Investigating the Impact of Maternal Residential Mobility on Identifying Critical Windows of Susceptibility to Ambient Air Pollution during Pregnancy

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Running head: Residential Mobility and Windows of Susceptibility

Abstract:

Identifying periods of increased vulnerability during pregnancy to air pollution with respect to the development of adverse birth outcomes can improve understanding of possible mechanisms of disease development and provide guidelines for protection of the child. Exposure to air pollution during pregnancy is typically based on the residence at delivery, potentially resulting in exposure misclassification and biasing the estimation of critical windows. In this work, we determine the impact of maternal residential mobility during pregnancy on defining weekly exposure to PM_{10} and the estimation of windows of susceptibility for term low birth weight utilizing birth cohort datasets from Connecticut (1988-2008) that include information on all residential addresses for each woman between conception and delivery. A simulation study is designed to investigate the impact of increasing levels of mobility on critical window identification. Increased PM_{10} exposure during pregnancy weeks 16-18 is associated with an increased probability of term low birth weight. Ignoring residential mobility when defining weekly exposure has only minor impact on the identification of critical windows for PM_{10} and term low birth weight in the data application and simulation study. Critical window identification is robust to exposure misclassification caused by ignoring residential mobility in these Connecticut birth cohorts.

Keywords: Bayesian statistics; critical pregnancy windows; exposure misclassification; term low birth weight.

Abbreviations: $PM_{2.5}$ (PM_{10}), particulate matter less than or equal to 2.5 (10) micrometers in aerodynamic diameter.

Exposure to ambient air pollution during pregnancy is associated with a number of adverse birth outcomes including but not limited to preterm birth, low birth weight, and congenital anomaly development (1, 2). The majority of past statistical models investigating these associations incorporate exposure to ambient pollution concentrations in a regression framework using averages based on pre-specified periods of the pregnancy such as specific pregnancy weeks, months, trimesters, and the entire pregnancy. Typically, separate models are fit for each exposure definition and multiple comparisons are made to test specific hypotheses regarding timing of exposure.

More recently, there is increasing interest in identifying more specific periods of increased vulnerability to environmental exposures, known as critical windows of pregnancy, within a single modeling framework. The National Institute of Environmental Health Sciences recently included the identification of critical windows of susceptibility as part of its set of strategic goals (3). A better understanding of the specific timing of exposure and outcome development could lead to improved mechanistic explanations for disease development as well as focused guidelines for protection of the fetus. A number of statistical methods have been developed to estimate these critical windows of development and have been successfully applied to adverse birth outcomes including preterm birth (4, 5), low birth weight (6, 7), and cardiac congenital anomalies (8, 9).

In the majority of these past studies, exposures throughout the pregnancy have been defined based on the residence at delivery of the women under the assumption(s) that only a small proportion of women move between conception and delivery and/or these women typically move only a short distance. Such exposure approaches are typically necessitated by datasets that only have residence information available for the time at birth. A recent review suggests that 9-

32% of women move at least once during pregnancy, though the majority moved a relatively small distance (< 10 kilometers), and that residential mobility can differ by individual characteristics including age, parity, socioeconomic status, and marital status (10). Ignoring maternal residential mobility during pregnancy can lead to exposure misclassification for these women. In related work, Pereira et al. (11) investigated the impact of this misclassification error when standard epidemiologic analyses based on pre-specified pollution averaging periods (e.g., trimester, entire pregnancy) are used in separately fit statistical models. Their findings suggested that results from these models are robust to the introduced error. However, when estimating critical windows of exposure, smaller pollution averaging periods (e.g., daily, weekly) are often considered jointly in a model. The impact that this misclassification has on finer scale averaging periods and the resulting critical window estimation is currently unknown and difficult to address given the limited availability of full residential histories.

In this work, we aim to determine what impact maternal residential mobility has on identification of critical windows of susceptibility. Working with multiple birth cohorts from Connecticut, 1988-2008, that include full residential histories, we define exposure based on (i) residence at delivery and (ii) accounting for full movement during pregnancy. These exposure definitions are compared and misclassification error is quantified across each pregnancy week. We then apply the critical window identification method of Warren et al. (5) to investigate the timing of term low birth weight development with respect to average weekly exposures to particulate matter less than or equal to 10 micrometers in aerodynamic diameter (PM_{10}). The method is applied to each exposure definition and results are compared. Finally, in a simulation study, we investigate the potential impact on critical window identification as the proportion of women who move during pregnancy increases.

METHODS

Data description

We utilized data from four birth cohorts collected in Connecticut, 1988-2008, consisting of information from the Environmental Tobacco Smoke study (12) (1988-1991; N=2,781), the Nutrition in Pregnancy study (13) (1996-1999; N=2,344), the Asthma in Pregnancy study (14) (1996-2000; N=2,255), and the Pink and Blue study of depression during pregnancy (15) (2005-2008; 2,645). Full geocoded residential history is available for each woman throughout the entire pregnancy. These data have been previously described (11). Yale University institutional review board approved the study protocol and participation of human subjects did not occur until after informed consent was obtained.

All analyses are limited to singleton, live, at or after term (gestational age of at least 37 weeks) births. 785 women were removed from the dataset as a result of not meeting each of these conditions. Weekly ambient PM_{10} concentrations (inverse distance weighted value of all monitors within 100 kilometers) are calculated for each woman in the study based on her specific calendar dates of pregnancy and spatial location. Gestational age was obtained from birth certificate records and represents the best available clinical estimate for each woman. When available, ultrasound estimates were used, otherwise, last menstrual period. PM_{10} was explored rather than $PM_{2.5}$ as $PM_{2.5}$ was not routinely measured during the study period. The spatial linking of exposures is done in two ways: (i) ignoring residential mobility by linking exposures based on residence at delivery and (ii) accounting for full residential history during the pregnancy. In the study, we focus on term low birth weight, occurring when the birth weight of an infant at 37 or more completed weeks of gestation is less than 2,500 grams. Term low birth weight is associated with a number of immediate health concerns in newborns as well as the development of adverse health outcomes later in life. Table 1 displays the available covariates in the final analysis dataset. 445 women were removed from the dataset due to missing outcome or covariate information, leaving 8,795 births for analysis.

Statistical model

We apply the previously established statistical model of Warren et al. (5) to identify critical windows of susceptibility with respect to weekly exposure to PM_{10} and development of term low birth weight. This method represents a probit regression model, fit in the Bayesian setting, that includes weekly PM_{10} exposure across the entire pregnancy for each woman within a single modeling framework while accounting for the correlation between the exposures through use of a temporally smoothed Gaussian process prior distribution for the risk parameters. Risk parameters associated with pregnancy weeks closer together in time are assumed to be more similar, allowing for smoothing of the estimation over the pregnancy weeks. This model helps overcome issues related to multicollinearity when dealing with highly correlated daily and weekly exposures. The form of the model is similar to a multivariable probit regression that accounts for exposure and covariates, but the introduced prior structure helps to stabilize parameter estimation and reduce uncertainty in the estimated parameters. Additional statistical model details, prior distribution specifications, and model fitting details are presented in Web Appendix 1.

Data application

We begin by creating two different PM_{10} exposure datasets for our Connecticut birth cohorts. The first defines weekly exposure throughout the pregnancy based only on the residence at delivery, ignoring the possibility that a portion of the women moved at some point between conception and delivery. This exposure definition represents the most common metric used in practice and mimics a dataset for which only the residence at birth is available. The second defines exposure based on the full set of residential addresses for each woman in the study and thereby accounts for changes in exposure that occur due to the women moving during pregnancy. These data are often unavailable due to data collection limitations such as the frequent use of birth registries. Using the Connecticut birth cohorts data and both exposure datasets, we quantify the number of women who moved between conception and delivery and how this movement changed the average exposure level during each pregnancy week.

Next, we apply the critical window statistical model to both exposure datasets in separate models and compare the estimated critical windows of susceptibility with respect to term low birth weight development.

Simulation study

We design a simulation study to investigate the impact of increasing levels of residential mobility on critical window estimation. We explore the impact on this estimation with simulations assuming that 25%, 50%, and 75% of the population moves at least once during pregnancy.

In order to create a dataset with the required proportion of population mobility, we begin by using our actual Connecticut birth cohorts data to establish the overall sample size and characteristics of the population. Next, we randomly sample the women who we designate as "movers" during the pregnancy. The number of selected women depends on the proportion of mobility we are currently working with (25%, 50%, 75% of the entire sample). We ensure that the selected group of movers are similar to our observed dataset by assigning higher sampling weights to women who are younger, less educated, non-White, and single (see Table 1). Once the movers are identified, we displace their true PM_{10} exposure at each pregnancy week to create misclassified exposures. To do this, we randomly sample from the true distribution of exposure differences at each pregnancy week that we observe in our actual data (see Figure 1). Displaced exposures less than zero and greater than the largest observed exposure are re-displaced in order to create realistic exposures. Those women designated as non-movers do not have their exposures altered from the original estimates. The women designated as movers and non-movers are re-selected for each simulated dataset.

We repeat this process 100 times for each of the three mobility pattern proportions, creating 100 datasets for analysis in each setting. For each dataset, we apply the critical window statistical model, ignoring the residential mobility of the population, and compare the estimated critical windows with the critical windows that would be estimated if we accounted for full residential mobility (full mobility results).

We estimate the bias, mean absolute error, and mean squared error for each weekly risk parameter estimator (posterior mean), lower 95% credible interval (0.025 posterior quantile), and upper 95% credible interval (0.975 posterior quantile), with respect to the full mobility results. We then average these metrics over all pregnancy weeks to get an average bias, average mean absolute error, and average mean squared error for each estimator. This process is repeated for each setting of the proportion of movers in the population. We also monitor the proportion of times (out of 100 simulated datasets) that each pregnancy week was identified as a critical window, meaning that its 95% credible interval failed to include zero, regardless of the sign of the estimate. In addition, the mean of the 100 posterior mean estimates of risk at each pregnancy week as well as the mean of the 100 lower and upper 95% credible interval limits at each pregnancy week are collected and compared graphically with the actual posterior means and quantiles in the full mobility results.

RESULTS

Data description

Table 1 describes the Connecticut birth cohorts and available covariates by mobility status as well as statistical testing results for comparing attributes between the two groups (t-tests for continuous variables and chi-squared tests for categorical variables). Overall, around 1.6% of the sample resulted in a term low birth weight, lower than the most recent reported prevalence in the United States of 2.8% (16). Women who moved during pregnancy were more likely to be younger, single, less educated, non-White, have a lower gravidity and parity, a longer gestational length, and a higher third trimester average exposure to PM_{10}. In Figure 2, we display the histograms of weekly PM_{10} exposures for all women across all pregnancy weeks by mobility status.

Data application

The median distance travelled was 5 kilometers with an interquartile range of 2-13 kilometers for the full set of women who moved during pregnancy (before removing women with missing covariates), with women moving to areas with lower levels of PM_{10} on average (11). In the final analysis dataset, 965 out of the 8,795 women (10.97%) moved at least once during pregnancy. For these 965 women, 45.05% of their weekly PM_{10} exposures based on full residential mobility did not differ compared to exposures based on residence at delivery alone. This indicates that the distance traveled may have been short for these women overall, in agreement with the review of Bell and Belanger (10). We compare the two exposure definitions for these women who moved at least once and where some change occurred in a weekly exposure, by calculating the absolute value of the difference in PM_{10} exposures on those particular pregnancy weeks. The average, standard deviation, and range of these absolute differences was 1.05, 1.84, and [0.00, 51.70] micrograms per cubic meter, respectively. The histogram of these absolute differences in the exposure metrics is displayed in Web Figure 1.

Next, we investigate how these exposure differences are distributed over each pregnancy week. In Figure 1, we display the differences in exposure definitions (residence at delivery - full residential mobility) for the women who moved at least once during the pregnancy, at each pregnancy week, while in Web Figure 2 we show the number of these women who have not given birth by each week of pregnancy. It is clear from Figure 1 that as gestational age increases, the exposure misclassification decreases. This may be a result of women moving earlier in the pregnancy and remaining stable later in the pregnancy. Web Figure 2 suggests that after week 37 of the pregnancy, the number of women who are still pregnant begins to decrease as expected. This would also lead to a smaller amount of misclassification error during these later pregnancy weeks.

Finally, we analyze results from the critical window identification statistical model fit to each exposure dataset. Figure 3 shows the estimated critical window results (posterior means and 95% credible intervals) for the model fit to both datasets as well as a scatterplot to compare estimates between the two models. Individual week risk parameters that have 95% credible intervals that are completely above zero are referred to as critical windows. Increased exposure to PM_{10} during these weeks is associated with an increased probability of term low birth weight. The results in Figure 3 from the different exposure datasets are nearly identical, with the same critical windows being identified; pregnancy weeks 16-18. Web Tables 1 and 2 display inference for the included covariates and remaining model parameters, respectively.

Simulation study

In Table 2, we present the average bias, mean absolute error, and mean squared error results for all estimators and for each setting of the proportion of movers in the population. There is a steady increase in average mean absolute error for each of three estimators as the proportion of movers increases from 25% to 75%. We also present the proportion of times (out of the 100 simulated datasets) that a pregnancy week was identified as a critical window. If estimation if not affected by the increased exposure misclassification, we would expect these proportions to be large during pregnancy weeks 16-18 (as seen in our data application) and low otherwise. This appears to be the case across each of the three proportion of movers though the probability of incorrectly identifying a critical window increases as the proportion of movers increases while remaining low overall.

In Figure 4, we display the results assuming 75% mobility of the population. Web Figures 3 and 4 display the results for 25% and 50% mobility, respectively (results consistent across mobility level). These figures are comparable to Figure 3 in their content. Overall, these findings suggest that even though estimation of the critical windows changes as the proportion of movers increases, the changes are minimal and do not greatly impact estimation and identification of statistically significant critical windows of susceptibility.

DISCUSSION

The results from our data application (i.e., analysis of the cohorts data) indicate an association between term low birth weight and exposure to PM_{10} during weeks 16-18 of pregnancy. In a Texas-based study of critical window estimation during 2001-2004, similar weeks of increased vulnerability to $PM_{2.5}$ were identified in the second trimester (weeks 19-21) using the same statistical model implemented in this analysis (6). In that work, the authors did not have access to full material residential histories needed to more accurately link weekly exposures to the pregnant women. Hao et al. (17) observed elevated risk of term low birth weight with increased exposure to $PM_{2.5}$ during the second trimester for women across the United States in an unadjusted analysis. General agreement in the estimated critical windows between these different populations, with a focus on different pollutants, strengthens the evidence suggesting that an association exists sometime in the second trimester between particulate matter exposure and term low birth weight. Exposures to PM_{10} and $PM_{2.5}$ throughout the pregnancy have been linked to decreases in birth weight in a number of past epidemiologic analyses using different populations, pollutant averaging periods, and statistical methods (1, 18-22).

The biological pathway by which prenatal air pollution exposure impacts birth weight is not yet fully understood. A recent study suggests that placental mitochondrial DNA may act as a mediator of the association between air pollution exposure during pregnancy and reduced birth weight (23). Prenatal air pollution exposure may deplete the placenta's mitochondria content through increased oxidative stress (23, 24). These mitochondria are important in ensuring that the placenta can support proper growth of the fetus, and their damage could result in a reduction in birth weight for a fetus (23-26).

Using the same cohorts of pregnant women presented in this study, Pereira et al. (11) investigated the association between exposure to PM_{10} during pregnancy and a number of adverse birth outcomes using separately fit standard epidemiologic statistical models with pre-specified pollution averaging periods. They also considered different exposure definitions based on (i) first recorded residential address, (ii) last recorded residential address, and (iii) accounting for full maternal residential mobility. Increased exposures were associated with reduced birth weight during the second trimester and across the entire pregnancy. Similarly, the authors found no substantial changes in risk effect estimation when the different exposure definitions were used. Their work established the adequacy of using residence at delivery for defining exposures for larger aggregated periods of pregnancy in the cohorts. Our work extends this by focusing on the joint estimation of critical windows of increased vulnerability using more advanced statistical methods.

The simulation study results suggest that the distance travelled may be a more important factor in terms of exposure misclassification than the proportion of the population who move during pregnancy. Moving larger distances would more greatly incorporate the geographic variability of ambient air pollution and therefore lead to larger exposure classification. Among the women who moved in our dataset, the exposure misclassification was relatively small and decreasing as the pregnancy progressed. Other subpopulations may have different mobility patterns during pregnancy. In this study, this minimal amount of error apparently has only minor impact on critical window estimation, even as a larger proportion of women move. It is possible that with different pollutants of interest, critical window estimation could be affected more severely; particularly if that pollutant has abrupt changes in composition or magnitude at shorter distances (e.g., greater spatial heterogeneity due to point sources). This would result in increased exposure misclassification and would tend to pull the estimation of critical windows towards the null (9). Our cohorts of women had smaller term low birth weight and pregnancy mobility rates than the general pregnant population. Future studies are needed to determine the robustness of our findings in populations with higher rates for both of these factors.

Changing the level of exposure aggregation (e.g., weekly to daily) could also result in different levels of exposure misclassification. In this study, we focused on weekly averages of air pollution exposure across the entire pregnancy based on similar critical window analyses of term low birth weight and preterm birth. However, for some health outcomes, the window of development is shorter than the entire pregnancy span and therefore, a finer scale of exposure timing may be needed. For example, Warren et al. (9) considered daily exposures during post-conception weeks 2-8 to $PM_{2.5}$ on the risk of development of a number of cardiac congenital anomalies based on the development period of the heart. Future work should consider how critical window estimation is impacted in different populations, using different adverse birth outcomes, pollutants, and exposure averaging periods, while carefully considering the biological plausibility of using such finer scaled exposures.

In conclusion, our study is the first to our knowledge to quantify the impact of maternal residential mobility on critical window estimation. Using our Connecticut birth cohorts with full maternal residential address histories, we were able to investigate this impact with respect to estimating the association between term low birth weight and PM_{10} weekly pregnancy exposures as well as characterize the periods of pregnancy with increased exposure misclassification. In line with past work, we observed an increased risk of low birth weight associated with PM exposure in the second trimester, but were able to more specifically identify pregnancy weeks 16-18 as particularly vulnerable. Simulation study results suggest that even for a larger proportion of the pregnant population moving between conception and delivery, there is relatively little impact on critical window identification for PM_{10} and term low birth weight for this study population, likely due to the small distances being travelled.

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Figure Legends:

Figure 1. Differences in exposure metrics by pregnancy week for the Connecticut birth cohorts, 1988-2008. Exposure Metric 1: Exposures based on full maternal residential address histories; Exposure Metric 2: Exposures based on residence at delivery. $\mu g/m^3$, micrograms per cubic meter. Differences shown as Exposure Metric 2 – Exposure Metric 1.

Figure 2. Histograms of weekly PM_{10} exposures by pregnancy mobility status for the Connecticut birth cohorts, 1988-2008. (A) Non-movers; (B) Movers.

Figure 3. Estimated critical windows of low birth weight development with respect to PM_{10} weekly pregnancy exposure for the Connecticut birth cohorts, 1988-2008; a comparison of the two exposure metrics. (A) Exposure Metric 1: Exposures based on full maternal residential address histories; (B) Exposure Metric 2: Exposures based on residence at delivery; (C) Scatterplot of parameter estimates from (A) and (B). CI, credible interval.

Figure 4. Simulation study results assuming 75% of the pregnant population moves between conception and delivery for the Connecticut birth cohorts, 1988-2008; a comparison of the two exposure metrics. (A) Exposure Metric 1: Exposures based on full maternal residential address histories; (B) Exposure Metric 2: Exposures based on residence at delivery; (C) Scatterplot of parameter estimates from (A) and (B). CI, credible interval.

Figure 1

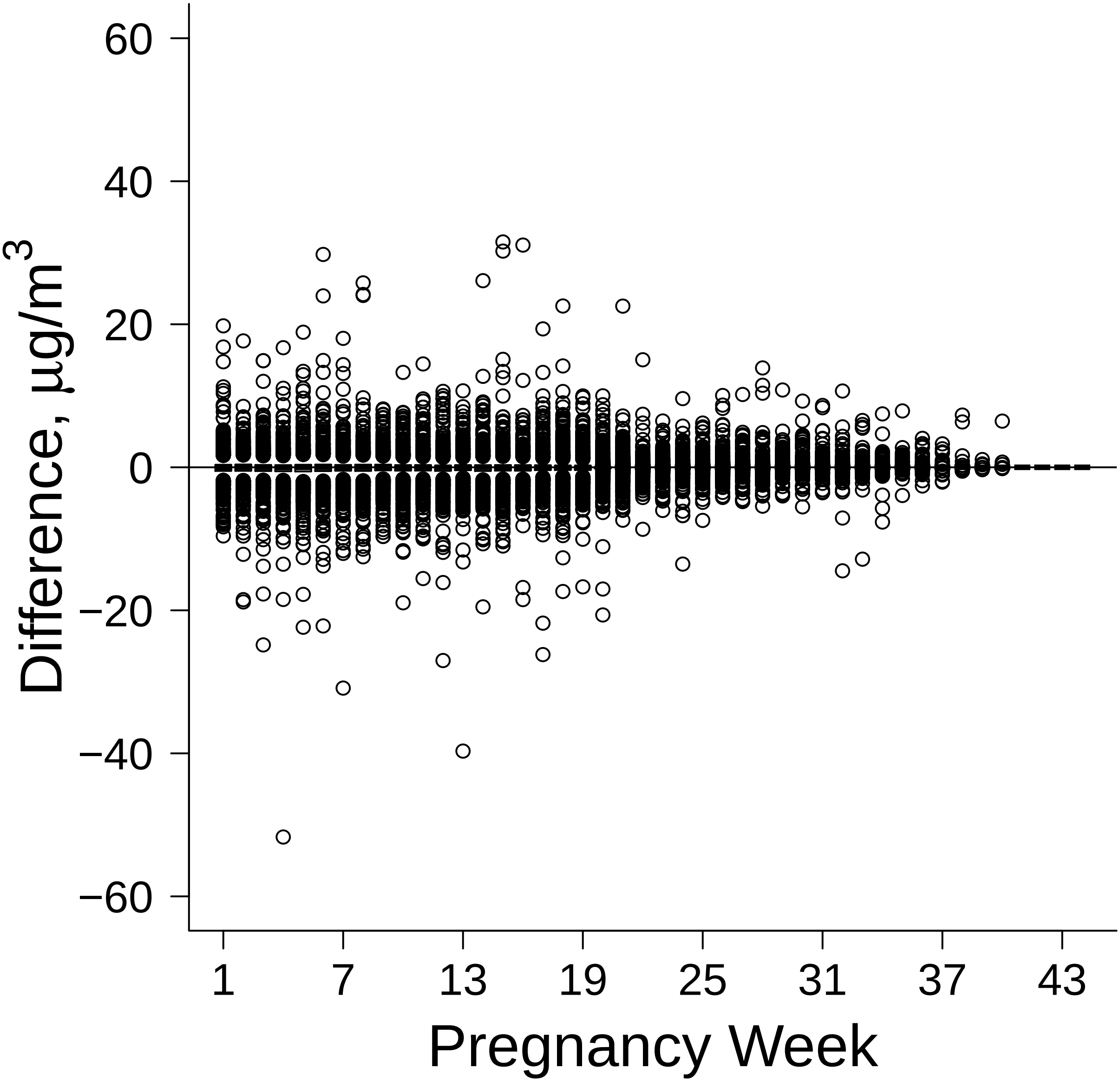
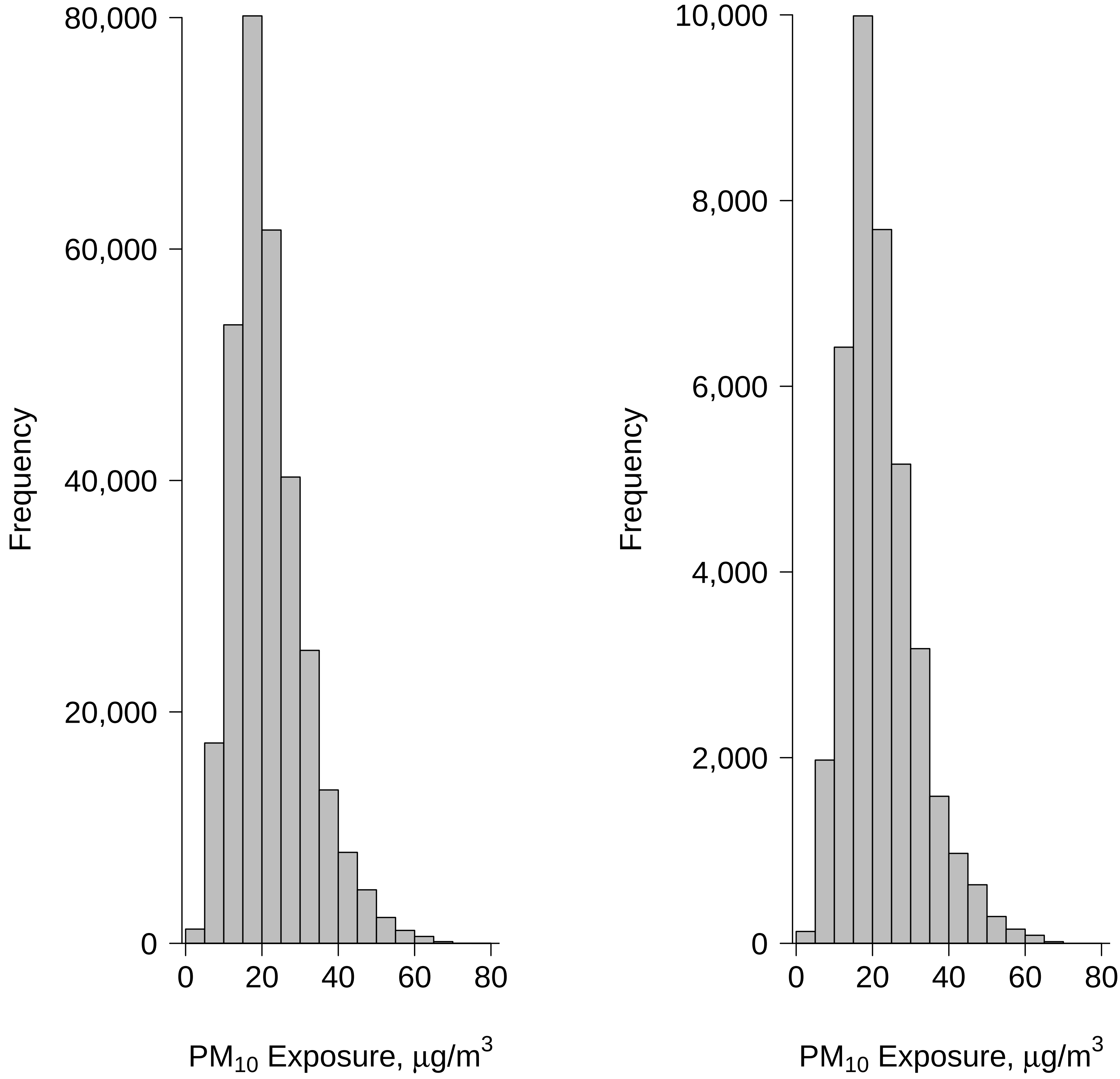
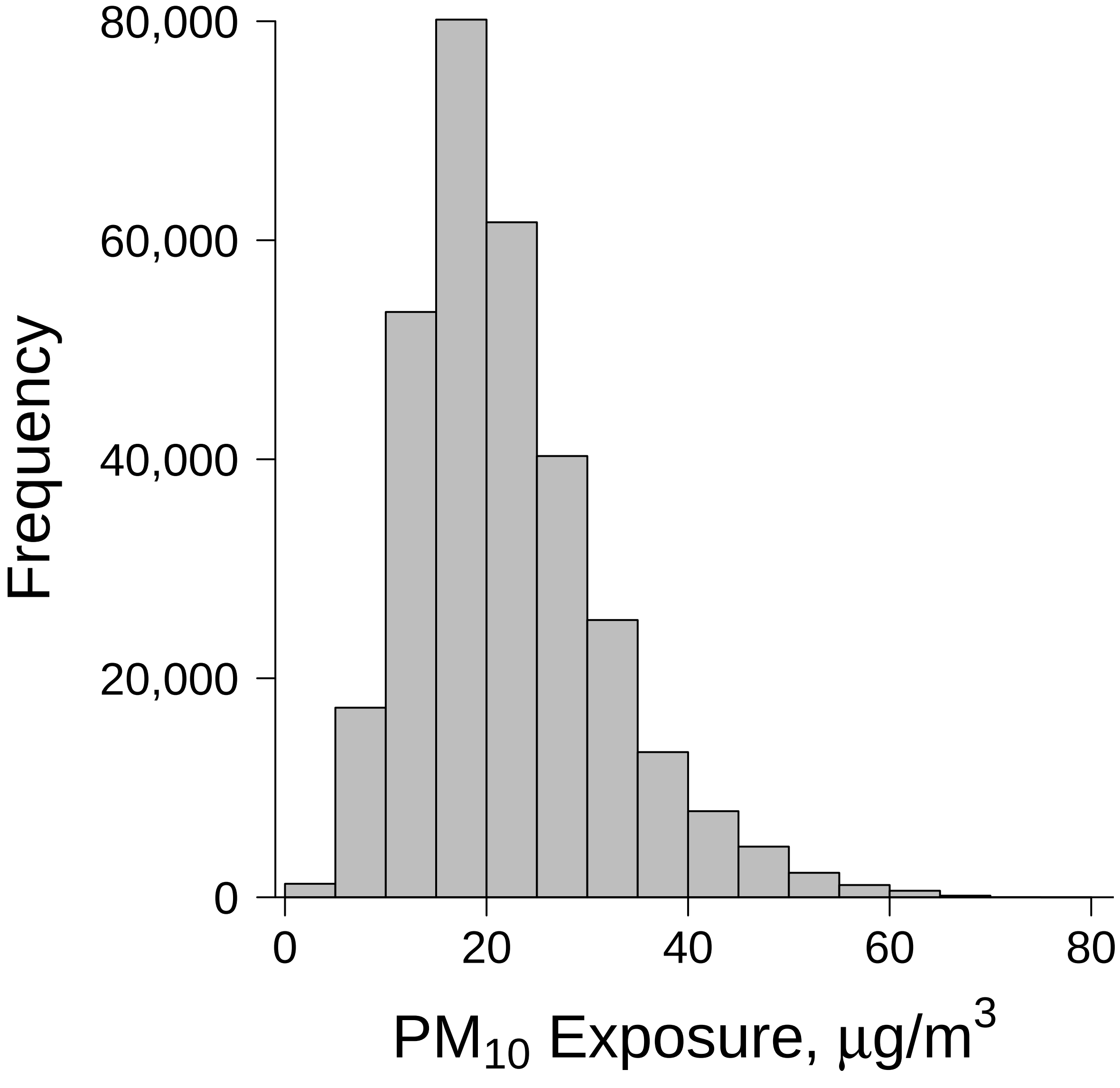

60
40
20
0
−20
−40
−60
Difference, μg/m3
1
7
13
19
25
31
37
43
Pregnancy Week

Figure 2



80,000
60,000
40,000
20,000
0
Frequency
0
20
40
60
80
PM10 Exposure, µg/m3
10,000
8,000
6,000
4,000
2,000
0
Frequency
0
20
40
60
80
PM10 Exposure, µg/m3

Figure 2A



80,000
60,000
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Frequency
0
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40
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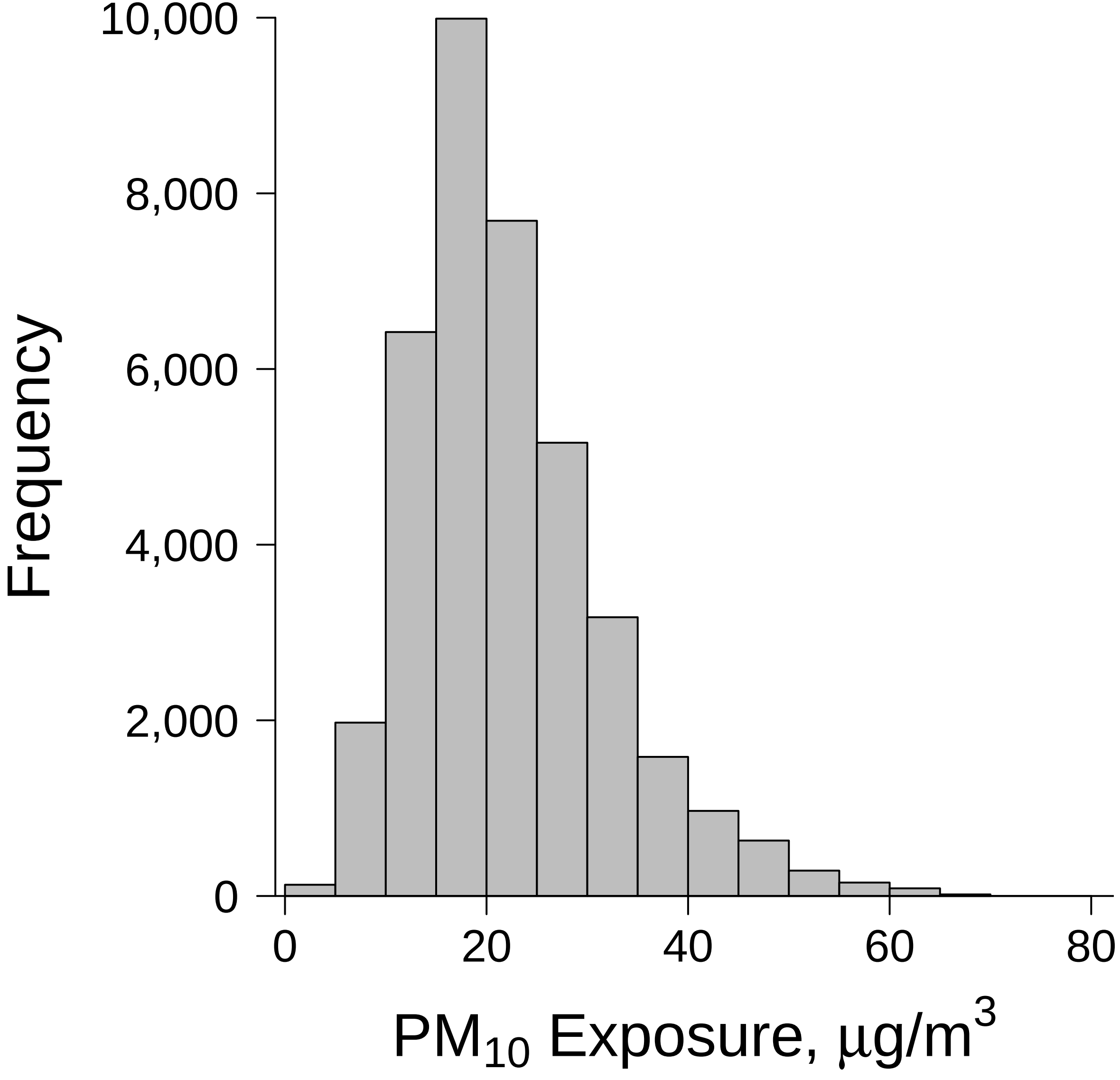
80
PM10 Exposure, µg/m3

Figure 2B



10,000
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4,000
2,000
0
Frequency
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60
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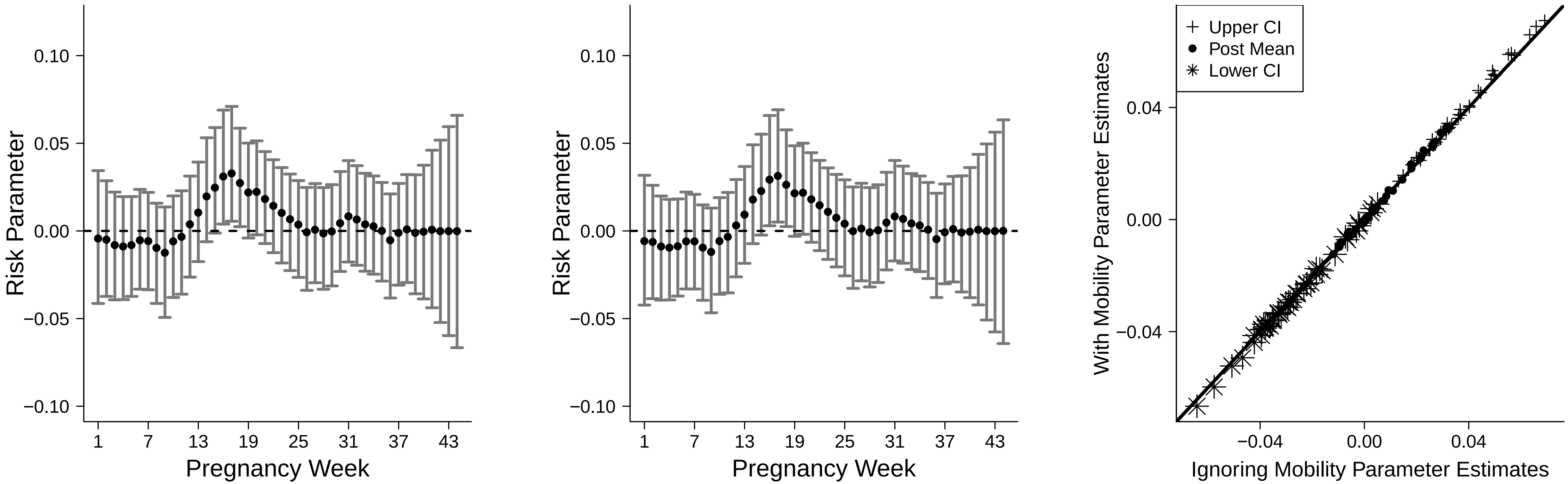
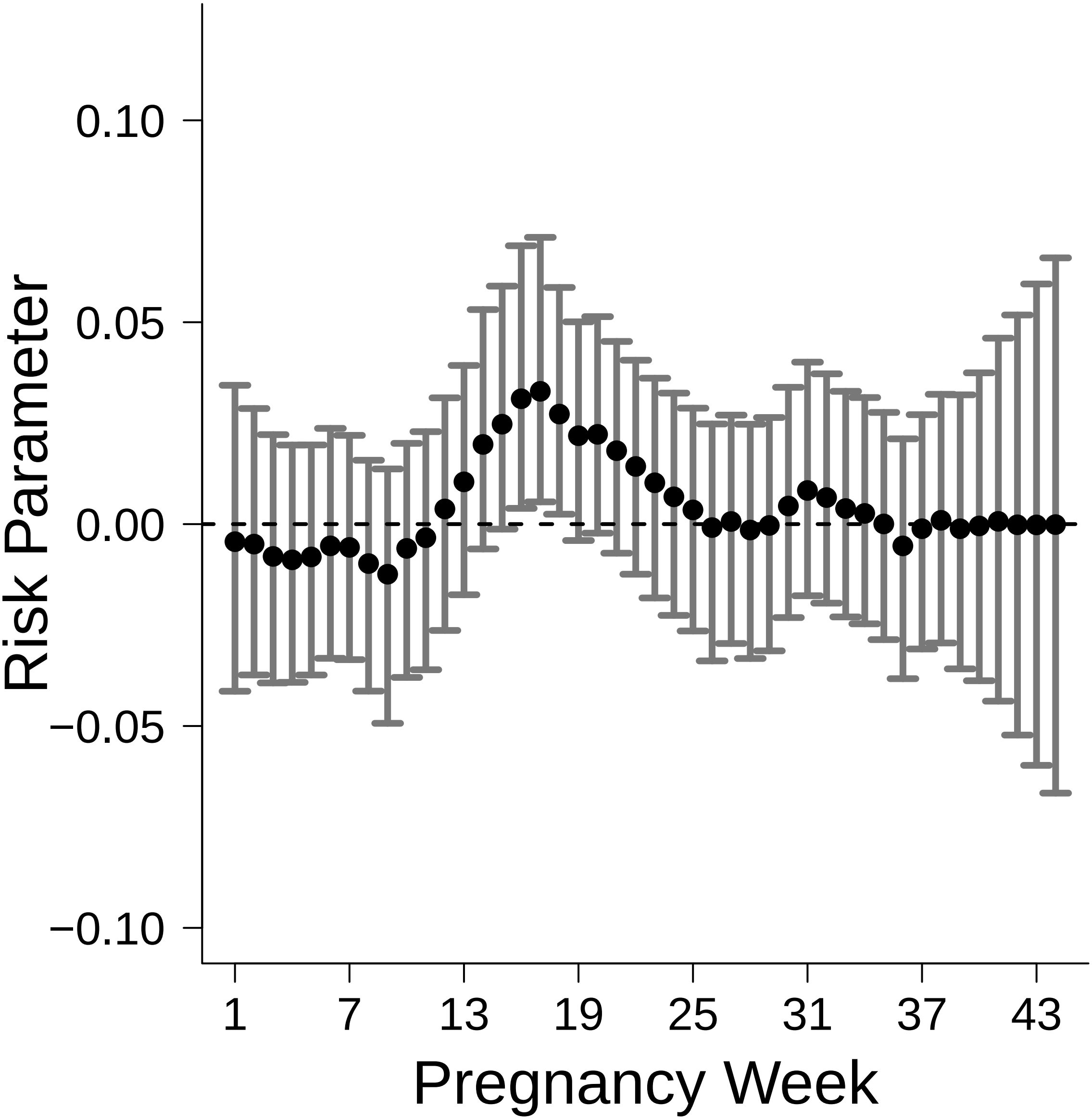
PM10 Exposure, μg/m3

Figure 3



Risk Parameter
0.10
0.05
0.00
−0.05
−0.10
1
7
13
19
25
31
37
43
Pregnancy Week
Risk Parameter
0.10
0.05
0.00
−0.05
−0.10
1
7
13
19
25
31
37
43
Pregnancy Week
Upper CI
Post Mean
Lower CI
With Mobility Parameter Estimates
0.04
0.00
−0.04
−0.04
0.00
0.04
Ignoring Mobility Parameter Estimates

Figure 3A



0.10
0.05
0.00
−0.05
−0.10
Risk Parameter
1
7
13
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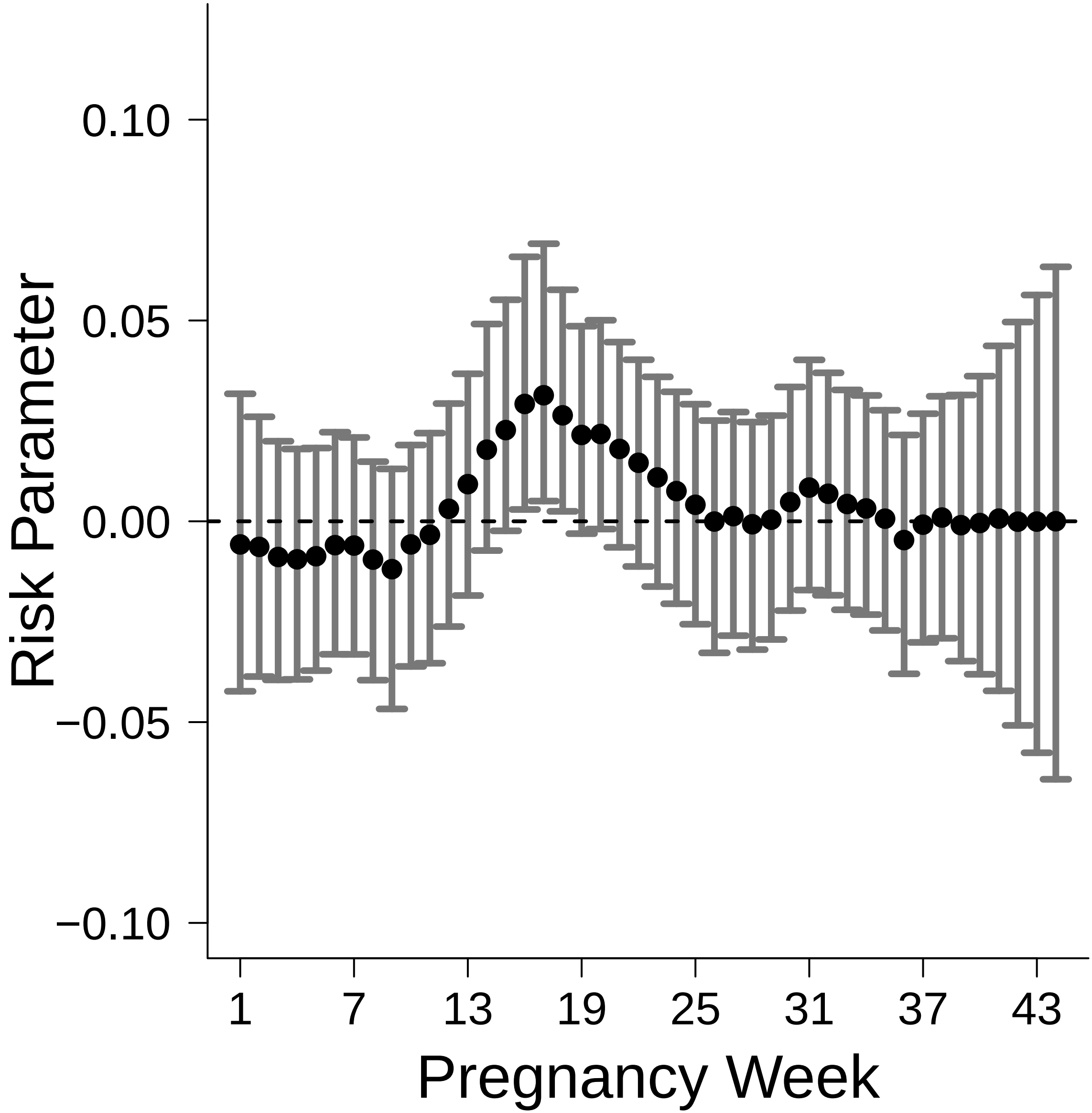
43
Pregnancy Week

Figure 3B



Risk Parameter
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0.05
0.00
−0.05
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43
Pregnancy Week

Figure 3C

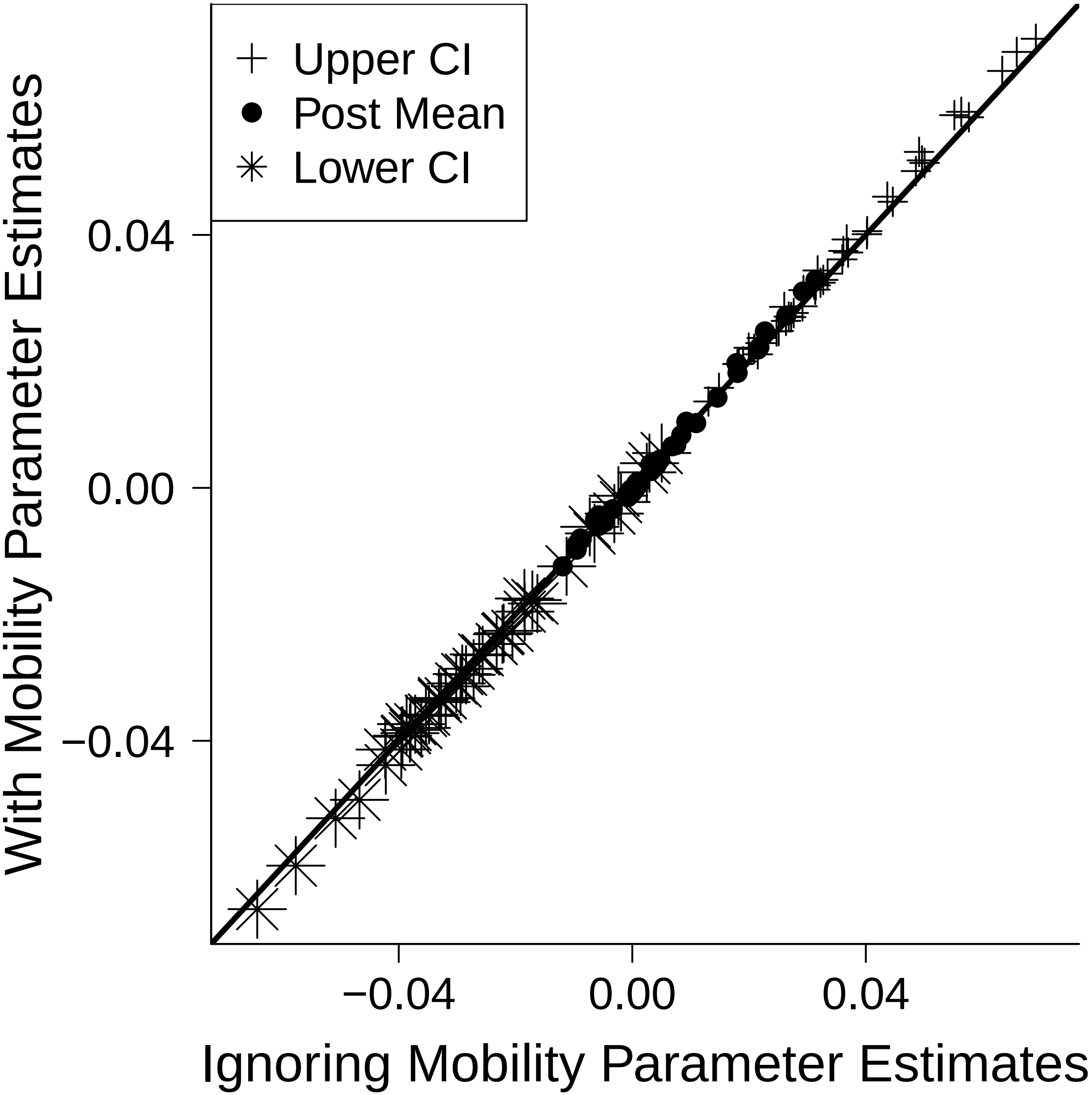
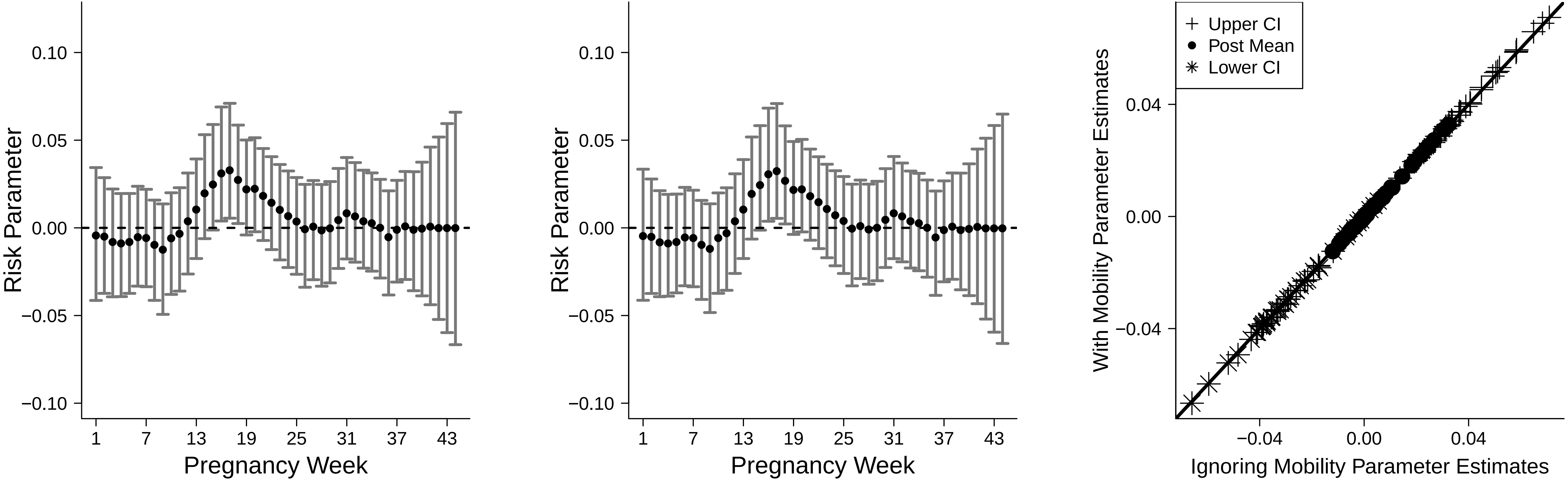
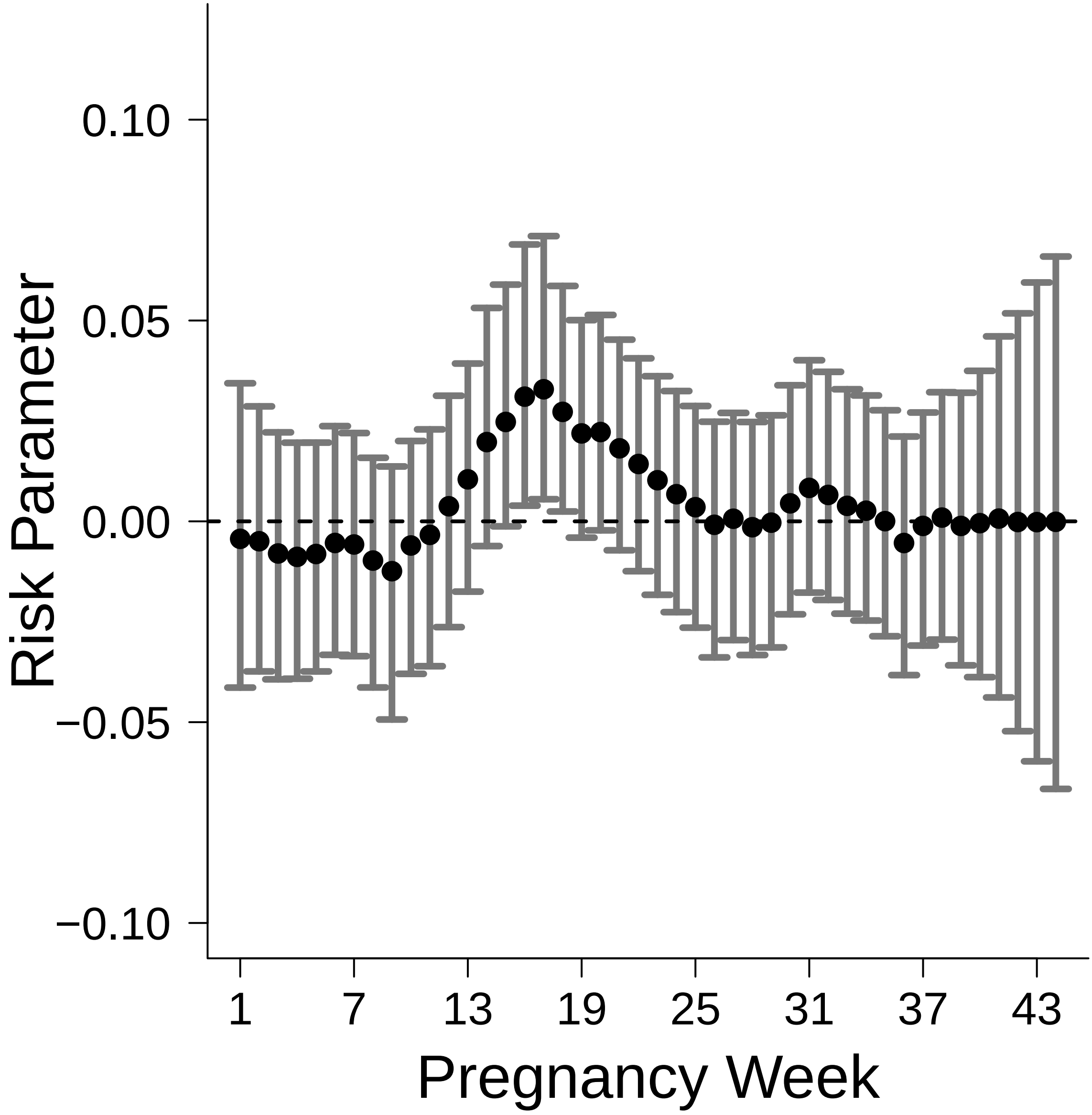

Upper CI
Post Mean
Lower CI
0.04
0.00
−0.04
With Mobility Parameter Estimates
−0.04
0.00
0.04
Ignoring Mobility Parameter Estimates

Figure 4



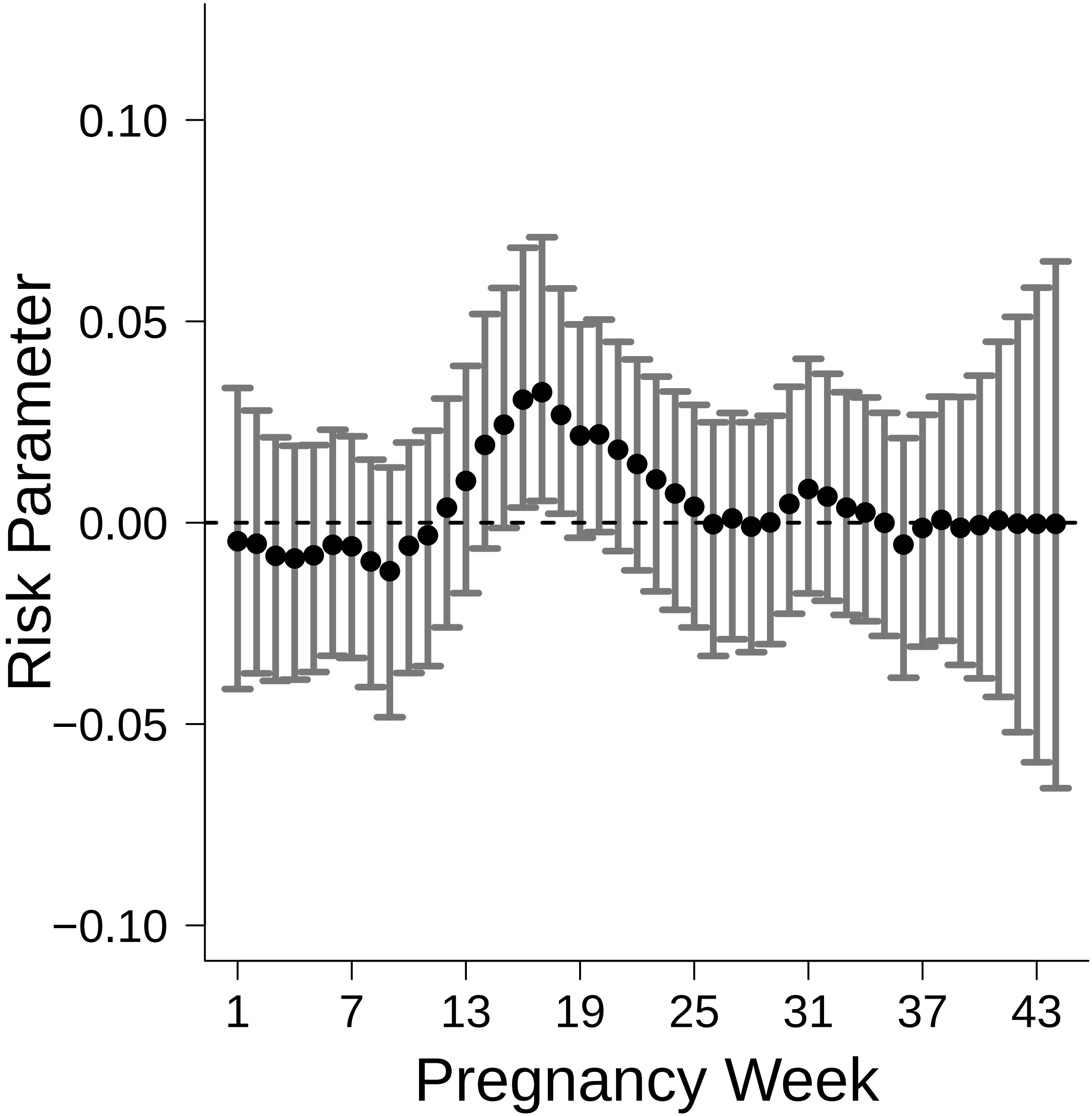
Risk Parameter
0.10
0.05
0.00
−0.05
−0.10
1
7
13
19
25
31
37
43
Pregnancy Week
Risk Parameter
0.10
0.05
0.00
−0.05
−0.10
1
7
13
19
25
31
37
43
Pregnancy Week
Upper CI
Post Mean
Lower CI
With Mobility Parameter Estimates
0.04
0.00
−0.04
−0.04
0.00
0.04
Ignoring Mobility Parameter Estimates

Figure 4A



0.10
0.05
0.00
−0.05
−0.10
Risk Parameter
1
7
13
19
25
31
37
43
Pregnancy Week

Figure 4B



Risk Parameter
0.10
0.05
0.00
−0.05
−0.10
1
7
13
19
25
31
37
43
Pregnancy Week

Figure 4C

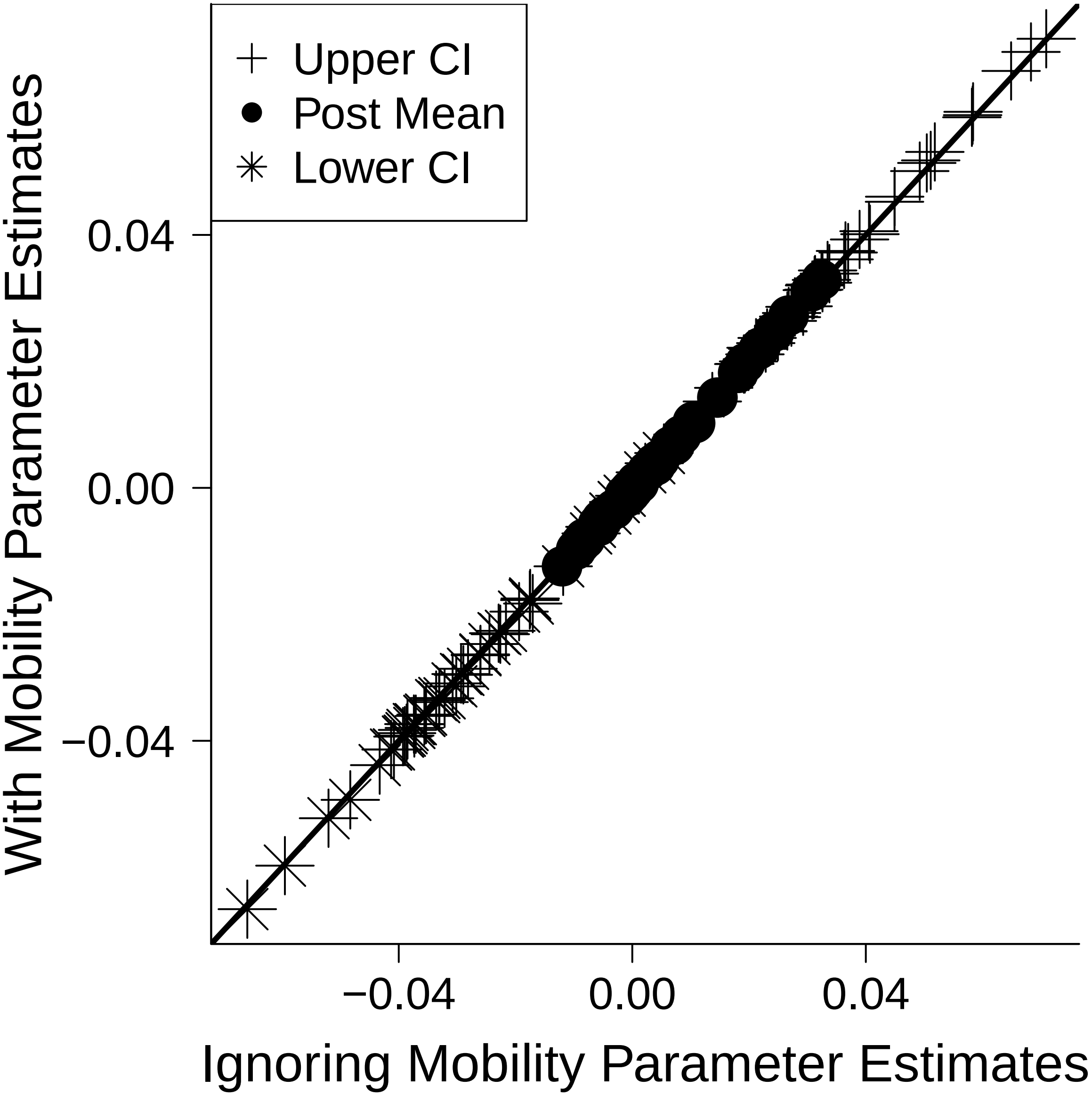

Upper CI
Post Mean
Lower CI
0.04
0.00
−0.04
−0.04
0.00
0.04
With Mobility Parameter Estimates
Ignoring Mobility Parameter Estimates

Table 1. Characteristics of the Connecticut Birth Cohorts, 1988-2008.

Characteristic	Movers (*n*=965)		Non-Movers (*n*=7,830)	
	Mean (SD)	%	Mean (SD)	%
Gravidity[a]	2.29 (1.40)		2.49 (1.46)	
Parity[a]	0.64 (0.90)		0.85 (0.92)	
Maternal Body Mass Index[b]	24.62 (5.52)		24.56 (5.52)	
Gestational Age (Weeks)[a]	39.65 (1.33)		39.50 (1.31)	
Previous Preterm Birth		0.03		0.03
Low Birth Weight Outcome		0.02		0.02
Previous Low Birth Weight Birth		0.05		0.05
Sex of Child (Female)		0.50		0.50
Marital Status (Single)[a]		0.43		0.19
Maternal Ethnicity[a]				
White		0.66		0.79
Black		0.11		0.07
Other		0.23		0.15
Maternal Education Level[a]				
Did not complete High School		0.15		0.07
Completed High School		0.21		0.16
Post-secondary		0.47		0.51
Graduate and Above		0.17		0.26
Maternal Age Category[a]				
< 25 years		0.33		0.15
[25, 29]		0.30		0.27
[30, 34]		0.27		0.37
> 34		0.10		0.21
Season of Birth				
Winter: December-February		0.26		0.25
Spring: March-May		0.23		0.26
Summer: June-August		0.24		0.24
Fall: September-November		0.28		0.25
PM_{10} Exposure (μg/m^3)				
Entire Pregnancy[a]	22.18 (9.58)		21.99 (9.55)	
Trimester 1	22.32 (9.68)		22.15 (9.68)	
Trimester 2	22.11 (9.66)		22.05 (9.66)	
Trimester 3[a]	22.11 (9.40)		21.77 (9.32)	

Abbreviations: μg/m3, micrograms per cubic meter; SD, standard deviation.

[a] Indicates a p-value < 0.05 for testing the variable between the two groups of women.

[b] Weight (kg)/height $(m)^2$

Table 2. Simulation Study Results for Critical Window Estimation; Connecticut Birth Cohorts, 1988-2008.

Estimator	25% Mobility	50% Mobility	75% Mobility
Posterior Mean			
Average Bias[a]	-0.03 (0.03)	-0.03 (0.03)	-0.01 (0.03)
Average MAE[a]	0.77 (0.03)	0.94 (0.04)	1.07 (0.04)
Average MSE[a]	0.001 (0.0000)	0.002 (0.0001)	0.002 (0.0002)
Posterior 0.975 Quantile			
Average Bias[a]	-0.42 (0.05)	-0.49 (0.05)	-0.39 (0.05)
Average MAE[a]	1.38 (0.06)	1.66 (0.08)	1.68 (0.07)
Average MSE[a]	0.004 (0.0003)	0.005 (0.0005)	0.005 (0.0004)
Posterior 0.025 Quantile			
Average Bias[a]	0.28 (0.04)	0.35 (0.04)	0.33 (0.04)
Average MAE[a]	1.38 (0.05)	1.61 (0.06)	1.69 (0.05)
Average MSE[a]	0.007 (0.0002)	0.005 (0.0003)	0.005 (0.0003)
Critical Window Estimation (Proportion of Times Significant)			
Week 16	1.00	1.00	1.00
Week 17	1.00	1.00	1.00
Week 18	1.00	1.00	0.97
Maximum at Any Other Week	0.05	0.08	0.20
Average Across Any Other Weeks	0.001	0.002	0.005

Abbreviations: MAE, mean absolute error; MSE, mean squared error.

[a] Estimates multiplied by 1,000 for display purposes.

[b] Standard errors are presented in parentheses where applicable.

Web Materials:

Title:

Investigating the Impact of Maternal Residential Mobility on Identifying Critical Windows of Susceptibility to Ambient Air Pollution during Pregnancy

Authors:

Joshua L. Warren, Ji-Young Son, Gavin Pereira, Brian P. Leaderer, and Michelle L. Bell

WEB APPENDIX 1

Statistical model details

We model the low birthweight (LBW) binary random variable using a probit regression framework such that $Y_i|p_i \sim \text{Bernoulli}(p_i), i = 1, \dots, n$ where Y_i is the LBW indicator for pregnancy *i* (equal to one if birth *i* results in a LBW outcome and equal to zero otherwise), p_i is the probability of LBW development for pregnancy *i*, and *n* represents the total number of pregnancies observed in the dataset. The probability of LBW development is modeled using the probit link such that $\Phi^{-1}(p_i) = \mathbf{x}_i^T \boldsymbol{\beta} + \sum_{w=1}^{\text{ga}_i} z_i(w)\theta(w)$ where $\Phi^{-1}(.)$ is the inverse cumulative distribution function of the standard normal distribution, $\mathbf{x}_i$ is the vector of covariates specific to pregnancy *i*, $\boldsymbol{\beta}$ is the vector of regression parameters that describes the association between the covariates and the probability of LBW, ga_i is the gestational age (weeks) for birth *i*, $z_i(w)$ is the average pollution exposure amount during pregnancy week *w* for pregnancy *i* (specific to the spatial location and calendar dates of pregnancy for pregnancy *i*), and $\theta(w)$ is the risk parameter that describes the association between pollution exposure on pregnancy week *w* and the probability of LBW.

We don't allow exposures experienced after the birth to impact the probability of a LBW outcome by limiting the exposures up to the gestational age for each pregnancy (ga_i). We note that different exposure definitions can be used for $z_i(w)$. In our data application, we define $z_i(w)$ based on (i) the residence at delivery and (ii) the full maternal residential address history. Changes in the spatial location of the pregnant women will potentially lead to differences in $z_i(w)$ across the pregnancy. Exposures at each pregnancy week are standardized for computational stability with zeroes used for exposures occurring after the birth.

The weekly risk parameters are modeled using a Gaussian process (GP) such that $\boldsymbol{\theta}|\sigma_\theta^2,\phi\sim\text{MVN}(\mathbf{0},\sigma_\theta^2\Sigma(\phi))$ where $\theta=\{\theta(1),\dots,\theta(44)\}^T$ (44 is the largest gestational age observed in our Connecticut birth cohorts), MVN(.,.) is the multivariate normal distribution, $\mathbf{0}$ is a column vector of 44 zeroes and the mean of the GP, σ_θ^2 is the variance of the GP, and $\Sigma(\phi)$ is a correlation matrix describing the correlation between the weekly risk parameters. We introduce an exponential functional form for this correlation matrix such that $\Sigma(\phi)_{ij}=\text{Corr}\{\theta(i),\theta(j)\}=\exp\{-\phi|i-j|\}$ where ϕ describes the smoothness of the GP across pregnancy weeks with smaller values of ϕ indicating that the risk parameters are more similar even at very different weeks of pregnancy.

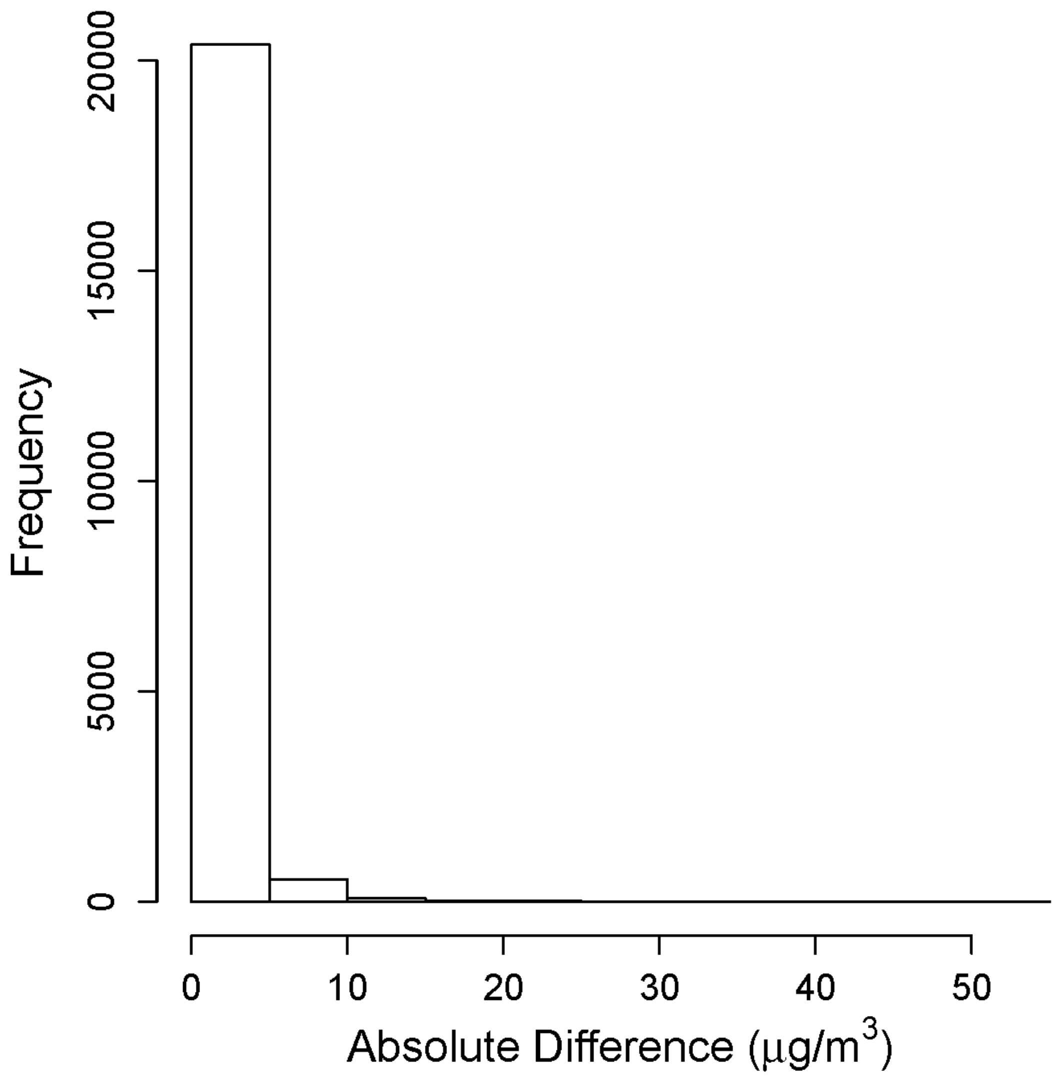
Prior specification

We specify prior distributions for all introduced model parameters in order to complete the model specification. For the regression parameters, we assign independent and identically distributed normal distributions centered at zero with a large, fixed prior variance such that $\beta_j\sim\text{N}(0,1e^{10}), j=0,\dots,p$ where p is the number of covariates included in the model. The variance of the GP is given a weakly informative Inverse Gamma prior distribution such that $\sigma_\theta^2\sim\text{Inverse Gamma}(0.10,0.10)$. Finally, the correlation parameter is given a weakly informative Uniform prior distribution that allows the correlation between weekly risk parameters to range from near zero (independence) to near one (perfect correlation) a priori such that $\phi\sim\text{Uniform}(a_\phi,b_\phi)$ with $a_\phi=-\ln(0.9999)/43$ and $b_\phi=-\ln(0.0001)/1$. The values of a_ϕ and b_ϕ are selected based on the effective range of correlation of the exponential correlation function to allow for complete flexibility in correlation values before observing any data. All of the prior specifications are chosen to be weakly informative in order to reflect our lack of prior knowledge regarding the true value of the parameters.

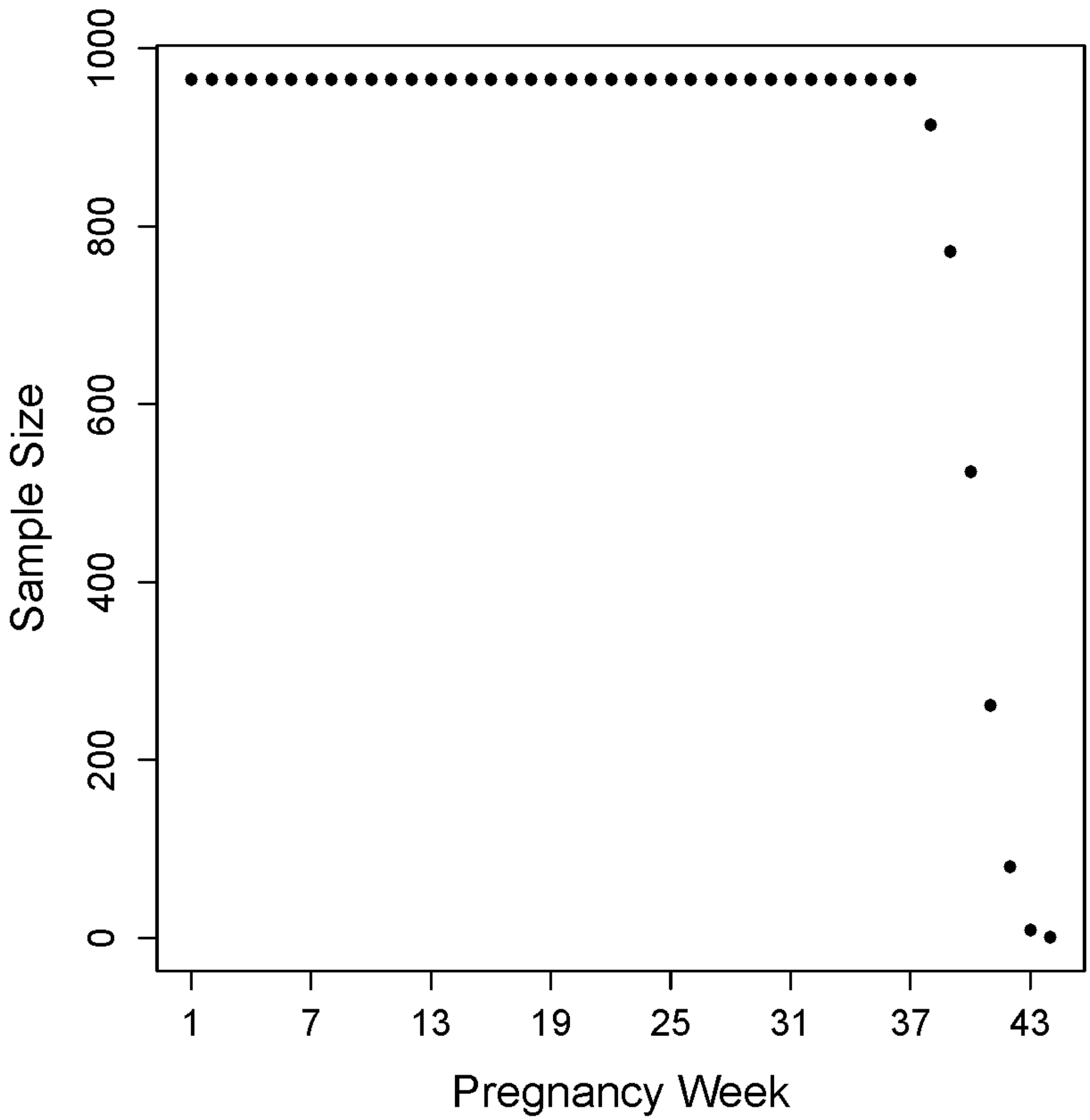
Model fitting details

The model is fit using Markov chain Monte Carlo sampling techniques in the R Statistical Software program (1). In the data application, inference is based on 90,000 samples from the posterior distributions of interest after discarding the first 10,000 iterations before the model converged. In the simulation study, inference is based on 15,000 posterior samples for each analyzed dataset, after discarding the first 10,000 iterations before the model converged.

Web Figure 1. Absolute differences in exposure metrics (non-zero) for the Connecticut birth cohorts, 1988-2008. Exposure Metric 1: Exposures based on residence at delivery; Exposure Metric 2: Exposures based on full maternal residential address histories. μg/m^3, micrograms per cubic meter.



Web Figure 2. Number of pregnant women by pregnancy week for the Connecticut birth cohorts, 1988-2008.



Web Table 1. Posterior Inference Using the full Residential Exposure Dataset, Connecticut Birth Cohorts, 1988-2008.

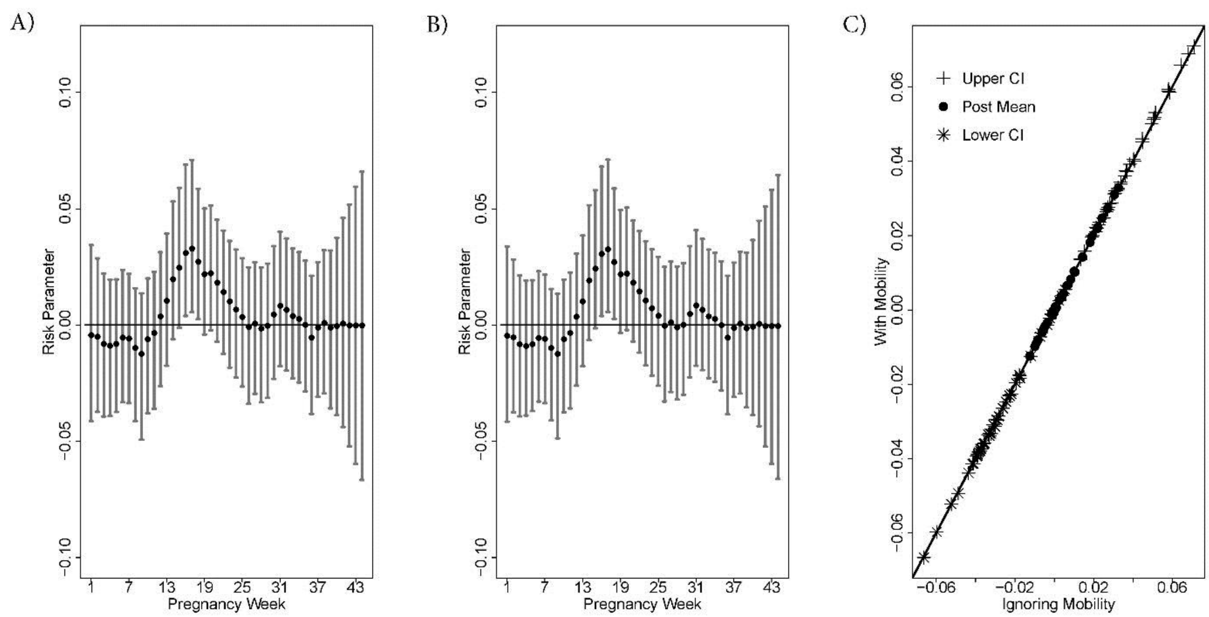
Parameter	Posterior Mean	Posterior SD	Posterior 95% Credible Interval
Intercept	--1.93	0.24	--2.40, --1.45
Gravidity (Count)	--0.05	0.04	--0.13, 0.02
Parity (Count)	--0.07	0.06	--0.19, 0.06
Maternal Body Mass Index	--0.01	0.01	--0.03, 0.00
Previous Preterm Birth (Yes)	--0.13	0.18	--0.49, 0.22
Previous Low Birth Weight Birth (Yes)	0.76	0.15	0.46, 1.04
Gender of Child (Female)	0.26	0.07	0.12, 0.41
Marital Status (Single)	0.46	0.12	0.23, 0.69
Maternal Ethnicity			
Black vs. White	0.07	0.11	--0.15, 0.29
Other vs. White	--0.14	0.14	--0.41, 0.14
Maternal Education Level			
Completed HS vs. Did not complete HS	--0.17	0.14	--0.45, 0.11
Post-secondary vs. Did not complete HS	--0.31	0.17	--0.64, 0.01
Graduate and above vs. Did not complete HS	0.11	0.11	--0.11, 0.31
Maternal Age Category			
[25, 29] vs. < 25	0.00	0.12	--0.24, 0.23
[30, 34] vs. < 25	0.08	0.13	--0.17, 0.33
> 34 vs. < 25	0.03	0.15	--0.26, 0.32
Season of Birth			
Spring vs. Winter	0.19	0.12	--0.04, 0.43
Summer vs. Winter	0.02	0.11	--0.19, 0.22
Fall vs. Winter	0.09	0.12	--0.15, 0.34

Web Table 2. Posterior inference using the full residential exposure dataset, Connecticut birth cohorts, 1988-2008.

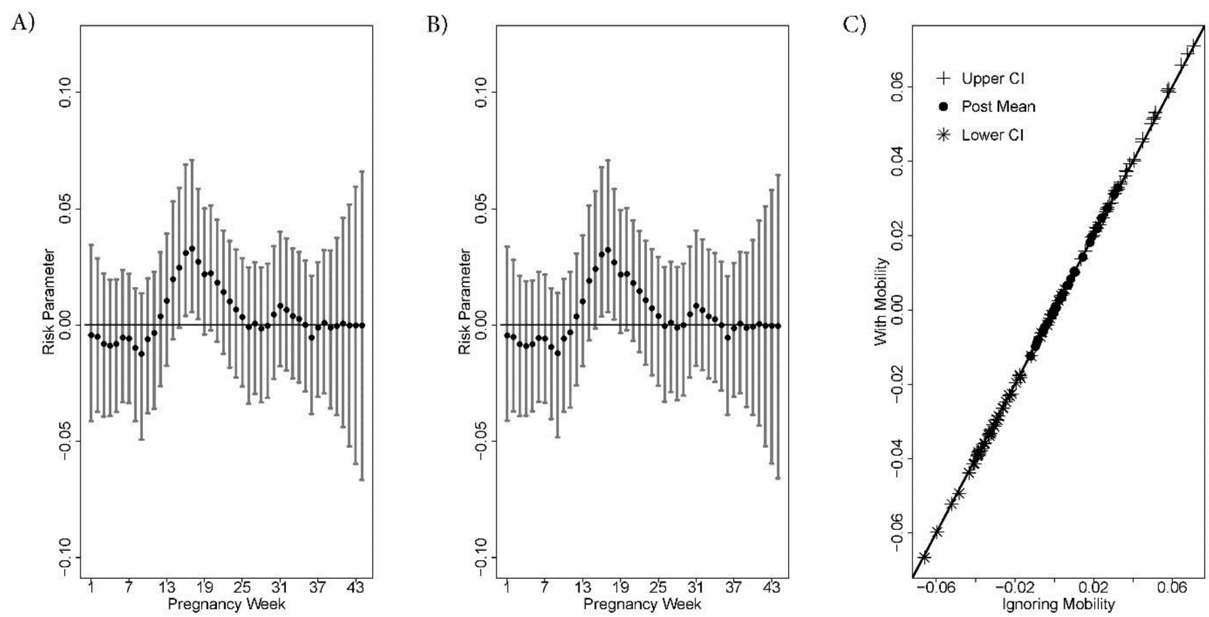
Parameter	Posterior Mean	Posterior SD	Posterior 95% Credible Interval
σ_θ^2: Variance of GP	0.15	0.36	0.02, 0.70
ϕ: Smoothness of GP	0.002	0.002	0.000, 0.008

Abbreviations: GP, Gaussian process.

Web Figure 3. Simulation study results assuming 25% of the pregnant population moves between conception and delivery for the Connecticut birth cohorts, 1988-2008; a comparison of the two exposure metrics. (A) Exposure Metric 1: Exposures based on full maternal residential address histories; (B) Exposure Metric 2: Exposures based on residence at delivery; (C) Scatterplot of parameter estimates from (A) and (B). CI, credible interval.



Web Figure 4. Simulation study results assuming 50% of the pregnant population moves between conception and delivery for the Connecticut birth cohorts, 1988-2008; a comparison of the two exposure metrics. (A) Exposure Metric 1: Exposures based on full maternal residential address histories; (B) Exposure Metric 2: Exposures based on residence at delivery; (C) Scatterplot of parameter estimates from (A) and (B). CI, credible interval.



REFERENCES

1. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing, 2016.