Journal of Exposure Science and Environmental Epidemiology (2010) 20, 469–477
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www.nature.com/jes

Assessing exposure metrics for PM and birth weight models

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The link between air pollution exposure and adverse birth outcomes is of public health concern due to the relationship between poor pregnancy outcomes and the onset of childhood and adult diseases. As personal exposure measurements are difficult and expensive to obtain, proximate measures of air pollution exposure are traditionally used. We explored how different air pollution exposure metrics affect birth weight regression models. We examined the effect of maternal exposure to ambient levels of particulate matter <10, $<2.5\,\mu m$ in aerodynamic diameter (PM_{10}, $PM_{2.5}$) on birth weight among infants in North Carolina. We linked maternal residence to the closest monitor during pregnancy for 2000–2002 ($n = 350{,}754$). County-level averages of air pollution concentrations were estimated for the entire pregnancy and each trimester. For a finer spatially resolved metric, we calculated exposure averages for women living within 20, 10, and 5 km of a monitor. Multiple linear regression was used to determine the association between exposure and birth weight, adjusting for standard covariates. In the county-level model, an interquartile increase in PM_{10} and $PM_{2.5}$ during the entire gestational period reduced the birth weight by 5.3 g (95% CI: 3.3–7.4) and 4.6 g (95% CI: 2.3–6.8), respectively. This model also showed a reduction in birth weight for PM_{10} (7.1 g, 95% CI: 1.0–13.2) and $PM_{2.5}$ (10.4 g, 95% CI: 6.4–14.4) during the third trimester. Proximity models for 20, 10, and 5 km distances showed results similar to the county-level models. County-level models assume that exposure is spatially homogeneous over a larger surface area than proximity models. Sensitivity analysis showed that at varying spatial resolutions, there is still a stable and negative association between air pollution and birth weight, despite North Carolina's consistent attainment of federal air quality standards.
Journal of Exposure Science and Environmental Epidemiology (2010) **20,** 469–477; doi:10.1038/jes.2009.52; published online 23 September 2009

Keywords: *air pollution, particulate matter, birth weight, birth outcomes, exposure metrics.*

Introduction

Many epidemiological studies have been conducted to investigate the effect of maternal exposure to air pollution on adverse pregnancy outcomes (Bobak, 2000; Ha et al., 2001; Chen et al., 2002; Dugandzic et al., 2006; Bell et al., 2007). Results of these studies have shown that exposure to air pollution may elevate the risk of adverse birth outcomes, including low birth weight (LBW), preterm delivery, and small for gestational age (Ritz et al., 2000; Vassilev et al., 2001; Lee et al., 2003; Yang et al., 2003; Lin et al., 2004; Mannes et al., 2005; Parker et al., 2005).

Poor birth outcomes are significant predictors of neonatal mortality and morbidity (McCormick, 1985). Evidence shows that children born LBW, preterm delivery, or small for gestational age are at an increased risk for both short-term neonatal morbidity and long-term health effects (Hack et al., 1995; Lemons et al., 2001). Such effects include mental retardation (Lorenz et al., 1998), severe vision loss (Crofts et al., 1998), deafness (Lorenz et al., 1998), learning disabilities (Resnick et al., 1999; Saigal et al., 2000), motor impairment (Ross et al., 1990), and cerebral palsy (Kuban and Leviton, 1994), as well as hypertension, cardiovascular disease, and type 2 diabetes in adulthood (Ashdown-Lambert, 2005).

Although the biological mechanisms by which air pollutants may influence birth weight and fetal growth are as yet unknown, studies suggest that air pollution exposure during pregnancy may lead to placental inflammation, which impairs placental function, and chronic inflammation may in turn result in growth restriction (Lee et al., 2003). Data also suggest that fetuses may be more prone to genetic damage and process toxicants less efficiently than adults (Perera et al., 1999). Perera et al. (1999) also propose that increased DNA adducts in the fetus relative to the mother could result in lower levels of detoxification enzymes and decreased DNA repair efficiency in the fetus.

Epidemiologists and policy makers are often interested in the effect of particulate air pollution on susceptible populations; (NRC, 1998) thus pregnant women are of particular concern. As the National Research Council (NRC) identified at-risk subpopulations as a high priority research task, several studies have been conducted to better examine the effects of PM exposure and adverse pregnancy outcomes (Resnick et al., 1999; Ritz et al., 2000; Bell et al., 2007).

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Received 21 April 2009; accepted 11 August 2009; published online 23 September 2009

In the last of the four reports produced by the NRC in 2004, the group determined that more research needs to be done to clarify uncertainties about impacts of maternal exposure to PM on pregnancy and to understand how environmental factors can affect adverse pregnancy outcomes (NRC, 2004).

Although much attention has been given to studying the relationship between adverse pregnancy outcomes and air pollution, many of these studies are limited to sparsely located monitoring station data (Bobak, 2000; Bell et al., 2007; Hansen et al., 2008). These studies use average measurements calculated from monitoring stations within city or county limits, or postal codes. Epidemiologists are aware that measurements obtained from ambient monitoring stations may not be representative of personal exposure for all subjects within a predetermined geographic area (Jerrett et al., 2005). Consequently, the use of personal exposure measures based on city or county levels may misclassify individual exposure.

While many studies have found significant results, the traditional analyses may misclassify exposure because of the way the exposure is measured and modeled (Thomas et al., 1993; Dominici et al., 2003). Using measurements based on residing either within a certain geographic area or proximity to a monitoring station as a proxy for personal exposure assumes that air pollution levels are spatially homogeneous across the defined geographic regions. Although lacking precision, this method of estimating exposure for an individual or a population has been used in air pollution and health effects studies (Dockery et al., 1993; Samet et al., 2000; Pope et al., 2002), as collection of accurate personal level exposures is often difficult and expensive to obtain. In the presence of potential measurement error, it is important to determine whether these measurements affect the exposure–response relationship.

In this paper, we evaluate how robust the air pollution and birth weight relationship is to different air pollution measurements. For comparability to other studies (Chen et al., 2002; Rogers and Dunlop, 2006; Bell et al., 2007), we use air pollution metrics based on county averages for the State of North Carolina. We then use buffering schemes associated with proximity models of 20-, 10-, and 5-km radii and compare how these different exposure metrics affect the birth weight model. As previous studies have used distances ranging from 2 to 50 km (Yang et al., 2003; Mannes et al., 2005; Ritz et al., 2006), we chose a range of distances for greater cross-study comparability. Our goal is to investigate how birth weight regression models change when different exposure metrics are used. Importantly, North Carolina communities are typically below the federal standards for both PM_{10} and $PM_{2.5}$, therefore these analyses have direct relevance to the policy debate regarding setting regulatory standards to protect public health.

Methods

Birth Data

The North Carolina Detailed Birth Record (NCDBR) data were obtained from the North Carolina State Center for Health Statistics. The NCDBR data contain information on both birth outcomes and parental demographics for all registered births in North Carolina. We limited our analysis to the years 2000–2002 ($n = 350{,}754$). The recorded birth information in the NCDBR used in this study included gestational age (weeks), infant sex, birth weight, congenital anomalies, and year of birth. The maternal characteristics recorded in the NCDBR included residential address, age, marital status, education, race and ethnicity, alcohol and tobacco use, plurality, birth order, and the trimester in which prenatal care began.

To link births from the NCDBR to the air pollution data, we street geocoded the residential addresses in the dataset at the individual record level (all spatial data management was performed using ArcGIS 9.2 produced by ESRI, Redlands, CA). The total births successfully geocoded using the maternal residence at the time of delivery in North Carolina can be seen in Figure 1. Approximately, 17% of the total births could not be geocoded due to unmatched address locations. To determine whether systematic differences exist between the full geocoded dataset and the subsets for which air pollution data were available, summary statistics (data not shown) were calculated using Census data from the zip code links and the DBR data. Differences were not significant enough to undermine the analytical work presented here.

We excluded multi-fetal births (3.3%), and infants characterized by congenital anomalies (0.9%). These exclusions were chosen, as we sought to focus on those pregnancies that could reasonably be expected to go to term and deliver at a normal birth weight. We also excluded women <15 and >44 years (0.3%) with reported alcohol consumption (0.6%). As 95% of the women in the dataset self-declared as non-Hispanic white, non-Hispanic black, or Hispanic, we excluded other races/ethnicities due to the small sample size for other minority groups. We excluded births with gestation <32 and >44 weeks (2.2%), birth weight <1000 and >5500 g (1.0%), impossible birth weight and gestation combinations (0.1%) (Alexander et al., 1996), and mothers with any missing data on covariates (1.0%), leaving 259,962 cases. For the county-level model, we focused on

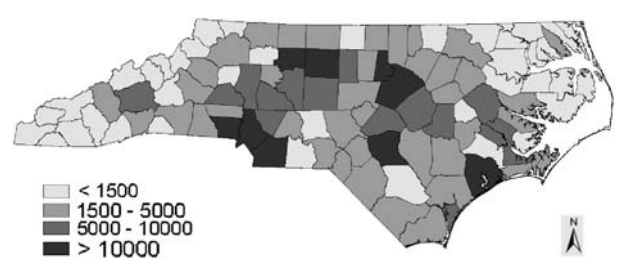

Figure 1. Total geocoded births in North Carolina.

women who lived in a county with an active monitoring station, whereas for the proximity models, we used only women within a 20-, 10-, and 5-km buffer of a monitoring station.

Air Pollution Data

The air pollution datasets for PM_{10} and $PM_{2.5}$ were obtained from the US EPA Air Quality System (AQS) for 1999–2002 (US Environmental Protection Agency, 2006a). The analyses used births between the years of 2000–2002, and air pollution exposures from 1999–2002, as exposures for some 2000 births occurred in 1999. The AQS data contained the daily 24-h average concentration ($\mu g/m^3$) for PM_{10} and $PM_{2.5}$. There were between 27 and 37 active PM_{10} monitors and between 37 and 41 active $PM_{2.5}$ monitors in North Carolina during 1999–2002. The monitors recorded pollution measurements everyday, every 3 days, or every 6 days with some monitors being added to or removed from operation during the years of the study. The difference in the frequency of recordings at certain monitoring stations is random and should not introduce any bias into the study. Locations of the PM_{10} and $PM_{2.5}$ monitors in North Carolina can be seen in Figure 2.

Maternal Exposure Assessment

To estimate air pollution exposure for the proximity models, each mother's residence at the time of delivery was linked to the closest active monitor. The weeks of exposure were calculated based on the actual weeks of pregnancy as recorded in the NCDBR. As birth date and gestational age were supplied as part of the NCDBR data, we calculated backwards the number of weeks of gestation from the delivery date to determine an estimated date of conception for each woman. Average maternal exposure was calculated for each pollutant by averaging the daily or weekly data of the closest monitoring station for each trimester. Trimesters were constructed based on the following categorization: 1–13 weeks of gestation, 14–26 weeks of gestations, and 27 weeks of gestation until birth. Exposure estimates averaged over the entire pregnancy were also calculated for each pollutant.

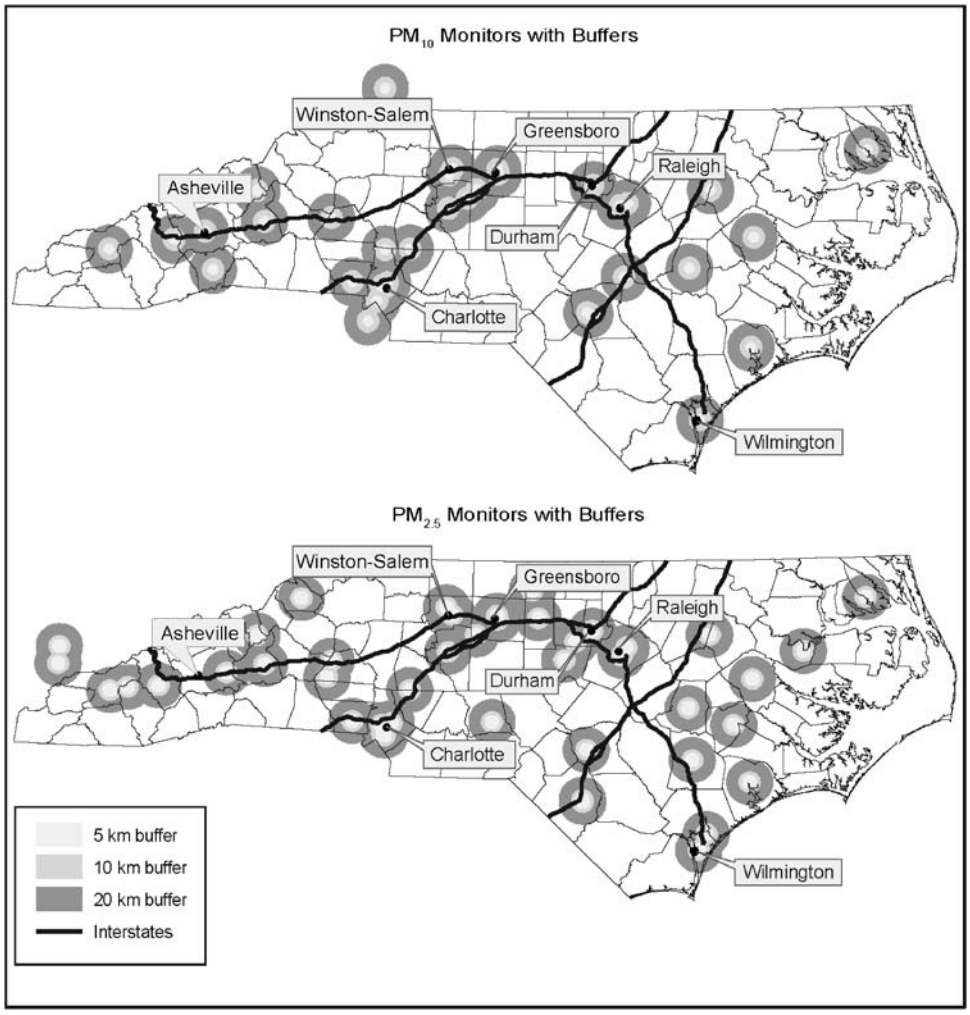

Figure 2. Location of PM_{10} and $PM_{2.5}$ monitors and distance buffers.

The AQS data were not available for every day and week of the years 1999–2002. For each birth, the completeness of the exposure dataset was identified by taking the number of weeks of gestation and dividing it by the number of AQS concentration values for that birth. If the birth had more than 75% of the data and there was no more than one consecutive missing concentration value for that birth, then the average of the concentrations for the weeks before and after the missing value were used as a proxy for the exposure concentration during that week. If there was more than one consecutive missing value for a birth, then that birth was not included in the dataset because a sufficient proxy for the 2 weeks or more of missing air quality data was not available. After all exclusion criteria, exposure estimates were calculated for 195,141 mothers for at least one of the pollutants of interest.

Statistical Analysis

Multiple linear regression modeling was used to determine the association between exposure to the pollutants of interest, PM_{10} and $PM_{2.5}$, and birth weight. Using birth weight as a continuous outcome variable, we controlled for gestational age (32–34, 35–36, 37–38, 39–40, 41–42, and 43–44 weeks), maternal race/ethnicity (non-Hispanic black, non-Hispanic white, or Hispanic), maternal education (<9, 9–11, 12, 13–15, and >15 years), maternal age (15–19, 20–24, 25–29, 30–34, 35–39, and 40–44 years), trimester prenatal care began, tobacco use during pregnancy (yes or no), marital status (married or unmarried), year of birth, firstborn (yes or no), and infant sex (male or female) for PM_{10} and $PM_{2.5}$. The exposure estimates were considered as continuous variables. We then examined the exposure–response relationship with county-wide estimates and the estimates for mothers within 20, 10, and 5 km of a monitoring station.

A baseline model without the air pollution variables was constructed to examine which of the standard covariates mentioned above affect birth weight in our sample. We then constructed separate models for PM_{10} and $PM_{2.5}$. For comparability with previous studies, we constructed models using all three trimester exposure estimates in the same model, as well as models with a pregnancy-long estimate (Maisonet et al., 2001; Glinianaia et al., 2004; Salam et al., 2005). All risk factors considered were observed as being associated with birth weight in recent literature. (Bobak, 2000; Maroziene and Grazuleviciene, 2002; Liu et al., 2003; Dugandzic et al., 2006; Bell et al., 2007),

Results

Our analysis included estimating pollution exposures for sample populations at the county level, and within the 20-, 10-, and 5-km radial buffers surrounding monitors. At the county level, there were 195,141 observations with the restrictions described above, and 167,851, 110,555, and 56,043 births at 20, 10, and 5 km, respectively. Table 1 shows the summary statistics for each of the four sample populations (county and 20-, 10-, and 5-km buffers). Among the 195,141 county-level births, the mean birth weight was 3368 g and the prevalence of LBW was 5.4%. Approximately, 11% reported smoking during pregnancy. Most of the mothers were non-Hispanic white (61%), married (68%), and with more than a high-school education (52.8%). The

Table 1. Summary statistics of the study population with exposure estimates for either PM_{10} or $PM_{2.5}$.

	20 km	10 km	5 km	County
Total births	167,851	110,555	56,043	195,141
Mean BWT (g) ± SD	3372 ± 528.4	3353 ± 530.5	3321 ± 531.9	3368 ± 530.9
% LBW	5.2	5.6	6.3	5.4
Mean gestation (weeks) ± SD	38.9 ± 1.6	38.9 ± 1.6	38.9 ± 1.7	38.9 ± 1.6
32–34 (%)	2.0	2.2	2.3	2.2
35–36 (%)	5.5	5.6	6.0	5.7
37–38 (%)	24.9	25.0	25.1	24.6
39–40 (%)	54.8	54.4	54.0	54.7
41–42 (%)	11.3	11.4	11.1	11.4
43–44 (%)	1.4	1.4	1.5	1.4
% Male	50.9	51.0	50.7	51.0
% Firstborn	42.8	43.3	42.3	42.9
% Trimester prenatal care				
First	86.2	84.6	81.2	86.0
Second	10.8	12.0	14.6	11.0
Third	1.7	2.0	2.5	1.7
None	0.7	0.9	1.2	0.8
Unknown	0.6	0.5	0.5	0.5
% Race/ethnicity				
NHW	61.7	52.9	41.9	61.1
NHB	25.7	32.2	39.4	26.1
HISP	12.6	14.9	18.8	12.8
% Maternal education (years)				
<9	5.5	6.6	9.0	5.7
9–11	13.8	15.1	19.2	13.9
12	27.5	28.0	29.3	27.7
13–15	22.3	21.5	19.5	22.3
>15	31.0	28.8	23.0	30.5
% Maternal age (years)				
15–19	10.6	11.6	13.9	10.8
20–24	25.4	27.4	30.3	25.7
25–29	26.8	26.3	25.2	26.9
30–34	24.7	23.0	20.1	24.4
35–39	10.7	9.9	8.9	10.5
40–44	1.8	1.7	1.6	1.8
% Tobacco use	11.2	10.7	11.4	10.9
% Married	68.4	63.1	54.0	68.2

BWT, birth weight; HISP, Hispanic; LBW, low birth weight; NHB, non-Hispanic black; NHW, non-Hispanic white.

mean PM_{10} and $PM_{2.5}$ levels are higher than the median, a phenomenon driven by a few geographic areas with higher pollution levels (e.g., the greater Charlotte area).

The descriptive characteristics of the mothers living within 20 and 10 km of a monitoring station are similar to those in the county-level dataset. Some maternal demographics change with proximity to the monitoring station, including maternal race/ethnicity, maternal education, and marital status. Moving from 20 km away to 5 km away from a monitoring station increases the non-Hispanic black population by approximately 14% and Hispanic population by 6.2%. There is also a decrease in the mothers having more than a high-school education, as well as those who are married, as residence gets closer to a monitor. The incidence of LBW increases from 5.2% at 20 km to 6.3% at the 5 km buffer. The means ± SD along with the interquartile range (IQR), and 25th, 50th and 75th percentiles of the average exposure of each pollutant are shown in Table 2 for the county and 20-km models. Summary statistics of the pollution averages for the 10- and 5-km models (not shown) were similar to the results at the 20-km level. For the 10-km buffer, there were 75,111 and 86,573 observations for PM_{10} and $PM_{2.5}$, respectively. At the 5-km level, there were 35,212 and 42,782 observations for PM_{10} and $PM_{2.5}$, respectively.

Average values of PM_{10} ($PM_{2.5}$) concentration levels were approximately 22.7 (14.3) $\mu g/m^3$. The $PM_{2.5}$ average is below the National Ambient Air Quality Standard (NAAQS) annual mean of 15 $\mu g/m^3$ and there is currently no annual PM_{10} standard. The correlations between PM_{10} and $PM_{2.5}$ during each trimester remain relatively consistent with $r^2 \sim 0.7$. The correlation between PM_{10} and $PM_{2.5}$ exposure during the entire pregnancy was 0.63. Table 3 shows the correlation coefficients among trimester exposures for PM_{10} and $PM_{2.5}$ at the county-level model. Similar correlations were obtained at the 20-, 10-, and 5-km level.

In all of the baseline models with no air pollution estimates, the standard covariates carried the expected signs with positive correlation between birth weight and longer gestation (>40 weeks), male sex, more than a high-school level education, and higher parity; and negative correlation between birth weight and tobacco use during pregnancy, unmarried status, less than high-school education, minority race groups, firstborns, mothers younger than 24 years and older than 40 years, and mothers who started prenatal care later in pregnancy. All covariates were statistically significant ($P<001$) and were included in the models with pollution estimates. Table 4 shows the baseline models for PM_{10} at the county level and the 20 km level. Similar results (not shown) were obtained for both pollutants at the county level and the 20-, 10-, and 5-km buffer levels.

In the multiple regression models for the county-level measure of air pollution exposure, PM_{10} and $PM_{2.5}$ exposure in the third trimester and during the entire pregnancy were negatively associated with birth weight (Figure 3). An IQR increase in PM_{10} and $PM_{2.5}$ during the entire gestational period reduced birth weight by 5.3 g (95% CI: 3.3–7.4) and 4.6 g (95% CI: 2.3–6.8), respectively. This model also showed a reduction in birth weight for PM_{10} (7.1 g, 95% CI: 1.0–13.2) and $PM_{2.5}$ (10.4 g, 95% CI: 6.4–14.4) during the third trimester.

Proximity models for 20, 10, and 5 km distances showed results similar to the county-level models (Figure 3). During the entire gestational period, there were birth weight reductions between 7 and 8 g for PM_{10} and 7 and 10 g for $PM_{2.5}$ per IQR increase in each pollutant. Exposure during the third trimester also showed significant results similar to

Table 3. Pearson's correlation coefficients between trimester pollutions estimates at the county level.

		PM_{10}					$PM_{2.5}$		
		T1	T2	T3			T1	T2	T3
PM_{10}	T1	1			$PM_{2.5}$	T1	1		
	T2	0.44	1			T2	0.23	1	
	T3	0.16	0.42	1		T3	−0.08	0.24	1

Table 2. Pollutant averages ± SD and IQR of pollutants by pregnancy period.

Exposure period	Pollutant	County level; PM_{10} ($n=178{,}356$); $PM_{2.5}$ ($n=174{,}933$)					20 km; PM_{10} ($n=117{,}279$); $PM_{2.5}$ ($n=134{,}232$)				
		Mean ± SD	IQR	Quartiles			Mean ± SD	IQR	Quartiles		
				25%	50%	75%			25%	50%	75%
Trimester 1	PM_{10}	19.6 ± 5.5	5.5	16.2	17.8	21.8	23.0 ± 5.4	7.2	19.0	22.5	26.2
	$PM_{2.5}$	13.5 ± 1.5	1.9	12.5	13.7	14.3	15.0 ± 3.0	4.2	12.7	12.5	16.8
Trimester 2	PM_{10}	25.1 ± 5.3	7.3	21.0	24.3	28.3	22.6 ± 4.9	6.6	19.1	22.4	25.6
	$PM_{2.5}$	15.3 ± 1.7	2.1	14.5	15.6	16.6	14.4 ± 2.6	3.9	12.7	14.4	16.7
Trimester 3	PM_{10}	26.5 ± 5.2	7.9	22.6	25.7	30.5	22.4 ± 4.9	6.4	19.0	22.3	25.4
	$PM_{2.5}$	18.2 ± 2.8	3.1	16.8	18.3	19.9	14.6 ± 2.6	3.9	12.3	14.3	16.5
Entire pregnancy	PM_{10}	23.7 ± 4.9	4.8	20.7	22.7	25.5	22.6 ± 3.8	3.8	20.5	22.2	24.3
	$PM_{2.5}$	15.7 ± 1.6	1.6	15.0	15.7	16.6	14.7 ± 1.7	2.2	13.7	14.9	15.9

IQR, interquartile range.

Table 4. Change in birth weight in the baseline models for PM_{10}.

	County PM_{10}	20 km PM_{10}
Male sex	127.3 (123.4 to 131.1)	126.4 (107.1 to 145.8)
Mat edu (years)		
< 9	−40.2 (−50.4 to −29.9)	−41.1 (−54.5 to −27.8)
9−11	−33.9 (−40.3 to −27.5)	−39.6 (−47.0 to −32.2)
12		
13−15	22.8 (17.1 to 28.5)	18.5 (11.9 to 25.1)
>15	24.6 (18.6 to 30.6)	21.9 (15.0 to 28.9)
Maternal tobacco use	−188.5 (−195.2 to −181.9)	−194.7 (−202.6 to −186.9)
Maternal race/ethnicity		
NHW		
NHB	−179.2 (−184.3 to −174.1)	−178.8 (−184.6 to −172.9)
HISP	−70.5 (−77.5 to −63.7)	−75.6 (−83.4 to −67.8)
Trimester of prenatal care		
First		
Second	−11.4 (−17.9 to −4.9)	−11.6 (−19.3 to −3.9)
Third	−35.2 (−50.1 to −20.3)	−18.1 (−36.0 to −0.1)
No care	−19.1 (−41.8 to 3.5)	−29.7 (−56.8 to −2.61)
Maternal age (years)		
15−19	−42.6 (−51.5 to −33.7)	−40.8 (−51.2 to −30.5)
20−24	−31.5 (−37.8 to −25.2)	−32.7 (−40.0 to −25.5)
25−29	−7.1 (−12.6 to −1.5)	−6.9 (−13.2 to −0.5)
30−34		
35−39	−2.8 (−9.9 to 4.4)	−3.7 (−12.0 to 4.6)
40−44	−34.9 (−49.8 to −19.9)	−28.5 (−45.6 to −11.3)
Firstborn non	114.4 (110.2 to 118.7)	115.1 (110.1 to 120.1)
Gestational length (weeks)		
32−34	−1285.1 (−1298.6 to −1271.7)	−1287.8 (−1303.9 to −1271.7)
35−36	−714.5 (−723.1 to −705.9)	−714.3 (−724.3 to −704.3)
37−38	−278.5 (−283.2 to −273.8)	−278.2 (−283.6 to −272.8)
39−40		
41−42	186.8 (180.5 to 193.1)	185.8 (178.5 to 193.1)
43−44	256.7 (240.4 to 273.0)	240.5 (221.1 to 259.8)

HISP, Hispanic; Mat edu, maternal education; NHB, non-Hispanic black; NHW, non-Hispanic white.

the county-level models for both pollutants. $PM_{2.5}$ showed birth weight reductions at 20 and 10 km, but not at 5 km or the county-level model. We also ran logistic models to see whether air pollution exposure predicted LBW or very LBW (results not shown here). The only statistically significant results were for pregnancy-long $PM_{2.5}$ exposure and the odds ratios were very close to 1.

Discussion

County-level models assume that air pollution exposure is spatially homogeneous over a larger surface area than city-wide or neighborhood-level models. If air pollution concentrations are heterogeneous, with variability that increases as distance from the pollution source increases, then the associated measurement error may also be larger in exposure measurements based on large geographic regions. This misclassification in the pollution concentration could underestimate the true effects of air pollution exposure. For this reason, we explored the relationship between both county and neighborhood-level averages of PM. This sensitivity analysis compared birth weight regression results using exposure metrics for PM_{10} and $PM_{2.5}$ at various spatial resolutions from 2000 to 2002 in North Carolina. We observe some differences in both the magnitude of the coefficients and the significance of the estimates as well. The model for the entire gestational period showed both significant and negative associations for PM_{10} and $PM_{2.5}$ with all the exposure metrics used.

Basu et al. (2004) explore the use of different spatial measures of exposure in birth weight regression models and also found differences between the various metrics in a study in California in 2000. Basu et al. found that county-level measures of $PM_{2.5}$ produced a stronger reduction in birth weight than exposure measures within a 5-mile radius of a

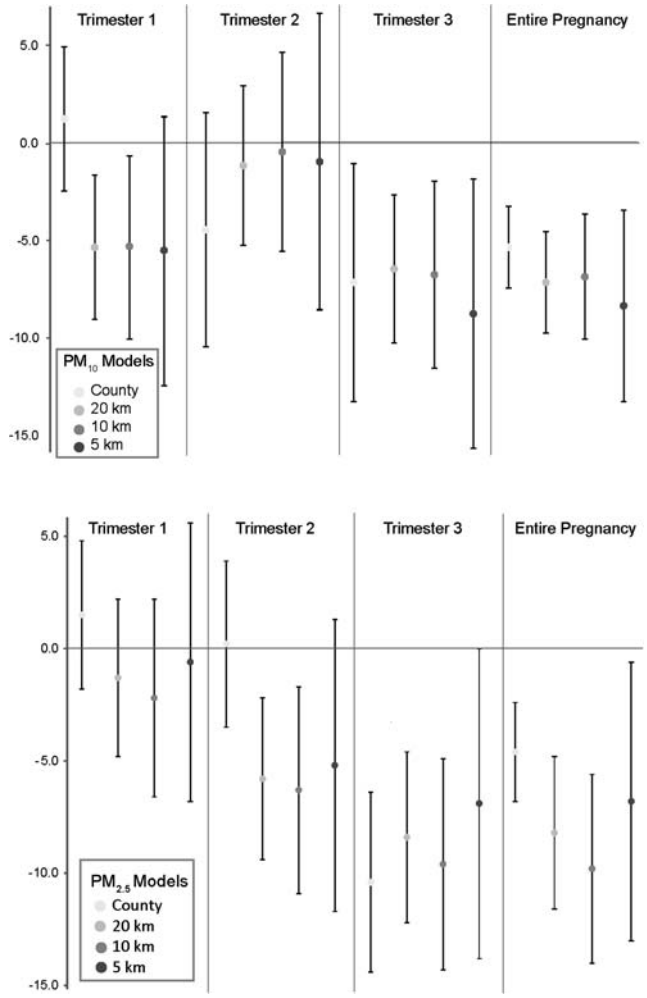

Figure 3. Changes in birth weight in the PM models.

monitoring station. This California study limited analysis to non-Hispanic white and Hispanic mothers in California, where air pollution levels are relatively high compared with North Carolina. Although there are differences in the demographic composition and the air pollution levels, similar results were seen when comparing county-level models to proximity models.

In another study using data from Connecticut and Massachusetts, Bell et al. (2007) saw reductions in birth weight at the county level during the entire pregnancy and the third trimester for both PM_{10} and $PM_{2.5}$, which is consistent with the results in our study. This study had average PM levels similar to those in NC, with means of 22.3 and 11.9 $\mu g/m^3$ for PM_{10} and $PM_{2.5}$, respectively. Comparable results in the reduction of birth weight per IQR increase in PM_{10} and $PM_{2.5}$ were seen in the North Carolina county-level models and the models presented in the Bell et al. analysis.

Other studies have also found an inverse relationship between exposure to PM and reduction in birth weight, using both county-level and neighborhood-level exposure metrics. Dugandzic et al. (2006), Gouveia et al. (2004), and Yang et al. (2003) all found a significant relationship in the first trimester for PM_{10} exposure and birth weight in a study in Taiwan, Canada, and Brazil, respectively. Salam et al. (2005) in a California study found that the exposure to PM_{10} during the third trimester was negatively associated with birth weight. Mannes et al. (2005) showed in a study in Australia that both PM_{10} and $PM_{2.5}$ were associated with reduced birth weight during the second trimester as well as during the last month of pregnancy. In California, Parker et al. (2005) found a negative effect of $PM_{2.5}$ on birth weight for all three trimesters when comparing the highest and lowest levels of $PM_{2.5}$. It is still unclear which exposure period is most affected and further analysis is certainly needed.

A limitation to this research is the quantity and placement of active PM monitoring sites each year. Monitoring sites are part of a long-term fixed network that was established for regulatory purposes, rather than for health effects research. In some geographic areas, such as those closer to major cities and roadways, there is a greater density of monitors.

Monitoring data from these areas are more representative of ambient maternal exposures than from areas where the monitors were more distal from maternal residences. Thus, the exposures of women who lived in more urban areas were more accurately captured than those women who were at the far range of the 20-km buffer set for this study. In addition, individual exposure measurements calculated using ambient concentration readings from monitoring stations introduce misclassification errors into the study. Without using personal monitors, one cannot truly capture actual exposure.

We also make the assumption that pregnant women did not relocate during their pregnancy. Other relevant maternal information such as gestational weight gain, maternal nutrition, and indoor and occupational exposure estimates are factors that may affect birth weight but could not be examined. In addition, use of assisted reproductive technology, even among singleton pregnancies, is a known risk factor for PTB (Myers et al., 2008), but cannot be controlled for in our analyses (data not available).

This study examined only PM_{10} and $PM_{2.5}$, which are highly correlated with each other and possibly with other pollutants. The PM_{10} monitors used in this study also measure ambient levels of $PM_{2.5}$. Consequently, the lower birth weight associated with PM_{10} may in fact be indistinguishable from the birth weight effects attributable to $PM_{2.5}$. To address this issue, the EPA's Clean Air Scientific Advisory Committee has recommended that the Agency develop a new indicator for particles between 2.5 and 10 μm in diameter ($PM_{2.5-10}$) because PM_{10} sampling is an imprecise measure of coarse particulate matter in this size range (US Environmental Protection Agency, 2006b). At present, there is inadequate information on $PM_{2.5-10}$ ambient levels, exposure, and health risks. In the October 2006 revision to the PM NAAQS, however, EPA retained PM_{10} as the indicator for coarse particles.

In North Carolina, the annual NAAQS for $PM_{2.5}$ is 15.0 μg/m^3 averaged over a 3-year period for each monitor (US Environmental Protection Agency, 2004). In October 2006, the EPA rescinded the 50 μg/m^3 annual standard for PM_{10}, citing a lack of association between long-term exposure to current ambient levels of PM_{10} and adverse health effects. Consequently, there is currently no annual standard for PM_{10}. Although average annual $PM_{2.5}$ levels in North Carolina are less than the standard of 15 μg/m^3, we still see robust relationships between $PM_{2.5}$ exposure and birth weight. Similarly, PM_{10} levels are less than half of the previous NAAQS of 50 μg/m^3, yet maternal exposure to PM_{10}, both during the third trimester and during the entire pregnancy, is negatively associated with birth weight. Although our results show a small reduction in birth weight for the entire pregnancy across both pollutants, average county levels of PM_{10} and $PM_{2.5}$ (22.7, 14.3) were associated with a reduction in mean birth weight of 25.1 g (95% CI: 20.2–29.9) and 41.0 g (95% CI: 30.9–51.1), respectively. These reductions are meaningful in North Carolina, and potentially even more so in regions with air quality below the NAAQS.

Exposure to PM pollution during pregnancy is an important public health issue. In our study, the county-level model produced consistent results with the proximity model for estimating reductions in birth weight during the entire pregnancy and in the third trimester for both PM_{10} and $PM_{2.5}$. There were some differences in the first trimester for PM_{10} and the second trimester for $PM_{2.5}$. In both cases, there was a reduction in birth weight at the 20- and 10-km level but not at the county level or the 5-km level.

Our study provides comparability to previous studies by examining the relationship between birth weight and average county levels of PM_{10} and $PM_{2.5}$. In addition, we go beyond the previous studies by constructing proximity models using 20-, 10-, and 5-km buffers around monitoring stations. These additional analyses indicate that the statistical significance and negative relationship between birth weight and air pollution is robust to the choice of air pollution metrics at substantially different geographic scales. Despite North Carolina's consistent attainment of federal air quality standards, we still see a stable and negative association between both pollutants and birth weight in the third trimester and during the entire pregnancy at various spatial resolutions.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

This work is supported by the Southern Center on Environmentally-Driven Disparities in Birth Outcomes, EPA grant RD 83329301-0 and by the Center for Geospatial Medicine, NIH grant 1-P20-RR020782-01. We acknowledge important advice and guidance provided by Alan Gelfand, Martha Keating, and Kerry Williams. This research was supported by funding from the National Institutes of Health (1-P20-RR020782-01) and the Environmental Protection Agency (RD-83329301-0).

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