 1).

We followed a standard PCA process to reduce the number of highly-correlated variables to the minimum number of uncorrelated components. Specifically, following initial extraction of components and corresponding eigenvalues, we selected the number of components based on eigenvalues >1, Scree plots, and proportion of variance $>5\%$. We then used the rotated (varimax) solution to identify SEP variables that loaded strongly ($>\pm 0.40$) on more than one component, suggesting that the variable captured more than one underlying construct, and could be omitted to increase between-factor differences. After generating a city-wide PCA solution, we repeated the above steps within each borough, to ensure that locally-important variables and relationships, possibly obscured in the city-wide PCA, could be retained and contribute to the final deprivation index. We tallied variables that loaded $>\pm 0.40$ in two or more borough-level PCA solutions, which were then included with those retained by the initial city-wide solution in a second city-wide PCA process.

The final socioeconomic deprivation index (SDI) solution based on census tracts retained seven ACS variables: population rates of residents with a college degree, unemployed, residential crowding, management or professional occupation, below 200% of the Federal Poverty Level (FPL), households receiving public assistance, and non-White racial composition. The first component factor explained 56% of overall variance in retained variables. The initial city-wide solution, in contrast, retained fewer, slightly different variables, and the first component explained only 41% of overall variance (Supplemental Table 1). We operationalized the SDI as tract-level factor scores for the first component of the PCA solution, in keeping with Messer et al. (2006), such that higher scores indicated greater tract-level socioeconomic deprivation (Fig. 1); tract SDI mean score$=0$, standard deviation (SD)$=1$, range -2.33 to 4.01. PCA was implemented in SAS v9 (Cary, NC).

2.4. Air pollution exposure assessment

Fine-scale ambient pollution data from the New York City Community Air Survey (NYCCAS) was used to derive near-residence maternal NO_2 and $PM_{2.5}$ exposure estimates. NYCCAS methods and results are detailed elsewhere (Matte et al., 2013; Clougherty et al., 2013). Briefly, NYCCAS utilized a spatial saturation design to measure multiple air pollutants across 150 locations, repeated across four seasons and over two years. Monitors were positioned at street-level (10–12 feet), and collected integrated two-week samples in each season from December 2008 through December 2010. Prior analyses reported greater spatial variability in NO_2 and greater temporal variability in $PM_{2.5}$ (Clougherty et al., 2013; Savitz et al., 2014). Because our SDI measure used multi-year census variables to maximize precision in spatial variability in SEP (which is not time-varying over the course of study), we focus here on the full-gestation period for NO_2 exposure assessment, and consider co-pollutant adjustment for full-gestation $PM_{2.5}$ in sensitivity analyses.

Births were geocoded to mother's residential address at delivery, and NYCCAS pollution concentration surfaces were used to estimate near-residence exposure as the mean concentration within a 300 m radial buffer. Exposure estimates were then temporally adjusted using regulatory monitoring data to match individual-level gestation periods, as detailed in Ross et al. (2013).

2.5. Statistical analyses

We used generalized additive mixed models to estimate associations between area-level deprivation, maternal air pollution exposure, and term birth weight, allowing for flexible estimation of non-linear exposure–response relationships using penalized splines (Wood, 2003). A random intercept accounted for the clustering of mothers within census tracts. We first considered mutually-adjusted non-linear effects of NO_2 and area-level deprivation (i.e., SDI) on term birth weight, with adjustment for maternal SEP and covariates (Model 1). We then examined differential NO_2-birth weight associations by SDI levels by allowing the smooth relationship between NO_2 and birth weight to differ by quartile of census tract-level SDI (Model 2). Cut-points for three-level SDI categories were set at the 25th and 75th percentiles of factor scores across mothers (-0.46 and 1.03, respectively). We

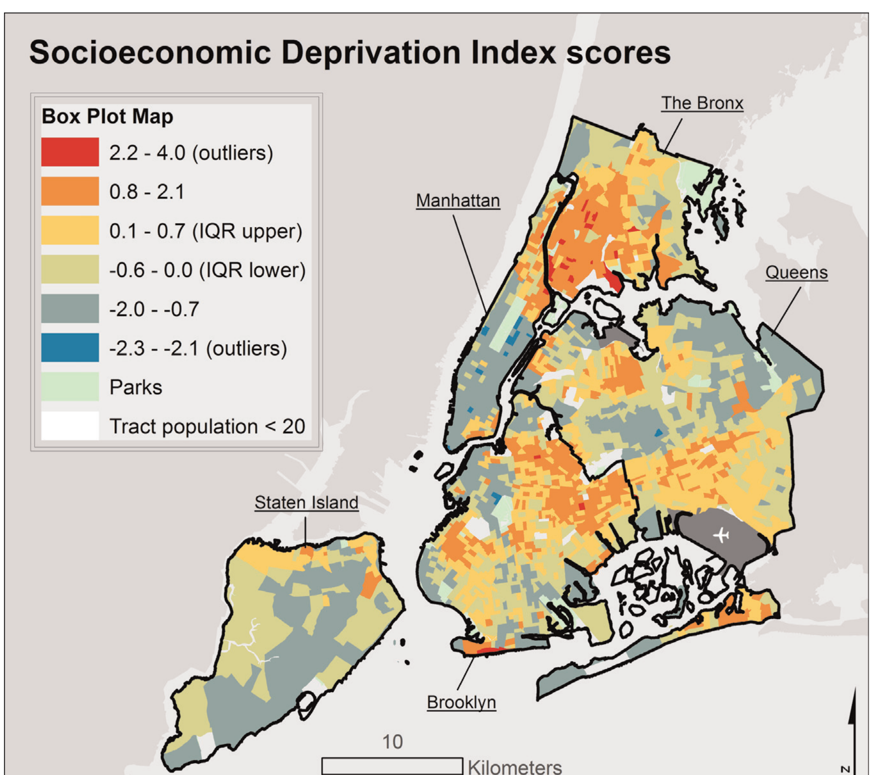

Fig. 1. Socioeconomic deprivation index scores, with higher scores indicating greater census tract-level deprivation.

Table 1
Study population characteristics, by SDI levels.

	Study Population *n=243,853*	High-SEP tracts (SDI Q1) *n=60,963*	Mid-range SEP tracts (SDI Q2+Q3) *n=121,809*	Low-SEP tracts (SDI Q4) *n=61,081*
Term birth weight (g)	% (*n*)	% (*n*)	% (*n*)	% (*n*)
< 1500	0.04 (88)	0.04 (26)	0.03 (32)	0.05 (30)
1500–2499	2.6 (6402)	2.2 (1361)	2.7 (3291)	2.9 (1750)
2500–3999	90.3 (220,156)	90.2 (54,978)	90.3 (110,017)	90.3 (55,161)
≥ 4000	7.1 (17,207)	7.5 (4598)	7.0 (8469)	6.8 (4140)
Maternal SEP	% (*n*)	% (*n*)	% (*n*)	% (*n*)
Education				
< 9 yrs	8.1 (19,731)	2.1 (1300)	8.8 (10,700)	12.7 (7731)
9–11 yrs	17.6 (42,819)	4.3 (2622)	17.8 (21,719)	30.3 (18,487)
12 yrs (High school)	23.9 (58,286)	10.3 (6266)	10.3 (6266)	28.7 (17,476)
13–15 yrs	21.9 (53,376)	16.8 (10,249)	24.9 (30,293)	21.0 (12,825)
16 yrs (BA)	16.3 (39,793)	33.2 (20,213)	13.2 (16,129)	5.7 (3451)
> 16 yrs	12.2 (29,857)	33.3 (20,213)	6.9 (8424)	1.8 (1120)
Medicaid status				
Yes	61.1 (149,106)	23.8 (14,485)	68.6 (83,582)	83.6 (51,039)
No	38.9 (94,747)	86.2 (46,478)	31.4 (38,227)	16.4 (10,042)
Ethnicity				
US-born White	19.4 (47,233)	44.3 (27,021)	14.6 (17,725)	4.1 (2496)
Foreign-born White	9.4 (22,912)	20.3 (12,387)	8.0 (9,763)	1.3 (762)
US-born Black	12.0 (29,339)	2.8 (1732)	13.8 (16,779)	17.7 (10,828)
Foreign-born Black	9.8 (23,856)	2.1 (1295)	13.4 (16,299)	10.3 (6,262)
US-born Hispanic	12.4 (30,346)	6.5 (3974)	11.3 (13,794)	20.6 (12,578)
Foreign-born Hispanic	21.8 (53,248)	7.4 (4529)	21.5 (26,161)	36.9 (22,558)
US-born Asian	1.2 (2899)	2.9 (1783)	0.8 (981)	0.2 (135)
Foreign-born Asian	14.0 (34,020)	13.5 (8251)	16.7 (20,307)	8.9 (5462)
Adjustment covariates	% (*n*)	% (*n*)	% (*n*)	% (*n*)
Maternal age (years)				
< 20	6.6 (16,108)	1.7 (1024)	6.6 (8056)	11.5 (7.028)
20– < 25	20.8 (50,608)	8.1 (4964)	23.4 (28,504)	28.1 (17,140)
25– < 30	26.6 (64,814)	20.0 (12,178)	28.9 (35,145)	28.6 (17,491)
30– < 35	26.4 (64,481)	37.8 (23,062)	24.3 (29,556)	19.4 (11,863)
35– < 40	15.3 (37,246)	25.1 (15,324)	13.2 (16,025)	9.7 (5897)
≥ 40	4.4 (10,596)	7.2 (4411)	3.7 (4523)	2.7 (1662)
Pre-pregnancy BMI				
< 18.5 (Underweight)	5.5 (13,445)	6.4 (4108)	5.3 (6456)	4.7 (2881)
18.5– < 25 (Normal)	54.3 (132,442)	68.7 (41,851)	51.6 (62,810)	45.5 (27,781)
25– < 30 (Overweight)	23.7 (57,842)	16.3 (9929)	25.5 (31,082)	27.6 (16,831)
≥ 30 (Obese)	16.5 (40,124)	8.3 (5075)	17.6 (21,461)	22.3 (13,588)
Prenatal care received				
Yes	99.5 (242,570)	99.6 (60,746)	99.5 (121,156)	99.3 (60,668)
No	0.5 (1283)	0.4 (217)	0.5 (653)	0.7 (413)
Previous live births				
0	46.6 (113,644)	56.3 (34,314)	44.0 (53,582)	42.2 (25,748)
1	29.5 (71,990)	29.3 (17,884)	29.9 (36,356)	29.1 (17,741)
2	13.5 (33,011)	9.4 (5727)	14.3 (17,433)	16.1 (9851)
≥ 3	10.3 (25,208)	5.0 (3038)	11.9 (14,429)	12.7 (7741)
Gestational age (weeks)				
37	8.1 (19,654)	7.0 (4284)	8.6 (10,147)	8.6 (5223)
38	18.5 (44,994)	17.6 (10,727)	18.7 (22,876)	18.7 (11,391)
39	34.5 (84,237)	35.0 (21,319)	34.7 (41,742)	34.7 (21,176)
40	29.6 (72,284)	31.7 (19,288)	28.7 (35,454)	28.7 (17,542)
41	8.6 (21,002)	8.2 (4975)	8.8 (10,569)	8.8 (5368)
42	0.7 (1682)	0.6 (370)	0.8 (931)	0.6 (381)
Conception season				
Dec–Feb	28.8 (70,242)	28.4 (17,305)	29.0 (35,326)	28.8 (17,611)
Mar–May	20.4 (49,686)	20.0 (12,200)	20.4 (24,839)	20.7 (12,647)
Jun–Aug	22.0 (53,670)	22.4 (13,654)	22.0 (26,787)	21.7 (13,229)
Sep–Nov	28.8 (70,255)	29.2 (17,804)	28.6 (34,857)	28.8 (17,594)
Conception year				
2007	16.7 (40,812)	16.8 (10,212)	16.7 (20,292)	16.9 (10,308)
2008	38.7 (94,238)	38.7 (23,562)	38.6 (47,042)	38.7 (23,634)
2009	37.2 (90,615)	37.2 (22,709)	37.2 (45,301)	37.0 (22,605)
2010	7.5 (18,188)	7.4 (4480)	7.5 (9174)	7.4 (4534)
Full-gestation air pollution exposure estimate	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
NO_2 near-residence mean concentration (ppb)	26.8 (5.3)	28.1 (8.0)	25.7 (3.9)	27.8 (3.6)
$PM_{2.5}$ near-residence mean concentration ($\mu g/m^3$)	11.8 (1.9)	12.3 (2.4)	11.3 (1.5)	12.2 (1.7)

also examined the linear interaction between NO_2 with SDI quartiles (Model 3), to quantitatively compare the estimated slopes across the SDI levels. For interaction models, we combined middle-range SDI quartiles (Q2 and Q3) due to similar observed relationships between pollutant exposures and birth weight in these quartiles. Regression models were implemented R statistical software v3.1.0.

2.6. Sensitivity analyses

First, to investigate whether the observed interaction between NO_2 and tract-level SDI was driven by clustering of similar-SEP mothers within a tract, we examined modification of the NO_2-birth weight association by maternal SEP characteristics, adjusted for area-level deprivation. Second, because NO_2 and $PM_{2.5}$ have some common sources, and thus may be spatially confounded, we re-fit all models with adjustment for maternal $PM_{2.5}$ exposure estimates.

This research protocol was approved by Institutional Review Boards at the NYC Department of Health and Mental Hygiene, Brown University and University of Pittsburgh.

3. Results

Mothers in the study population reflected the socio-demographic diversity of NYC (Table 1). Overall, 71.5% of mothers reported fewer than 16 years of education [roughly the equivalent of a college degree (BA)] and 61.1% of deliveries were eligible for Medicaid coverage. Mothers living in least-deprived (high-SEP, SDI Q1) tracts had higher mean educational attainment (33.5% < BA) and lower mean Medicaid eligibility rates (23.8%), compared to mothers living in the most-deprived (low-SEP, SDI Q4) tracts (92.7% < BA, 83.6% Medicaid eligibility). Overall, 55% of mothers were foreign-born, with the highest proportion of non-native mothers reporting Hispanic and Asian ethnicities. Ethnicity varied across SDI levels; more foreign- and US-born White and foreign-born Asian mothers lived in high-SEP tracts (20.3, 44.3, and 13.5%, respectively), versus higher proportions of foreign- and US-born Black and Hispanic mothers in low-SEP tracts (10.3, 17.7, 36.9, and 20.6, respectively). Mothers in high-SEP tracts were generally older, with lower parity, and lower pre-pregnancy BMI, compared to mothers in low-SEP tracts. The majority of mothers across SDI levels received prenatal care (overall 99.5%). Few births were less than 2500 g (2.64%), which were slightly less common (2.24%, $p < 0.001$) among mothers in high-SEP tracts.

Maternal air pollution exposures varied spatially, and by the SDI; the distribution of NO_2 across SDI levels exhibited an inverted J-shaped relationship, with highest, and most variable, exposures in high-SEP tracts forming a negative relationship within SDI Q1, while, in the middle- and lower-SEP tracts (SDI Q2–Q4), NO_2 and SDI showed a weak but positive correlation (Fig. 2). The inter-quartile range for full-gestation maternal NO_2 exposure was 6.25 ppb. NO_2 and $PM_{2.5}$ exposure estimates were correlated [Pearson $\rho = 0.81$ ($p < 0.001$)], and both were weakly inversely correlated with SDI [NO_2 $\rho = -0.12$ ($p < 0.05$), $PM_{2.5}$ $\rho = -0.11$ ($p < 0.05$)].

3.1. Mutually-adjusted associations of SDI and NO_2 with term birth weight

In Model 1, SDI showed a negative linear association with term birth weight, while NO_2 exhibited negative non-linear associations with birth weight (Supplemental Fig. 2), with strongest associations below approximately 20 ppb, flat between 20 and 30 ppb, and a shallow slope above 30 ppb. Gestational age, receipt of prenatal care, pre-pregnancy BMI, maternal age, and maternal education were positively associated with birth weight (Table 2). Offspring of US- and foreign-born Black, US-born Hispanic, and US-and foreign-born Asian mothers had lower average birth weights, as did births in later study years. Medicaid status and conception season did not significantly predict birth weight.

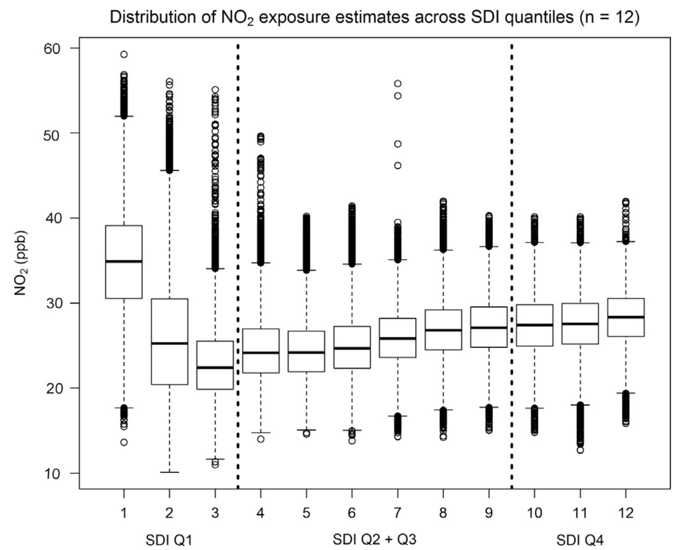

Fig. 2. Maternal NO_2 exposure estimates, by SDI quantiles. The most affluent quartile of tracts (SDI Q1) contains the highest and most varying NO_2 levels.

3.2. Modification of the NO_2-birth weight association by SDI levels

In Model 2, we observed decreasing term birth weight with increasing pollution exposures in the highest- and lowest-SDI quartiles, and a flat association in the middle-range SDI level (Q2+Q3) (Fig. 3). Among high-SEP tracts (SDI Q1), increasing NO_2 below approximately 20 ppb, and above approximately 30 ppb, was associated with lower birth weights (p-value < 0.001). Among lower-SEP tracts (SDI Q4), there was a near-linear negative relationship between NO_2 and birth weights ($p = 0.05$), and no association in the mid-range SDI group (p-value = 0.8).

In Model 3, linear NO_2-birth weight slopes (i.e., birth weight reductions) were −16.2 g (95% CI: −21.9, −10.5), 0.5 g (95% CI: −7.7, 8.7), and −11.0 g (95% CI: −22.7, 0.9) per 10 ppb increase in NO_2, for the lowest, middle, and highest SDI groups (SDI Q1, SDI Q2+Q3, and SDI Q4), respectively. Compared to the mid-range SDI group (reference), p-values for interaction for SDI Q1 and Q4 were < 0.001 and 0.09, respectively. Covariate estimates in Models 2 and 3 were unchanged from Models 1 (Table 2).

3.3. Sensitivity analyses

Tests for modification of the NO_2-birth weight association by individual-level SEP indicators with adjustment for area-level deprivation were null or weak (Supplemental Table 3). We observed no evidence for modification by educational attainment, and modest non-significant modification by Medicaid status; among Medicaid-eligible mothers, each 10 ppb increase in NO_2 conferred a 6.6 g decrement (95% CI: −13.1, −0.1) in birth weight, versus −14.0 g (95% CI: −19.3, −8.7) among non-eligible mothers. Similarly, we observed attenuated NO_2-birth weight associations among foreign-born White and Asian mothers – a 10 ppb increase in NO_2 was associated with birth weight decrements of 4.9 g (95% CI: −14.1, 4.3) and 0.3 g (95% CI: -9.6, 9.0), respectively – versus greater decrements among US-born White and US- and foreign-born Black and Hispanic mothers [−15.8 g (95% CI −22.4,

Table 2
Linear coefficient estimates for change in term birth weight (g) for covariates from Models 1–3.

	Model 1		Model 2		Model 3	
Covariates	**Effect estimate (g)**	**95% CIs**	**Effect estimate (g)**	**95% CIs**	**Effect estimate (g)**	**95% CIs**
Intercept	2773.4	2746.2, 2800.6	2773.2	2746.0, 2800.4	2774.0	2739.2, 2808.7
Ethnicity						
US-born White [REF]	–	–	–	–	–	–
Foreign-born White	5.7	−1.2, 12.6	5.8	−1.1, 12.7	5.2	−1.5, 12.0
US-born Black	−113.8	−121.2, −106.3	−113.3	−120.7, −105.8	−113.8	−121.1, −106.4
Foreign-born Black	−78.5	−86.3, −70.8	−77.9	−85.6, −70.1	−78.6	−86.2, −70.9
US-born Hispanic	−38.2	−45.4, −30.9	−37.9	−45.1, −30.6	−38.3	−45.4, −31.1
Foreign-born Hispanic	−1.4	−8.1, 5.3	−1.0	−7.7, 5.7	−1.6	−8.1, 5.0
US-born Asian	−104.5	−120.3, −88.6	−104.3	−120.2, −88.4	−104.8	−120.4, −89.2
Foreign-born Asian	−87.7	−94.5, −80.8	−87.5	−94.4, −80.7	−88.4	−95.2, −81.7
Maternal education						
< 9 yrs [REF]	–	–	–	–	–	–
9–11 yrs	12.2	10.1, 25.6	12.2	4.9, 19.5	12.2	5.0, 19.4
12 yrs. (High school)	17.5	41.0, 57.1	17.5	10.5, 24.6	17.5	10.7, 24.4
13–15 yrs	34.7	57.2, 74.2	34.8	27.3, 42.2	34.7	27.4, 41.9
16 yrs. (BA)	36.9	66.1, 84.4	37.1	28.8, 45.4	37.1	28.9, 45.2
> 16 yrs	36.1	50.8, 73.6	36.2	27.1, 45.4	36.3	27.3, 45.2
Medicaid status						
No [REF]	–	–	–	–	–	–
Yes	1.5	−3.0, 5.9	1.5	−3.0, 5.9	1.3	−3.1, 5.0
Maternal age (years)						
< 20 [REF]	–	–	–	–	–	–
20– < 25	17.8	10.4, 24.6	17.8	10.0, 25.5	17.7	10.0, 25.3
25– < 30	49.0	27.3, 42.1	48.9	40.8, 56.9	48.9	40.8, 56.9
30– < 35	65.7	28.6, 45.3	65.5	57.1, 74.0	65.7	57.3, 74.2
35– < 40	75.2	27.0, 45.2	75.1	65.9, 84.2	75.2	65.9, 84.2
≥40	62.2	−3.0, 5.9	62.1	50.6, 73.5	62.2	51.0, 73.4
Pre-pregnancy BMI						
< 18.5 (Underweight) [REF]	–	–	–	–	–	–
18.5– < 25 (Normal)	95.3	87.8, 102.8	95.3	87.8, 102.8	95.3	87.9, 102.6
25– < 30 (Overweight)	159.7	151.6, 167.8	159.7	151.6, 167.8	159.7	151.8, 167.6
≥30 (Obese)	215.5	207.0, 224.0	215.5	207.0, 224.0	215.6	207.2, 223.9
Prenatal care received						
No [REF]	–	–	–	–	–	–
Yes	32.2	9.1, 55.2	32.2	9.2, 55.3	32.1	9.5, 54.7
Previous live births						
0 [REF]	–	–	–	–	–	–
1	68.4	64.3, 72.5	68.4	64.3, 72.5	68.3	64.3, 72.4
2	77.2	71.6, 82.8	77.3	71.7, 82.8	77.2	71.7, 82.7
≥ 3	76.9	70.3, 83.5	77.0	70.3, 83.6	76.7	70.2, 83.2
Gestational age (weeks)						
37 [REF]	–	–	–	–	–	–
38	198.8	191.7, 205.8	198.8	191.8, 205.8	198.8	191.9, 205.7
39	347.5	341.0, 354.0	347.5	341.0, 354.1	347.6	341.2, 354.0
40	454.8	448.2, 461.5	454.9	448.3, 461.6	454.9	448.1, 461.4
41	585.9	577.7, 594.1	585.9	577.7, 594.1	585.9	577.7, 594.1
42	648.5	627.6, 669.4	648.7	627.8, 669.7	648.5	628.0, 669.0
Conception season						
Dec–Feb [REF]	–	–	–	–	–	–
Mar–May	1.4	−3.6, 6.4	1.4	−3.6, 6.3	1.5	−3.4, 6.4
Jun–Aug	4.4	−0.6, 9.3	4.2	−0.7, 9.2	4.1	−0.7, 9.0
Sep–Nov	−2.3	−7.1, 2.4	−2.5	−7.2, 2.3	−2.5	−7.2, 2.1
Conception year						
2007 [REF]	–	–	–	–	–	–
2008	−11.7	−16.9, −6.5	−11.4	−16.6, −6.2	−11.3	−16.4, −6.3
2009	−17.8	−23.4, −12.2	−17.3	−23.0, −11.6	−16.8	−22.4, −11.3
2010	−30.4	−38.9, −22.0	−29.8	−38.4, −21.2	−28.7	−37.1, −20.3

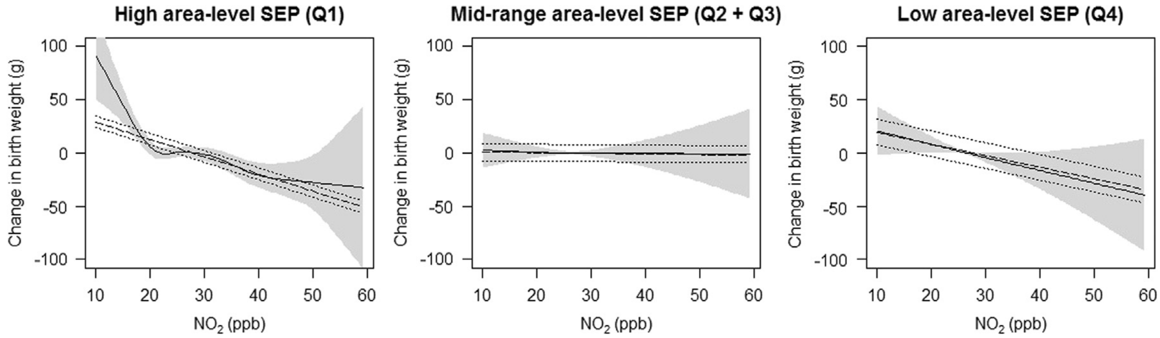

Fig. 3. Exposure–response functions of NO_2 with birth weight, at different levels of area-level SDI, adjusted for maternal SEP and covariates (Models 2 and 3). Shaded areas indicate 95% confidence intervals for non-linear association (Model 2). For comparison, linear slope and 95% confidence intervals in dashed lines (Model 3). Linear NO_2-birth weight slopes (i.e., birth weight reduction) were -16.2 g (95% CI: −21.9, −10.5), 0.5 g (95% CI: −7.7, 8.7), and −11.0 g (95% CI: −22.8, 0.9) per 10 ppb increase in NO_2, for SDI Q1, SDI Q2+Q3, and SDI Q4 groups, respectively.

−9.2); −15.4 g (95% CI: −28.5, −2.3); −16.5 g (−30.1, −2.9); −14.8 g (95% CI: −25.8, −3.8); and −11.6 g (95% CI: −21.2, −2.0), respectively].

Adjusting for $PM_{2.5}$ co-exposures did not change covariate coefficient estimates across all models (Supplemental Table 4). A smooth term for $PM_{2.5}$ added to Model 1 appeared slightly protective above approximately 20 $\mu g/m^3$, but was not statistically significant (Supplemental Fig. 3). In Model 2, adding a smooth term for $PM_{2.5}$ was not statistically significant (p-value$=$0.6), and did not substantively alter the NO_2-SDI interaction result (see Supplemental Fig. 4); non-linear inverse association between NO_2 and birth weight, which was most pronounced in the least-deprived areas, null in the mid-range of deprivation, and inverse (near-significant) among the most-deprived areas (p-values $<$ 0.001, 0.9, and 0.08, respectively). Likewise in Model 3, adding a linear term for $PM_{2.5}$ produced similar NO_2-birth weight slopes (i.e., birth weight reductions): −16.8 g (95% CI: −24.1, −8.0), −0.8 g (95% CI: −10.5, 9.0), and −11.7 g (95% CI: −24.3, 2.4) per 10 ppb increase in NO_2, for the lowest, middle, and highest SDI groups, respectively. Compared to the mid-range SDI group (reference), p-values for interaction for SDI Q1 and Q4 were $<$ 0.001 and 0.08, respectively.

4. Discussion

Our findings indicate complex spatial patterning of air pollution and deprivation in NYC. The non-linear relationship between gestational air pollution exposure and area-level deprivation we observed are consistent with the one other NYC analysis of their joint spatial distribution (Hajat et al., 2013), and echo other studies reporting higher air pollution concentrations in more affluent urban areas of Los Angeles County (Molitor et al., 2011) and Rome, Italy (Forastiere et al., 2007). While the spatial heterogeneity in deprivation and air pollution vary across cities and regions, they appear to be positively correlated in many US cities (Bell and Ebisu, 2012; Miranda et al., 2011; Gray et al., 2014); better understanding their joint distributions may be important for discerning mixed evidence for deprivation as a modifier of the air pollution-birth weight association.

Our interaction results indicate differences in birth weight decrements along different parts of the exposure–response curve, in linear and non-linear models. The relatively steep exposure–response function describing mothers in the most-affluent quartile of census tracts (SDI Q1) may be due to higher average and more variable near-residence pollution exposures among this group. By comparison, the NO_2-birthweight slope was somewhat lower (though not significantly so) in the most-deprived quartile (SDI Q4), where pollution exposures were also lower. Alternately, this differential association by SDI may be due to unmeasured deprivation-related behavioral (e.g., time-activity patterns) or structural factors, potentially associated with both air pollution and birth outcomes. However, the varying distribution of the estimated NO_2 exposures across the SDI gradient raises challenges for interpreting the differences in NO_2-birth weight slopes as "modification," because the observed differences in the slopes may also be due to the difference in NO_2's variance and concentration ranges.

The magnitude of our findings for linear effects of NO_2 on birth weight, across deprivation levels, are comparable to some US studies (Bell et al., 2007; Darrow et al., 2011). Though few studies have examined modification of air pollution effects on birth outcomes by area-level SEP, the majority have found heightened associations in lower-SEP areas (Wilhelm and Ritz 2003; Morello-Frosch et al., 2010; Gray et al. 2014). Specifically, Morello-Frosch et al. (2010) found approximately 13 g decrements, on average, in birth weight per 10 ppb increase in NO_2 among mothers living in census tracts with $\geq$22% of residents living in households with income under the FPL, vs. lesser, but statistically significant, negative associations in areas with 0–22% of residents living in poverty (approximately 6–9 g decrements per 10 ppb NO_2). In comparison to this step-wise exposure–response relationship, we observed similar magnitude decrements in higher-SEP tracts [−16.2 g (95% CI: −21.9, −10.5) per 10 ppb increase in NO_2], but null and weaker effects in mid-range and lower-SEP tracts. Gray et al. (2014) found increased odds of adverse birth outcomes among mothers residing in census tracts with lower mean household income, but found no significant interaction with $PM_{2.5}$ or O_3, potentially due to low variability in modeled air pollution exposures by area-level SEP across North Carolina. In contrast, Généreux et al. (2008) found that closer residential proximity to a highway conferred greater odds of low birth weight only among mothers in the wealthiest areas of Montréal, Canada, though mothers in the poorest areas were more likely to live within 200 m of a highway. Further studies are needed to understand whether these mixed results are a function of locally-specific differences in exposure and/or susceptibility patterns, or to different deprivation metrics and/or air pollution exposure assignment methods.

4.1. Limitations

Though we sought to minimize uncertainty in exposure assignment, our air pollution exposure assessment was limited because near-residence estimates (a) do not encompass daily activities, and (b) assume that the mother maintained the same residential location recorded at the time of birth for the full gestation. Though we tested adjustment for co-pollutant $PM_{2.5}$ exposures, our use of the total mass concentration, instead of specific constituents, may have obscured impacts of key elevated $PM_{2.5}$

constituents in NYC, the spatial distributions of which may not be accurately captured by the total mass distribution [e.g., nickel (NYC DOHMH, 2010)]. Likewise, our area-level deprivation assessment was conducted using census tract units, which may be poor proxies for lived neighborhood spaces (Diez Roux, 2001).

4.2. Strengths

The primary strength of this analysis is our fine-scale, spatially-informed exposure assignment for both air pollution and contextual deprivation. Adapting Morello-Frosch and Shenassa, (2006) method for calculating the socioeconomic deprivation index bolsters comparability with other investigations of area-level deprivation and birth outcomes. Here, we employ spatial regimes for improving accuracy and local-specificity in estimating contextual deprivation, potentially of particular interest in studies of joint effects of social and environmental exposures. Importantly, spatial regimes can be identified and evaluated empirically using geostatistical techniques (e.g., LISA) commonly used in econometrics (Paelinck and Klaassen, 1979; Anselin, 2009), and more recently in air pollution modeling (Sampson et al., 2013). These methods offer promising approaches for environmental health research, especially where exposure–outcome relationships may be heterogeneous across space. Another strength is our consideration of non-linear exposure–response relationships and non-linear interactions, and our comparison to linear models. We adjusted for multiple maternal SEP indicators, and tested whether our observed area-level deprivation modification was driven by compositional, rather than contextual, factors. In keeping with the "ethnic framework" for birth outcomes research (Janevic et al., 2010), we included both maternal ethnicity and nativity (i.e., US-vs. foreign-born).

5. Conclusion

Our findings suggest possible differential associations between air pollution and fetal growth by area-level socioeconomic deprivation, but also illustrate the complexity in determining the "interaction" of these risk factors because of their uneven joint distribution. Spatially-refined exposure assessment and a flexible modeling approach suggest where adverse birth outcomes may arise from disproportionate exposure burdens, or from differential susceptibility to exposures. The apparent role of contextual deprivation impacts, as distinct from individual-level and compositional impacts, reinforces the need to design studies to disentangle which components of area-level deprivation may be driving differential susceptibility, and to elucidate their physiological and/or behavioral mechanisms (Clougherty et al., 2014).

Funding

This research was supported by the National Institute of Environmental Health Sciences (Grant # 1R01ES019955-01 to Brown University) and by the U.S. Environmental Protection Agency (Grant # R834576 to the University of Pittsburgh).

Conflict of interest

The authors declare no competing financial or non-financial interests.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2015.08.019.

References

Anselin, L., 1995. Local indicators of spatial association – LISA. Geogr. Anal. 27, 93–115.
Anselin, L., 2009. Thirty Years of Spatial Econometrics. GeoDa Center for Geospatial Analysis and Computation, Tempe, AZ.
Barker, D.J., Eriksson, J.G., Forsen, T., Osmond, C., 2002. Fetal origins of adult disease: strength of effects and biological basis. Int. J. Epidemiol. 31 (6), 1235–1239.
Bell, M.L., Ebisu, K., Belanger, K., 2007. Ambient air pollution and low birth weight in Connecticut and Massachusetts. Environ. Health Perspect. 115 (7), 1118–1124.
Bell, M.L., Ebisu, K., 2012. Environmental inequality in exposures to airborne particulate matter components in the United States. Environ. Health Perspect. 120 (12), 1699–1704.
Blumenshine, P., Egerter, S., Barclay, C.J., Cubbin, C., Braveman, P., 2010. Socioeconomic disparities in adverse birth outcomes: a systematic review. Am. J. Prev. Med. 39 (3), 263–272.
Burton, G.J., Jauniaux, E., 2011. Oxidative stress. Best Pract. Res. Clin. Obstet. Gynaecol. 25, 287–299.
Clark, L.P., Millet, D.B., Marshall, J.D., 2014. National patterns in environmental injustice and inequality: outdoor NO_2 air pollution in the United States. PLoS One 15 (4), e94431. http://dx.doi.org/10.1371/journal.pone.0094431 9.
Clougherty, J.E., Kubzansky, L.D., 2009. A framework for examining social stress and susceptibility to air pollution in respiratory health. Environ. Health Perspect. 117 (9), 1351–1358.
Clougherty, J.E., Kheirbek, I., Eisl, H.M., Ross, Z., Pezeshki, G., Gorzynski, J.E., et al., 2013. Intra-urban spatial variability in wintertime street-level concentrations of multiple combustion-related air pollutants: the New York City community air survey (NYCCAS). J. Expo Sci. Environ. Epidemiol. 23 (3), 232–240.
Clougherty, J.E., Shmool, J.L.C., Kubzansky, L.D., 2014. The role of non-chemical stressors in mediating the socioeconomic susceptibility to environmental chemicals. Curr. Environ. Health Rep. . http://dx.doi.org/10.1007/s40572-014-0031-y
Dadvand, P., Parker, J., Bell, M.L., Bonzini, M., Brauer, M., Darrow, L.A., et al., 2013. Maternal exposure to particulate air pollution and term birth weight: a multi-country evaluation of effect and heterogeneity. Environ. Health Perspect. 121 (3), 267–373.
Darrow, L.A., Klein, M., Strickland, M.J., et al., 2011. Ambient air pollution and birth weight in full-term infants in Atlanta, 1994–2004. Environ. Health Perspect. 119 (5), 731–737.
Diez Roux, A.V., 2001. Investigating neighborhood and area effects on health. Am. J. Public Health 91 (11), 1783–1789.
Forastiere, F., Stafoggia, M., Tasco, C., Picciotto, S., Agabiti, N., Cesaroni, G., et al., 2007. Socioeconomic status, particulate air pollution and daily mortality: differential exposure or differential susceptibility. Am. J. Ind. Med. 50 (3), 208–216.
Gee, G.C., Payne-Sturges, D.C., 2004. Environmental health disparities: a framework for integrating psychosocial and environmental concepts. Environ. Health Perspect. 112 (17), 1645–1653.
Généreux, M., Auger, N., Goneau, M., Daniel, M., 2008. Neighborhood socioeconomic status, maternal education and adverse birth outcomes among mothers living near highways. J. Epidemiol. Community Health 62 (8), 695–700.
Gray, S.C., Edwards, S.E., Schultz, B.D., Miranda, M.L., 2014. Assessing the impact of race, social factors and air pollution on birth outcomes: a population-based study. Environ. Health 13 (4). http://dx.doi.org/10.1186/1476-069X-13-4.
Hajat, A., Diez-Roux, A.V., Adar, S.D., Auchincloss, A.H., Lovasi, G.S., O'Neill, M.S., Sheppard, L., Kaufman, J.D., 2013. Air pollution and individual and neighborhood socioeconomic status: evidence from the multi-ethnic study of atherosclerosis (MESA). Environ. Health Perspect. 121 (11–12), 1325–1333.
Institute of Medicine (IOM), 1999. Toward Environmental Justice: Research, Education, and Health Policy Needs. The National Academies Press, Washington DC.
Janevic, T., Stein, C.R., Savitz, D.A., Kaufman, J.S., Mason, S.M., Herring, A.H., 2010. Neighborhood deprivation and adverse birth outcomes among diverse ethnic groups. Ann. Epidemiol. 20 (6), 445–451.
Kannan, S., Misra, D.P., Dvonch, J.T., Krishnakumar, A., 2006. Exposures to airborne particulate matter and adverse perinatal outcomes: a biologically plausible mechanistic framework for exploring potential effect modification by nutrition. Environ. Health Perspect. 114 (11), 1636–1641.
Krieger, N., Chen, J.T., Waterman, P.D., Rehkopf, D.H., Subramanian, S.V., 2003. Race/ethnicity, gender, and monitoring socioeconomic gradients in health: a comparison of area-based socioeconomic measures – the public health disparities geocoding project. Am. J. Public Health 93 (10), 1655–1671.
Matte, T.D., Ross, Z., Kheirbek, I., Eisl, H., Johnson, S., Gorczynski, J.E., et al., 2013. Monitoring intraurban spatial patterns of multiple combustion air pollutants in New York City: design and implementation. J. Expo Sci. Environ. Epidemiol. 23 (3), 223–231.
McEwen, B.S., Seeman, T., 1999. Protective and damaging effects of mediators of

stress. Elaborating and testing the concepts of allostasis and allostatic load. Ann. N. Y. Acad. Sci. 896, 30–47.
Messer, L.C., Laraia, B.A., Kaufman, J.S., Eyster, J., Holzman, C., Culhane, J., et al., 2006. The development of a standardized neighborhood deprivation index. J. Urban Health 83 (6), 1041–1062.
Miranda, M.L., Edwards, S.E., Keating, M.H., Paul, C.J., 2011. Making the environmental justice grade: the relative burden of air pollution exposure in the United States. Int. J. Res. Public Health 8 (6), 1755–1771.
Molitor, J., Su, J.G., Molitor, N.T., Rubio, V.T., Richardson, S., Hastie, D., et al., 2011. Identifying vulnerable populations through an examination of the association between multipollutant profiles and poverty. Environ. Sci. Technol. 45 (18), 7754–7760.
Morello-Frosch, R., Shenassa, E.D., 2006. The environmental “riskscape” and social inequality: implications for explaining maternal and child health disparities. Environ. Health Perspect. 114 (8), 1150–1153.
Morello-Frosch, R., Jesdale, B.M., Sadd, J.L., Pastor, M., 2010. Ambient air pollution exposure and full-term birth weight in California. Environ. Health 9 (44), http://dx.doi. org/10.1186/1476-069X-9-44.
Munoz-Suano, A., Hamilton, A.B., Betz, 2011. Gimme shelter: the immune system during pregnancy. Immunol. Rev. 241 (1), 20–38.
Ness, R.B., Bodnar, L., Holzman, C., Platt, R.W., Savitz, D.A., Shaw, G.M., et al., 2013. Thoughts on the future of reproductive and perinatal epidemiology. Pediatr. Perinat. Epidemiol. 27 (1), 11–19.
New York City Department of Health and Mental Hygiene (NYC DOHMH), 2010. New York City Community Air Survey. Nickel Concentrations in Ambient Fine Particles: Winter Monitoring, 2008–2009. New York, NY.
Nweke, O.C., Payne-Sturges, D., Garcia, L., Lee, C., Zenick, H., Grevatt, P., et al., 2011. Symposium on integrating the science of environmental justice into decision-making at the environmental protection agency. Am. J. Public Health 101 (S1), S19–S29.
O'Campo, P., Burke, J.G., Culhane, J., Elo, I.T., Eyster, J., Holzman, C., et al., 2008. Neighborhood deprivation and preterm birth among non-Hispanic Black and White women in eight geographic areas in the United States. Am. J. Epidemiol. 167 (2), 155–163.
Paelinck, J., Klaassen, L., 1979. Spatial Econometrics. Saxon House, Farnborough, England.
Pickett, K.E., Pearl, M., 2001. Multilevel analyses of neighborhood socioeconomic context and health outcomes: a critical review. J. Epidemiol. Community Health 55 (2), 111–122.
Ross, Z., Ito, K., Johnson, S., Yee, M., Pezeshki, G., Clougherty, J.E., et al., 2013. Spatial and temporal estimation of air pollutants in New York City: exposure assignment for use in a birth outcomes study. Environ. Health 12 (51). http://dx.doi.org/10.1186/1476-069X-12-51.
Sampson, P.D., Richards, M., Szpiro, A.A., Bergen, S., Sheppard, L., Larson, T.V., Kaufman, J.D., 2013. A regionalized national universal kriging model using partial least squares regression for estimating annual $PM_{2.5}$ concentrations in epidemiology. Atmos. Environ. 75, 383–392.
Savitz, D.A., Bobb, J.F., Carr, J.L., Clougherty, J.E., Dominici, F., Elston, B., et al., 2014. Ambient fine particulate matter, nitrogen dioxide, and term birth weight in New York, New York. Am. J. Epidemiol. 179 (4), 457–466.
Sexton, K., Linder, S.H., 2011. Cumulative risk assessment for combined health effects from chemical and nonchemical stressors. Am. J.Public Health 101S (1), S81–S88.
Schwartz, J., Bellinger, D., Glass, T., 2011. Exploring potential sources of differential vulnerability and susceptibility in risk from environmental hazards to expand the scope of risk assessment. Am. J. Public Health 101 (Suppl. 1), S94–S101.
Shah, P.S., Balkhair, T., 2011. Knowledge Synthesis Group on Determinants of Preterm/LBW births. Air pollution and birth outcomes: a systematic review. Environ. Int. 37 (2), 498–516.
Stieb, D.M., Chen, L., Eshoul, M., Judek, S., 2012. Ambient air pollution, birth weight and preterm birth: a systematic review and meta-analysis. Environ. Res. 117 (2012), 100–111.
Strand, L.D., Barnett, A.G., Tong, S., 2011. Methodological challenges when estimating the effects of season and seasonal exposures on birth outcomes. BMC Med. Res. Methodol. 11, 49–57.
Tian, N., Xue, J., Barzyk, T.M., 2013. Evaluating socioeconomic and racial differences in traffic-related metrics in the United States using a GIS approach. J. Expos. Sci. Environ. Epidemiol. 23 (2), 215–222.
Wilhelm, M., Ritz, B., 2003. Residential proximity to traffic and adverse birth outcomes in Los Angeles county, California, 1994–1996. Environ. Health Perspect. 111 (2), 207–216.
Wood, S.N., 2003. Thin plate regression splines. J. R. Stat. Soc. B 65 (1), 95–114.
Woodruff, T.J., Parker, J.D., Darrow, L.A., Slama, R., Bell, M., Choi, H., et al., 2009. Methodological issues in studies of air pollution and reproductive health. Environ. Res. 109 (3), 311–320.