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The association of PM_{2.5} with full term low birth weight at different spatial scales

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Abstract

There is interest in determining the relationship between fine particulate matter air pollution and various health outcomes, including birth outcomes such as term low birth weight. Previous studies have come to different conclusions. In this study we consider whether the effect may vary by location and gestational period. We also compare results when using different spatial resolutions for the air concentration estimates. Among the seven states considered, New Jersey and New York had the highest PM_{2.5} levels (average full gestation period exposures of 13 µg/m³) and the largest rate of low birth weight births (2.6 and 2.8%, respectively); conversely Utah and Minnesota had the lowest PM_{2.5} levels (9 µg/m³) and the lowest rates of low birth weight births (2.1 and 1.9%, respectively). There is an association between PM_{2.5} exposure and low birth weight in New York for the full gestation period and all three trimesters, in Minnesota for the full gestation period and the first and third trimesters, and in New Jersey for the full gestation period and the first trimester. When we pooled the data across states, the OR for the full gestation period was 1.030 (95% CI: 1.022–1.037) and it was highest for the first trimester (OR 1.018; CI: 1.013–1.022) and decreasing during the later trimesters. When we used a finer spatial resolution, the strengths of the associations tended to diminish and were no longer statistically significant. We consider reasons why these differences may occur and their implications for evaluating the effects of PM_{2.5} on birth outcomes.

Keywords

low birth weight; birth outcomes; fine particulate matter; PM_{2.5}; spatial resolution; temporal resolution

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The study was approved by the Institutional Review Board of the University of Medicine and Dentistry of New Jersey (now part of Rutgers University). The study also had approvals with the states from which grid-level data were obtained (New Jersey, New York, and Utah). The data used by the authors did not include personal identifiers (e.g., names, social security numbers), nor was such information sought, nor was any contact with the subjects attempted.

1. Introduction

While the United States has made great strides in reducing air pollution since the 1970s, regions continue to consistently exceed ambient air quality standards. While the most excessive levels of pollutants have been reined in, the breadth of the health effects of lower exposures is still not well understood. This is particularly true of fine particulate matter, which is not a single chemical but rather a complex of chemicals that varies depending upon regional and local sources. Certain health effects of exposure to particulate matter, such as overall mortality and cardiovascular disease, have been widely studied, and the associations are well established (U.S. EPA, 2009). Adverse birth outcomes such as low birth weight are less well studied and have mixed results.

Fine particulate matter (PM_{2.5}) is a common pollutant that is regularly monitored throughout the US. It consists of particles less than 2.5 µm in aerodynamic diameter. The major sources of PM_{2.5} vary by geographic location, but are typically from dust, fuel combustion, and industrial emissions. PM_{2.5} can go deep into lung tissue and get into the bloodstream. The EPA has concluded that exposure to PM_{2.5} causes mortality and cardiovascular effects, and is likely to cause respiratory effects (U.S. EPA, 2009).

However, whether there is a positive association between exposure to particulate matter and adverse birth outcomes is less clear. In their most recent Integrated Science Assessment, the EPA find that the evidence suggests that PM_{2.5} causes reproductive and developmental effects (U.S. EPA, 2009).

Low birth weight is a major predictor of perinatal mortality and morbidity and therefore of public health importance. Low birth weight (LBW) infants have mortality rates more than 20 times those of normal weight infants (MacDorman and Atkinson, 1999). They are at increased risk for neurological outcomes, particularly cerebral palsy (Goldenberg and Culhane, 2007). Low birth weight is associated with health issues in adolescence and beyond, including asthma, low IQ, and hypertension (Ashdown-Lambert, 2005; Barker, 1995; Godfrey and Barker, 2000; Richards et al., 2001; Steffensen et al., 2000). Hospital costs associated with LBW infants are also large: Almond (2005) estimates the excess hospital costs for a 2 – 2.5 kg birth at \$600, \$6,800 for a 1.5 – 2 kg birth, and over \$20,000 for lower birth weights.

Full-term low birth weight (LBW) babies are those that are born at 37 to 41 weeks of gestation but weigh less than 2,500 g. Among full-term births, 3.1% were LBW in the U.S. in 2012 (Martin et al., 2013), and ranged between 2.9% and 3.2% between 1997 and 2012 (source: National Vital Statistics Reports, “Births: Final Data” for each of the years). Well-established risk factors for LBW births include race, young maternal age, high parity, maternal smoking, alcohol and/or drug use, poor nutrition, and stress (Ashdown-Lambert, 2005).

While it is understood that fetal health can be impacted by environmental pollution, studies of the impact of pollutants on LBW have had mixed results. Recent reviews have come to different conclusions. Bosetti et al. (2010) found that current evidence does not support an association between exposure to ambient particulate matter and adverse birth outcomes (low

birth weight and preterm birth). Stieb et al. (2012) found that PM_{2.5} was associated with LBW. Through a meta-analysis, they estimated an OR of 1.05 (99% CI: 0.99 – 1.12) per 10 µg/m³ increase in PM_{2.5}. The authors found that the heterogeneity among studies was primarily due to differences in study designs and varying definitions of exposure periods. In a multi-country study, Dadvand et al. (2013) found ambient exposure to PM_{2.5} was significantly associated with LBW (OR 1.10, 95% CI 1.03 – 1.18) per 10 µg/m³ increase in PM_{2.5}. They reported that the heterogeneity among studies was due to median PM_{2.5} exposure levels and temporal versus spatiotemporal exposure contrasts. Sapkota et al. (2012) did a meta-analysis of 20 studies of LBW, and calculated a combined OR of 1.09 (95% CI: 0.90–1.32) per 10 µg/m³ increase in PM_{2.5}.

With PM_{2.5}, it may also be that different compositions can lead to different health outcomes. Because PM_{2.5} is made of a mixture of sources and the sources will vary by location, it may be unreasonable to expect the effect of PM_{2.5} on birth outcomes to be constant across geography. Studies have found associations between specific components of PM_{2.5} and low birth weight. Bell et al. (2010, 2012) found Al, elemental C, K, Ni, Si, Ti, V, and Zn to be associated with LBW. Ebisu and Bell (2012) found associations of LBW with Al, Ca, Cd, elemental C, Ni, Si, Ti, and Zn. Darrow et al. (2011) found associations of LBW with elemental carbon and PM_{2.5} water soluble metals in the Atlanta region. Wilhelm et al. (2012), however, did not find associations of LBW with nitrate, sulfate, elemental C, organic C, nor V.

The impact that a pollutant has on fetal growth may depend upon the stage of fetal development when the exposure occurs. Multiple studies have found effects to be confined to exposure during specific trimesters. Bell et al. (2007) found associations during the second and third trimesters using data from Massachusetts and Connecticut. Rich et al. (2009) found associations of PM_{2.5} and small for gestational age during the first and third trimesters using New Jersey births. Morello-Frosch et al. (2010) studied births in California and the associations of PM_{2.5} and reduction in birth weight varied in size by trimester. Parker et al. (2005) did find an association between PM_{2.5} and birth weight for exposures across the full pregnancy, but did not see differences in the associations by trimester. Parker and Woodruff (2008) also did not find an association between PM_{2.5} and birth weight for any trimester, nor for the full pregnancy. Hyder et al. (2014) found significant associations between low birth weight and PM_{2.5} in the first trimester, but not the second or third trimester, using satellite and monitor data of PM_{2.5} concentrations in Connecticut and Massachusetts. Savitz et al. (2014) found reductions in birth weight with increases in PM_{2.5} concentrations during all three trimesters in New York City. Ebisu and Bell (2012) found associations of PM_{2.5} components with LBW differed by trimester, but did not find an overall association with total PM_{2.5} in northeastern and mid-Atlantic United States.

An important issue in assessing these effects of air pollution is the assignment of dose values to individual births (Waller and Gotway, 2004). Direct monitoring of the air pollution levels to which individual pregnant women are exposed is not feasible for large-scale epidemiologic studies. Actual monitor data are routinely collected only at fairly scattered locations. Consequently, studies differ in terms of how air concentration values from the monitors in the region of each mother's residence are utilized for the assignment of exposure

values. Furthermore, issues of confidentiality often preclude investigators from obtaining exact geographic locations of the residences of the women whose births are studied. Consequently, if, for example, the only information available concerning location is county of residence, then exposure values ascribed to individual births must be based on some sort of average or interpolated measure at the county level rather than on some more individualized values.

Our study was conducted within the Centers for Disease Control and Prevention's Environmental Public Health Tracking Program. Several state health departments in the Tracking Program expressed interest in assessing whether variation in PM_{2.5} within their states was associated with adverse birth outcomes. Public health officials in all the participating states, and particularly in those states that share borders with other participating states, were interested to learn whether combining and comparing data across states might help to clarify these effects of PM_{2.5}.

The study was conducted within the framework of public health surveillance, which is defined as "the ongoing systematic collection, analysis, and interpretation of outcome-specific data for use in the planning, implementation, and evaluation of public health practice" (Thacker and Berkelman, 1988). In that context, a key goal was to assess whether associations between PM_{2.5} and birth outcomes could be validly evaluated with currently available databases that are routinely collected over time and do not require special permissions and extensive time commitments of research staff. In that way, the states would be able to evaluate the efficacy of interventions designed to reduce exposure of pregnant women via assessment of changes over time in the contribution of PM_{2.5} to adverse birth outcomes in the population.

Consequently, the goal of our study was to assess if there is an association between exposure to PM_{2.5} and low birth weight, and whether that association varied according to spatial and temporal resolution of the exposure or according to timing of the exposure during the pregnancy.

2. Methods

2.1 Data Sources

2.1.1 Birth certificate data—Birth certificate data for CT, ME, MN, NJ, NY, UT, and WI were obtained from the National Center for Health Statistics's vital statistics Public Use Micro Data (NCHS, 2013). Additionally, NY, UT, and NJ provided birth certificate data from their own vital statistics departments.

The NCHS birth certificates are restricted to county of maternal residence and month of birth for the period under study, 2001 to 2004. Birth certificate data provided by the states included the date of birth and a more precise maternal residence location, with the degree of location precision varying by state: NJ data were geocoded to the latitude and longitude of the maternal residence; UT data were geocoded to the latitude and longitude of the centroid of the town of maternal residence; NY provided data that pre-linked the maternal residence to the exposure based on the nearest grid point (discussed below).

Low birth weight was defined as <2,500 grams among full-term singleton births. Since the NCHS birth certificate data only gives month of birth and not date of birth, we assume that the birth is on the 15th of the month. The analysis was limited to early term and full term births (births with gestational ages between 37 and 40 weeks, ACOG, 2013) so that the full gestation periods in the NCHS analysis were all based on 9 months of exposure.

2.1.2 Air pollution data—Daily PM_{2.5} air concentrations for the period 2001 to 2004 were obtained from the EPA. The modeled values were based on the Community Multi-scale Air Quality (CMAQ) model which uses monitoring data to estimate values along a regular grid. Grid spacing was 12 km for all but UT, which had a grid spacing of 36 km. The CMAQ is a widely used model that combines atmospheric transport models with emission models and meteorological models to aid air quality management (Byun and Schere, 2006; Binkowski and Roselle, 2003). It is periodically peer reviewed (Brown, et al., 2011) and its performance has been evaluated (Appel et al., 2012). Appel et al. (2012) found the bias for estimating PM_{2.5} concentrations across North American in 2006 depended upon season – overestimated in the winter and fall with an average Normalized Mean Bias of –30% and an average NMB of –4.6% in the summer. Bravo et al. (2012) compared CMAQ results to monitor data for the eastern United States in 2002, and found an annual NMB of –2.1% for PM_{2.5}, varying by season from 32% in November to –27% in July.

The CMAQ calculated concentrations were adjusted using a hierarchical Bayesian model to improve the accuracy of the forecasted values (McMillan et al., 2010). The hierarchical Bayesian model combines the CMAQ estimate with observed data from the U.S. EPA Federal Reference Method PM_{2.5} monitoring data. McMillan et al. (2010) validated the procedure by comparing the hierarchical model results to kriging results for a set of independent monitor data and found the hierarchical results to be superior. Sahu et al. (2009) used a similar model for ozone and also concluded that the results were superior to just using the monitoring data alone.

2.2 Exposure estimates

We considered four exposure periods at two spatial and temporal resolutions. The four exposure periods were the full gestation period and the three trimesters. The gestation period was determined by the last menstrual period (with conception beginning 2 weeks after LMP), when available, and otherwise by the clinical estimate. Trimesters were defined as 1–13 weeks, 14–26 weeks, and 27–40 weeks. The spatial/temporal resolution is determined by the source of the birth certificate data.

For the analyses using the NCHS Public Use Micro Data files, the spatial resolution is limited to the county of the maternal residence at the time of the birth and the temporal resolution is limited to birth month. The NCHS Public Use birth certificates do not identify the county of birth for births in counties with populations under 100,000. Births in these counties were combined into a single “county” for the analyses. For the full gestation period, the average PM_{2.5} concentration is determined by averaging the daily concentrations from all grid points in the maternal residence county across all months of gestation, with the month of birth being the ninth month of gestation. Similarly, the trimester averages are

calculated by averaging over the grid points in the maternal residence county for the three months of the trimester. The number of grid points per county ranged from 1 to 123; and the average number of grid points per county ranged from a high of 24.6 in Maine to a low of 2.5 in Utah. All seven states are included in this analysis.

A second analysis was performed using only NJ, NY, and UT. For these three states with more precise spatial and temporal data on the birth, the spatial resolution was the grid point nearest the maternal residence, and the temporal resolution was day. These exposure estimates and their association with low birth weight were compared to the results using the county-level exposure estimates.

2.3 Statistical Methods

We used logistic regression models to estimate the association (as odds ratios) of $PM_{2.5}$ exposure with full term low birth weight. We initially ran the data from each state separately. Then we pooled all the state data together to get overall estimates of the association. Finally, we included a state by PM exposure interaction term in the pooled data model so that we could estimate the association in each state. These pooled state estimates are contrasted with the individual state estimates.

We tested the goodness-of-fit of the models using the Hosmer-Lemeshow test. We also checked for non-linearity by testing if a quadratic term significantly improved the fit of the model. Otherwise, the exposure/response relationship was modeled as loglinear, with the slope (i.e., log odds ratio) corresponding to a $1 \mu g/m^3$ increase in daily exposure.

Logistic regression modeling was done using PROC LOGISTIC in the SAS system. Plots were generated using R.

Models were adjusted for the age, marital status, education, race/ethnicity of the mother, Kessner measure of prenatal care, sex of the child, mother's smoking status, and whether there were any pregnancy complications. We also used census 2000 data to adjust for county-level socioeconomic variables, but these variables (percent white, percent Hispanic, percent less than high school education, percent with at least a B.S. degree, median household income, and percent below the poverty level) did not add significantly to the model fit, so are not included in the final models presented here.

3. Results

Table 1 summarizes the birth certificate data and the exposure estimates by state. For the period 2001 to 2004, we include 1,374,875 full-term births. The fewest births occurred in Maine, 19,486, and the most occurred in New York, 565,439. The percent of births that were LBW ranged from 1.89 (Minnesota) to 2.85 (New York). New Jersey had the highest full-term average daily exposures at 13.5 ($sd=1.4$) $\mu g/m^3$ and Utah had the lowest at 9.2 (2.8) $\mu g/m^3$. Overall, 2.53% of the full-term births were LBW, and the average full gestation period daily exposure was 11.9 (2.9) $\mu g/m^3$. The average daily exposure ascribed to an individual birth ranged from $4.5 \mu g/m^3$ for a birth in UT to $16.6 \mu g/m^3$ for a birth in New Jersey.

Table 1 also shows a positive association between PM_{2.5} exposure and %TLBW, at least at a crude level. The correlation between the mean PM_{2.5} exposure and %TLBW is 0.91.

The results of fitting logistic regression models to the county-level data are shown in Table 2. When the states are analyzed separately, there is a significant increase in risk of LBW with an increase in PM_{2.5} exposure in New York for all exposure periods considered, in Minnesota for the full gestation period exposure and for the first and third trimesters, in Wisconsin for the second and third trimesters, and in New Jersey during the first trimester. Connecticut, Maine, and Utah did not show significant associations for any exposure period.

When all the state data are pooled into a large analysis to get an overall estimate of risk from PM_{2.5} exposure across all the states, there is a consistent effect that is largest for the full gestation exposure periods, and decreases with increasing trimester. The effect size per 1 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5}, as measured by the odds ratio, is 1.030 (95% CI: 1.022, 1.037) for the full gestation period exposure, 1.018 (1.013, 1.022) for the first trimester exposure, 1.012 (1.007, 1.017) and 1.009 (1.005, 1.014) for the second and third trimester exposures.

When all the state data are pooled into a large analysis and we include an interaction term between state and PM_{2.5} exposure levels, New York shows consistent positive associations between PM_{2.5} exposure and LBW for all exposure periods. Minnesota shows a positive association for the full gestation period and the first and third trimester exposure periods. Wisconsin also shows a positive association for the full gestation, and for the second and third trimester exposure periods. New Jersey shows a significant positive association for the full gestation period and first trimester exposure periods. Connecticut, Maine, and Utah do not show significant associations for any exposure period when the data are pooled together.

The OR estimates by state for the pooled data analyses were similar to the estimates when using only the individual state data. There is no obvious pattern in how the estimates differ depending upon if from the pooled data or not. The ORs for Wisconsin and Maine tended to differ the most between the pooled and individual state results. For example, for the full gestation period exposure, the Wisconsin OR per 1 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} using the pooled analysis is 1.031 (1.010, 1.052) and using the individual state data only is 1.022 (0.999, 1.046) and the Maine OR using the pooled analysis is 1.002 (0.886, 1.133) and using the individual state data only is 1.015 (0.899, 1.146). These were the two largest differences in OR estimates seen across all states and exposure periods.

When we used the pooled data, with over a million births, the models consistently failed the Hosmer-Lemeshow goodness of fit test. For the individual state analyses, only Connecticut and to a lesser extent, New Jersey, consistently passed the goodness of fit test for all exposure periods. New York, Utah, and Wisconsin consistently did not pass the goodness of fit test for all exposure periods. Adding interaction terms to the models did not impact the goodness of fit results.

We also tested to see if there may be some curvature in the relationship between PM_{2.5} and LBW by adding a quadratic term to the model. As shown in Table 2, the quadratic term did not differ significantly from 0 in all the models except for the individual trimester models

for New York state. Here there was a slight, but significant, negative curvature in the relationship.

To assess whether the association between $PM_{2.5}$ and LBW varied by state, we tested whether the interaction terms of exposure and state added significantly to the model. We found that for all exposure periods the interaction terms were highly significant, indicating that the relationship between $PM_{2.5}$ and LBW varied by state (data not shown).

For three of the states (New Jersey, New York, and Utah) we obtained more precise information about the maternal residence location and the date of birth. The “county”-level analysis uses maternal county of residence as the exposure location and month of birth as the date of birth. The “grid”-level analysis uses the exposure model grid point closest to the maternal street address residence location (New Jersey, New York) or town centroid (Utah) as the exposure location and actual date of birth.

Table 3 summarizes the full gestation period exposure estimates by state and level of analysis. In New Jersey and New York the mean exposures tended to be about $0.5 \mu\text{g}/\text{m}^3$ lower in the grid level analysis and in Utah the mean exposure was about $0.2 \mu\text{g}/\text{m}^3$ higher in the grid level analysis. In all states, the grid-level exposure estimates varied more than the county-level exposure estimates. We see similar results for the other gestation periods (results not shown).

Table 4 shows the correlation between the county-level and grid-level exposure estimates by state and gestation period. For New Jersey, the correlations ranged between 0.68 to 0.73 with the lowest correlation for the full gestation period and the highest for the first trimester. For New York, the correlations ranged between 0.60 and 0.68, with the lowest correlation for the full gestation period and the highest for the first trimester. For Utah, the correlations ranged between 0.88 and 0.91 with the lowest correlations for the second and third trimesters and the highest for the full gestation period and first trimester.

Figure 1 compares the modeled odds ratios for LBW by analysis level, state, and exposure period. For New Jersey and New York the ORs for the grid level analyses tended to be closer to 1 than the ORs for the county level analyses. The single exception was the second trimester exposure for New Jersey, where the county level OR was closer to one. Those ORs whose confidence intervals did not include 1 in the county level analysis, did include 1 in the grid level analyses. This pattern tended to be more due to the reduction in the OR rather than a change in the width of the confidence interval, which are similar in the two levels of analysis. For Utah, the analysis level had little effect on the estimates of the ORs.

4. Discussion

In this study, we are interested in study factors that could influence the association between $PM_{2.5}$ and low birth weight. We studied the association between exposure to $PM_{2.5}$ during gestation and low birth weight using relatively easily available data. We used data from seven states for a broad analysis of the association. We found that the association depended upon state, period of gestation when the exposure is assessed, and on the precision of the spatial and temporal exposure estimates. Due to the many uncertainties in the exposure

analysis – for example, using modeled results, variation with respect to the last menstrual period and actual birth date, exposure estimates on a large geographic scale - we cannot rule out that the results are due to chance or unaccounted for confounders.

Recent reviews of studies of associations of PM_{2.5} with low birth weight (U.S. EPA, 2009; Stieb et al., 2012) have concluded that there is an association. However the review by Bosetti et al. (2010) finds the evidence less convincing.

Specific biological mechanisms for how PM_{2.5} may impact birth weight are not fully understood. Reviews of possible mechanisms are given by Kannan et al. (2006), Slama et al. (2008), and Xu et al. (2011). Kadiiska et al. (1997) and Prahalad et al. (2001) found evidence of PM_{2.5} causing oxidative stress. PM_{2.5} exposure has been associated with increased C-reactive protein concentrations in early pregnancy which indicates inflammation that could impact gestation (Lee et al., 2011).

Unlike other air quality standards, fine particulate matter is not a homogeneous chemical. Its composition will depend upon what sources are contributing to it in a given area. It can be composed of different chemicals and have varying particle size distributions. Both of these factors may explain some of the location differences in PM_{2.5} effects on adverse birth outcomes. Particle size distribution will impact the ability of the particles to become biologically active as it affects lung deposition (Oberdörster et al., 1994; Carvalho et al., 2011). Chemical composition will in part determine the toxicological profile of the particulate matter. Some of the components that may be of interest include elemental carbon, organic carbon, ammonium, nitrate, sulfate, and the trace elements.

The models consistently failed the Hosmer-Lemeshow goodness of fit test. This is not unusual with large datasets where even minor discrepancies from the model may yield significance, although the Hosmer-Lemeshow test is considered to have low power for detecting certain model misspecifications, including interactions (Hosmer, et al., 1997).

We also compare the results when we use two levels of exposure assessment. The county level uses exposure estimates based on the county of the maternal residence and the month of birth. This level was chosen because the data are freely available to the public. The grid level uses exposure estimates based on the model grid point nearest the street address of the maternal residence or the centroid of the town of the maternal residence and the actual date of birth.

We find the average exposure estimates are nearly the same for the two levels of analyses, but they vary more for the grid-level analysis. This occurs because the county-level exposure estimate is based on an average of grid points in the county, while the grid-level exposure is based on a single grid point. The correlations between the county-level and grid-level exposure estimates are lower in NY and NJ (range 0.60 to 0.73) than in UT (range 0.88 to 0.91). This difference is in part probably due to the use of a 36 km grid for UT exposure estimates compared to a 12 km grid for NJ and NY.

Our statistical modeling regarded each birth as an independent event and, although we obviously used location in assigning exposure values, we did not take explicit analytic

account of the spatial distribution of births. Consequently, some of the standard errors used in calculating our confidence intervals may be underestimated.

There were important differences in some of the estimates of the odds ratios depending upon the exposure analysis level. The grid-level analysis estimates tended to have ORs closer to one, and their confidence intervals were more likely to include one. It is not clear why this should be.

Basu et al. (2004) had a similar result when, using full term births from California in 2000, they compared three levels of exposure to PM_{2.5}: the nearest monitor to the maternal residence, average of all monitors within a 5 mile radius of maternal residence, and average all monitors within the county of the maternal residence. The county-average estimate gave a consistently stronger negative association of PM_{2.5} on birth weight than the other two exposure measures. They suggest that the county-level measure better captures the exposures the mother experiences than the neighborhood level exposures.

The grid-level exposure analysis determines the exposures by the actual date of birth and the grid point nearest the maternal residence, while the county-level exposure analysis uses only the month of birth and the county of the maternal residence. Using the actual date of birth should provide a more representative estimate of the exposure than using the 15th day of the month as the date of birth, so the grid-level exposure should be less prone to exposure misclassification than the county-level exposure.

It is less clear whether using the nearest grid point is more or less representative of maternal exposure during gestation than using county estimates. If the person spends the majority of her time within about 12 km (36 km for Utah) of the grid point nearest their residence, the grid level exposure estimate is more representative than the county level estimate. If the person spends the majority of her time outside that area, but inside the county, then the county level estimate would be more representative. While we are not aware of maternal mobility data, it seems reasonable to assume that the grid level exposure estimate is more representative and less prone to exposure misclassification than the county level estimate.

Since the exposure misclassification is probably greater in the county-level analyses and since that misclassification is probably non-differential with respect to the outcome, we would expect from the point of view of misclassification only that the ORs for the county-level analyses would be closer to 1 than the grid-level analyses, but what our results indicate is that the county-level analysis ORs are further from one than the grid level analyses. However, the observed pattern is consistent with findings of Thompson and Wartenberg (2007), who have shown that multiplicative modeling of ecologic-level exposure data can bias relative risk estimates away from the null value, and with Basu et al. (2004).

Residence information is important in assigning exposure values and some confounders such as socio-economic variables. In order to accommodate data confidentiality concerns both Utah and New York took appropriate precautions when providing data to us. Utah geocoded the maternal residence to the centroid of the town. New York matched the nearest grid point to the maternal street address and calculated the exposures before returning the exposure assignments to us, so that we never had to handle confidential information for New York.

We feel that both of these arrangements were reasonable ways for us to access more precise exposure and maternal data without compromising the privacy of the individuals in the study.

This study is not without its limitations. We have already discussed the temporal and spatial exposure measurement errors. Additionally the ambient measures may not characterize the indoor home or workplace exposures. We only have maternal residence for the date of birth so if the mother moved during the pregnancy, we cannot account for that. Previous studies have shown between 12 to 35% of mothers move during pregnancy (Brauer et al., 2008). While we did adjust for mother's smoking status, we do not know if other family members may smoke, exposing the pregnant mother to environmental tobacco smoke. Since PM_{2.5} may be correlated with other pollutants, we may actually be estimating the effect of those other pollutants (or combination of pollutants). We were limited to adjusting for only the SES factors available on the birth certificate. We did include county-level SES information in our models, but they did not improve the fit of the models and so were dropped from the models. Neighborhood SES information would probably reduce the likelihood of confounding in our results.

5. Conclusion

Our results indicate that associations of PM_{2.5} and LBW depend upon location. Possible reasons for differences by locations include differences in the populations, differences in the environment, or differences in the composition of the PM_{2.5}. If the composition of the PM_{2.5} is a major factor in the toxicity of PM_{2.5}, then more precise monitoring of PM_{2.5} components may be needed to protect the public's health.

We also found that the association of PM_{2.5} and LBW depended upon the period during gestation when the exposure occurred, which may indicate different vulnerabilities during different periods of gestation.

Our results depend upon the scale of the analyses. It would seem the "individual" level is better in some sense, but it may also be that too fine a scale may misrepresent exposures more than a larger scale. The characteristics of mixed level studies (grid level birth data and ecologic exposure data) need to be better understood if they are to be used more widely in a tracking/surveillance context.

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Abbreviations

PM_{2.5} Particulate matter with aerodynamic diameter smaller than 2.5 µm

LBW	Low birth weight
TLBW	Term low birth weight
EPA	U.S. Environmental Protection Agency
OR	Odds ratio
NCHS	National Center for Health Statistics
CT	Connecticut
ME	Maine
MN	Minnesota
NJ	New Jersey
NY	New York
UT	Utah
WI	Wisconsin
CMAQ	Community Multi-scale Air Quality model
CI	Confidence interval
NMB	Normalized mean bias
LMP	Last menstrual period

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Figure 1.

Odds ratios and confidence intervals for low birth weight per 1 µg/m³ change in average PM_{2.5} concentration over the exposure period (full gestation, 1st, 2nd, and 3rd trimesters) by state (NJ, NY, and UT) and exposure analysis level (Cty = county, Gri = grid).

Summary statistics of the births used in the county level study for the period 2001 to 2004 by state, sorted by proportion of TLBW births.

Table 1

State	# of Births	% TLBW	Full Gestation Period PM2.5 Exposure (µg/m ³)		
			Mean (sd)	Min.	Max
MN	158,677	1.89	9.7 (1.2)	5.3	11.8
UT	127,260	2.10	9.2 (2.8)	4.5	15.3
ME	19,486	2.15	10.1 (0.8)	7.8	11.6
WI	155,120	2.28	10.5 (1.7)	7.0	14.3
CT	98,385	2.53	12.1 (0.9)	10.0	14.1
NJ	250,508	2.61	13.5 (1.4)	9.3	16.6
NY	565,439	2.85	12.9 (1.8)	7.4	16.4
Total	1,374,875	2.53	11.9 (2.3)	4.5	16.6

Table 2

Results of the county-level analyses associating PM_{2.5} with full-term low birth weight. Odds ratios are for a 1 µg/m³ increase in PM_{2.5}.

Exposure Period	Model	Pooled Analysis				Individual State Analysis			
		P(GoF) ^a	OR	95% CI	OR	95% CI	P(Quad) ^b		
Full	PM	<0.0001	1.075	(1.070,1.081)					
	PM, confounders ^c	<0.0001	1.033	(1.027,1.039)					
	PM, confounders, state	<0.0001	1.030	(1.022,1.037)					
	PM, confounders, state, state*PM	<0.0001							
	CT	0.6951	0.980	(0.935,1.028)	0.975	(0.933,1.025)	0.6716		
	ME	0.4315	1.002	(0.886,1.133)	1.015	(0.899,1.146)	0.8690		
	MN	0.0855	1.051	(1.017,1.087)	1.047	(1.011,1.084)	0.7353		
	NJ	0.1267	1.019	(1.001,1.037)	1.015	(0.997,1.034)	0.7393		
	NY	0.0010	1.055	(1.043,1.066)	1.056	(1.045,1.068)	0.8708		
	UT	0.0038	0.991	(0.977,1.006)	0.994	(0.980,1.009)	0.3196		
Tri1	WI	0.0002	1.031	(1.010,1.052)	1.022	(0.999,1.046)	0.6713		
	PM	<0.0001	1.048	(1.044,1.052)					
	PM, confounders	<0.0001	1.022	(1.018,1.027)					
	PM, confounders, state	<0.0001	1.018	(1.013,1.022)					
	PM, confounders, state, state*PM	<0.0001							
	CT	0.4316	0.999	(0.972,1.026)	0.998	(0.973,1.025)	0.5388		
	ME	0.1189	0.986	(0.915,1.063)	0.991	(0.921,1.066)	0.0624		
	MN	0.1678	1.026	(1.002,1.050)	1.024	(1.000,1.048)	0.1260		
	NJ	0.1545	1.014	(1.001,1.028)	1.013	(1.001,1.025)	0.5390		
	NY	0.0139	1.034	(1.026,1.042)	1.033	(1.025,1.042)	0.0004		
Tri2	UT	0.0326	1.004	(0.993,1.014)	1.005	(0.997,1.013)	0.4552		
	WI	<0.0001	1.015	(0.997,1.033)	1.009	(0.991,1.026)	0.9137		
	PM	<0.0001	1.043	(1.039,1.047)					
	PM, confounders	<0.0001	1.018	(1.014,1.022)					
	PM, confounders, state	<0.0001	1.012	(1.007,1.017)					
	PM, confounders, state, state*PM	<0.0001							
	CT	0.4168	0.993	(0.967,1.020)	0.992	(0.966,1.019)	0.2305		

Exposure Period	Model	Pooled Analysis			Individual State Analysis		
		P(GoF) ^a	OR	95% CI	OR	95% CI	P(Quad) ^b
Tri3	ME	0.3546	1.057	(0.981,1.138)	1.063	(0.988,1.144)	0.8348
	MN	0.0540	1.019	(0.993,1.046)	1.017	(0.991,1.044)	0.9523
	NJ	0.0963	1.007	(0.996,1.017)	1.006	(0.994,1.017)	0.1944
	NY	0.0003	1.029	(1.021,1.037)	1.029	(1.020,1.037)	0.0002
	UT	0.0074	0.994	(0.987,1.000)	0.995	(0.986,1.003)	0.6657
	WI	0.0001	1.023	(1.004,1.042)	1.018	(1.000,1.037)	0.5573
	PM	<0.0001	1.041	(1.037,1.045)			
	PM, confounders	<0.0001	1.016	(1.011,1.020)			
	PM, confounders, state	<0.0001	1.009	(1.005,1.014)			
	PM, confounders, state, state*PM	<0.0001					
	CT	0.6517	0.989	(0.964,1.015)	0.989	(0.963,1.015)	0.2016
	ME	0.0367	0.962	(0.893,1.037)	0.966	(0.898,1.040)	0.3394
	MN	0.2527	1.035	(1.008,1.063)	1.033	(1.006,1.060)	0.9448
	NJ	0.0575	1.001	(0.991,1.011)	1.000	(0.989,1.011)	0.4477
	NY	0.0003	1.025	(1.017,1.034)	1.024	(1.016,1.032)	<0.0001
	UT	0.0124	0.993	(0.986,1.000)	0.994	(0.985,1.003)	0.4236
	WI	0.0001	1.021	(1.002,1.040)	1.016	(0.997,1.035)	0.4373

^aProbability associated with Hosmer-Lemeshow Goodness of fit test. Small p-values (say, < 0.05) indicate that the distribution of predicted values differs significantly from the distribution of observed values. Probabilities shown for the individual states correspond to individual state analyses; the remaining probabilities correspond to the pooled analyses.

^bProbability associated with the null hypothesis that a quadratic exposure coefficient is zero.

^cModels were adjusted for age, marital status, education, race/ethnicity of the mother, Kessner measure of prenatal care, sex of the child, mother's smoking status, and whether there were any pregnancy complications.

Table 3

Summary statistics comparing the full gestation period exposures ($\mu\text{g}/\text{m}^3$) by analysis level and state.

State	# Births	Level	Mean	Std. Dev.	Min.	Max.
New Jersey	57,039	County Grid	14.3	1.3	9.3	17.2
			13.8	1.7	7.6	18.7
New York	400,033	County Grid	11.6	1.7	5.9	17.3
			11.0	1.8	4.5	17.6
Utah	162,367	County Grid	9.5	2.8	2.9	18.9
			9.7	3.0	2.7	19.7

Table 4

Correlation of grid level and county level exposures of PM_{2.5} by gestation period.

State	Gestation Period			
	Full	Tri. 1	Tri. 2	Tri. 3
New Jersey	0.682	0.729	0.697	0.690
New York	0.606	0.676	0.651	0.665
Utah	0.905	0.907	0.884	0.883