

NIH Public Access

Author Manuscript

Epidemiology. Author manuscript; available in PMC 2011 March 11.

Published in final edited form as:

Epidemiology. 2010 November ; 21(6): 884–891. doi:10.1097/EDE.0b013e3181f2f405.

Prenatal Exposure to Fine Particulate Matter and Birth Weight:

Variations by Particulate Constituents and Sources

Michelle L. Bell^a, Kathleen Belanger^b, Keita Ebisu^a, Janneane F. Gent^b, Hyung Joo Lee^c, Petros Koutrakis^c, and Brian P. Leaderer^b

^aYale University, School of Forestry and Environmental Studies, New Haven, CT

^bDepartment of Epidemiology and Public Health, Yale University, School of Medicine, New Haven, CT

^cHarvard University, School of Public Health, Boston, MA

Abstract

Background—Exposure to fine particles ($PM_{2.5}$) during pregnancy has been linked to lower birth weight; however, the chemical composition of $PM_{2.5}$ varies widely. The health effects of $PM_{2.5}$ constituents are unknown.

Methods—We investigated whether $PM_{2.5}$ mass, constituents, and sources are associated with birth weight for term births. $PM_{2.5}$ filters collected in 3 Connecticut counties and 1 Massachusetts county from August 2000 through February 2004 were analyzed for more than 50 elements. Source apportionment was used to estimate daily contributions of $PM_{2.5}$ sources, including traffic, road dust/crustal, oil combustion, salt, and regional (sulfur) sources. Gestational and trimester exposure to $PM_{2.5}$ mass, constituents, and source contributions were examined in relation to birth weight and risk of small-at-term birth (term birth <2500 g) for 76,788 infants.

Results—Road dust and related constituents such as silicon and aluminum were associated with lower birth weight, as were the motor-vehicle-related species such as elemental carbon and zinc, and the oil-combustion-associated elements vanadium and nickel. An interquartile range increase in exposure was associated with low birthweight for zinc (12% increase in risk), elemental carbon (13%), silicon (10%), aluminum (11%), vanadium (8%), and nickel (11%). Analysis by trimester showed effects of third-trimester exposure to elemental carbon, nickel, vanadium, and oil-combustion PM_{2.5}.

Conclusions—Exposures of pregnant women to higher levels of certain $PM_{2.5}$ chemical constituents originating from specific sources are associated with lower birth weight.

Birthweight is a common indicator of fetal health, and low birth weight (LBW) is associated with risk of infant mortality,1 childhood morbidity,1 and diabetes.2 Links between mother's exposure to particulate matter (PM) during pregnancy and birth weight have been observed in numerous epidemiologic studies. Several particle-size distributions have been considered. Exposure to particles with aerodynamic diameter $\leq 2.5 \,\mu$ m (PM_{2.5}) has been associated with lower birth weight in North America (eg, California, Vancouver)^{3–6} and Europe.7 Exposure to particles with aerodynamic diameter $\leq 10 \,\mu$ m (PM₁₀) exhibited similar associations in multiple locations,^{4–6} but not in all areas studied.⁸ Third-trimester PM₁₀ exposure has been

Copyright © 2010 by Lippincott Williams & Wilkins

Correspondence: Michelle L. Bell, Yale University, 195 Prospect St, New Haven, CT 06511. michelle.bell@yale.edu. Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.epidem.com).

associated with lower birth weight in Southern California, but the effect was not robust to adjustment for ozone.⁹ Comparison across studies is hindered by differences in study designs,¹⁰ and the effects of prenatal exposures to particles on fetal growth are still not fully understood.¹¹ However, collectively the results indicate a relationship between exposure to airborne particles during pregnancy and birth weight.

The above-mentioned studies examine particles' total mass although particles' chemical composition varies substantially by season and region.¹² For example, sulfate levels are higher in the Northeast than other US regions. Scientific evidence on which PM sources or chemical constituents have higher toxicity is one of the largest research gaps with respect to PM.¹³ Characterizing the health effects of PM components and sources was identified as a priority by a US National Research Council Committee.¹⁴ Health effects of various PM sources and constituents have been studied primarily for mortality and hospital admissions.^{15,16} To date, few studies have considered PM composition in relation to pregnancy outcomes. Some have investigated traffic-related air pollution more generally, using a traffic measure or indicator as a surrogate of exposure to traffic emissions. Lower birth weight has been linked to residence <50 m from a highway⁴ and to residential distance to major highways.¹⁷ PM_{2.5} absorbance (used to measure black carbon, a marker of traffic-related pollution)⁷ and distance-weighted traffic density18 have been associated with lower birth weight.

We investigated whether exposures to $PM_{2.5}$ sources and elemental constituents were associated with birth weight at term. Our previous work found higher effect estimates for an association between $PM_{2.5}$ and lower birth weight among infants of African-American mothers than among infants of white mothers.⁶ Changes in birth weight may be particularly important for some minorities who are at higher risk of LBW.¹⁹ Therefore, we investigated whether any observed effect estimates differ by race.

METHODS

This research aims to identify which $PM_{2.5}$ constituents or sources are most strongly associated with birth weight. To aid in this goal, we identified which constituents were most associated with specific sources to assist interpretation of estimates for constituents.

Exposure Estimates for PM_{2.5} Sources and Constituents

We estimated exposures for 2 $PM_{2.5}$ exposure metrics: (1) elemental constituent concentrations (eg, nickel) and (2) source contributions (eg, traffic). Certain elements are mostly associated with a single source, and thus these tracer elements ("indicator" constituents) can be used to investigate the toxicity of the respective sources.

Teflon filters from PM_{2.5} regulatory monitors were obtained for the study period (August 2000–February 2004) from the Connecticut and Massachusetts Departments of Environmental Protection. For each location, we identified a primary monitoring site and filters from other sites were used for days missing data from the primary site. eTable 1 (http://links.lww.com/EDE/A423) provides information on primary and supplemental monitoring sites.

 $PM_{2.5}$ filter samples were available for 92%, 90%, 57%, 32%, and 30% of days in the study for Hartford, CT; New Haven, CT; Springfield, MA; Bridgeport, CT; and Danbury, CT, respectively. We used filters to obtain daily levels of $PM_{2.5}$ constituents, which were then used in source-apportionment analysis. Elemental carbon was measured by optical reflectance.^{20,21} Levels of 51 chemical elements were determined by x-ray fluorescence²² Bell et al.

by the Desert Research Institute. $PM_{2.5}$ mass values were obtained from the Connecticut and Massachusetts Departments of Environmental Protection.

Positive matrix factorization²³ was applied to data from each monitor separately to convert daily levels of elemental constituents into daily estimated source profiles and source contributions for motor vehicles, road dust/crustal, oil combustion, salt, and other regional sources. The approach is related to the following mass balance equation:

$$m_{ct} = \sum_{k=1}^{p} f_{ck} S_{kt}$$

where m = level of constituent c for day t

- f = gravimetric concentration as mass of constituent c per mass of PM_{2.5} from source k
- $s = PM_{2.5}$ from source k on day t
- p = number of sources

Positive matrix factorization uses an algorithm²³ to estimate the contribution of $PM_{2.5}$ sources to constituent levels, based on measured constituent data, by solving a matrix form of the above equation:

$$X(n \times j) = G(n \times p)F(p \times j) + E(n \times j)$$

where X is a matrix of measured constituent levels with dimensions of n (number of measurements) $\times j$ (number of chemical species), and E includes residuals. Concentrations and source contributions are constrained as zero or larger. The positive-matrix-factorization approach produces source factors that generally have low correlations with each other. We conducted positive-matrix-factorization models with various numbers of source factors (p), and we evaluated goodness-of-fit through multiple approaches, including the root-mean-squared error of predicted and measured concentrations.

Positive matrix factorization was repeated for each set of monitoring filters from a given location. The method produces estimates of the $PM_{2.5}$ from each source for each day and location, which were then combined to estimate exposure over the gestational period (ie, pregnancy) and each trimester for each study subject. Source-factorization approaches have been applied in other air pollution and health studies.²¹

Analysis of exposures included traffic, oil combustion, road dust, salt, and regional sources. The regional-source factor is dominated by sulfur and likely reflects coal combustion. Constituents used in positive-matrix-factorization analysis included elements that were readily detected by x-ray fluorescence, such as elemental carbon, zinc, lead, copper, bromine (present in the form of bromide), silicon, iron, aluminum, calcium, barium, titanium, sulfur, potassium, vanadium, nickel, sodium, chlorine (present in the form of chloride), and manganese. Daily values for source factor scores for each sampling site were estimated and rescaled to $\mu g/m^3$ units. This method generates a time-series of estimated PM_{2.5} levels from each source. Further information on positive matrix factorization can be found elsewhere.²⁴ Additional information on optical reflectance and x-ray fluorescence are presented in an earlier study,²¹ which used these methods for New Haven County, CT, to examine risk of symptoms and medication use in asthmatic children.

County-average pollutant levels were used to estimate exposure for each study subject. Fairfield County had 2 monitors, located in Bridgeport and Danbury. A population-weighted exposure was calculated using 2000 US Census tract populations. We calculated the distance

from each monitor to the centroid of each of the 209 census tracts, and assigned population from each tract to the closest monitor. Most of the population (74%) lived closer to Bridgeport than Danbury. The largest distance from any point in a county to a monitor in that county (or the midpoint of Bridgeport and Danbury monitors for Fairfield County) was 42.1, 44.6, 44.8, and 45.0 km for New Haven, Fairfield, Hampden, and Hartford Counties, respectively.

Constituents contributing the most to each source factor were identified for each county, based on percentage mass. To identify constituents that are closely linked to particular sources, the distribution of constituents (percentage) in each source was calculated, and each constituent was then assigned to an individual source to which it contributed the highest percentage. We calculated the ratio of the highest percentage contribution to any source to the second highest contribution to identify constituents that were more likely to originate from a specific source. All constituents originate from multiple sources; however, this approach identifies constituents more likely to be from one particular source. Effect estimates for a particular indicator component (eg, nickel) can thereby inform our understanding of PM_{2.5} sources (eg, nickel as indicator of oil combustion), and can be compared with effect estimates from a particular source (eg, oil combustion).

Weather Data

Daily temperature and dew-point temperature data were obtained from the National Climatic Data Center. Previous studies have identified links between temperature and birth weight.²⁵ Apparent temperature for the gestational period and each trimester for each study subject was calculated to represent overall response to temperature,²⁶ and was used as a confounder in models, as applied in earlier work.^{5,6}

Study Subject Data

Birth weight, demographic, and other variables were obtained from birth-certificate data from the National Center for Health Statistics. We based gestational periods on the date of birth and last menstrual period (LMP), corrected for an average 2 weeks between LMP and conception. In the 4 counties, 232,347 births occurred during 1999 and 2000. We eliminated births with missing data for LMP (17%). Of the remaining births, 121,589 (63%) had gestational periods matching our measurement data. We omitted subjects with infeasible delivery dates6 or birth-weight and gestation combinations27 (0.4%). Births were excluded if counties of residence and delivery were not identical or adjacent (1%) or if data for covariates used in analysis were missing (31%). Analysis was restricted to singleton births (excluding 3.4%), term births (gestational period \geq 37 weeks) with gestational period \leq 44 weeks (excluding 8.5%), and those weighing 1000–5500 g (excluding <0.1%). Note that an observation may be omitted for more than one exclusion criteria. The final dataset included 76,788 births. Mother's race was categorized as African-American, white, or other. Analysis of other racial categories (eg, Vietnamese) was not possible due to small sample size.

Data Analysis

Exposure was calculated for each study subject for weather and $PM_{2.5}$ total mass, constituents, and sources by first calculating weekly averages and then combining these values to generate an overall exposure for the pregnancy and trimesters (1–13 weeks, 14–26 weeks, and 27 weeks to birth). This approach avoids bias from differences in sampling frequency. Analysis was conducted separately for $PM_{2.5}$ mass, selected constituents, and sources. Not all study subjects had data available for all pollutant constituents or sources.

Linear regression was performed to relate birth weight to PM_{2.5} total mass, sources, and constituents in separate models. Each model included one of the following as the exposure

variable: a single constituent, single source, or $PM_{2.5}$ total mass. The association between pollutants and risk of small-at-term (term birth <2500 g) compared with non-small-at-term (term birth ≥2500 g) births was estimated with logistic regression. Models adjusted for apparent temperature by trimester; infant's sex; parity (first in birth order, not first in birth order); nature of delivery (vaginal, primary cesarean section, repeat cesarean section); trimester prenatal care began (first, second, or third trimester, no care, unknown); length of gestation in weeks; indicator variables for year of birth; and mother's age (<20, 20–24, 25– 29, 30–34, 35–39, >39 years), marital status (unmarried, married), education (<12, 12, 13– 15, >15 years, or unknown), tobacco use during pregnancy (yes, no), alcohol use during

pregnancy (yes, no), and race (white, African-American, other). Earlier research used similar approaches.^{3,5,6,8,18} Results are presented as the change in birth weight or risk of small-at-term birth per interquartile range (IQR) increase in exposure (source, constituent, or PM_{2.5}).

We repeated the linear analysis with a model that simultaneously included all 3 separate trimester exposure variables, rather than overall gestational exposure. Because trimester exposures can be correlated, we also performed second-stage analysis with adjusted variables of trimester exposure to estimate the association between a given trimester's exposure and birth weight, adjusted for other trimesters' exposures. This method accounts for the correlation among trimester exposures and is described in more detail in our previous studies.⁶

An interaction model was used to investigate whether associations differed by race. Interaction terms were added for pollutant level over the gestational period and indicator variables of mother's race.

RESULTS

After exclusions, 76,788 births were included: 22,911 (30%) in New Haven County, CT; 21,947 (29%) in Hartford County, CT; 25,450 (33%) in Fairfield County, CT; and 6480 (8%) in Hampden County, MA. Table 1 summarizes the study population overall and by county. Mothers were primarily white and married, with a mean age of 29.3 years and 13.8 years of education. Fairfield County had the lowest risk of term LBW, highest fraction of births as a first child, lowest tobacco or alcohol use during pregnancy, highest maternal education, and oldest mothers.

eTable 2 (http://links.lww.com/EDE/A423) provides the largest and second largest constituent contributions to each source from positive-matrix-factorization analysis, for each county. Elemental carbon and sulfur are the main contributors to almost all source factors for almost all counties, comprising an average of 86%–90% of contributions to the motor-vehicle, oil-combustion, and regional-source factors. These constituents comprise an average 56% of the road-dust factor. Chloride and sodium comprise most (61%) of the salt-source factor.

Because of the dominance of a small number of constituents across most sources, we did not identify indicator constituents based on the largest contributor to each source, but rather on constituents that were more closely linked to each source. In other words, for each source, we identified source tracer constituents that most likely originated from that particular source. Whereas eTable 2 shows the main constituents for each source factor, eTable 3 (http://links.lww.com/EDE/A423) shows the main sources resulting from each constituent. Zinc, copper, lead, elemental carbon, bromide, and potassium tended to be associated with the motor-vehicle source more than with any other source. Crustal elements (silicon, aluminum, titanium, manganese, calcium, and iron) and barium mostly originated from the

road-dust-source factor. Vanadium and nickel were most associated with oil combustion, chloride with salt, and sulfur and sodium with the regional-source category. These results were used to identify constituents to function as approximate indicators of source categories, so that associations of PM_{2.5} source exposures and birth weight could be examined.

For each constituent, we calculated the ratio of the highest percentage contribution to a source to the second highest percentage, to identify constituents that are more closely linked to a particular source. For example, the ratio for bromide was 1.6 (= 41.6/26.6) indicating that bromide is about 1.6 times more likely to be in the motor-vehicle-source than the regional-source factor (the sources with the highest and second highest percentage contributions of bromide). Indicator constituents were selected as zinc and elemental carbon for motor vehicles as zinc is about 6 times and elemental carbon 3 times more likely to be in motor vehicle $PM_{2.5}$ than the source with the next highest percentage. Silicon and aluminum were selected for road dust; vanadium and nickel for oil combustion; chloride for salt; and sulfur for the regional-source factor. The selected indicator constituents (ie, those with the highest ratios) were chloride, vanadium, and silicon.

Table 2 summarizes study subject exposures for these selected constituents and source factors. Exposures were highest for the motor-vehicle and regional sources and lowest for salt. Based on the constituents' relative mean standard deviation (standard deviation/mean × 100%), the largest variations in exposures were for chloride and vanadium and the smallest for sulfur and zinc. Based on relative mean standard deviation, the salt factor had the largest variation in exposures of the 5 identified sources, and the regional source factor the lowest. eTable 4 (http://links.lww.com/EDE/A423) shows correlations among gestational exposures to the constituents, with the highest correlation between aluminum and silicon (0.98).

Table 3 shows the association between IQR increase in gestational exposure to $PM_{2.5}$ mass, constituents and sources, and birth weight. For each exposure, separate analyses were performed for a linear model using birth weight as a continuous variable (Table 3, column 3) and a logistic model comparing risk of small-at-term to not small-at-term births (Table 3, column 4). Central estimates indicated a decrease in birth weight and higher risk of small-atterm birth for all sources and constituents except for oil combustion and risk of small-atterm birth. Higher levels of all road-dust indicators (silicon and aluminum) and oilcombustion indicators (vanadium and nickel) were associated with lower birth weight for both models. Higher levels of zinc were associated with lower birth weight and increased risk of small-at-term birth. Elemental carbon was associated with increased risk of small-atterm birth. The linear model results for elemental carbon showed an association with decreased birth weight for the central estimate, although results were imprecise. Higher PM_{2.5} levels from all sources were associated with lower birth weight based on central estimates. All source factors other than oil combustion were associated with higher risk of small-at-term birth in terms of central estimates, although the only strong association was for road dust. The central estimates for PM2.5 total mass indicate that higher levels are associated with lower birth weight, although findings are marginal for the logistic model. Previous work did find such an association,⁶ and the current study's findings may result from lower statistical power.

Table 4 shows associations between trimester exposures to $PM_{2.5}$ sources and constituents and birth weight. Associations were observed in the third trimester for oil combustion, elemental carbon, zinc, nickel, and vanadium. For most exposures, trimester values were not highly correlated (average correlation 0.29), although there were exceptions (elemental carbon correlations among trimesters 0.82–0.90). Using models adjusted for correlation among trimesters' exposures, consistent effects were observed across models in the third trimester for oil combustion, elemental carbon, nickel, and vanadium (Table 4).

Effect modification by race was investigated for pollutants and sources exhibiting associations in the main model (road dust source, zinc, elemental carbon, silicon, aluminum, nickel, and vanadium). Table 5 shows associations between these pollutants or sources and birth weight for infants of African-American mothers and infants of white mothers. For all pollutants, a given increment in exposure had larger associations among infants of African-American mothers (approximately, 35%–100% higher). However, these differences by race did not reach statistical significance for any given pollutant.

DISCUSSION

This study provides one of the first investigations of $PM_{2.5}$ composition and sources and pregnancy outcomes. Decrements in birth weight were related to road dust, oil combustion, and motor vehicles, but not sea salt or regional/sulfur sources. Higher levels of $PM_{2.5}$ from zinc, elemental carbon, silicon, aluminum, vanadium, and nickel were associated with lower birth weight or increased risk of LBW. Third-trimester effects were consistently observed for elemental carbon, nickel, vanadium, and oil combustion. Higher effect estimates for infants of African-American mothers, compared with infants of white mothers, is of particular public health relevance given that this group is at higher risk of lower birth weight.²⁸

Several PM constituents have been linked to health in previous research. Elemental carbon levels were associated with risk of several respiratory symptoms in a cohort of asthmatic children.²¹ PM_{2.5} nickel and vanadium levels were associated with wheeze, whereas elemental carbon levels were associated with cough during the cold and flu season among children 2 years or younger.²⁹ Elemental carbon levels were associated with increased risk of same-day cardiovascular hospital admissions for a Medicare population, but other constituents considered, including sodium and sulfate, were not.¹⁶ Effect estimates for PM_{2.5} and mortality were higher when the PM_{2.5} chemical composition had higher contributions from aluminum, silicon, or nickel.¹⁵ Communities with higher PM_{2.5} contributions from nickel and vanadium had higher effect estimates for PM₁₀ and mortality³⁰; however, results were sensitive to the New York City community.³¹ Higher PM_{2.5} composition of nickel, vanadium, or elemental carbon was associated with higher cardiovascular or respiratory hospital admissions for persons 65 years and older.³²

Source-apportionment results indicate that a small number of constituents comprise the majority of several source factors, with elemental carbon and sulfur (2 of the more abundant constituents) contributing 86%–90% of motor-vehicle, oil-combustion, and regional sources. For analyses, we selected indicator constituents (source tracer elements) that are characteristic of individual sources. Previous work has used similar approaches. For example, elemental carbon has been used as a marker for diesel pollution or traffic pollution in general.³³ Most PM_{2.5} constituents have multiple sources. For instance, we used zinc and elemental carbon as indicator constituents for traffic, although zinc in PM2.5 can result from vehicles, oil combustion, coal combustion, and industry, and elemental carbon can be produced from traffic as well as industrial sources and combustion of oil and coal.³⁴ A study of primary PM found that elemental carbon is not a unique indicator of diesel air pollution.³⁵ Although the indicator approach is useful, results should be interpreted with an understanding that they are not exclusive source markers. Similarly, an indentified constituent may function as a marker for other constituents with similar sources. For instance, although nickel and vanadium are good proxies for oil combustion (eTable 3, http://links.lww.com/EDE/A423), the constituents represent a combination of sources and perhaps harmful properties. Additional research is needed to further illuminate the health effects of PM characteristics and sources.

An additional limitation of analyses presented here is the use of county-wide exposure estimates. Spatial heterogeneity of $PM_{2.5}$ constituents and sources can vary, potentially introducing exposure misclassification. Because the spatial variation is larger for some constituents and sources than others, the degree of misclassification may differ by constituent or source.36^{,37} Within-community variation in pollutant levels can affect results in epidemiological studies,36^{,38} and exposure misclassification may result in an underestimation of effects. Ambient monitors do not capture differences in personal exposures, which may reflect personal activity patterns (eg, movement indoors and outdoors, occupational exposure).

Further, exposure estimates were based on residence location at delivery. While studies of residential mobility and pregnancy are limited, research suggests that most mothers who move during pregnancy move short distances within the same community and that gestational exposures for PM_{10} and ozone are similar when based on address at delivery versus addresses from interviews during pregnancy.³⁹ Additional research is needed to address this issue for PM constituents.

Future work could investigate other model structures (eg, nonlinear terms) or variables for which we did not have sufficient data. As an example, a 1 kg/m increase in mothers' body mass index (BMI) has been shown to be associated with a 20-g increase in birth weight.⁴⁰ As BMI can follow community patterns, it may be associated with pollutant exposures. In our dataset, the rate of smoking during pregnancy was 6% and did not differ by race; however, detailed information on smoking during pregnancy could be applied to investigate differences in effects by community or subpopulation.

The biologic pathways through which $PM_{2.5}$ constituents and sources or other air pollutants might affect fetal growth are not fully understood. Possibilities include altered placental vascular function, altered heart rate variability impairing cardiac function, and alveolar inflammation.11 There has been progress in understanding how particles can affect cardiovascular and respiratory health13; however, further research is needed to disentangle the effects of various particle mixtures. Studies on biologic mechanisms are needed with respect to what particular constituents or sources are relevant to various health outcomes. Discussion of potential physiologic mechanisms through which PM could affect human health, including a summary of human studies of the association of PM with pulmonary or systematic inflammation and other markers of cardiovascular risk, is provided elsewhere.¹³ Our study does not investigate biologic pathways; however, results on which constituents or sources and windows of exposure (eg, third trimester) are most associated with birth weight can help guide future research.

The US Environmental Protection Agency established National Ambient Air Quality Criteria standards for PM_{10} and $PM_{2.5}$ mass. Two counties in this study, Fairfield and New Haven Counties, CT, are out of attainment with the $PM_{2.5}$ standards. All counties comply with the PM_{10} standards. PM remains the only air pollutant regulated without regard to chemical form. While PM is a robust predictor of health endpoints, growing evidence suggests that PM's chemical structure affects its toxicity. Better understanding regarding which PM sources or chemical mixtures are most toxic will aid decision makers in setting policies to protect public health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported by the National Institutes of Health (NIH), National Institute of Environmental Health Sciences (NIEHS) R01ES016317 and NIH/NIEHS ES11013 and the U.S. Environmental Protection Agency STAR grant RD832417.

REFERENCES

- McCormick MC. The contribution of low birth weight to infant mortality and childhood morbidity. New Eng J Med 1985;312:82–90. [PubMed: 3880598]
- 2. Whincup PH, Kaye SJ, Owen CG, et al. Birth weight and risk of type 2 diabetes: a systematic review. J Am Med Assoc 2008;300:2886–2897.
- 3. Parker JD, Woodruff TJ, Basu R, Schoendorf KC. Air pollution and birth weight among term infants in California. Pediatrics 2005;115:121–128. [PubMed: 15629991]
- Brauer M, Lencar C, Tamburic L, Koehoorn M, Demers P, Karr C. A cohort study of traffic-related air pollution impacts on birth outcomes. Environ Health Perspect 2008;116:680–686. [PubMed: 18470315]
- 5. Bell ML, Ebisu K, Belanger K. The relationship between air pollution and low birth weight: effects by mother's age, infant sex, co-pollutants, and pre-term births. Environ Res Lett 2008;3 Art. No. 044003.
- Bell ML, Ebisu K, Belanger K. Ambient air pollution and low birth weight in Connecticut and Massachusetts. Environ Health Perspect 2007;115:1118–1125. [PubMed: 17637932]
- Slama R, Morgenstern V, Cyrys J, et al. LISA Study Group. Traffic-related atmospheric pollutants levels during pregnancy and offspring's term birth weight: a study relying on a land-use regression exposure model. Environ Health Perspect 2007;115:1283–1292. [PubMed: 17805417]
- Maisonet M, Bush TJ, Correa A, Jaakkola JJ. Relation between ambient air pollution and low birth weight in the northeastern United States. Environ Health Perspect 2001;109:S351–S356.
- 9. Salam MT, Millstein J, Li YF, Lurmann FW, Margolis HG, Gilliland FD. Birth outcomes and prenatal exposure to ozone, carbon monoxide, and particulate matter: results from the Children's Health Study. Environ Health Perspect 2005;113:1638–1644. [PubMed: 16263524]
- 10. Woodruff TJ, Parker JD, Darrow LA, et al. Methodological issues in studies of air pollution and reproductive health. Environ Res 2009;109:311–320. [PubMed: 19215915]
- Glinianaia SV, Rankin J, Bell R, Pless-Mulloli T, Howel D. Particulate air pollution and fetal health: a systematic review of the epidemiologic evidence. Epidemiology 2004;15:36–45. [PubMed: 14712145]
- Bell ML, Dominici F, Ebisu K, Zeger SL, Samet JM. Spatial and temporal variation in PM_{2.5} chemical composition in the United States for health effects studies. Environ Health Perspect 2007;115:989–995. [PubMed: 17637911]
- Pope CA, Dockery DW. Health effects of fine particulate air pollution: lines that connect. J Air Waste Manag Assoc 2006;56:709–742. [PubMed: 16805397]
- Research Priorities for Airborne Particulate Matter: IV. Continuing Research Progress. Washington, DC: National Academies Press; 2004. National Research Council of the National Academies.
- Franklin M, Koutrakis P, Schwartz J. The role of particle composition on the association between PM_{2.5} and mortality. Epidemiology 2008;19:680–689. [PubMed: 18714438]
- Peng RD, Bell ML, Geyh AS, et al. Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution. Environ Health Perspect 2009;117:957–963. [PubMed: 19590690]
- Zeka A, Melly SJ, Schwartz J. The effects of socioeconomic status and indices of physical environment on reduced birth weight and preterm birth in Eastern Massachusetts. Environ Health 2008;7:60. [PubMed: 19032747]
- Wilhelm M, Ritz B. Residential proximity to traffic and adverse birth outcomes in Los Angeles County, California, 1994–1996. Environ Health Perspect 2003;111:207–216. [PubMed: 12573907]
- Nepomnyaschy L. Socioeconomic gradients in infant health across race and ethnicity. Matern Child Health J 2009;13:720–761. [PubMed: 19557507]

Bell et al.

- Cyrys J, Heinrich J, Hoek G, et al. Comparison between different traffic-related particle indicators: elemental carbon (EC), PM_{2.5} mass, and absorbance. J Expo Anal Environ Epidemiol 2003;13:134–1473. [PubMed: 12679793]
- Gent JF, Koutrakis P, Belanger K, et al. Symptoms and medication use in children with asthma and traffic-related sources of fine particle pollution. Environ Health Perspect 2009;117:1168–1174. [PubMed: 19654929]
- Watson, JG.; Chow, JC.; Frazier, CA. X-ray fluorescence analysis of ambient air samples. In: Landsberger, S.; Creatchman, M., editors. Elemental Analysis of Airborne Particles. Amsterdam: Gordon and Breach Science Publishers; 1999.
- 23. Paatero P, Tapper U. Positive matrix factorization: a non-negative factor model with optimal utilization of error estimates of data values. Environmetrics 1994;5:111–126.
- 24. Norris, G.; Vedantham, R.; Wade, K.; Brown, S.; Prouty, J.; Foley, C. EPA Positive Matrix Factorization (PMF) 3.0 Fundamentals and User Guide. Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development; 2008.
- 25. Lawlor DA, Ronalds G, Clark H, Smith GD, Leon DA. Birth weight is inversely associated with incident coronary heart disease and stroke among individuals born in the 1950s: findings from the Aberdeen children of the 1950s prospective cohort study. Circulation 2005;112:1414–1418. [PubMed: 16129799]
- 26. Kalkstein LS, Valimont KM. An evaluation of summer discomfort in the United States using a relative climatological index. Bull Am Meteorological Soc 1986;67:842–848.
- 27. Alexander GR, Himes JR, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. Obstet Gynecol 1996;87:163–168. [PubMed: 8559516]
- Collins JW Jr, David RJ. Racial disparity in low birth weight and infant mortality. Clin Perinatol 2009;36:63–67. [PubMed: 19161865]
- Patel MM, Hoepner L, Garfinkel R, et al. Ambient metals, elemental carbon, and wheeze and cough in New York City children through age 24 months. Am J Respir Crit Care Med 2009;180:1107–1113. [PubMed: 19745205]
- Lippmann M, Ito K, Hwang JS, Maciejczyk P, Chen LC. Cardiovascular effects of nickel in ambient air. Environ Health Perspect 2006;114:1662–1669. [PubMed: 17107850]
- Dominici F, Peng RD, Ebisu K, Zeger SL, Samet JM, Bell ML. Does the effect of PM₁₀ on mortality depend on PM nickel and vanadium content? A reanalysis of the NMMAPS data. Environ Health Perspect 2007;115:1701–1703. [PubMed: 18087586]
- Bell ML, Ebisu K, Peng RD, Samet JM, Dominici F. Hospital admissions and chemical composition of fine particle air pollution. Am J Respir Crit Care Med 2009;179:1115–1120. [PubMed: 19299499]
- Narváez RF, Hoepner L, Chillrud SN, et al. Spatial and temporal trends of polycyclic aromatic hydrocarbons and other traffic-related airborne pollutants in New York City. Environ Sci Technol 2008;42:7330–7335. [PubMed: 18939566]
- Kim E, Hopke PK. Identification of fine particle sources in mid-Atlantic US area. Water Air Soil Poll 2005;168:391–421.
- 35. Schauer JJ. Evaluation of elemental carbon as a marker for diesel particulate matter. J Expo Anal Environ Epidemiol 2003;13:443–453. [PubMed: 14603345]
- 36. Peng RD, Bell ML. Spatial misalignment in time series analyses of air pollution and health data. Biostatistics. In press.
- Bell ML, Ebisu K, Peng RD. Community-level spatial heterogeneity of chemical constituent levels of fine particulates and implications for epidemiological research. J Expo Sci Environ Epidemiol. In press.
- Jerrett M, Burnett RT, Ma R, et al. Spatial analysis of air pollution and mortality in Los Angeles. Epidemiology 2005;16:727–736. [PubMed: 16222161]
- Chen L, Bell EM, Caton AR, Druschel CM, Lin S. Residential mobility during pregnancy and the potential for ambient air pollution exposure misclassification. Environ Res 2010;110:162–168. [PubMed: 19963212]
- 40. Fleten C, Stigum H, Magnus P, Nystad W. Exercise during pregnancy, maternal pregnancy body mass index, and birth weight. Obstet Gynecol 2010;115:331–337. [PubMed: 20093907]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Subject's Characteristics	Overall (n = 76,788)	New Haven County, CT (n = 22,911)	Hartford County, CT (n = 21,947)	Fairfield County, CT (n = 25,450)	Hampden County, MA (n = 6480)
Term low birth weight (<2500 g)	2.2	2.5	2.4	1.7	2.4
Birth weight (g); mean (SD)	3434 (470)	3423 (476)	3416 (464)	3466 (464)	3408 (473)
Male	51.1	50.4	51.5	51.6	50.4
First child	34.6	34.2	34.4	36.0	30.6
Gestational duration (weeks)	39.3 (1.4)	39.4 (1.4)	39.3 (1.4)	39.3 (1.3)	39.5 (1.5)
Mother's characteristics					
Tobacco use during pregnancy	5.8	7.2	6.3	2.4	13
Alcohol use during pregnancy	$\overline{\nabla}$	\sim	<1	~	1.8
Married	69	67	67	78	53
Race					
White	82	81	81	83	88
African-American	13	14	14	11	10
Age (years)	29.3 (6.2)	28.9 (6.1)	28.8 (6.1)	30.7 (5.9)	27.2 (6.3)
Education (years)	13.8 (2.7)	13.7 (2.6)	13.8 (2.5)	14.3 (2.8)	12.8 (2.6)

Percent, unless otherwise indicated.

Summary of Study Population Exposures ($\mu g/m^3$) During Pregnancy to PM_{2.5} Mass, Constituents, and Sources (n = 76,788)

Gestational Pollution Exposure	Mean (SD)
Motor vehicles	3.82 (1.02)
Zinc	0.017 (0.004)
Elemental carbon	1.04 (0.60)
Road dust	1.73 (0.92)
Silicon	0.073 (0.034)
Aluminum	0.042 (0.020)
Oil combustion	1.60 (0.62)
Vanadium	0.0048 (0.0036)
Nickel	0.0031 (0.0015)
Salt	0.21 (0.15)
Chloride	0.013 (0.013)
Other regional sources	6.04 (1.20)
Sulfur	1.31 (0.16)
PM _{2.5} mass	14.0 (2.13)

Chemical constituents are divided into key sources, although all constituents listed result from multiple sources.

Change in Birthweight (g) per Interquartile Range (IQR) Increase in Gestational Exposure to $PM_{2.5}$ Mass, Constituents, and Sources

Constituent	IQR (µg/m ³)	Change in Birthweight (95% CI)	Percent Increase in Risk of Small- at-term Birth (95% CI)
Motor vehicles	1.4	-2 (-7 to 4)	8 (-1 to 18)
Zinc	0.006	-7 (-13 to -2)	12 (3 to 21)
Elemental carbon	1.1	-6 (-11 to 0)	13 (3 to 24)
Road dust	1.6	-4 (-10 to 1)	10 (1 to 19)
Silicon	0.05	-5 (-10 to 0)	10 (3 to 19)
Aluminum	0.03	-5 (-10 to 0)	11 (3 to 20)
Oil combustion	0.74	-4 (-10 to 1)	-3 (-11 to 6)
Vanadium	0.004	-5 (-8 to -1)	8 (2 to 15)
Nickel	0.002	-7 (-12 to -3)	11 (3 to 19)
Salt	0.17	-3 (-7 to 1)	5 (-2 to 12)
Chloride	0.009	-2 (-4 to 1)	3 (-1 to 7)
Regional sources	1.5	-3 (-8 to 2)	7 (-1 to 16)
Sulfur	0.3	-3 (-10 to 4)	7 (-5 to 20)
PM _{2.5} mass	3.6	-3 (-9 to 2)	7 (-1 to 17)

Chemical constituents are divided into key sources, although all constituents listed result from multiple sources. Data were restricted to term births. Models were adjusted for apparent temperature, infant's sex, parity, nature of delivery, prenatal care, length of gestation, year of birth, tobacco and alcohol use during pregnancy, and mother's age, race, and education.

Change in Birthweight (g) per IQR Increase in Trimester Exposure to PM2.5 Mass, Constituents, and Sources

]	Trimester of Expo	sure
Constituent	IQR (µg/m ³)	First Change in Birthweight (95% CI)	Second Change in Birthweight (95% CI)	Third Change in Birthweight (95% CI)
Motor vehicles	1.4	2 (-3 to 6)	1 (-4 to 5)	-4 (-9 to 0)
Zinc	0.006	-1 (-6 to 4)	0 (-5 to 5)	-6 (-11 to -1)
Elemental carbon	1.1	17 (-5 to 40)	2 (-19 to 23)	$-25 (-47 \text{ to } -3)^a$
Road dust	1.6	-1 (-12 to 10)	-10 (-21 to 1)	6 (-4 to 17)
Silicon	0.05	-5 (-11 to 1)	-3 (-10 to 3)	4 (-3 to 10)
Aluminum	0.03	-4 (-12 to 4)	-5 (-13 to 3)	4 (-4 to 12)
Oil combustion	0.74	-2 (-5 to 1)	3 (-1 to 6)	$-7 (-12 \text{ to } -1)^b$
Vanadium	0.004	-1 (-5 to 2)	2 (-3 to 7)	$-6 (-12 \text{ to } 0)^{C}$
Nickel	0.002	-1 (-6 to 3)	2 (-3 to 7)	$-9 (-15 \text{ to } -2)^d$
Salt	0.17	-3 (-5 to 0)	0 (-3 to 3)	-1 (-3 to 2)
Chloride	0.009	-2 (-3 to 0)	0 (-1 to 2)	-1 (-2 to 1)
Regional sources	1.5	-1 (-5 to 4)	-1 (-7 to 4)	0 (-5 to 4)
Sulfur	0.3	-0 (-6 to 6)	-1 (-7 to 5)	-1 (-99 to 4)
PM _{2.5} mass	3.6	-1 (-6 to 5)	0 (-5 to 5)	-2 (-8 to 3)

Table results are unadjusted for correlation among trimester exposures; results for adjusted models are provided in footnotes. Chemical constituents are divided into key sources, although all constituents listed result from multiple sources. Data were restricted to term births. Models were adjusted for apparent temperature, infant's sex, parity, nature of delivery, prenatal care, length of gestation, year of birth, tobacco and alcohol use during pregnancy, and mother's age, race, and education.

^{*a*}Change in birth weight per IQR increase in third trimester elemental carbon for models adjusted for correlation among trimesters: range -25 to -8.

 b Change in birth weight per IQR increase in third trimester oil combustion for models adjusted for correlation among trimesters: range -7 to -5.

 c Change in birth weight per IQR increase in third trimester vanadium for models adjusted for correlation among trimesters: range -5 to -6.

 d Change in birth weight per IQR increase in third trimester nickel for models adjusted for correlation among trimesters: range -8 to -9.

Change in Birthweight (g) per IQR Increase in Gestational Exposure to Specific $PM_{2.5}$ Constituents and Sources, by Race of Infant's Mother

	Race of Mother		
Constituent	White Change in Birthweight (95% CI)	African-American Change in Birthweight (95% CI)	
Zinc	-7 (-13 to -2)	-10 (-22 to 3)	
Elemental carbon	-6 (-13 to 1)	-9 (-24 to 7)	
Road dust	-5 (-11 to 1)	-7 (-22 to 7)	
Silicon	-5 (-10 to 0)	-9 (-22 to 3)	
Aluminum	-5 (-11 to 0)	-9 (-22 to 5)	
Vanadium	-4 (-8 to 0)	-9 (-18 to 1)	
Nickel	-6 (-12 to -1)	-12 (-24 to 0)	

Chemical constituents are divided into key sources, although all constituents listed result from multiple sources. IQR values are provided in Table 3. Data were restricted to term births. Models were adjusted for apparent temperature, infant's sex, parity, nature of delivery, prenatal care, length of gestation, year of birth, tobacco and alcohol use during pregnancy, and mother's age, race, and education.