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Exposure to Coarse Particulate Matter during Gestation and Birth Weight in the U.S.

Keita Ebisu[a], **Jesse D. Berman**[a], and **Michelle L. Bell**[a]

Keita Ebisu: keita.ebisu@aya.yale.edu; Jesse D. Berman: jesse.berman@yale.edu; Michelle L. Bell: michelle.bell@yale.edu

[a] Yale University, School of Forestry and Environmental Studies, 195 Prospect Street, New Haven, CT 06511 USA

Abstract

Few studies have explored the relationship between coarse particles ($PM_{10-2.5}$) and adverse birth outcomes. We examined associations between gestational exposure of $PM_{10-2.5}$ and birth weight. U.S. birth certificates data (1999-2007) were acquired for 8,017,865 births. Gestational and trimester exposures of $PM_{10-2.5}$ were estimated using co-located PM_{10} and $PM_{2.5}$ monitors ≤ 35 km from the population-weighted centroid of mothers' residential counties. A linear regression model was applied, adjusted by potential confounders. As sensitivity analyses, we explored alternative $PM_{10-2.5}$ estimations, adjustment for $PM_{2.5}$, and stratification by regions. Gestational exposure to $PM_{10-2.5}$ was associated with 6.6 g (95% Confidence Interval: 5.9, 7.2) lower birth weight per interquartile range increase (7.8 $\mu g/m^3$) in $PM_{10-2.5}$ exposures. All three trimesters showed associations. Under different exposure methods for $PM_{10-2.5}$, associations remained consistent but with different magnitudes. Results were robust after adjusting for $PM_{2.5}$, and regional analyses showed associations in all four regions with larger estimates in the South. Our results suggest that $PM_{10-2.5}$ is associated with birth weight in addition to $PM_{2.5}$. Regional heterogeneity may reflect differences in population, measurement error, region-specific emission pattern, or different chemical composition within $PM_{10-2.5}$. Most countries do not set health-based standards for $PM_{10-2.5}$, but our findings indicate potentially important health effects of $PM_{10-2.5}$.

Keywords

air pollution; birth weight; coarse PM; particulate matter

1. Introduction

In scientific research and policy, particulate matter (PM) is often defined by size range, but not chemical constituents. There are many size types of PM (PM with aerodynamic diameter

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Corresponding Author: Keita Ebisu, 195 Prospect Street, New Haven, CT 06511 USA, Phone: (203) 432-9869, Fax: (203) 436-9158, keita.ebisu@aya.yale.edu.

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≤ 10 μm (PM_{10}), ≤ 2.5 μm ($PM_{2.5}$), etc.), and many studies reported associations between these PM metrics and adverse health outcomes, including pregnancy outcomes, across the world. For instance, gestational exposure to PM_{10} and $PM_{2.5}$ were associated with low birth weight in U.S. and Europe (1, 2). Furthermore, short-term exposure to PM_{10} and $PM_{2.5}$ were associated with mortality and morbidity (3, 4).

Consistent findings have accumulated for linking PM_{10} and $PM_{2.5}$ with health, as summarized in systematic reviews (5-7), and the U.S. Environmental Protection Agency (EPA) set National Ambient Air Quality Standards (NAAQS) for these PM metrics. On the other hand, coarse particulate matter (PM with aerodynamic diameter between 2.5 μm and 10 μm: $PM_{10-2.5}$) is not directly regulated (although is indirectly regulated through the separate regulations for PM_{10} and $PM_{2.5}$). While EPA concluded that scientific evidence of $PM_{10-2.5}$ and health outcomes are suggestive of a causal relationship, the agency notes that the number of studies is limited, and knowledge of biological plausibility is insufficient (8).

Several multi-city studies have been performed for short-term exposure to $PM_{10-2.5}$ and various health outcomes. While many studies identify associations, findings are inconsistent. Peng et al. did not find associations of $PM_{10-2.5}$ with cardiovascular and respiratory disease hospital admissions in 108 U.S. counties after controlling for $PM_{2.5}$ (9). However, Powell et al., with additional data to the study by Peng et al., observed increased cardiovascular hospitalization in association with $PM_{10-2.5}$ (10). A study using 47 U.S. counties found that $PM_{10-2.5}$ was associated with mortality (11), but a study conducted in 12 European cities did not observe a statistically significant association with mortality (12).

Only a few studies have explored birth outcomes in association with $PM_{10-2.5}$. Three of them examined a single city or state (i.e. Florida, Atlanta, and Barcelona) (13-15), and only one national study has been conducted (16). Results of these studies are inconsistent and they evaluated different exposure windows. EPA concluded that “evidence is inadequate to determine if a causal relationship exists between long-term exposure to $PM_{10-2.5}$ and developmental and reproductive outcomes,” and that further studies are warranted (8).

One of the challenging issues of $PM_{10-2.5}$ is how to estimate $PM_{10-2.5}$ levels. A direct measurement using dichotomous samplers is preferred. There are several studies used that sampling method, but the monitors were set by investigators (17, 18). Therefore, such an approach may be practical for single-city study, but not for a multi-city study. EPA does not measure $PM_{10-2.5}$ directly, resulting in $PM_{10-2.5}$ estimation based on the difference of the same location monitor of PM_{10} and $PM_{2.5}$ (co-located monitor) values for many multi-city studies (9, 10). Another approach is averaging county-wide PM_{10} and $PM_{2.5}$ levels including nearby monitors that are not co-located monitors, and taking the difference (11, 16). Both approaches have strengths and limitations. The number of co-located monitor varies by time and location, which impacts the former approach. Spatial heterogeneity of PM_{10} and $PM_{10-2.5}$, especially $PM_{10-2.5}$, is a potential concern in the latter approach (19-21). This could be particularly problematic in the western U.S., where the size of counties can be large compared to the east, and air monitor networks are far more disperse.

We explored associations between $PM_{10\text{-}2.5}$ gestational exposure and birth weight. We investigated the robustness of associations by different exposure approaches for $PM_{10\text{-}2.5}$ and by adjustment for $PM_{2.5}$ exposure. Analysis stratified by geographical region was conducted. Previous studies found heterogeneous associations of PM on health outcomes (3, 16). Birth weight is an important predictor for mortality and morbidity during childhood (1), therefore it is important to investigate whether exposure to $PM_{10\text{-}2.5}$ is associated with birth weight. As scientific evidence of linking $PM_{10\text{-}2.5}$ with adverse health, particularly birth weight, is limited, our study will inform further understanding of $PM_{10\text{-}2.5}$. Further, as direct measurement of $PM_{10\text{-}2.5}$ is not available nationwide, our sensitivity analysis of different $PM_{10\text{-}2.5}$ exposure estimations adds important insights on exposure approaches.

2. Material and methods

2.1 Birth data

Birth certificate data of the U.S. mainland from January 1999 to December 2007 were obtained from the National Center for Health Statistics. Data included variables relating to mothers and infants, such as maternal residential county at delivery, gestational length, and birth weight. We also obtained variables relating county socio-economic status (SES) from 2000 Census and 2006 American Community Survey to represent neighborhood SES: percentage of educational attainment less than a high school degree for population ≥25 years, and percentage of households with income below the poverty line as defined by family income and size and price index (22).

Delivery date was estimated based on last menstrual period (LMP) and gestational length, assuming conception two weeks after LMP. If the estimated delivery date was >30 days from the midday of the birth month reported on the birth certificate, that birth was excluded from analysis. Furthermore, births were excluded from analysis if gestational age was <37 or >44 weeks, plural deliveries, or impossible gestational age and birth weight combinations (23). These selection criteria were used in previous studies, and further description is available elsewhere (24, 25).

2.2 Exposure assessment

$PM_{2.5}$ and PM_{10} monitor values from January 1998 to December 2007 were obtained from the U.S. EPA Air Quality Systems networks. We excluded monitors if their observation frequency is less than 120 days within the study period or if the observation period (time between first and last observation within the study period) is less than one year, to avoid seasonal bias. $PM_{10\text{-}2.5}$ level was estimated by subtracting the $PM_{2.5}$ value from PM_{10} value at the co-located monitor on the same day. $PM_{10\text{-}2.5}$ values were removed from data if calculated values were negative (6.7%).

Each day, $PM_{10\text{-}2.5}$ exposure levels were assigned to counties, based on the nearest co-located PM_{10} and $PM_{2.5}$ monitors within 35 km of the county's population weighted centroid, which was calculated using the Census 2010 population. The 35 km buffer distance was based on assessments of spatial correlation across PM_{10} concentrations calculated with semivariograms. We found that for more than 75% of days, the minimum semivariance among monitor pairs fell within a 0 to 40km distance. Because our exposure of interest is $PM_{10\text{-}2.5}$, ideally the initial buffer size for analyses would be determined based on $PM_{10\text{-}2.5}$ concentrations. However, due to the sparse number of co-located monitors, we lack the power to calculate spatial dependence using semivariograms. Therefore, we determined the buffer size using estimated semivariance of PM_{10}, which is more heterogeneous compared to $PM_{2.5}$ (26).

Gestational and trimester exposures of $PM_{10\text{-}2.5}$ were estimated based on residential county of the mother at time of birth. First, second, and third trimester were defined as 1-13 weeks, 14-26 weeks, and week 27 to delivery, respectively. We first estimated weekly-averaged $PM_{10\text{-}2.5}$ levels, which were calculated to avoid observational frequency bias (1, 24). Gestational and trimester $PM_{10\text{-}2.5}$ levels were estimated by averaging weekly levels. Births were excluded if more than 25% of weekly-averaged $PM_{10\text{-}2.5}$ levels were unavailable in any trimester. This will prevent seasonally biased air pollution sampling (1). Counties were excluded if the available length of data (time between first and last daily $PM_{10\text{-}2.5}$ estimate in that county) was less than 4 years or the number of births within that county during the study period is less than 100, so that we exclude counties with a short observation period. To control for overall weather discomfort, apparent temperature for each trimester was calculated following same approach used to estimate trimester $PM_{10\text{-}2.5}$ exposures. Daily apparent temperature was estimated by combing daily temperature and dew point, which were obtained from closest weather station from county's population-weighted centroid (27).

2.3 Statistical analysis

A linear model with birth weight as a continuous variable was used. We explored separate models of 1) $PM_{10\text{-}2.5}$ gestational exposure, and 2) $PM_{10\text{-}2.5}$ trimester exposures: all three trimester exposures included simultaneously. Adjusted variables include sex of infant; gestational length; maternal age, race, educational attainment, and marital status; birth order; the trimester in which prenatal care began; alcohol and/or tobacco consumption during pregnancy; indicator variables of birth year, season, and state; neighborhood SES (% less than high school education and % of households below poverty line); and apparent temperature for each trimester. When these variables were missing on birth certificate, we labeled as unknown and included in the analyses. The statistical model and covariates are chosen following our earlier studies (1, 24). For the trimester exposures model, we conducted a trimester residual model to address correlation of exposures among trimesters. In brief, a specific trimester exposure level was used to predict the remaining trimester exposures. We took residuals of actual exposure levels from predicted values, and included them in the model in addition to the referenced trimester. Detail explanations of the trimester residual model can be found elsewhere (1, 28).

A number of sensitivity analyses were conducted. First, we applied two alternative methods of estimating $PM_{10\text{-}2.5}$ ($PM_{10\text{-}2.5\_alt1}$ and $PM_{10\text{-}2.5\_alt2}$). For daily $PM_{10\text{-}2.5alt1}$ values, we averaged available co-located monitors within the county; an approach that has been applied in many previous births outcome studies for estimating gestational exposures for air pollutants (29, 30). As another approach, $PM_{10\text{-}2.5\_alt2}$, we subtracted the daily county average $PM_{2.5}$ from the daily county average PM_{10}, regardless of whether the monitors were co-located. Several studies used this definition to explore relationships with adverse health outcomes (11, 16). Second, we explored whether the gestational $PM_{10-2.5}$ association, using our original $PM_{10-2.5}$ exposure estimate, is robust to adjustment by gestational exposure of $PM_{2.5}$ by adding this variable to the main model. Gestational exposure of $PM_{2.5}$ was estimated in the same way as $PM_{10-2.5}$ exposure. Furthermore, we stratified the analysis by region (East, South, North, and West), based on U.S. EPA regions (Supplementary Figure 1) (31). In addition to the 35 km buffer, we performed analyses with two other buffer sizes (20 and 50 km). Moreover, instead of removing negative values of $PM_{10-2.5}$, we retained these negative values and included them in the analyses. For comparison purpose, all results of $PM_{10-2.5}$ associations were expressed in birth weight change (g) per interquartile range (IQR) increase in gestational $PM_{10-2.5}$ exposures using the original $PM_{10-2.5}$ estimation.

3. Results

There were 12,066,006 births, who had at least one $PM_{10-2.5}$ estimation. Among them, 102,844 births (0.8%) were excluded, because their estimated delivery date was >30 days from the midday of the birth month on the birth certificate. Birth exclusion criteria (e.g. plural, preterm births, etc.) omitted 1,951,164 births (14.3%), and 2,245,421 births (16.5%) did not meet air pollution criteria (i.e. missing > 25% $PM_{10-2.5}$ observations in any trimester). More than one exclusion criteria could be applied for some births. After applying these exclusion criteria, analysis included 8,017,865 births from 224 counties. Average birth weight was 3,394.0 g (standard deviation (SD): 467.9), and mean $PM_{10-2.5}$ and $PM_{2.5}$ levels during gestation were 13.7 $\mu g/m^3$ (SD: 5.7, IQR: 7.8) and 12.9 $\mu g/m^3$ (SD: 3.6, IQR: 5.3), respectively. Correlation between gestational exposures of $PM_{10-2.5}$ and $PM_{2.5}$ was 0.11. Distribution of pregnancy-related variables is summarized in Table 1. The population included 720,670 births from the East (43 counties), 2,054,373 from the North (73 counties), 1,992,041 from the South (58 counties), and 3,250,781 from the West (50 counties) region. Supplementary Table 1 shows summary statistics, including $PM_{10-2.5}$ and $PM_{2.5}$ gestational exposure, stratified by region.

Our main model showed association between gestational $PM_{10-2.\ 5}$ exposure and birth weight. Birth weight decreased 6.6 g (95% Confidence Interval (CI): 5.9, 7.2) per IQR increase (7.8 $\mu g/m^3$) of $PM_{10-2.5}$ gestational exposure (Table 2). Sensitivity analysis using alternative estimations of $PM_{10-2.5}$ also exhibited associations, although with different magnitudes. An IQR increase of $PM_{10-2.5\_alt1}$ and $PM_{10-2.5\_alt2}$ were associated with lowering birth weight by 10.4g (95% CI: 9.6, 11.2) and 3.4 g (95% CI: 2.8, 4.1), respectively. Correlation between original $PM_{10-2.5}$ estimation and $PM_{10-2.5\_alt1}$, and original $PM_{10-2.5}$ estimation and $PM_{10-2.5\_alt2}$ were 0.90 and 0.76, respectively. The association between $PM_{10-2.5}$ and birth weight was robust after adjusting for $PM_{2.5}$ gestational exposure: 5.4 g (95% CI: 4.7, 6.1). In same model, exposure to $PM_{2.5}$ also showed an association with birth weight: 4.4 g (95% CI: 3.6, 5.2) decrease of birth weight per IQR increase (5.3 $\mu g/m^3$) in $PM_{2.5}$ gestational exposure. We also observed an association for $PM_{2.5}$ gestational exposure in a model without $PM_{10-2.5}$: 6.4 g (95% CI: 5.6, 7.1).

Associations were found in all three trimesters (Table 2) with a 2.0 g (95% CI: 1.3, 2.6), 2.1 g (95% CI: 1.4, 2.8), and 2.6 g (95% CI: 2.0, 3.2) decrease in birth weight per IQR increase (7.8 μg/m^3) for the first, second, and third trimester $PM_{10\text{-}2.5}$ exposures, respectively. Correlations among trimester exposures are 0.61 to 0.74. Results were consistent under the trimester residual model (results not shown). Results of the trimester model were robust after controlling for $PM_{2.5}$ trimester exposures: the birth weight decrease per IQR increase in $PM_{10\text{-}2.5}$ exposure was 1.5 g (95% CI: 0.8, 2.2), 1.8 g (95% CI: 1.1, 2.5), and 2.1 g (95% CI: 1.5,2.8) for the first, second, and third trimesters, respectively (Table 2). Figure 1 shows results stratified by region. All four regions indicated reductions in birth weight by $PM_{10\text{-}2.5}$ gestational exposure, and estimates were particularly high in South (14.3g (95% CI: 13.0, 15.7)). Applying different buffer sizes showed similar results: 4.9g (95% CI: 5.6, 6.3) for the 20 km buffer, and 6.5g (95% CI: 5.8, 7.2) for the 50 km buffer. Similarly, replacing negative values to zero did not impact our results: 5.8g (95% CI: 5.3, 6.3).

4. Discussion

While evidence of PM_{10} and $PM_{2.5}$ impacts on birth outcomes have been frequently reported (1, 15), far less research is known regarding the potential health burden of $PM_{10\text{-}2.5}$ on birth weight. To our knowledge, this research is the largest national study investigating the association between $PM_{10\text{-}2.5}$ and birth outcomes to date. Our results indicated that gestational exposure to $PM_{10\text{-}2.5}$, as well as exposure in all three trimesters, was associated with lower birth weight. The association was retained after adjusting for $PM_{2.5}$. Notably, $PM_{2.5}$ was also associated with birth weight in a two-pollutant model, suggesting that $PM_{10\text{-}2.5}$ and $PM_{2.5}$ are independent risk factors for lower birth weight. While PM_{10} and $PM_{2.5}$ are regulated by many government agencies, most of them, including EPA, do not set a health-based standard for $PM_{10\text{-}2.5}$. Our findings indicate that mothers living in high $PM_{10\text{-}2.5}$ area may have higher risk of experiencing adverse birth outcomes.

In this study, heterogeneous effect estimates were found by region, with particularly high estimates in the Southern U.S. (Figure 1). This might be explained by exposure measurement error (32), or differences in populations by region, such as BMI (33). Alternatively, this may result from differences in $PM_{10\text{-}2.5}$ chemical constituents, which relates to the sources. Other work has demonstrated that the distribution of $PM_{2.5}$ chemical constituents differ by region (34), which is linked to heterogeneous health effect estimates for $PM_{2.5}$ (11, 24, 30). A large portion of $PM_{10\text{-}2.5}$ chemical constituents is crustal elements (i.e. aluminum, silicon etc.) and organic carbon (OC) (35-38). However, $PM_{2.5}$'s detailed spatial-temporal distribution throughout the U.S. remains unknown, because a U.S. national monitoring network for $PM_{10\text{-}2.5}$ chemical constituents' concentrations or for $PM_{10\text{-}2.5}$ total mass does not exist. There are a few studies that have explored the spatial-temporal distribution of $PM_{10\text{-}2.5}$ in selected cities. For instance, a recent EPA pilot study revealed the distribution for selected locations (8). The study measured $PM_{10\text{-}2.5}$ and selected $PM_{10\text{-}2.5}$ chemical constituents in Phoenix, Arizona, and East St. Louis, Illinois, from June 2010 to May 2011. The annual average of $PM_{10\text{-}2.5}$ total mass value was much higher in Phoenix (18.7 μg/m^3) than East St. Louis (9.4 μg/m^3). Local environments and sources could contribute to difference in $PM_{10\text{-}2.5}$ composition with higher silicon concentrations observed in Phoenix and higher OC in East St. Louis. Phoenix is surrounded by desert, while emissions from traffic and industrial plants, sources of OC, play a major role in East St. Louis (34). Heterogeneous $PM_{10\text{-}2.5}$ levels in 20 European areas were also observed in ESCAPE project (39). Furthermore, variability of $PM_{10\text{-}2.5}$ and its chemical constituents was observed across cities and within cities according to a study conducted in three U.S. cities (40). Further data collection across U.S. is needed to better understanding for seasonal variations within a city or between cities.

A U.S. national study by Parker et al. explored associations between gestational/trimester exposures to $PM_{10\text{-}2.5}$ and PM_{10} with birth weight (16). Birth weight was associated with $PM_{10\text{-}2.5}$ for gestational and all three trimester exposures. For instance, their result showed that gestational exposure to $PM_{10\text{-}2.5}$ was associated with 9.9 g (95% CI: 5.8, 14.0) lower birth weight per our IQR increase, which is higher than our estimate (6.6 g (95% CI: 5.9, 7.2)). These associations were robust after controlling for $PM_{2.5}$, although their $PM_{2.5}$ estimate showed protective associations with birth weight. The study by Parker et al. also conducted regional stratification analyses, but findings differed from ours. They did not find associations in some regions, and the association was the strongest in Northwest, which corresponds to the northern part of our West region plus the western part of our North region, whereas we observed associations in all regions with the highest estimate in the South region. Several factors likely contributed to the varying results. We only used monitors with observation frequency ≥120 days and observation period ≥1 years to avoid seasonally biased sampling. Our study period was longer than the Parker et al. study (9 years vs. 3 years), leading to more subjects and counties available for analyses. Counties included in analyses were different, which could lead to a different distribution of $PM_{10\text{-}2.5}$ chemical constituents. Finally, adjusted variables were different: we included gestational length, neighborhood SES variables, etc.

A few other studies have explored the relationship between $PM_{10\text{-}2.5}$ and birth outcomes (13-16). Gestational exposure to $PM_{10\text{-}2.5}$ was linked to increased risk of low birth weight in Florida (13). A study in Atlanta found that third trimester exposure to $PM_{10\text{-}2.5}$ was associated with lower birth weight for non-Hispanic Blacks and Hispanics, but not for non-Hispanic Whites (14). They did not investigate the association with gestational, first trimester, or second trimester exposures. Dadvand et al. conducted a study in Barcelona, Spain, and found an association between third trimester exposure to $PM_{10\text{-}2.5}$ and low birth weight (15); however, this association became null after adjusting for proximity to major roads.

Attention should be paid to the estimation of $PM_{10\text{-}2.5}$, as the methods differ by studies. Our original estimation was calculated by subtracting daily $PM_{2.5}$ values from PM_{10} values at the nearest co-located monitor within 35 km from the residential county's population weighted centroid. In Parker et al., $PM_{10\text{-}2.5}$ was based on daily values calculated as the difference between county averaged PM_{10} and $PM_{2.5}$, which corresponds to our $PM_{10\text{-}2.5\_alt2}$. Both $PM_{10\text{-}2.5}$ estimations showed associations with lower birth weight in our analyses, but with different estimates (Table 2). Our method of $PM_{10\text{-}2.5\_alt1}$, similar to $PM_{10\text{-}2.5\_alt2}$ but only using co-located monitors, was applied in handful studies (9, 10). Results using $PM_{10\text{-}2.5\_alt1}$ supported associations, but magnitudes differed. Both $PM_{10\text{-}2.5\_alt1}$ and $PM_{10\text{-}2.5\_alt2}$ have limitations; exposure misclassification is a problematic in large counties for $PM_{10\text{-}2.5\_alt1}$, and inaccurate measurement for $PM_{10\text{-}2.5}$ due to different sampling locations for PM_{10} and $PM_{2.5}$ is an issue for $PM_{10\text{-}2.5\_alt2}$. EPA recommends direct measurement of $PM_{10\text{-}2.5}$ using dichotomous sampling method, which minimizes the measurement error by segregating fine and coarse particles onto separate filters (8, 41). EPA regards the direct measurements of $PM_{10\text{-}2.5}$ as preferable to estimations based on PM_{10} and $PM_{2.5}$ measurements due to uncertainties (8, 42). Nevertheless, most of current $PM_{10\text{-}2.5}$ literatures rely on $PM_{10\text{-}2.5}$ estimation due to limited availability of $PM_{10\text{-}2.5}$ dichotomous sampling (9, 11).

Our original $PM_{10\text{-}2.5}$ estimation, based on co-located monitor, avoids spatial exposure misclassification. The spatial heterogeneity of pollutants can vary by pollutant (e.g., PM_{10}, $PM_{2.5}$, and $PM_{10\text{-}2.5}$) (19, 25, 40). Supplementary Figure 2 presents correlations of $PM_{2.5}$ or PM_{10} monitor pairs against distances between monitors. The plot indicated more homogeneous levels of $PM_{2.5}$ over long distances compared to PM_{10}, which exhibited higher heterogeneity over short distances. Although the spatial heterogeneity of $PM_{10\text{-}2.5}$ is not fully understood due to the lack of a large ambient monitoring network, this study only assigned $PM_{10\text{-}2.5}$ exposure estimates to counties with population weighted centroid ≤ 35 km from the co-located monitor to minimize exposure misclassification. Using other buffer sizes (20 and 50 km) showed similar results, though results should be interpreted with caution since population characteristics could differ by different buffer sizes (25). Nevertheless, some exposure misclassification may exist due to the spatial heterogeneity of $PM_{10\text{-}2.5}$, measurement error, and relying on to ambient monitors, which do not account for individual behavior patterns. Additional research is needed to better understand the implications of methods to estimate $PM_{10\text{-}2.5}$ exposure and their implications for exposure misclassification, health effects, etc.

The lack of direct measurements for $PM_{10\text{-}2.5}$ contributes to key limitations for all large studies on $PM_{10\text{-}2.5}$ including this study. For instance, calculated $PM_{10\text{-}2.5}$ values were occasionally negative as mentioned above, indicating measurement error. However, according to EPA committee, negative values for PM_{10}-$PM_{2.5}$ are not a serious concern if they constitute a small fraction of data and are spatially unbiased (43). In our analysis, we removed negative $PM_{10\text{-}2.5}$ dates from data, and results were similar when these negative values were included in analysis. A further challenge is that the number of U.S. air quality monitors has declined over recent years for several states (e.g. New York), particularly for $PM_{10,}$ hindering the estimation of $PM_{10\text{-}2.5}$: PM_{10} monitors in U.S. decreased from 1,055 in 1999 to 872 in 2007. In fact, available monitor numbers were less in East region compared to other regions (Supplementary Table 1), resulting in less subjects in this region.

These challenges in assessing exposure likely contribute to the lack of studies on this topic, which also highlights the need for such research. We addressed these limitations by investigating multiple exposure estimations, and identified associations under all methods. Still, there is a possibility that $PM_{10\text{-}2.5}$ served as surrogates for other unmeasured pollutants. Our study also faces limitations that are typical of national studies. For example, we could only access to limited maternal information; we cannot adjust maternal BMI or neighborhood SES levels in census tract unit. We also cannot access maternal residential history; some mothers could move during pregnancy, leading to exposure misclassification.

A recent study, however, found that changes in effect estimates were negligible even after taking account for maternal mobility (44). Second, attention should be paid to some variables (e.g. tobacco and alcohol consumption) on birth certificate for their reliability and validity (45). The reliability and validity of these variables are not fully known, but one study concluded that variables on birth certificate are adequate to use for adjustment purpose (46). Indeed, associations between $PM_{10-2.5}$ and birth weight were retained after excluding mothers with smoking and/or alcohol consumption status during pregnancy (results now shown). Another limitation is that the monitors used in this study are not equally distributed and tend to be located in urban areas (47). Therefore, mothers who are exposed to higher pollutants than others are more likely to be included in our analyses. In addition, average birth weight for births within the 35km buffer (3394.0g) is slightly lower than for those who lived outside the buffer (3,403.4g), and maternal characteristics and SES are also different (25). Depending on the population patterns, selection of buffer size can introduce selection bias; however, we present analyses with two other buffer sizes (20 and 50 km), and results were robust.

Several plausible biological mechanisms have been proposed for an impact of $PM_{10-2.5}$ on birth weight. Animal experiments found that exposure to $PM_{10-2.5}$ evokes lung inflammation (48, 49), and the estimate of $PM_{10-2.5}$ was stronger than that of $PM_{2.5}$ per mass (50). Inflammation may change blood viscosity, which eventually alters placenta vascular function (51). An alternative explanation is that nutrition transfer and/or placenta development is prevented by placental mitochondrial alterations, which could be caused by $PM_{10-2.5}$ exposure (52). Exposure to $PM_{10-2.5}$ induces oxidative stress, which may contribute to lower birth weight (53). Similar to $PM_{2.5}$ chemical constituents, various combinations of $PM_{10-2.5}$ chemical constituents may involve different biological pathway in different trimesters (24, 25). Further investigations are necessary to investigate potential biological mechanism for $PM_{10-2.5}$ exposure and birth outcomes.

A handful of studies explored associations of $PM_{10-2.5}$ with mortality and morbidity outcomes (10, 54), but studies linking to adverse birth outcomes remain scarce and inconclusive (14, 16). Our study found that exposures to $PM_{10-2.5}$ during gestation and all three trimesters are associated with lower birth weight among term birth infants, in addition to the association of $PM_{2.5}$ and birth weight. Heterogeneous results by region could relate to region-specific emission patterns and different $PM_{10-2.5}$ chemical constituents, as well as exposure measurement error and differences in populations. $PM_{10-2.5}$ is not directly regulated, but our findings indicate potentially important health effects of $PM_{10-2.5}$. Since every pregnant woman is at risk, exposure to $PM_{10-2.5}$ is a public health concern. Research on $PM_{10-2.5}$ has been hindered by the lack of widespread direct measurement of $PM_{10-2.5}$. Future studies may apply further alternative estimation (e.g. combining satellite imagery) or sophisticated statistical modeling, such as generalized linear mixed models. As the U.S. EPA prepares to expand the $PM_{10-2.5}$ monitoring network, which measure $PM_{10-2.5}$ total mass and chemical constituents (8), additional research could evaluate the results identified here. This will shed light on spatio-temporal distribution of $PM_{10-2.5}$, and aid identification of the regions and populations with higher health risks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviation

EPA	U.S. Environmental Protection Agency
IQR	interquartile range
LMP	last menstrual period
NAAQS	National Ambient Air Quality Standards
PM	particulate matter
PM_{10}	particulate matter with aerodynamic diameter ≤ 10 μm
$PM_{10\text{-}2.5}$	coarse particulate matter
$PM_{2.5}$	particulate matter with aerodynamic diameter ≤ 2.5 μm
OC	organic carbon
SES	socio-economic status

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Highlights

- Only a few studies have explored birth outcomes in association with $PM_{10-2.5}$
- We explored associations between $PM_{10-2.5}$ gestational exposure and birth weight
- $PM_{10-2.5}$ is associated with birth weight in addition to $PM_{2.5}$
- Our findings indicate potentially important health effects of $PM_{10-2.5}$

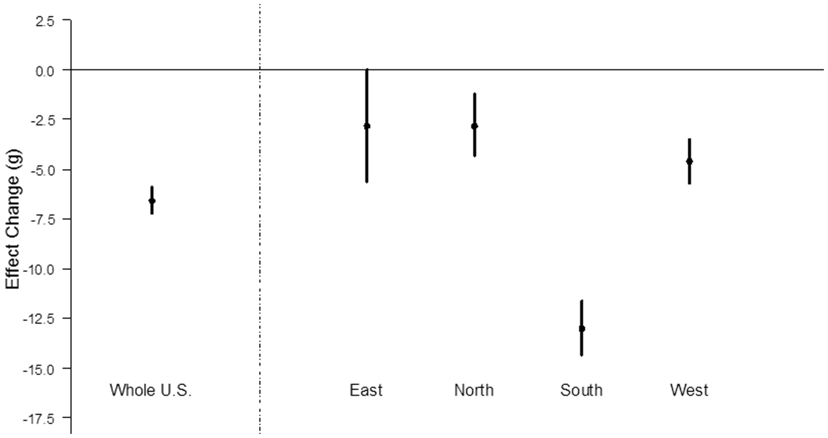

Figure 1.

Associations between $PM_{10-2.5}$ and Birth Weight: Overall and Stratified by Region. Change in birth weight (g) per IQR increase (7.8 μg/m^3) of $PM_{10-2.5}$ gestational exposure. For comparison purpose, the same IQR values were applied to estimates in all regions. The points represent the central estimated effects, and the vertical lines the 95% CIs.

Table 1

Summary Statistics of Population and Exposures

Total Number of Births		8,017,865
PM Gestational Exposures		
$PM_{10-2.5}$ Gestational Exposure[a]	mean (SD)	13.72 µg (5.67)
$PM_{2.5}$ Gestational Exposure	mean (SD)	12.87 µg (3.58)
Mother and Infant Characteristics		
Birth Weight	mean (SD)	3,394.0 g (467.9)
Gestational Length	37-38 weeks	2,421,380 (30.2%)
	39-40	4,185,847 (52.2%)
	41-44	1,410,638 (17.6%)
Maternal Age	<20 years	841,790 (10.5%)
	20-24	1,976,411 (24.7%)
	25-29	2,175,054 (27.1%)
	30-34	1,884,789 (23.5%)
	35-39	934,974 (11.7%)
	>40	204,847 (2.6%)
Maternal Race	White	6,149,190 (76.7%)
	Black	1,221,968 (15.2%)
	Other	646,707 (8.1%)
Maternal Educational Attainment	Less than High School	1,980,837 (24.7%)
	High School	2,195,200 (27.4%)
	Some College	1,671,202 (20.8%)
	College	2,037,459 (25.4%)
	Unknown	133,167 (1.7%)
Maternal Marital Status	Married	5,050,811 (63.0%)
	Unmarried	2,967,054 (37.0%)
Infant's Sex	Male	4,079,206 (50.9%)
	Female	3,938,659 (49.1%)
Parity	First Birth	2,749,952 (34.3%)
	Second or Later Birth	5,243,384 (65.4%)
	Unknown	24,529 (0.3%)
Trimester Prenatal Care Begin	First	6,498,200 (81.0%)
	Second	1,088,782 (13.6%)
	Third	227,415 (2.8%)

	Never	71,847 (0.9%)
	Unknown	131,621 (1.6%)
Tobacco Consumption During Pregnancy	Yes	489,034 (6.1%)
	No	5,177,739 (64.6%)
	Unknown	2,351,092 (29.3%)
Alcohol Consumption During Pregnancy	Yes	32,248 (0.4%)
	No	4,154,003 (51.8%)
	Unknown	3,831,614 (47.8%)
SES Levels of Residential County		
Less than High School Education (%)	mean (SD)	18.5 % (6.4)
Below Poverty Line (%)	mean (SD)	13.8 % (4.3)

[a] $PM_{10-2.5}$ is based on original estimation.

Table 2

Change in Birth Weight (95% CI) per IQR Increase of $PM_{10\text{-}2.5}$

Pollutant	N	Exposure Period	Change in Birth Weight (g)[a]
$PM_{10\text{-}2.5}$	8,017,865	Whole Gestation	−6.6 (−7.2, −5.9)
		1st trimester	−2.0 (−2.6, −1.3)
		2nd trimester	−2.1 (−2.8, −1.4)
		3rd trimester	−2.6 (−3.3, −2.0)
$PM_{10\text{-}2.5\_alt1}$[b]	8,799,256	Whole Gestation	−10.4 (−11.2, −9.6)
$PM_{10\text{-}2.5\_alt2}$[c]	10,597,927	Whole Gestation	−3.4 (−4.1, −2.8)
$PM_{10\text{-}2.5}$ (adjusted by $PM_{2.5}$)	8,017,865	Whole Gestation	−5.4 (−6.1, −4.7)
		1st trimester	−1.5 (−2.2, −0.8)
		2nd trimester	−1.8 (−2.5, −1.1)
		3rd trimester	−2.1 (−2.8, −1.5)

[a] IQRs are 7.8 μg/m^3 for $PM_{10\text{-}2.5}$; for comparison purpose, the same IQR values were applied for $PM_{10\text{-}2.5}$, $PM_{10\text{-}2.5\_alt1}$, and $PM_{10\text{-}2.5\_alt2}$ estimates. Included adjusted variables were sex of infant, gestational length, maternal age, race, educational attainment, and marital status, birth order, the trimester in which prenatal care began, alcohol and/or tobacco consumption during pregnancy, indicator variable of birth year, season, and state, neighborhood SES (% less than high school education and % of households below poverty line), and apparent temperature for each trimester.

[b] $PM_{10\text{-}2.5\_alt1}$ is estimated by averaging the $PM_{10\text{-}2.5}$ values estimated only from co-located monitors within a county.

[c] $PM_{10\text{-}2.5\_alt2}$ is based on daily estimates based on using all PM monitors to estimate county levels of PM_{10} and $PM_{2.5}$ separately and then subtracting them.