Original article

# Acute air pollution exposure and NICU admission: a case-crossover analysis

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ABSTRACT

*Purpose:* Neonatal intensive care unit (NICU) admission rates have increased over time. Air pollution is associated with adverse pregnancy outcomes, but the relationship between prenatal air pollution exposure and NICU admission has not been investigated.
*Methods:* In the Consortium on Safe Labor (2002−2008), 27,189 singletons were admitted to the NICU. Modified Community Multiscale Air Quality models estimated exposures for criteria air pollutants and constituents of particles less than or equal to 2.5 microns ($PM_{2.5}$). Case-crossover analyses calculated odds ratios and 95% confidence intervals for interquartile range increases in pollutant exposure, comparing exposures during the week of delivery to control periods before and after delivery.
*Results:* In models that adjusted for $PM_{2.5}$, exposure to $PM_{2.5}$ constituents during the week before delivery was significantly associated with increased odds of NICU admission: elemental carbon (35%), ammonium ions (37%), nitrate compounds (16%), organic compounds (147%), and sulfate compounds (35%). Odds were also significantly increased by day of and day before delivery exposures to carbon monoxide (4%−5%), nitrogen dioxide (13%), nitrogen oxides (4%−8%), particles less than or equal to 10 microns (2%), particles less than or equal to 2.5 microns (2%), and sulfur dioxide (3%−6%). No associations were observed for ozone.
*Conclusions:* Acute exposures to $PM_{2.5}$ constituents and several traffic-related pollutants during the week before delivery, the day of delivery, and day before delivery appear to increase the odds of NICU admissions. These novel associations suggest infants exposed in utero to common air pollutants may require additional care during the newborn hospital admission.

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## Introduction

Neonatal intensive care unit (NICU) admission rates have been on the rise in the United States independent of changes in gestational age or birth weight, with a 23% increase in admissions from 2007 to 2012 [1]. These rising rates pose many challenges for families. NICU admission can cause psychological distress to parents and interferes with early bonding between parent and child [2]. NICU admission also limits parent-child interaction, a challenge that potentially has negative implications in the child's cognitive (executive and visual-spatial skills), lingual, and socioemotional (responsiveness and attentiveness) development in infancy through early childhood [2,3]. Rising admission rates also pose financial challenges on both families and society, as average daily NICU costs can total $3000 [4]. Furthermore, NICU patients constitute 0.15% of patients in the US population but 0.45% of national health care costs [4].

These long-term health and social implications as well as the financial burdens of NICU admission motivate identifying potentially modifiable causes underlying admission. Obstetric and neonatal factors that increase risk of NICU admission have been identified [5,6], but NICU admission rates continue to increase.

Maternal conditions such as diabetes, gestational diabetes, kidney disease, maternal bleeding, premature rupture of the membrane, and hypertension appear to increase the risk of NICU

admission [6—10]. Adverse neonatal outcomes such as preterm birth, low birth weight, and respiratory conditions are also factors that lead to NICU admission [5,11]. Although these maternal conditions, neonatal conditions, and genetics can all be independent risk factors for NICU admission [12], they are more complex in origin and less amenable to intervention. However, one potentially modifiable risk factor for NICU admission could be ambient air pollution.

Air pollution has been linked with many adverse maternal and neonatal outcomes. Specifically, chronic and acute exposures to pollution have increased risk of preeclampsia and gestational diabetes mellitus [13]. Several criteria air pollutants have also been associated with an increased risk of preterm birth, low birth weight, small for gestational age, and intrauterine growth restriction [14—17]. However, to the best of our knowledge, the direct relationship between prenatal exposure to air pollution and NICU admission is unexamined.

Acute exposures to pollution have also been associated with infant outcomes. Several studies have found an association between late pregnancy exposures (third trimester, month before delivery, or 6 weeks before delivery) and lower birth weight, small for gestational age, fetal growth restriction, and preterm birth [18—23]. Acute exposures on the day of delivery and days before delivery were associated with an increased risk of preterm birth in Australia [22]. There is also evidence that prenatal exposure to pollution can increase the long-term vulnerability of a child's respiratory, cardiovascular, and immune systems [24].

Given this important data gap on a potentially modifiable risk, the purpose of this study was to investigate the potential acute effect of prenatal air pollution exposure on NICU admission in a US obstetric cohort.

## Methods

### Participants

Participants of this study were from the Consortium on Safe Labor (CSL: 2002—2008), a retrospective cohort study conducted at 12 clinical sites across the United States. The sites included 19 hospitals that all used electronic medical records to extract data for deliveries at 23 weeks or later. Hospitals in the CSL were chosen to represent American College of Obstetricians and Gynecologists regions in the United States [25]. Maternal sociodemographic characteristics, medical, reproductive, and prenatal history, labor and delivery summaries, and postpartum and newborn data were available. There were 223,385 singleton births in the CSL, and 27,193 singleton infants were admitted to a NICU. We excluded four infants with missing air pollution data, resulting in a final analytical sample of 27,189 (11.6%) neonates. Each study site received approval from the institutional review board, and data were anonymized.

### Outcome variable

NICU admission was recorded in the neonate medical record or in discharge summaries.

### Exposure assessment

The Air Quality and Reproductive Health Study linked modified Community Multiscale Air Quality (CMAQ) data with the CSL study to assign pollutant concentrations for each mother [26]. The CMAQ is a three-dimensional multipollutant air quality model that uses emissions data (from National Emissions Inventories) and meteorological data (from Weather Research Forecasting model) to predict ambient pollutant levels. The model predicted hourly estimates of ambient pollutant concentrations within hospital referral regions because maternal residence was not available in CSL data [26,27]. These estimates were weighted to reflect population concentration and accounted for places where women were unlikely to reside. Model performance is described in additional detail elsewhere [26].

Average pollutant concentrations were calculated for the following hazard periods: the average week before delivery (7 days), the day of delivery, and the day before delivery. Average pollutant concentrations were also estimated for two control periods: two weeks (14 days) before the week of delivery and two weeks after delivery for the criteria air pollutants (CO, carbon monoxide; $NO_x$, nitrogen oxides; $NO_2$, nitrogen dioxide; $O_3$, ozone; $PM_{10}$, particulate matter $\leq 10$ microns; $PM_{2.5}$, particulate matter $\leq 2.5$ microns; $SO_2$, sulfur dioxide) and 5 $PM_{2.5}$ constituents (AEC, elemental carbon; $ANH_4$, ammonium compounds; $ANO_3$, nitrate compounds; AOC, organic compounds; $ASO_4$, sulfate compounds).

### Study design and statistical analysis

The case-crossover design assesses the odds of a neonate being admitted to the NICU associated with maternal exposure to air pollution during the hazard period in the week before delivery in comparison to exposure levels during two control periods (two weeks before the week of delivery and two weeks after delivery). This study design is ideal as we were interested in the acute occurrence of NICU admission in relation to an acute exposure to air pollution [28]. The advantage of this study design is that each mother serves as her own control, which controls for non—time-varying factors such as maternal health and unmeasured risk factors, eliminating the potential for control-selection bias [28]. Non—time-varying confounders are thus held constant, and the model anticipates indications for NICU admission before and after the hazard period. The use of bidirectional control windows accounts for seasonal and temporal trends and accounts for some autocorrelation in environmental exposures over a short period [29]. Thus, the risks detected in the model are more likely to be explained by the changes over time in air pollutant exposure.

NICU admission was the outcome of interest. The neonate was the unit of analysis for statistical testing. Multivariate logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) for NICU admission based on an interquartile range (IQR) increase in pollutant concentration. The $PM_{2.5}$ constituent models were adjusted for $PM_{2.5}$ concentration in the respective window. All models were adjusted for temperature (Celsius) and relative humidity. Because women serve as their own controls in the case-crossover design, there was no additional covariate adjustment.

We stratified the case-crossover models by preterm status and mode of delivery to assess whether the relation with air pollution would vary based on common indications for NICU admission (Supplemental Table 4).

Finally, the Benjamini-Hochberg procedure was used to adjust *P*-values as a control for any falsely discovered significance. All analyses were conducted using SAS 9.4 (Cary, NC).

## Results

The prevalence of NICU admission among neonates in the CSL was 10% ($n = 27,189$). Preterm neonates comprised 49.1% ($n = 13,362$) of this NICU-admitted population. A majority of NICU admission of neonates occurred among mothers who had vaginal deliveries (53.7%) or were privately insured (52.5%). The plurality of NICU admissions was among white/non-Hispanic mothers (43.4%),

and among neonates who were their mother's first live birth (47.7%) (Table 1). Each pollutant's distribution (minimum, maximum, and IQR) and Spearmen's correlation coefficients between time windows are respectively presented in Supplemental Tables 1 and 2.

*Day of delivery and day before delivery*

On the day of delivery, each of the criteria air pollutants except ozone was associated with higher odds of NICU admission (Fig. 1 and Supplemental Table 3). Each IQR increase in CO exposure increased odds of NICU admission by 5% (OR: 1.05, 95% CI: 1.02, 1.07), $NO_x$ by 8% (OR: 1.08, 95% CI: 1.05, 1.10), and $SO_2$ by 3% (OR: 1.03, 95% CI: 1.01, 1.06). $PM_{10}$ and $PM_{2.5}$ both increased the odds of

admission by 2% (OR: 1.02, 95% CI: 1.00, 1.04) and (OR: 1.02, 95% CI: 1.00, 1.04), respectively. $NO_2$ exposure was associated with the greatest increase in odds of NICU admission (OR: 1.13, 95% CI: 1.10, 1.17). Estimates were similar for each pollutant for the day before delivery (Fig. 1 and Supplemental Table 3).

Exposure to each of the particulate matter constituents was also associated with increased odds of NICU admission. Elemental carbons, ammonium compounds, nitrate compounds, and sulfate compounds increased odds by 13%−35%, while organic compounds increased odds by 127% (Fig. 2, Supplemental Table 3).

*Average week before delivery*

Results for exposures averaged for the week before delivery for criteria pollutants were attenuated and null (Fig. 3 and Supplemental Table 3).

By contrast, exposure to $PM_{2.5}$ constituents in the week before delivery generally continued to be associated with increased odds of NICU admission (Fig. 4 and Supplemental Table 3). Increases in odds of NICU admission ranged from 16% (OR: 1.16, 95% CI: 1.14−1.18) for nitrate compounds to 147% (OR: 2.47, 95% CI: 2.40−2.54) for organic compounds (Fig. 4 and Supplemental Table 3).

*Supplemental analyses*

In a sensitivity analysis, we examined stratified case-crossover models for preterm or term status and for mode of delivery (vaginal/cesarean). We also examined cesarean delivery after excluding prelabor cases which are less likely to be related to exposure. Although less precise due to smaller numbers of cases, results from these stratified analyses were generally similar to the main findings (data not shown).

All results remained significant after correcting for false-discovery rate.

## Discussion

This case-crossover analysis on a nationwide US cohort found that acute prenatal exposure to air pollution increased the odds of NICU admission. NICU admission was associated with exposure to all criteria air pollutants, except ozone, on the day of delivery and day before delivery, and with each $PM_{2.5}$ constituent exposure on the day of delivery, day before delivery, and average week before delivery. These novel findings are important to consider amid rising rates of NICU admissions and the associated financial burden and psychological distress on families [1−4].

To our knowledge, the relationship between prenatal exposure to air pollution and NICU admissions has not been examined before this study. Our findings are in line with previous studies that found an association between prenatal air pollution and adverse maternal and neonatal outcomes that are associated with an upstream increased risk [16] of NICU admission. A review of 41 studies found that chronic exposure to $PM_{2.5}$ increases the risk of several neonatal outcomes, such as preterm birth, low birth weight, and small for gestational age [13,14]. $PM_{2.5}$ has also been associated with reduced fetal growth and rapid postnatal growth [15,30] as well as increased risk of preeclampsia and gestational diabetes mellitus [31]. Short-term exposure to certain criteria air pollutants in the third trimester or month of delivery can decrease birth weight, increase odds of preterm birth, and increase odds of health care utilization after birth [18−23].

In addition, although we observed strong increased odds of NICU admission due to exposure to $PM_{2.5}$ constituents over the week before delivery, we only observed increased odds due to

**Table 1**
Characteristics of singleton neonates admitted to NICUs and their mothers in the Consortium on Safe Labor, 2002−2008 ($n = 27,189$)

| Characteristics | Neonates in the NICU (n = 27,189) |
|---|---|
| | n (%) |
| Maternal age | |
| <20 | 2927 (10.8) |
| 20−24 | 7011 (25.8) |
| 25−29 | 7023 (25.8) |
| 30−34 | 5795 (21.3) |
| ≥35 | 4433 (16.3) |
| Prepregnancy body mass index (BMI, kg/m$^2$) | |
| <18.5 | 859 (3.2) |
| 18.5−24.9 | 7578 (27.9) |
| 25.0−29.9 | 3902 (14.4) |
| 30−34.9 | 2070 (7.6) |
| ≥35 | 1897 (7.0) |
| Unknown | 10,883 (40.0) |
| Maternal race | |
| White/Non-Hispanic | 11,807 (43.4) |
| Black/Non-Hispanic | 8192 (30.1) |
| Hispanic | 4399 (16.2) |
| Other/unknown | 2791 (10.3) |
| Mode of delivery | |
| Vaginal | 14,593 (53.7) |
| Caesarean | 12,600 (46.3) |
| Birth status | |
| Term | 13,827 (50.9) |
| Preterm | 13,362 (49.1) |
| Parity (number of live births) | |
| 1 | 7278 (26.8) |
| 2 | 4234 (15.6) |
| 3+ | 1987 (7.3) |
| Unknown | 13,690 (50.4) |
| Marital status | |
| Married | 13,746 (50.6) |
| Divorced/widowed | 12,456 (45.8) |
| Single | 987 (3.6) |
| Smoking/alcohol | |
| No | 24,497 (90.1) |
| Yes | 2692 (9.9) |
| Insurance | |
| Private | 14,276 (52.5) |
| Public | 11,170 (41.1) |
| Other | 1743 (6.4) |
| Site | |
| 1 | 2562 (9.4) |
| 2 | 1131 (4.2) |
| 3 | 2203 (8.1) |
| 4 | 884 (3.3) |
| 5 | 5190 (19.1) |
| 6 | 1886 (6.9) |
| 7 | 4370 (16.1) |
| 8 | 892 (3.3) |
| 9 | 352 (1.3) |
| 10 | 2377 (8.7) |
| 11 | 1854 (6.8) |
| 12 | 3492 (12.8) |

**Fig. 1.** Adjusted relative risks between exposure to criteria air pollutants (day of delivery and day before delivery) and risk of NICU admission ($n = 27,189$). *Denotes statistical significance at $P < .05$.

$PM_{2.5}$ itself on the day of delivery and day before delivery. However, these findings are similar to a previous study on $PM_{2.5}$ and its constituents that found that gestational and trimester exposures to constituents were associated with a greater decrease in birth weight than $PM_{2.5}$ was itself [32]. The constituents we measured are the primary components of $PM_{2.5}$, but there are other constituents that may be lowering estimates for total $PM_{2.5}$.

The exact biologic mechanisms linking exposure to air pollution and NICU admission are likely to be multifactorial. For example, prenatal exposure to air pollution affects lung development and function in neonates, which can lead to respiratory problems and subsequent NICU admission [33,34]. $PM_{2.5}$ constituents and other criteria air pollutants apparently cause oxidative stress that leads to inflammation that can then negatively impact placental vasculature, growth, and function [35–38]. Impaired placental function can lead to nutrient deprivation that limits fetal growth and health [39]. The placenta is also responsible for monitoring environmental exchanges between the mother and child, and its altered development can result in harmful environmental pollutants to enter the womb and adversely affect fetal development [40]. The placenta also moderates the availability of hormones and neurotransmitters to the fetus [41]. Long-term effects are also possible because the inflammation caused by pollution could cause the placenta to convert more tryptophan into serotonin resulting in adverse effects on fetal neurodevelopment [42].

There is limited literature on the acute prenatal effects of air pollution on neonates. One study in the United States found a nonsignificant but increased risk of preterm birth due to $PM_{10}$ and $SO_2$ exposures in the days before delivery. However, this study was a time-series analysis that estimated risks for a 50 µg per m³ increase in $PM_{10}$ and a 15 ppb increase in $SO_2$ in contrast to this study's odds ratio estimates for interquartile range increases in exposure [22]. A case-crossover study in Australia also estimated risks for a 50 µg/m³ increase in $PM_{10}$ and a 15 ppb increase in $SO_2$ but did find significant increased risk of preterm birth due to acute exposures on the day of delivery and days before delivery [23].

To the best of our knowledge, no previous study has examined the potential economic cost of air pollution exposure-related NICU
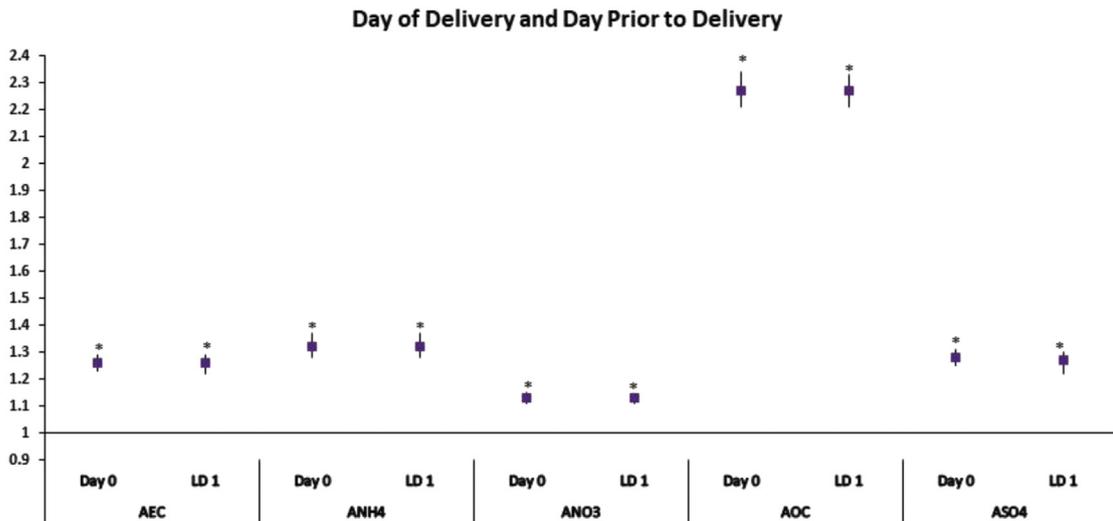


**Fig. 2.** Adjusted relative risks between exposure to PM constituents (day of delivery and day before delivery) and risk of NICU admission ($n = 27,189$). *Denotes statistical significance at $P < .05$.

## Week Prior to Delivery



**Fig. 3.** Adjusted relative risks between criteria air pollutants (week before delivery) and risk of NICU admission ($n = 27,189$). *Denotes statistical significance at $P < .05$.

admission. However, if our findings are replicated, there is likely a substantial economic cost. Exposure to high levels of air pollution has been linked with preterm birth [43,44], a key indicator for NICU admission, and previous work has estimated the attributable economic cost (combined medical expenses and estimated lifetime economic productivity) of air pollution among preterm births [15]. For example, the lifetime estimated attributable cost of preterm birth related to high levels of air pollution in 2010 was 5.09 billion US dollars, or approximately 322,000 US dollars per preterm birth [15]. Whereas the rate of NICU admission was higher for preterm infants, approximately half of the cases in our study were babies born at term, suggesting even further economic impacts. NICU admission cases are among the highest per-case cost of any health outcome [4]; the attributable economic cost of air pollution

exposure in NICU admission cases is likely considerable. Although an economic cost analysis of air pollution and NICU admission is beyond the scope of this study, further work in this area is warranted.

The case-crossover design is a strength of this study as we were interested in association between acute exposure to air pollution and NICU admission [28]. Individuals are self-matched, which controls for non–time-varying confounders such as genetic risks and unmeasured susceptibilities to poor outcomes as well as demographic factors such as maternal age and race. This eliminates control-selection bias, while accounting for indications for NICU admission before and after the hazard period [28]. The bidirectional selection of control periods also adjusts for seasonal and temporal trends, avoiding a potential bias associated with trends over time,

## Week Prior to Delivery



**Fig. 4.** Adjusted relative risks between $PM_{2.5}$ constituents (week before delivery) and risk of NICU admission ($n = 27,189$). * Denotes statistical significance at $P < .05$.

even when that time frame is short [45]. Even when the outcome risk might vary by time (e.g., by gestational age), the difference between the hazard and control periods of exposure remains valid.

Whereas our novel findings merit attention, it is important to consider the limitations of our study. The hospital referral region is the geographic unit of analysis, as maternal residential address was not available in the anonymized data. Ambient pollutant concentrations were averaged across hospital referral regions, which limits extreme values and results in less variation than ambient pollutant concentrations measured at the residence potentially limiting our ability to identify statistically significant associations. Our observations may be biased toward the null, as we would expect higher concentrations measured at a more localized geographic level to result in stronger associations. Although there is a potential for exposure misclassification, most mothers will reside near their hospital of delivery near the end of their pregnancy and a broader exposure region accounts for local mobility. We also lack data on other environmental exposures that may be associated with NICU admission, such as indoor air pollution, noise pollution, and exposure to vibration. As such, we assume these exposures are average in our data. In addition, poor obstetric outcomes may increase risk of NICU admission [6] and our previous analyses of the Consortium on Safe Labor data found air pollution is associated with increased risk for neonatal outcomes including TTN [46], but criteria air pollutants did not increase the risk of preeclampsia and had little impact on preterm birth [43,47]. We examined NICU admission as an aggregate indicator of poor neonatal health, which could derive from a number of causes.

## Conclusions

This case-crossover analysis demonstrated that acute prenatal exposures to most criteria air pollutants and $PM_{2.5}$ constituents increase the odds of NICU admission. With increasing rates of NICU admission, these novel findings suggest that prenatal exposure to air pollution is a potentially modifiable risk factor. If these findings are replicated, women should consider avoiding exposure to ambient air pollution near the end of pregnancy.

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# Appendix

**Supplemental Table 1**
Distribution of pollutant concentrations by exposure windows

| Pollutant | Day of delivery | | | Day before delivery | | | Week before delivery | | |
|---|---|---|---|---|---|---|---|---|---|
| | Min | Max | IQR | Min | Max | IQR | Min | Max | IQR |
| CO (ppm) | 84.11145 | 2264.29 | 303.8322 | 82.38535 | 2694.22 | 303.409 | 95.39043 | 1629.63 | 278.2813 |
| $NO_2$ | 0.844771 | 81.37503 | 12.10341 | 0.844771 | 81.37503 | 11.97993 | 2.999747 | 48.82488 | 10.18299 |
| $NO_x$ (ppb) | 1.773109 | 258.3488 | 26.36542 | 1.773109 | 258.3488 | 26.21495 | 4.119 | 134.9031 | 25.13483 |
| $O_3$ (ppb) | 0.114521 | 76.66985 | 17.82243 | 0.114521 | 76.66985 | 17.75439 | 2.970658 | 53.87552 | 15.44131 |
| $PM_{10}$ ($mg/m^3$) | 0 | 98.65399 | 13.55622 | 0 | 98.65399 | 13.62173 | 2.643697 | 78.05894 | 10.03166 |
| $PM_{2.5}$ ($mg/m^3$) | 0 | 63.87037 | 9.079654 | 0 | 63.87037 | 9.06313 | 0.462488 | 52.87287 | 6.700632 |
| $SO_2$ (ppb) | 0.04451 | 40.54167 | 2.907514 | 0.009573 | 40.54167 | 2.968034 | 0.704536 | 30.91781 | 2.656709 |
| AEC | 0 | 4.23963 | 0.510594 | 0 | 4.740969 | 0.510189 | 0.000987 | 3.067944 | 0.456802 |
| $ANH_4$ | 0 | 15.56368 | 1.616399 | 0 | 16.8751 | 1.624582 | 0.011633 | 14.28334 | 1.350504 |
| $ANO_3$ | 0 | 37.82798 | 1.754802 | 0 | 40.18651 | 1.770021 | 0.00065 | 34.79125 | 1.702881 |
| AOC | 0 | 20.84417 | 2.143069 | 0 | 21.36243 | 2.134894 | 0.221622 | 14.76249 | 1.865971 |
| $ASO_4$ | 0 | 28.46037 | 3.293612 | 0 | 29.40855 | 3.31363 | 0.008832 | 18.99348 | 2.687326 |

**Supplemental Table 2**
Spearman's correlation coefficients between pollutants over the average week before delivery

| Pollutant | CO | $NO_2$ | $NO_X$ | $O_3$ | $PM_{10}$ | $PM_{2.5}$ | $SO_2$ | AEC | $ANH_4$ | $ANO_3$ | AOC | $ASO_4$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CO | 1 | | | | | | | | | | | |
| $NO_2$ | **0.52161** | 1 | | | | | | | | | | |
| $NO_X$ | **0.56056** | **0.88434** | 1 | | | | | | | | | |
| $O_3$ | **−0.29301** | **−0.24712** | **−0.39632** | 1 | | | | | | | | |
| $PM_{10}$ | 0.00541 | **0.12153** | 0.00326 | **0.17789** | 1 | | | | | | | |
| $PM_{2.5}$ | **0.21579** | **0.32491** | **0.24334** | −0.08766 | **0.54399** | 1 | | | | | | |
| $SO_2$ | **0.21377** | **0.37133** | **0.33179** | **−0.2639** | −0.04126 | **0.41804** | 1 | | | | | |
| AEC | **0.43919** | **0.54702** | **0.52254** | **−0.35967** | **0.17249** | **0.40319** | **0.36756** | 1 | | | | |
| $ANH_4$ | **0.4089** | **0.59518** | **0.59925** | **−0.37257** | 0.07521 | **0.39867** | **0.36712** | **0.44148** | 1 | | | |
| $ANO_3$ | **0.25075** | **0.3674** | **0.31067** | **−0.18018** | **0.33278** | **0.78705** | **0.50502** | **0.45603** | **0.66225** | 1 | | |
| AOC | **0.23602** | **0.34659** | **0.29193** | −0.03286 | **0.373** | **0.49825** | **0.20572** | **0.48048** | **0.39102** | **0.4974** | 1 | |
| $ASO_4$ | **0.05776** | 0.02056 | −0.04436 | −0.06069 | **0.33139** | **0.69876** | **0.44118** | **0.30013** | 0.20087 | **0.7853** | **0.3728** | 1 |

Bolded numbers indicate significant correlations.

**Supplemental Table 3**
Associations between criteria air pollutants, $PM_{2.5}$ constituents, and NICU admissions ($n = 27,189$)

| Pollutant | Day of delivery | Day before delivery | Lag week 1 |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| CO | **1.05 (1.02, 1.07)** | **1.04 (1.01, 1.07)** | 1.02 (0.98, 1.05) |
| $NO_2$ | **1.13 (1.10, 1.17)** | **1.13 (1.10, 1.17)** | 1.03 (0.99, 1.07) |
| $NO_X$ | **1.08 (1.05, 1.10)** | **1.04 (1.02, 1.08)** | 1.01 (0.98, 1.05) |
| $O_3$ | 0.99 (0.96, 1.02) | 1.00 (0.96, 1.03) | 1.03 (0.98, 1.07) |
| $PM_{10}$ | **1.02 (1.00, 1.04)** | **1.02 (1.01, 1.04)** | 1.00 (0.98, 1.02) |
| $PM_{2.5}$ | **1.02 (1.00, 1.04)** | **1.02 (1.01, 1.04)** | 1.00 (0.98, 1.02) |
| $SO_2$ | **1.03 (1.01, 1.06)** | **1.03 (1.00, 1.06)** | 1.02 (0.99, 1.05) |
| AEC | **1.26 (1.23, 1.29)** | **1.36 (1.32, 1.39)** | **1.35 (1.32, 1.38)** |
| $ANH_4$ | **1.32 (1.28, 1.37)** | **1.32 (1.28, 1.37)** | **1.37 (1.33, 1.42)** |
| $ANO_3$ | **1.13 (1.11, 1.14)** | **1.13 (1.11, 1.15)** | **1.16 (1.14, 1.18)** |
| AOC | **2.27 (2.21, 2.34)** | **2.27 (2.21, 2.33)** | **2.47 (2.40, 2.54)** |
| $ASO_4$ | **1.28 (1.25, 1.31)** | **1.27 (1.22, 1.30)** | **1.35 (1.31, 1.39)** |

Bolded numbers indicate significant associations. All values remained significant after using the Benjamini-Hochberg false-discovery rate controlling method.

**Supplementary Table 4**
Common indicators[*] of NICU admission (N: 27,189)

| | Cases | Percent |
|---|---|---|
| Preterm Birth | 13,362 | 49.1 |
| Cesarean Delivery | 12,600 | 46.3 |
| Transient tachypnea of newborn | 5060 | 18.6 |
| Small for Gestational Age | 4415 | 16.2 |
| Neonatal respiratory distress | 3508 | 12.9 |
| Other maternal comorbidities | 2692 | 9.9 |
| Gestational diabetes | 1963 | 7.2 |
| Chronic diabetes | 1043 | 3.8 |
| Chronic hypertension | 825 | 3.0 |
| Gestational hypertension | 749 | 2.7 |
| Asphyxia | 577 | 2.1 |
| Neonatal Abstinence Syndrome | 390 | 1.4 |
| Chronic renal disease | 341 | 1.2 |

[*]  Indicators are not mutually exclusive.