The purpose of the present study was to examine the risk of stillbirth associated with ambient air pollution during pregnancy. Using live birth and fetal death data from New Jersey from 1998 to 2004, the authors assigned daily concentrations of air pollution to each birth or fetal death. Generalized estimating equation models were used to estimate the relative odds of stillbirth associated with interquartile range increases in mean air pollutant concentrations in the first, second, and third trimesters and throughout the entire pregnancy. The relative odds of stillbirth were significantly increased with each 10-ppb increase in mean nitrogen dioxide concentration in the first trimester (odds ratio (OR) = 1.16, 95% confidence interval (CI): 1.03, 1.31), each 3-ppb increase in mean sulfur dioxide concentration in the first (OR = 1.13, 95% CI: 1.01, 1.28) and third (OR = 1.26, 95% CI: 1.03, 1.37) trimesters, and each 0.4-ppm increase in mean carbon monoxide concentration in the second (OR = 1.14, 95% CI: 1.01, 1.28) and third (OR = 1.14, 95% CI: 1.06, 1.24) trimesters. Although ambient air pollution during pregnancy appeared to increase the relative odds of stillbirth, further studies are needed to confirm these findings and examine mechanistic explanations.

Abbreviations: IQR, interquartile range; LMP, last menstrual period; PM$_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 µm.

Several studies have examined the association between ambient air pollution and adverse pregnancy outcomes, including preterm birth (1–6), low birth weight (1, 2, 4, 6–10), and intrauterine growth restriction (1, 2, 11). However, studies in which the associations between ambient air pollution and stillbirth have been examined are limited (7, 12, 13), and the period(s) of gestation when ambient air pollution may be associated with fetal death is also unclear.

We examined the association between stillbirth and the mean concentrations of ambient air pollutants, including particulate matter with an aerodynamic diameter less than or equal to 2.5 µm (PM$_{2.5}$), sulfur dioxide, nitrogen dioxide, and carbon monoxide, across the entire length of pregnancy and during each trimester of pregnancy. We also examined effect modification of these associations by risk factors for stillbirth.

MATERIALS AND METHODS

Data sources and study population

We used New Jersey electronic birth certificate records for live births and fetal death certificates for stillbirths linked to their corresponding hospital delivery discharge records from 1998 to 2004. This data set is maintained by the Division of Family Health Services of the New Jersey Department of Health and Senior Services. We included all singleton births in New Jersey that occurred between 20 and 42 completed weeks of gestation (140–294 days of pregnancy) with birth weight of 500 g or more. The state of New Jersey requires all stillbirths at 20 or more completed weeks of gestation to be reported to the New Jersey Department of Health and Senior Services for registration purposes.
The linked perinatal data set provided information from birth certificates, fetal death certificates, and hospital discharge records for mothers and newborns. Linkage of records was obtained by using probabilistic matching with Automatch probabilistic software (14). Records were matched using the mother’s first and last name, the offspring’s date of birth, the medical record number, and the insurance identifier of the mother. The linkage success rate was 97% for this data set. Although our data set contained live births and stillbirths between January 1, 1998, and December 31, 2004, we limited our cohort to include only those pregnancies with conception dates (between 20 weeks before the study period started and 42 weeks before the study period ended) between August 8, 1997, and March 12, 2004, to avoid fixed cohort bias (15, 16).

Maternal and fetal characteristics were derived from birth and fetal death certificates. Both birth certificate and hospital discharge data were utilized to identify pregnancy complications, as this has been shown to provide higher sensitivity and specificity than birth certificate or hospital discharge data alone (17, 18).

The maternal characteristics we studied were age (<25, 25–34, 35–44, or ≥45 years), race/ethnicity (non-Hispanic white, non-Hispanic black, other non-Hispanic, or Hispanic), educational level (less than high school, high school graduate, or postsecondary education), time of prenatal care initiation (in the first trimester, after the first trimester, or never), and self-reported smoking during pregnancy (yes or no). The offspring characteristics were birth weight (<2,499, 2,500–3,999, or ≥4,000 g) and gestational age (21–24, 25–28, 29–32, 33–36, or ≥37 weeks). Gestational age was estimated in completed weeks using the first day of the last menstrual period (LMP) and the date of birth with the National Center for Health Statistics algorithm (19). The clinical estimate of gestational age was used when data were missing for the month or year of the LMP or if the entire LMP was missing. In cases in which both data on the LMP and clinical estimates were missing, gestational age was set to missing. Pregnancy complications, including chronic hypertension, pregnancy-induced hypertension, diabetes mellitus, gestational diabetes, placental abruption, preeclampsia, and eclampsia, were indicated if the birth certificate, fetal death certificate, or the hospital discharge data indicated the complication.

To determine maternal socioeconomic status, in addition to factors thought to represent the individual socioeconomic status of the mother (e.g., maternal educational level), we also calculated a neighborhood index for area-based socioeconomic status. We used selected area-based socioeconomic status measures that were previously validated for use as proxy individual socioeconomic status indicators (20). For each birth or fetal death, the geocoded residential address of the mother was used to assign a census tract using ArcGIS software (Esri, Redlands, California). Six variables were extracted from the 2000 US Census for each census tract: median household income, median home value, proportion of households receiving interest, dividend, or net rental income, percentage of adults 25 years of age or older with a high school diploma, percentage of adults 25 years of age or older who had completed college, and percentage of people employed in an executive, management, or professional specialty occupation. For each variable, a population mean and standard deviation were obtained by averaging the values from all census tracts in the entire state of New Jersey, and a z score for each variable for each census tract included in our sample was calculated. The z scores for all 6 variables were then summed to obtain the neighborhood score for a given census tract.

Ambient air pollutants

We retrieved concentrations of PM$_{2.5}$ from January 1, 1999, to December 31, 2004, and concentrations of nitrogen dioxide, sulfur dioxide, and carbon monoxide from January 1, 1998, to December 31, 2004. All pollutant measurements made by the New Jersey Department of Environmental Protection were retrieved from the US Environmental Protection Agency Air Quality System (21). Statewide, there were 25 monitoring stations that measured PM$_{2.5}$ every third day. There were 11 stations that monitored nitrogen dioxide, 16 that monitored sulfur dioxide, and 16 that monitored carbon monoxide, each with hourly measurements. The map with the locations of the monitors and the buffer regions is shown in the Web Figure 1 (available at http://aje.oxfordjournals.org/). We assigned PM$_{2.5}$ concentration data from the closest monitoring station within 10 km of the maternal residence for each live birth and stillbirth. All live births and stillbirths from women whose residences were more than 10 km from a monitoring site were excluded from the PM$_{2.5}$ analyses. We repeated this matching process separately for nitrogen dioxide, sulfur dioxide, and carbon monoxide monitoring sites.

We retrieved hourly temperature measurements from weather-monitoring sites at the Newark, Caldwell, Somerset, and Trenton, New Jersey, airports from January 1, 1998, to December 31, 2004. The weather monitoring site closest to each maternal residence at the time of the birth of the offspring was used to assign temperature measurements for that pregnancy. We then calculated apparent temperature as a measure of perceived temperature (22).

The trimester-specific mean pollutant concentration was calculated as the mean of all available pollutant concentrations associated with the length of each pregnancy for each trimester. The mean pollutant concentration for the entire pregnancy was calculated as the mean of all available pollutant concentrations associated with each pregnancy for the length of entire pregnancy. If more than 30% of a pollutant’s scheduled measurements (e.g., 30% of the PM$_{2.5}$ measurements taken every third day) for that trimester or for entire pregnancy were missing, we set that trimester-specific pollutant or entire pregnancy concentration to missing. We used the same method to calculate the mean apparent temperature for each trimester and for the entire length of the pregnancy.

Statistical analysis

We calculated Pearson correlation coefficients between trimester-specific and entire pregnancy mean pollutant concentrations. We used generalized estimating equation
models to estimate the relative odds of stillbirth associated with each interquartile range (IQR) increase in the mean concentration of each pollutant for each trimester and for the entire pregnancy length. The exchangeable correlation structure was used to account for the spatial correlation within the same air pollution monitor in the generalized

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Stillbirths</th>
<th>Total Births</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PM$_{2.5}$ ($n = 980$)</td>
<td>Nitrogen Dioxide ($n = 926$)</td>
</tr>
<tr>
<td>Maternal age, years</td>
<td>959</td>
<td>907</td>
</tr>
<tr>
<td>&lt;20</td>
<td>69</td>
<td>71</td>
</tr>
<tr>
<td>20–24</td>
<td>223</td>
<td>204</td>
</tr>
<tr>
<td>25–29</td>
<td>213</td>
<td>200</td>
</tr>
<tr>
<td>30–34</td>
<td>240</td>
<td>233</td>
</tr>
<tr>
<td>35–39</td>
<td>171</td>
<td>158</td>
</tr>
<tr>
<td>&gt;40</td>
<td>43</td>
<td>41</td>
</tr>
<tr>
<td>Maternal race</td>
<td>976</td>
<td>921</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>287</td>
<td>253</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>369</td>
<td>395</td>
</tr>
<tr>
<td>Other non-Hispanic</td>
<td>68</td>
<td>61</td>
</tr>
<tr>
<td>Hispanic</td>
<td>252</td>
<td>212</td>
</tr>
<tr>
<td>Maternal educational level</td>
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<td>926</td>
</tr>
<tr>
<td>Less than high school</td>
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<td>153</td>
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<tr>
<td>High school graduate</td>
<td>332</td>
<td>318</td>
</tr>
<tr>
<td>Some postsecondary education</td>
<td>481</td>
<td>455</td>
</tr>
<tr>
<td>Prenatal care initiation</td>
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<td>844</td>
</tr>
<tr>
<td>First trimester</td>
<td>648</td>
<td>593</td>
</tr>
<tr>
<td>Second trimester</td>
<td>150</td>
<td>155</td>
</tr>
<tr>
<td>Third trimester</td>
<td>44</td>
<td>40</td>
</tr>
<tr>
<td>Never</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>Self-reported smoking</td>
<td>955</td>
<td>894</td>
</tr>
<tr>
<td>Yes</td>
<td>115</td>
<td>111</td>
</tr>
<tr>
<td>No</td>
<td>840</td>
<td>783</td>
</tr>
<tr>
<td>Gestational week</td>
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<td>926</td>
</tr>
<tr>
<td>21–24</td>
<td>189</td>
<td>184</td>
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<td>25–28</td>
<td>134</td>
<td>131</td>
</tr>
<tr>
<td>29–32</td>
<td>150</td>
<td>147</td>
</tr>
<tr>
<td>33–36</td>
<td>213</td>
<td>185</td>
</tr>
<tr>
<td>≥37</td>
<td>294</td>
<td>279</td>
</tr>
<tr>
<td>Birthweight, g</td>
<td>909</td>
<td>847</td>
</tr>
<tr>
<td>500–2,499</td>
<td>638</td>
<td>610</td>
</tr>
<tr>
<td>2,500–3,999</td>
<td>243</td>
<td>211</td>
</tr>
<tr>
<td>≥4,000</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>Neighborhood socioeconomic status</td>
<td>967</td>
<td>921</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>–2.5 (3.7)</td>
<td>–2.6 (3.7)</td>
</tr>
</tbody>
</table>

Abbreviations: PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 µm; SD, standard deviation.

* The numbers of participants vary because of missing values.
estimating equation estimation. We also adjusted for the maternal characteristics that were known risk factors for the association between ambient air pollution and stillbirth. These included maternal age, maternal race/ethnicity, maternal educational level, prenatal care initiation, and self-reported smoking. The neighborhood index, indicator variables for calendar month and year of the date of conception (date of last menstrual period plus 14 days), and mean apparent temperature during the first trimester were also included in the model. Using this model, the relative odds of stillbirth and its 95% confidence interval for the mean first trimester PM$_{2.5}$ concentration were estimated. We then re-ran the same model for exposure in the second and third trimesters and during the entire pregnancy. Similar models were constructed for carbon monoxide, sulfur dioxide, and nitrogen dioxide concentrations.

To examine effect modification of the pollutant/stillbirth association by maternal educational level (high school graduate or less vs. more than high school), prenatal care (at any time during pregnancy or never), and self-reported smoking (yes vs. no), we added an interaction term (e.g., PM$_{2.5}$ x maternal educational level) to the same model described above. To examine the effect modification of the pollutant/stillbirth association by maternal age (<25, 25–34, or ≥35 years), race/ethnicity (non-Hispanic white, non-Hispanic black, other non-Hispanic, or Hispanic), we included an interaction term with a contrast statement for each level of the variable in the same model.

For carbon monoxide and nitrogen dioxide, pollutants that are related to traffic density, we performed sensitivity analyses limited to live births and stillbirths with maternal residence no more than 5 km from monitoring stations. All analyses were done using SAS, version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

There were 756,562 total singleton births, including 5,381 stillbirths, during the study period. After excluding births that occurred after 42 weeks of gestation and offspring with birth weights less than 500 g, there were 718,974 births, including 3,034 stillbirths. The mean annual rate of stillbirth during 20 and 42 weeks of gestation was 4.2 per 1,000 total births. After limiting the cohort to include offspring who were conceived between 20 weeks before the study period started and 42 weeks before the study period ended and excluding births to women who resided more than 10 km from a monitoring site and those with missing trimester-specific mean air pollutant concentrations, there were 343,077 total births and 1,446 stillbirths available for analysis. This included 980 stillbirths for PM$_{2.5}$ analyses, 926 stillbirths for nitrogen dioxide analyses, 994 stillbirths for sulfur dioxide analyses, and 992 stillbirths for carbon monoxide analyses. Thirty-six percent of pregnancies ending in fetal death and 13% of all pregnancies had 1 or more pregnancy complications.

For all 4 pollutant-specific stillbirth analyses, the risk of stillbirth was highest in non-Hispanic blacks and lowest in other non-Hispanics. Women who had stillbirths were less educated, less likely to have had any prenatal care, and more likely to report smoking during pregnancy. Less than one third of women who had a stillbirth reached term gestation, and approximately three quarters of these women had offspring with a birth weight less than 2,500 g or more than 4,000 g. In contrast, about 12% of total births were preterm, and 16% of offspring had a birth weight less than 2,500 g or more than 4,000 g (Table 1).

The differences in mean trimester-specific pollutant concentrations for stillbirths and live births are shown in Table 2. The subjects’ trimester-specific mean concentrations for PM$_{2.5}$, nitrogen dioxide, sulfur dioxide, and carbon monoxide were higher for stillbirths than for live births for all 3 trimesters of pregnancy and for the entire length of pregnancy (Table 2).

The trimester-specific mean concentrations of pollutants in subjects were highly correlated for nitrogen dioxide and carbon monoxide ($r = 0.76$–0.89) but not for sulfur dioxide ($r = 0.10$–0.46) and PM$_{2.5}$ ($r = 0.07$ to 0.14). Subjects’ trimester-specific mean carbon monoxide and nitrogen dioxide concentrations were moderately correlated ($r = 0.47$–0.55), but the other pollutants varied more across trimesters. Mean concentrations for the entire pregnancy were highly correlated with trimester-specific mean concentrations for nitrogen dioxide and carbon monoxide ($r = 0.93$–0.97) and moderately correlated for sulfur dioxide and PM$_{2.5}$

<table>
<thead>
<tr>
<th>Table 2. Mean Pollutant Concentrations Associated With Stillbirths and Live Births, New Jersey, 1998–2004</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pollutant</strong></td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>PM$_{2.5}$, µg/m³</td>
</tr>
<tr>
<td>Entire pregnancy</td>
</tr>
<tr>
<td>First trimester</td>
</tr>
<tr>
<td>Second trimester</td>
</tr>
<tr>
<td>Third trimester</td>
</tr>
<tr>
<td>Nitrogen dioxide, ppb</td>
</tr>
<tr>
<td>Entire pregnancy</td>
</tr>
<tr>
<td>First trimester</td>
</tr>
<tr>
<td>Second trimester</td>
</tr>
<tr>
<td>Third trimester</td>
</tr>
<tr>
<td>Sulfur dioxide, ppb</td>
</tr>
<tr>
<td>Entire pregnancy</td>
</tr>
<tr>
<td>First trimester</td>
</tr>
<tr>
<td>Second trimester</td>
</tr>
<tr>
<td>Third trimester</td>
</tr>
<tr>
<td>Carbon monoxide, ppm</td>
</tr>
<tr>
<td>Entire pregnancy</td>
</tr>
<tr>
<td>First trimester</td>
</tr>
<tr>
<td>Second trimester</td>
</tr>
<tr>
<td>Third trimester</td>
</tr>
</tbody>
</table>

Abbreviations: PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 µm; SD, standard deviation.
Table 3. Correlation Matrix of Mean Trimester-Specific and Entire Pregnancy Pollutant Concentrations, New Jersey, 1998–2004

<table>
<thead>
<tr>
<th>Pollutant and Trimester</th>
<th>PM$_{2.5}$</th>
<th>Nitrogen Dioxide</th>
<th>Sulfur Dioxide</th>
<th>Carbon Monoxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>1.00</td>
<td>0.15</td>
<td>0.07</td>
<td>0.26</td>
</tr>
<tr>
<td>Second</td>
<td>0.00</td>
<td>0.15</td>
<td>0.31</td>
<td>0.25</td>
</tr>
<tr>
<td>Third</td>
<td>0.14</td>
<td>0.21</td>
<td>0.10</td>
<td>0.24</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.67</td>
<td>0.54</td>
<td>0.58</td>
<td>0.52</td>
</tr>
<tr>
<td>First</td>
<td>0.15</td>
<td>0.24</td>
<td>0.31</td>
<td>0.30</td>
</tr>
<tr>
<td>Second</td>
<td>0.24</td>
<td>0.14</td>
<td>0.23</td>
<td>0.30</td>
</tr>
<tr>
<td>Third</td>
<td>0.39</td>
<td>0.22</td>
<td>0.12</td>
<td>0.25</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.27</td>
<td>0.21</td>
<td>0.24</td>
<td>0.30</td>
</tr>
<tr>
<td>First</td>
<td>0.15</td>
<td>0.41</td>
<td>0.33</td>
<td>0.30</td>
</tr>
<tr>
<td>Second</td>
<td>0.17</td>
<td>0.10</td>
<td>0.33</td>
<td>0.30</td>
</tr>
<tr>
<td>Third</td>
<td>0.40</td>
<td>0.04</td>
<td>0.30</td>
<td>0.30</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.40</td>
<td>0.04</td>
<td>0.30</td>
<td>0.30</td>
</tr>
<tr>
<td>First</td>
<td>0.26</td>
<td>0.34</td>
<td>0.25</td>
<td>0.49</td>
</tr>
<tr>
<td>Second</td>
<td>0.18</td>
<td>0.32</td>
<td>0.45</td>
<td>0.53</td>
</tr>
<tr>
<td>Third</td>
<td>0.25</td>
<td>0.18</td>
<td>0.23</td>
<td>0.42</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.24</td>
<td>0.27</td>
<td>0.29</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Abbreviation: PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 µm.
The entire pregnancy mean concentrations of the pollutants (PM$_{2.5}$, nitrogen dioxide, sulfur dioxide, and carbon monoxide) were found to have low to moderate correlations with each other ($r = 0.28$–$0.56$) (Table 3).

In unadjusted analyses, IQR increases in the first trimester mean nitrogen dioxide concentration, second trimester sulfur dioxide concentration, and entire pregnancy mean sulfur dioxide concentration were associated with significantly increased relative odds of stillbirth (Table 4). After adjustment for known risk factors and neighborhood socioeconomic status and mean apparent temperature, IQR increases in the mean concentrations of nitrogen dioxide in the first trimester, sulfur dioxide in the first and third trimesters, carbon monoxide in the second and third trimesters, and nitrogen dioxide across the entire pregnancy were still associated with significantly increased relative odds of stillbirth. After adjustment, there were also increased relative odds of stillbirth associated with each IQR increase in the mean PM$_{2.5}$ concentration in each trimester, but none were statistically significant (Table 4). The relative odds of stillbirth associated with each IQR increase in the mean concentration of PM$_{2.5}$ over the entire pregnancy were not significantly modified by maternal age, race/ethnicity, educational level, prenatal care, or smoking (Table 5).

We conducted sensitivity analyses for carbon monoxide and nitrogen dioxide, restricting the distance of maternal residence to 5 km from monitoring stations. The relative odds for mean carbon monoxide concentration were 1.27 for the first trimester, 1.25 for both the second and third trimesters, and 1.14 for the third trimester. The relative odds for mean nitrogen dioxide concentration were 1.26 for both the first and second trimesters, 1.14 for the third trimester, and 1.40 for the entire pregnancy. All relative odds were statistically significant ($P < 0.01$) except for the entire pregnancy mean nitrogen dioxide concentration ($P > 0.05$).

**DISCUSSION**

Increased concentrations of ambient air pollutants during pregnancy were associated with increased relative odds of stillbirth after adjustment for known risk factors for stillbirth, mean temperature, and a neighborhood level measure of socioeconomic status. Specifically, increased concentrations of nitrogen dioxide in the first trimester, sulfur dioxide in the first and third trimesters, and carbon monoxide in second and third trimesters were each independently associated with increased relative odds of stillbirth. Increased concentrations of nitrogen dioxide during the entire period of gestation were also associated with increased relative odds of stillbirth. However, we did not observe significant effect modification by maternal age, maternal

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**Table 4.** Unadjusted and Adjusted Relative Odds of Stillbirth Associated With Each Interquartile Range Increase in Ambient Air Pollutant Concentration by Time of Pregnancy, New Jersey, 1998–2004

<table>
<thead>
<tr>
<th>Pollutant (IQR) and Trimester</th>
<th>Unadjusted</th>
<th></th>
<th></th>
<th>Adjusted</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total No. of Births</td>
<td>No. of Stillbirths</td>
<td>OR</td>
<td>95% CI</td>
<td>Total Births</td>
<td>Stillbirths</td>
</tr>
<tr>
<td>PM$_{2.5}$ (4 µg/m$^3$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pregnancy</td>
<td>181,477</td>
<td>809</td>
<td>0.86</td>
<td>0.72, 1.03</td>
<td>172,596</td>
<td>696</td>
</tr>
<tr>
<td>First trimester</td>
<td>197,001</td>
<td>856</td>
<td>1.01</td>
<td>0.88, 1.15</td>
<td>187,829</td>
<td>738</td>
</tr>
<tr>
<td>Second trimester</td>
<td>182,086</td>
<td>807</td>
<td>1.00</td>
<td>0.94, 1.07</td>
<td>172,815</td>
<td>692</td>
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<tr>
<td>Third trimester</td>
<td>174,611</td>
<td>585</td>
<td>1.07</td>
<td>0.87, 1.31</td>
<td>165,405</td>
<td>512</td>
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<tr>
<td>Nitrogen dioxide (10 ppb)</td>
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<tr>
<td>Pregnancy</td>
<td>176,625</td>
<td>862</td>
<td>1.22</td>
<td>0.98, 1.52</td>
<td>161,805</td>
<td>719</td>
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<tr>
<td>First trimester</td>
<td>187,840</td>
<td>894</td>
<td>1.19</td>
<td>1.07, 1.31</td>
<td>173,528</td>
<td>742</td>
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<tr>
<td>Second trimester</td>
<td>180,546</td>
<td>862</td>
<td>1.08</td>
<td>0.93, 1.27</td>
<td>165,724</td>
<td>720</td>
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<tr>
<td>Third trimester</td>
<td>172,705</td>
<td>628</td>
<td>1.06</td>
<td>0.85, 1.33</td>
<td>158,214</td>
<td>542</td>
</tr>
<tr>
<td>Sulfur dioxide (3 ppb)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Pregnancy</td>
<td>203,958</td>
<td>947</td>
<td>1.29</td>
<td>1.07, 1.57</td>
<td>187,942</td>
<td>789</td>
</tr>
<tr>
<td>First trimester</td>
<td>216,020</td>
<td>987</td>
<td>1.02</td>
<td>0.95, 1.10</td>
<td>200,564</td>
<td>828</td>
</tr>
<tr>
<td>Second trimester</td>
<td>207,228</td>
<td>949</td>
<td>1.17</td>
<td>1.02, 1.24</td>
<td>191,305</td>
<td>794</td>
</tr>
<tr>
<td>Third trimester</td>
<td>198,110</td>
<td>668</td>
<td>1.10</td>
<td>0.98, 1.17</td>
<td>182,483</td>
<td>569</td>
</tr>
<tr>
<td>Carbon monoxide (0.4 ppm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>209,133</td>
<td>937</td>
<td>1.05</td>
<td>0.92, 1.21</td>
<td>191,446</td>
<td>770</td>
</tr>
<tr>
<td>First trimester</td>
<td>224,770</td>
<td>974</td>
<td>0.99</td>
<td>0.89, 1.10</td>
<td>207,414</td>
<td>805</td>
</tr>
<tr>
<td>Second trimester</td>
<td>214,461</td>
<td>939</td>
<td>1.07</td>
<td>0.95, 1.20</td>
<td>196,692</td>
<td>776</td>
</tr>
<tr>
<td>Third trimester</td>
<td>202,999</td>
<td>671</td>
<td>1.09</td>
<td>0.96, 1.23</td>
<td>185,646</td>
<td>568</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio; PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 µm.

* Adjusted for maternal age, race/ethnicity, educational level, prenatal care, and smoking, as well as neighborhood socioeconomic status and calendar year and month of conception and mean temperature.
Our findings are consistent with studies that reported a greater risk of adverse pregnancy outcomes associated with increases in ambient air pollution (1–13). However, there is limited evidence of an association between ambient air pollution and stillbirth, and the results have been inconsistent. In a study in the Czech Republic in fetuses over 28 weeks of gestation or with a birth weight greater than 1,000 g, Bobak and Leon (7) reported no significant association of stillbirth with 50-µg/m³ increase in the annual mean concentrations of nitrogen dioxide (odds ratio = 1.21, 95% confidence interval: 0.89, 1.64) and sulfur dioxide (odds ratio = 0.90, 95% confidence interval: 0.70, 1.16). Another study in Sao Pãulo, Brazil, reported a significantly increased risk of stillbirth associated with increases in the mean nitrogen dioxide concentration in the 5 days before delivery, sulfur dioxide on the same day as delivery, and carbon monoxide in the 3 days before delivery in fetuses over 28 weeks of gestation (13). Our results are consistent with this Brazilian study in that both reported an increase in stillbirths associated with increased ambient pollutant concentrations, although we examined trimester-long and pregnancy-long ambient pollutant concentrations rather than ambient pollutant concentrations in the few days before delivery. Future analyses should examine the associations between stillbirth and the acute effect of ambient pollutant concentrations few days before delivery.

Table 5. Adjusted Relative Odds of Stillbirth for the Effect Modification With Each Interquartile Range Increase in the Concentration of Particulate Matter With an Aerodynamic Diameter ≤2.5 µm Across the Entire Pregnancy, New Jersey, 1998–2004

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Total No. of Births</th>
<th>No. of Stillbirths</th>
<th>OR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>172,596</td>
<td>696</td>
<td>0.82</td>
<td>0.56, 1.21</td>
<td>0.32a</td>
</tr>
<tr>
<td>25–34</td>
<td></td>
<td></td>
<td>1.10</td>
<td>0.81, 1.48</td>
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</tr>
<tr>
<td>≥35</td>
<td></td>
<td></td>
<td>1.28</td>
<td>0.81, 2.02</td>
<td>0.28a</td>
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<tr>
<td>Maternal race</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>172,596</td>
<td>696</td>
<td>1.47</td>
<td>1.08, 1.99</td>
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</tr>
<tr>
<td>Non-Hispanic black</td>
<td></td>
<td></td>
<td>0.93</td>
<td>0.59, 1.48</td>
<td>0.76b</td>
</tr>
<tr>
<td>Other non-Hispanic</td>
<td></td>
<td></td>
<td>1.66</td>
<td>0.56, 4.94</td>
<td>0.36b</td>
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<tr>
<td>Hispanic</td>
<td></td>
<td></td>
<td>0.66</td>
<td>0.43, 1.02</td>
<td>0.06b</td>
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<tr>
<td>Maternal educational level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school graduate or less</td>
<td>172,596</td>
<td>696</td>
<td>1.00</td>
<td>0.73, 1.38</td>
<td>0.98</td>
</tr>
<tr>
<td>More than high school</td>
<td></td>
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<td>1.14</td>
<td>0.85, 1.52</td>
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<tr>
<td>Prenatal care</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>175,023</td>
<td>751</td>
<td>1.16</td>
<td>0.54, 2.50</td>
<td>0.71</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td>1.06</td>
<td>0.87, 1.30</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>172,596</td>
<td>696</td>
<td>0.93</td>
<td>0.60, 1.45</td>
<td>0.76</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td>1.08</td>
<td>0.87, 1.35</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio.

a P values for interaction terms comparing the age groups with age group 25–34 years.
b P values for interaction terms comparing the race/ethnicity groups with non-Hispanic whites.

Although the biologic mechanism(s) by which ambient air pollutants may affect fetal survival is not clear, there are several mechanisms that have been proposed to explain associations between ambient air pollution and adverse pregnancy outcomes (23, 24). Direct transfer of pollutants across the placenta causing irreversible damage to the dividing cells of the growing fetus and hypoxic damage or immune-mediated injury during critical periods of development are possible mechanisms that may lead to stillbirth. The transplacental exposure of the fetus to ambient air pollutants at different periods of development may have different effects because of differences in exposure pattern and/or physiologic maturity of the fetus (23, 24). Perhaps exposure to certain pollutants in early pregnancy is harmful for fetal survival, whereas other pollutants cause fatal damage in late pregnancy and still others are harmful throughout pregnancy. To properly examine the potential mechanistic explanations, further analyses are needed to confirm these findings and to explore more thoroughly the times during pregnancy when pollutants may impact the fetus resulting in stillbirth.

There are certain limitations in our analyses that should be considered when interpreting our results. First, we used maternal residence reported at birth to assign the pollutant concentration from the closest monitoring site within 10 km of the maternal residence. However, previous studies have reported that 12%–33% of women move during pregnancy, and maternal residence reported at birth may be different.
from the maternal residence used for most of the pregnancy (25, 26). This may have resulted in mismatching of monitoring sites to subjects if the mother moved a reasonably large distance during pregnancy. Second, we assigned mean concentrations of air pollutants from the monitoring sites to all women residing in a large area rather than prospectively measuring each woman’s exposure for each pollutant during pregnancy. However, both of these exposure errors should result in biases toward the null and underestimation of risk. It is possible that unmeasured confounding influenced the results of this observational study, although the consistency with earlier work is somewhat reassuring in this regard.

In conclusion, we found an increased risk of stillbirth associated with increased ambient concentrations of nitrogen dioxide and sulfur dioxide in early pregnancy and sulfur dioxide and carbon monoxide in late pregnancy. Our study confirms the findings of previous studies, but molecular studies with specific biomarkers are needed to define more clearly the roles of specific pollutants and to investigate possible biologic mechanisms that lead to stillbirth.

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Conflict of interest: none declared.

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