HHS Public Access

Author manuscript

J Expo Sci Environ Epidemiol. Author manuscript; available in PMC 2015 April 09.

Published in final edited form as:

J Expo Sci Environ Epidemiol. 2013 ; 23(3): 315–321. doi:10.1038/jes.2012.124.

Exploring prenatal outdoor air pollution, birth outcomes and neonatal health care utilization in a nationally representative sample

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Abstract

The impact of air pollution on fetal growth remains controversial, in part, because studies have been limited to sub-regions of the United States with limited variability. No study has examined air pollution impacts on neonatal health care utilization. We performed descriptive, univariate and multivariable analyses on administrative hospital record data from 222,359 births in the 2000, 2003 and 2006 Kids Inpatient Database linked to air pollution data drawn from the US Environmental Protection Agency's Aerometric Information Retrieval System. In this study, air pollution exposure during the birth month was estimated based on birth hospital address. Although air pollutants were not individually associated with mean birth weight, a three-pollutant model controlling for hospital characteristics, demographics, and birth month identified 9.3% and 7.2% increases in odds of low birth weight and very low birth weight for each μg/m^3 increase in $PM_{2.5}$ (both $P<0.0001$). $PM_{2.5}$ and NO_2 were associated with −3.0% odds/p.p.m. and +2.5% odds/p.p.b. of preterm birth, respectively (both $P<0.0001$). A four-pollutant multivariable model indicated a 0.05 days/p.p.m. NO_2 decrease in length of the birth hospitalization ($P=0.0061$) and a 0.13 days increase/p.p.m. CO ($P=0.0416$). A $1166 increase in per child costs was estimated for the birth hospitalization per p.p.m. CO ($P=0.0002$) and $964 per unit increase in O_3 ($P=0.0448$). A reduction from the 75th to the 25th percentile in the highest CO quartile for births predicts annual

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

savings of $134.7 million in direct health care costs. In a national, predominantly urban, sample, air pollutant exposures during the month of birth are associated with increased low birth weight and neonatal health care utilization. Further study of this database, with enhanced control for confounding, improved exposure assessment, examination of exposures across multiple time windows in pregnancy, and in the entire national sample, is supported by these initial investigations.

Keywords

outdoor air pollution; low birth weight; preterm birth; health care utilization

INTRODUCTION

Fetal growth measures, especially low birth weight, are important predictors of infant and childhood mortality,[1] as well as cardiovascular function, hypertension, and diabetes in adulthood,[2,3] and psychological, behavioral, and educational outcomes in later life.[4,5] Risks of low birth weight (8.2% in 2009 per National Center for Health Statistics data) and preterm birth (12.3% in 2008) remain above their Healthy People 2010 goals of <5% and <7.6%, respectively.[6]

Despite multiple, US-based, studies of prenatal outdoor air pollution exposure,[7–11] the impact of prenatal air pollution exposure on fetal growth, independent of other risk factors, such as maternal age, prenatal care, environmental tobacco smoke exposure, race, socioeconomic status, preterm delivery, and pre-eclampsia,[12] remains unresolved.[13] Although these studies are suggestive of adverse effects, they are difficult to combine due to differences in pollutants measured, timing of measurements (with variability in the pregnancy time windows examined), and restriction to one or more regions of the United States.[14–18] Because spatial and temporal heterogeneity of effects by particulate matter of diameter ≤2.5 μm ($PM_{2.5}$) has been documented for cardiovascular admissions in adults and may reflect different chemical composition of pollutants at the regional level, inconsistency in results may be due to variability in particle constituents.[19,20] Few studies have analyzed the impact of air pollution on birth weight nationally, which limits the degree to which these past studies can inform federal policy.[21,22] A national study would further permit examination of effects within certain regions of the United States and may better identify the sources and/or characteristics of air pollutants that pose particular risk.

The Kids Inpatient Database (KID) constitutes the largest all-payer data set for in-hospital births in the United States. It not only includes birth weight and diagnostic/procedure codes that identify adverse outcomes detected at birth or during the early neonatal period but also contains rich information about utilization (length of stay (LOS) and hospital charges) and sociodemographic and hospital characteristics that can influence health care delivery. The US Environmental Protection Agency (USEPA) Aerometric Information Retrieval System (AIRS) documents concentrations of criteria air pollutants across the nation.

Coupling the AIRS and the KID databases permits the first nationwide examination of relationships between prenatal outdoor air pollutant exposure during pregnancy and birth

weight and other perinatal outcomes. This data linkage provides major opportunities to extrapolate findings to inform both clinical practice and federal regulatory policy and to examine variation in the effects of outdoor air pollutants on a regional basis. A further benefit is that economic costs associated with prenatal exposure can be quantified, and the projected cost savings associated with pollution reduction can be estimated for comparison with the costs of technologies to reduce exposure.

In this manuscript, we present findings from an exploratory study linking mean monthly air pollutant data for the month of birth using the USEPA AIRS to a subsample of the 2000, 2003 and 2006 KID. We examined whether gestational month-specific exposures to ozone (O_3), particulate matter <2.5 μm ($PM_{2.5}$), particulate matter <10 μm in diameter (PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO) was associated with reductions in mean birth weight and increases in preterm birth, low birth weight, and very low birth weight. We also examined whether air pollution in the month of birth was associated with increases in LOS, charges, and costs for birth hospitalizations.

METHODS

This was a multiyear, cross-sectional study, linking two already collected and de-identified data sets, the KID and the USEPA AIRS, and was exempted from review by the Institutional Review Boards of New York University and Mount Sinai Schools of Medicine. Subsequent sections describe the databases and their linkage.

KID

The KID is a product of the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. The KID includes a sample of pediatric discharges from all hospitals in states that agree to participate in the KID (an increasing number of states participated over the years of the KID, from 22 in 1997 to 27 in 2000, 36 in 2003 and 38 in 2006).[23]

Pediatric discharges were stratified as: (1) uncomplicated (term) in-hospital birth; (2) complicated in-hospital birth; or (3) all other pediatric cases. Systematic random sampling was used to select 10% of uncomplicated in-hospital births and 80% of complicated in-hospital births and other pediatric cases from each hospital sampled in the KID. In the 2000, 2003, and 2006 KID, observations were available for a total of 2,675,679 births.

Data provided in the KID for each hospitalization include: LOS, hospital charges, associated diagnoses and procedures, race, primary expected payer, median income quartile for patient zip code, hospital region (Northeast, South, West, Midwest), admission month, teaching hospital status, and gender. Privacy issues prohibit access to hospitalization (birth) date and patient zip code in the publicly available and deidentified version of the KID, which derive from inpatient databases transmitted pursuant to agreements with each individual State.

Birth weight is provided by some states as a continuous variable, whereas others categorically do not include birth weight as part of data sets provided to the Healthcare Cost and Utilization Project. When the continuous measure was available, we used it to

categorize low birth weight as <2500 g and very low birth weight as <1500 g. To augment sample size, we used diagnostic codes (International Classification of Diseases and Related Health Problems version 9 (ICD-9-CM), 764.01–09, 764.11–19, 764.21–29, 764.91–99, 765.01–09, and 765.11–19) to identify low birth weight, very low birth weight, and/or normal weight births when a continuous measure of birth weight was not provided.

Gestational age is provided in the KID through diagnostic codes that identify preterm birth as birth at <37 weeks gestation (ICD-9-CM, 765.21–28). Term births were identified with Diagnosis Related Group of 391 indicating "Normal Newborn," and further designated by the categorical uncomplicated birth or UNCBRTH variable in the KID. The validity of using diagnostic code to account for gestational length and birth weight has been confirmed in multiple studies of neonates.[24–26] Recognizing the heterogeneity that exists in the origins of low birth weight, we examined term-low birth weight and preterm-low birth weight as outcomes to distinguish intrauterine growth retardation from preterm delivery in origins of low birth weight.

Due to their skewed distribution, univariate and multivariable analyses of LOS, charges and costs were performed after log(base 10)-transformation. Charges were adjusted to 2005 dollars to account for inflation using the Healthcare Consumer Price Index[27] and were converted to costs using cost-to-charge ratio files from the Center for Medicare and Medicaid Services.[28] The cost-to-charge files are constructed using all-payer, inpatient cost and charge information from detailed reports by hospitals to the Center for Medicare and Medicaid Services. Because the cost-to-charge ratios at the hospital level are for all admissions, including non-pediatric admissions, this does not account for Cesarean *versus* vaginal deliveries or other characteristics that influence complexity of maternal and/or neonatal care.

USEPA AIRS

AIRS is the national, publicly available, repository for information about airborne pollution in the United States (available at www.epa.gov/ttn/airs/airsaqs/detaildata/downloadaqsdata.htm). States are required to report data for eight criteria pollutants (lead, PM_{10}, NO_2, SO_2, CO and $PM_{2.5}$, and reactive volatile organic compounds). Concentrations of pollutants are recorded on a regular basis ranging from hourly to every few days, depending on the regulatory requirements. From the EPA AIRS database, text files were obtained for six air pollutants (O_3, PM_{10}, NO_2, SO_2, CO and $PM_{2.5}$) for 1999–2000, 2002–2003, and 2005–2006 in order to merge with the hospitalization data. We used the hospital address as the point from which to identify monitors that would appropriately represent individual child air pollutant exposure. Recognizing this is a key limitation, in the context of an exploratory study, we suggest hospital location as a reasonable proxy, on average, for residential location.

The latitude and longitude grid points of the address of each birth hospital was calculated and crosschecked using a geocoding website (http://stevemorse.org/jcal/latlonbatch.html?direction=forward), as well as Google Maps (http://maps.google.com). We determined distance between hospital zip codes provided in the KID database and AIRS monitors using latitude and longitude for the AIRS monitors, which are available on a publicly available

website (http://www.epa.gov/air/data/monvals.html). When multiple air monitors were identified within the 10-mile radius that we set for inclusion of air monitoring data, we computed a mathematical average of available data points to calculate mean O_3, PM_{10}, NO_2, SO_2, CO, and $PM_{2.5}$ for the appropriate month.

Linkage of KID to AIRS

The present study capitalized upon a data linkage of AIRS to the Nationwide Inpatient Sample, a nationally representative data set of pediatric and adult hospitalizations (like the KID, produced by the Healthcare Utilization Project of the Agency for Health Care Research and Quality), for the now-published studies in which we have previously assessed the role of subchronic and chronic air pollution in pediatric hospitalization with asthma[29] and bronchiolitis.[30] Given that not all Nationwide Inpatient Sample hospitals are included in the KID, we were able to aggregate air pollution with hospitalization data for approximately one-third of births in the KID. Our existing linkages for this exploratory study were also limited by availability of air pollution measurements only for the month of birth and utilized the hospital address as the basis for estimating exposure.

Statistical Analysis

We performed univariate and multivariate regression analyses using SAS 9.2 and SUDAAN 10.0.1 (Research Triangle Institute, Cary, NC) to account for the complex sample design used in the KID, using sample weights provided with the KID. All regression analyses utilized the SUBPOPN command, which analyzes the subsample of births in the KID while maintaining the integrity of the weighting in the analytic output. Race, primary expected payer, median income quartile for patient zip code, hospital region (Northeast, South, West, Midwest), admission month, teaching hospital status, and gender were included in the multivariable model. Each of the six pollutants was examined in single-pollutant multivariable models, before constructing a full multivariable model simultaneously examining multiple pollutants. To determine which pollutants to include in the final multivariable model, we used Spearman correlations to examine auto-correlation among the pollutants, recognizing that there can be strong correlations among pollutants arising from the same source (e.g. motor vehicles). Any two pollutants with $r \geq$absolute value of 0.25 were excluded from each other initially. This resulted in three separate models also controlling for sociodemographic and hospital characteristics: one multivariable model containing $PM_{2.5}$, NO_2, and CO, another with O_3 and PM_{10}, and a third with SO_2. We added any significant pollutant variables from the second and third models to the first in final multivariable models.

To account for multiple testing, we applied Bonferroni corrections[31] to account for multiple comparisons of air pollutants (applying a cut point of P=0.167 or 0.05 divided by 3). Retransformation of increments of total charges and LOS from the log base followed the technique described by Duan.[32]

Economic Analysis

We limited our extrapolation to statistically significant associations of air pollutants with costs after Bonferroni correction. We assumed the effects only to occur in urban centers, and

used data from the US Health Resources Services Administration and the Centers for Disease Control to identify number of annual births in US cities with population >100,000.[33] We then quantified the reduction of air pollutant exposure for those births with the highest air pollutant quartile (75th to 100th percentile, assuming all these births have 75th percentile exposures) down to the 25th percentile, and estimated the savings in costs associated with that reduction in air pollution by multiplying one-fourth of the annual births by the cost savings per unit air pollution and the unit reduction in the air pollution. This produced an estimate of direct health care cost savings that could be produced annually through reduction of air pollution in the most highly polluted regions of the United States.

RESULTS

Consistent with the sampling design for the KID, the study population has a predominance of low birth weight (37.0%) and preterm birth (26.9%), well above national rates (Table 1). Of the 222,359 births with available $PM_{2.5}$, NO_2, and CO data for the month of birth, 68,953 had a continuous measure of birth weight available. Availability of pollutant data was not significantly associated with low birth weight, preterm birth, or birth weight, on univariate regression analysis ($P>0.2$), while births lacking pollutant data had significantly shorter LOS ($P=0.0022$) and lower charges ($P=0.0002$). To account for potential confounding due to missing pollution data for these latter outcomes, we added a covariate for missing air pollution to multivariable regression models of LOS and charges.

Table 2 presents significant results for single-pollutant, multivariable models for the study outcomes. For each μg/m^3 increase in PM_{10}, a 1.9 g increase in birth weight was identified ($P=0.026$), while increased odds of low birth weight were associated with $PM_{2.5}$ in the month of birth (odds ratio (OR) +9.6%/p.p.m. increase, $P<0.0001$). $PM_{2.5}$, O_3, and CO were all significantly associated with very low birth weight in single pollutant models. NO_2 in the month of birth was associated with increased preterm birth (OR +2.4%/p.p.b. increase, $P=0.002$), while $PM_{2.5}$ was inversely associated with preterm birth (OR −3.0%/μg/m^3 increase, $P<0.0001$). $PM_{2.5}$ and CO in the month of birth were associated with increases in term-low birth weight, while $PM_{2.5}$, CO, NO_2, and PM_{10} were all associated with increases in preterm-low birth weight.

NO_2, CO, and O_3 were each associated with increases in charges for the neonatal hospitalization, though only CO was associated with increases in costs ($1350/p.p.m., $P<0.0001$). CO was also associated with increased LOS (+0.18 days/p.p.m., $P=0.0021$), whereas NO_2 (−0.04 days/p.p.b., $P=0.01$) and PM_{10} (−0.008 days/μg/m^3 increase, $P=0.01$) were associated with shorter hospital stays.

Spearman correlation coefficients revealed high potential for collinearity in multivariable modeling simultaneously including $PM_{2.5}$ and PM_{10} ($r=0.395$, Table 3), SO_2 and O_3 ($r=-0.296$) and CO and O_3 ($r=-0.297$). We therefore proceeded with a three-pollutant model including $PM_{2.5}$, NO_2, and CO in the multivariable regressions of all outcomes. Completely separate sets of multivariable regressions were performed for O_3 and PM_{10}, and for SO_2.

Among the 62,906 neonates for whom complete data were available, none of the three pollutants were individually associated with decrements in mean birth weight (Table 4). Among the 82,379 births that could be analyzed for categorical outcomes, however, 9.3% and 7.2% increases (both $P<0.0001$) in odds of low birth weight and very low birth weight were associated with each $\mu g/m^3$ increase in $PM_{2.5}$. This association could not be explained by increased preterm birth, as $PM_{2.5}$ was inversely associated with preterm birth (−3.0% odds per $\mu g/m^3$ increase, $P<0.0001$). Increases in NO_2 were also associated with 2.5% increased odds of preterm birth per p.p.b. increase ($P<0.0001$). $PM_{2.5}$ was significantly associated both with preterm-low birth weight (+9.1% odds per $\mu g/m^3$ increase, $P=0.0007$) and term-low birth weight (+11.6% odds per $\mu g/m^3$ increase, $P<0.0001$). Neither the model examining SO_2 in the month of birth nor the model examining PM_{10} and O_3, after adjusting for demographic and hospital characteristics, revealed any significant association with birth outcomes.

Significant differences in health care utilization were also associated with outdoor air pollutants. In the three-pollutant multivariable model ($PM_{2.5}$, NO_2, and CO), we found that a 1 p.p.b. increase in average NO_2 during the month of hospitalization was associated with a $463 ($P=0.0001$) increase in charges, and a 1 p.p.m. in average CO was associated with a $3646 ($P<0.0001$) increase. Among the smaller sample of hospitalizations for which cost data could be calculated, in a three-pollutant model controlling for sociodemographic and hospital characteristics, $PM_{2.5}$ and NO_2 were not significantly associated with costs for the neonatal hospitalization, while CO concentration was associated with an increase in costs ($1163, $P=0.0002$). CO concentrations during the birth month were associated with a 0.06-day lengthening of hospital stay ($P=0.0411$, $P>0.0167$ accounting for Bonferroni correction), while average NO_2 during the month of hospitalization was associated with a shortening of LOS (0.02 days/p.p.b. increase, $P=0.061$). Missing data were not significantly associated with LOS, charges, or costs in the multivariable models of costs, charges, and LOS ($P>0.2$).

SO_2 was not significantly associated with any health care utilization outcome, while the models performed for O_3 and PM_{10} revealed only a significant association of O_3 with increased birth hospitalization charges ($4716/p.p.m. increase). To assess separate influences of $PM_{2.5}$, O_3, NO_2, and CO, the final, full multivariable regressions modeled log-transformed total charges with a four-pollutant model. This model, presented in Table 5, associated a $462 increase in charges for the birth admission per p.p.b. increase in NO_2 ($P=0.0002$); a $3677 increase in charges per p.p.m. increase in CO ($P<0.0001$); and a $4877 increase in charges per p.p.m. increase in O_3. A significant 0.05 days/p.p.b. NO_2 decrease in LOS was identified ($P=0.0061$), as was a concomitant increase in LOS per unit CO (+0.13 days/p.p.m., $P=0.0416$). In final multipollutant models, only two pollutants were significantly associated with costs in the birth hospitalization: a $1166 increase per p.p.m. CO ($P=0.0002$) and a $964 increase per unit increase in O_3 ($P=0.0448$, not significant after Bonferroni correction).

In extrapolating to economic costs, we assume the effects only to occur in urban centers, which comprise 99.0% of the studied hospitalizations. Data from the US Health Resources Services Administration and the Centers for Disease Control suggest 1.4 million births in

US cities with population >100,000. A reduction from the 75th to the 25th percentile in those births in the highest CO quartile would reduce CO 0.33 p.p.m. (from 0.78 to 0.45), with savings of $134.7 million (=0.33 × 350,000 births × $1166/p.p.m.) in direct health care costs.

DISCUSSION

In an exploratory analysis of the KID and AIRS databases, we demonstrate utility and capacity in linking these two nationally representative data sets to examine air pollution impacts on birth outcomes. Although the results are limited in their extrapolation to the national experience, because they were performed in a limited subset of the nationally representative sample, they are consistent with and support past reported associations of outdoor air pollutants with adverse birth outcomes.[7–11]

The present study does identify associations of birth outcomes with different pollutants than some previous studies to date, which have implicated SO_2 and PM_{10} as a risk factor for preterm birth.[7–9,34,35] Our study also differs from other previous studies[7,36–38] in that we did not identify associations of PM_{10} or CO with low birth weight. We note key differences in that our exploratory study examined air pollutant exposure in the month of birth, which will require further study with the larger data set along with better control for confounding, and emphasize the uniqueness of this study in its examination of consequences for health care utilization during the neonatal hospitalization.

Divergent results in directionality, as identified for preterm birth with $PM_{2.5}$ and NO_2 and for LOS with CO and NO_2, are not uncommon in multi-pollutant models and could be artifacts of including correlated pollutants in the same model.[34,39] These merit further examination in larger, more detailed studies of the KID across the entire pregnancy. If PM toxicity varies with its composition, as expected, then these variations in air pollutant–preterm birth associations may also be more interpretable if evaluated in terms of variations in the PM pollution source mix. The CO and NO_2 associations with health care utilization outcomes also suggest a role by traffic pollution in these neonatal impacts, which can be further corroborated through addition of source apportionment data available from the USEPA's Chemical Speciation Network.[40] Use of the state-of-the-art source apportionment methods in studies of cardiovascular outcomes in adults has been of high utility.[41,42] The inverse association of NO_2 with LOS but increased charges is striking. We hypothesize that increased hospital costs could still occur in shorter LOS, due to additional procedures and medications that exceed the daily cost of the hospital bed. Yet, we exercise caution in further interpretation.

It might be argued that the effects identified here might suffer from an error of misattribution given that urban areas have more expensive medical care. However, air pollution monitoring data are almost exclusively available for urban areas (99% of all hospitalizations we analyzed for preliminary data were urban), and this analysis therefore represents effects within urban areas where pollution is greater. This analysis therefore controls for urbanicity and examines the effects of differences in air pollution within that context. We also recognize that we analyzed data from approximately 10% of urban births in

the data set, and so our economic estimates should be replicated using results of analyses of the entire sample. Our calculations of potential costs associated with air pollution exposure are predicated on causality and on the assumption that reducing the pollutant levels would lead to reduction in those outcomes. We also note that we were not able to use the day of birth to capture air pollution measurements in the month preceding birth. However, this exposure imprecision should bias towards the null,[43] suggesting that the true pollutant effect sizes may be larger than indicated here.

We recognize the absence of important individual-level data in the KID. These include lack of data on maternal obesity, tobacco exposure, substance abuse, and alcohol intake. Future analyses can control for these factors using regional-level data from publicly available sources such as the Behavioral Risk Factor Surveillance System[44] and the Department of Justice (e.g., drug arrests as a proxy for drug use) on these exposures, to create variables that approximate variability in the confounders that might otherwise explain effects of air pollution. Although this does not completely resolve individual-level data gaps, multiple imputation techniques[45] can be utilized to account more completely for missing data. Besides the obvious absence of other data on other environmental exposures that may alter fetal growth, including stress[46–48] as well as lead,[49] perfluorinated compounds,[50] and other chemical exposures,[51] variability in obstetric care (and seeking of care) and maternal conditions (especially preeclampsia) are other unmeasured confounders not available in an administrative data set containing only neonatal records. Another important covariate not available in the KID is climate, which is known to influence characteristics and effects of air pollution.[52]

Although there are limits to control for confounding using the KID for studies of air pollution effects, linking the AIRS to the KID permits examination of exposures in each gestational month and the average for the entire pregnancy, as well as on the day of birth, all of which may be related to birth weight and other adverse perinatal outcomes. Past studies have failed to measure pollution exposures comprehensively across pregnancy, assuming that either first/third trimester exposures are best suited to study exposure–outcome relationships.[14,17] The KID–AIRS linkage therefore has the potential to improve greatly upon previous studies by considering a large, nationwide database; developing and studying air pollution exposures in rural as well as urban areas; using gestational month measures of exposure to capture and isolate more relevant fetal development periods; and examining exposures over the complete course of pregnancy to address the hypothesis that specific early and/or late pregnancy time windows of exposure are of the greatest importance. Examination of peak air pollutant exposures or criteria more closely corresponding to National Ambient Air Quality Standards would also be possible.[53]

We conservatively limited our analyses to those births with monitoring data within a 10-mile radius of the hospital of birth. A larger radius of inclusion coupled to linkage to the entire KID would have greatly improved sample size and external validity of our analyses. Subsequent analyses can also account for the existence of data multiple monitors using more sophisticated approaches that give greater weight to monitors proximate to the home address, which is available in the restricted-use data file. Linkage of the data sets based upon the home zip code presents concerns about imprecision produced by mobility of the mother

during pregnancy, as well as use of zip code rather than address to model air pollutant exposures.[54] Linking with AIRS alone will also not be sufficient for future studies, as relatively few monitors exist in rural locations. Fortunately, innovative geo-spatial land use regression modeling estimates have been successfully applied in studies of exposure to air pollutants and associations with other health outcomes.[54,55] Together, these data sources have great potential to achieve linkage in a large proportion of KID births.

Given the known spatial and temporal heterogeneity for the impact of $PM_{2.5}$ exposure on adult cardiovascular health,[19,20] as well as pediatric asthma and bronchiolitis,[29,30] further work can also use the hospital region variable in the KID to assess heterogeneity of air pollutant effects. In addition, the KID–AIRS data linkage can examine effects within term *versus* preterm births, and within preterm-low birth weight, term-low birth weight, and very low birth weight births. The latter is especially important as term-low birth weight generally represents intrauterine growth retardation, as opposed to prematurity (preterm-low birth weight). All of the concerns having been raised about absence of individual-level confounding data, the large sample size proffers the benefit of stratified modeling with statistical power not readily attained, even in large international pools.[13]

CONCLUSION

In a large and predominantly urban population oversampled with complicated and potentially sicker newborns, outdoor air pollution exposure in the month of birth is associated with increases in low birth weight, as well as increased health care utilization during the birth hospitalization. Although further control for confounding and linkage to the entire nationwide database is needed, the result suggest significant economic, in addition to health, consequences of preventable prenatal exposure. Further study of this database, with enhanced control for confounding, improved exposure assessment, examination of exposures across multiple time windows in pregnancy, and in the entire national sample, is supported by these initial investigations.

ABBREVIATIONS

AIRS	Aerometric Information Retrieval System
BRFSS	behavioral risk factor surveillance system
CO	carbon monoxide
ICD-9-CM	International Classification of Diseases and Related Health Problems version 9
KID	Kids Inpatient Database
NIS	Nationwide Inpatient Sample
NO_2	nitrogen dioxide
LOS	length of stay
$PM_{2.5}$	particulate matter of diameter ≤2.5 μm

PM_{10}	particulate matter <10 μm in diameter
SO_2	sulfur dioxide
USEPA	US Environmental Protection Agency

REFERENCES

1. McCormick MC. The contribution of low birth weight to infant mortality and childhood morbidity. N Engl J Med. 1985; 312:82–90. [PubMed: 3880598]
2. Frankel S, Elwood P, Sweetnam P, Yarnell J, Smith GD. Birthweight, body-mass index in middle age, and incident coronary heart disease. Lancet. 1996; 348:1478–1480. [PubMed: 8942776]
3. Vos L, Oren A, Bots M, Gorissen W, Grobbee D, Uiterwaal C. Birth Size and Coronary Heart Disease Risk Score in young adulthood. The Atherosclerosis Risk in Young Adults (ARYA) Study. Eur J Epidemiol. 2006; 21:33–38. [PubMed: 16450204]
4. Hack M, Flannery DJ, Schluchter M, Cartar L, Borawski E, Klein N. Outcomes in young adulthood for very-low-birth-weight infants. N Engl J Med. 2002; 346:149–157. [PubMed: 11796848]
5. Hack M, Klein NK, Taylor HG. Long-term developmental outcomes of low birth weight infants. Future Child. 1995; 5:176–196. [PubMed: 7543353]
6. Martin JA, Hamilton BE, Ventura SJ, Osterman MJ, Kirmeyer S, Mathews TJ, et al. Births: final data for 2009. Natl Vital Stat Rep. 2011; 60:1–70. [PubMed: 22670489]
7. Ritz B, Yu F, Chapa G, Fruin S. Effect of air pollution on preterm birth among children born in Southern California between 1989 and 1993. Epidemiology. 2000; 11:502–511. [PubMed: 10955401]
8. Sagiv SK, Mendola P, Loomis D, Herring AH, Neas LM, Savitz DA, et al. A time series analysis of air pollution and preterm birth in Pennsylvania, 1997–2001. Environ Health Perspect. 2005; 113:602–606. [PubMed: 15866770]
9. Xu X, Ding H, Wang X. Acute effects of total suspended particles and sulfur dioxides on preterm delivery: a community-based cohort study. Arch Environ Health. 1995; 50:407–415. [PubMed: 8572718]
10. Huynh M, Woodruff TJ, Parker JD, Schoendorf KC. Relationships between air pollution and preterm birth in California. Paediatr Perinat Epidemiol. 2006; 20:454–461. [PubMed: 17052280]
11. Wu J, Ren C, Delfino RJ, Chung J, Wilhelm M, Ritz B. Association between local traffic-generated air pollution and preterm delivery in the south coast air basin of California. Environ Health Perspect. 2009; 117:1773–1779. [PubMed: 20049131]
12. de Bernabé V. Risk factors for low birth weight: a review. Eur J Obstet Gynecol Reprod Biol. 2004; 116:3–15. [PubMed: 15294360]
13. Parker JD, Rich DQ, Glinianaia SV, Leem JH, Wartenberg D, Bell ML, et al. The International Collaboration on air pollution and pregnancy outcomes: initial results. Environ Health Perspect. 2011; 119:1023–1028. [PubMed: 21306972]
14. Woodruff TJ, Parker JD, Darrow LA, Slama R, Bell ML, Choi H, et al. Methodological issues in studies of air pollution and reproductive health. Environ Res. 2009; 109:311–320. [PubMed: 19215915]
15. Slama R, Darrow L, Parker J, Woodruff TJ, Strickland M, Nieuwenhuijsen M, et al. Meeting Report: atmospheric pollution and human reproduction. Environ Health Perspect. 2008; 116:791–798. [PubMed: 18560536]
16. Sram RJ, Binkova B, Dejmek J, Bobak M. Ambient air pollution and pregnancy outcomes: a review of the literature. Environ Health Perspect. 2005; 113:375–382. [PubMed: 15811825]
17. Maisonet M, Correa A, Misra D, Jaakkola JJK. A review of the literature on the effects of ambient air pollution on fetal growth. Environ Res. 2004; 95:106–115. [PubMed: 15068936]
18. Glinianaia SV, Rankin J, Bell R, Pless-Mulloli T, Howel D. Particulate air pollution and fetal health: a systematic review of the epidemiologic evidence. Epidemiology. 2004; 15:36–45. [PubMed: 14712145]

19. Bell ML, Ebisu K, Peng RD, Walker J, Samet JM, Zeger SL, et al. Seasonal and regional short-term effects of fine particles on hospital admissions in 202 US counties, 1999–2005. Am J Epidemiol. 2008; 168:1301–1310. [PubMed: 18854492]
20. Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, et al. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA. 2006; 295:1127–1134. [PubMed: 16522832]
21. Woodruff TJ, Grillo J, Schoendorf KC. The relationship between selected causes of postneonatal infant mortality and particulate air pollution in the United States. Environ Health Perspect. 1997; 105:608. [PubMed: 9288495]
22. Woodruff TJ, Parker JD, Kyle AD, Schoendorf KC. Disparities in exposure to air pollution during pregnancy. Environ Health Perspect. 2003; 111:942. [PubMed: 12782496]
23. Steiner C, Elixhauser A, Schnaier J. The healthcare cost and utilization project: an overview. Eff Clin Pract. 2002; 5:143. [PubMed: 12088294]
24. Beeby PJ. How well do diagnosis-related groups perform in the case of extremely low birthweight neonates? J Paediatr Child Health. 2003; 39:602–605. [PubMed: 14629526]
25. Krawczyk-Wyrwicka I, Piotrowski A, Rydlewska-Liszkowska I, Hanke W. Calculating costs of premature infants' intensive care in the United States of America, Canada and Australia. Przegla § d epidemiologiczny. 2005; 59:781.
26. Ford J, Roberts C, Algert C, Bowen J, Bajuk B, Henderson-Smart D. Using hospital discharge data for determining neonatal morbidity and mortality: a validation study. BMC Health Serv Res. 2007; 7:188. [PubMed: 18021458]
27. Gold, MR.; Siegel, JE.; Russel, LB.; Weinstein, MC. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press; 1996.
28. [Accessed March 1, 2008] Agency for Healthcare Quality and Research. 2006. Available at http://www.hcup-us.ahrq.gov/db/state/costtocharge.jsp#user
29. Roy A, Sheffield P, Wong K, Trasande L. Incremental costs and charges for childhood asthma hospitalizations associated with outdoor air pollutants. Med Care. 2011; 49:810–817. [PubMed: 21430578]
30. Sheffield P, Roy A, Wong K, Trasande L. Fine particulate matter pollution linked to respiratory illness in infants and increased hospital costs. Health Aff. 2011; 30:871–878.
31. Bonferroni, CE. Il calcolo delle assicurazioni su gruppi di teste. In: Carboni, SO., editor. Studi in Onore del Professore Salvatore Ortu Carboni. Rome. Italy: 1935. p. 13-60.
32. Duan N. Smearing estimate: a nonparametric retransformation method. J Am Stat Assoc. 1983; 78:605–610.
33. Maternal Child Health Bureau. [Accessed 19 June 2012] Child Health USA 2008–2009. 2009. Available at http://mchb.hrsa.gov/chusa08/pdfs/c08cd.pdf
34. Liu S, Krewski D, Shi Y, Chen Y, Burnett RT. Association between gaseous ambient air pollutants and adverse pregnancy outcomes in Vancouver, Canada. Environ Health Perspect. 2003; 111:1773. [PubMed: 14594630]
35. Bobak M. Outdoor air pollution, low birth weight, and prematurity. Environ Health Perspect. 2000; 108:173. [PubMed: 10656859]
36. Maisonet M, Bush TJ, Correa A, Jaakkola JJ. Relation between ambient air pollution and low birth weight in the Northeastern United States. Environ Health Perspect. 2001; 109(Suppl 3):351. [PubMed: 11427384]
37. Salam MT, Millstein J, Li YF, Lurmann FW, Margolis HG, Gilliland FD. Birth outcomes and prenatal exposure to ozone, carbon monoxide, and particulate matter: results from the Children's Health Study. Environ Health Perspect. 2005; 113:1638. [PubMed: 16263524]
38. Bell ML, Ebisu K, Belanger K. Ambient air pollution and low birth weight in Connecticut and Massachusetts. Environ Health Perspect. 2007; 115:1118. [PubMed: 17637932]
39. Liu S, Krewski D, Shi Y, Chen Y, Burnett RT. Association between maternal exposure to ambient air pollutants during pregnancy and fetal growth restriction. J Expo Sci Environ Epidemiol. 2006; 17:426–432. [PubMed: 16736056]
40. U.S. Environmental Protection Agency. Available at http://www.epa.gov/ttnamti1/files/ambient/pm25/spec/spec997.pdf1997.

41. Thurston GD, Spengler JD. A quantitative assessment of source contribution to inhalable particulate matter in metropolitan Boston, MA. Atmos Environ. 1985; 19:9–25.
42. Thurston GD, Ito K, Mar T, Christensen WF, Eatough DJ, Henry RC, et al. Workgroup report: workshop on source apportionment of particulate matter health effects--intercomparison of results and implications. Environ Health Perspect. 2005; 113:1768–1774. [PubMed: 16330361]
43. Fuller, WA. Measurement error models. New York: Wiley; 1987.
44. Nelson DE, Holtzman D, Bolen J, Stanwyck CA, Mack KA. Reliability and validity of measures from the Behavioral Risk Factor Surveillance System (BRFSS). Sozial- und Praventivmedizin. 2001; 46(Suppl 1):S3–S42. [PubMed: 11851091]
45. Rubin, DB. Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons, Inc.; 1987.
46. Wright RJ, Cohen S, Carey V, Weiss ST, Gold DR. Parental stress as a predictor of wheezing in infancy: a Prospective Birth-Cohort Study. Am J Respir Crit Care Med. 2002; 165:358–365. [PubMed: 11818321]
47. Wright RJ, Cohen RT, Cohen S. The impact of stress on the development and expression of atopy. Curr Opin Allergy Clin Immunol. 2005; 5:23–29. [PubMed: 15643340]
48. Wright RJ. Stress and atopic disorders. J Allergy Clin Immunol. 2005; 116:1301–1306. [PubMed: 16337463]
49. Zhu M, Fitzgerald EF, Gelberg KH, Lin S, Druschel CM. Maternal low-level lead exposure and fetal growth. Environ Health Perspect. 2010; 118:1471–1475. [PubMed: 20562053]
50. Fei C, McLaughlin JK, Tarone RE, Olsen J. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. Environ Health Perspect. 2007; 115:1677–1682. [PubMed: 18008003]
51. Sathyanarayana S, Focareta J, Dailey T, Buchanan S. Environmental exposures: how to counsel preconception and prenatal patients in the clinical setting. Am J Obstet Gynecol. 2012; 207:463–470. [PubMed: 22440197]
52. Bernard SM, Samet JM, Grambsch A, Ebi KL, Romieu I. The potential impacts of climate variability and change on air pollution-related health effects in the United States. Environ Health Perspect. 2001; 109(Suppl 2):199–209. [PubMed: 11359687]
53. USEPA. [Accessed 18 September 2009] National Ambient Air Quality Standards (NAAQS). 2009. http://www. epa.gov/air/criteria.html
54. Jerrett M, Burnett RT, Ma R, Pope CA 3rd, Krewski D, Newbold KB, et al. Spatial analysis of air pollution and mortality in Los Angeles. Epidemiology. 2005; 16:727–736. [PubMed: 16222161]
55. Ross Z, Jerrett M, Ito K, Tempalski B, Thurston GD. A land use regression for predicting fine particulate matter concentrations in the New York City region. Atmos Environ. 2007; 41:2255–2269.

Table 1

Kids Inpatient Database study sample description.

All births in 2000, 2003, and 2006	*Median (IQR)*	*Unweighted* N (%)
Birth weight (IQR), g	3324 (2976, 3656)	660,826
Low birth weight (*n* = 1,138,222)		431,725 (37.9%)
Preterm (*n* = 951,800)		218,500 (22.9%)
Total charges, 2005$	1603 (1058, 2647)	2,674,941
Total costs, 2005$	793 (527, 1283)	2,674,941
Length of stay, days	1.60 (1.11, 2.27)	2,543,584
Mean $PM_{2.5}$, month of birth ($\mu g/m^3$)	12.17 (9.29, 15.20)	319,506
Mean PM_{10}, month of birth ($\mu g/m^3$)	25.10 (19.43, 32.33)	278,428
Mean O_3, month of birth (p.p.m.)	0.026 (0.017, 0.033)	272,282
Mean SO_2, month of birth (p.p.m.)	0.0031 (0.0017, 0.0048)	213,981
Mean NO_2, month of birth (p.p.b.)	0.017 (0.013, 0.024)	244,545
Mean CO, month of birth (p.p.m.)	0.58 (0.43, 0.77)	269,683
All births with available $PM_{2.5}$, NO_2, and CO data	*Median (IQR)*	*Unweighted* N (%)
Birth weight (IQR), g	3334 (2974, 3669)	68,953
Low birth weight		39,207 (37.0%)
Preterm (*n* = 75,878)		15,567 (26.9%)
Total charges, 2005 $	1855 (1203, 3271)	222,359
Total costs, 2005 $	996 (649, 1674)	222,359
Length of stay, days	1.64 (1.13, 2.45)	222,354
Mean $PM_{2.5}$, month of birth ($\mu g/m^3$)	12.63 (9.88, 15.91)	222,359
Mean PM_{10}, month of birth ($\mu g/m^3$)	26.31 (20.72, 34.00)	205,142
Mean O_3, month of birth (p.p.m.)	0.025 (0.017, 0.032)	198,990
Mean SO_2, month of birth (p.p.m.)	0.0032 (0.0017, 0.0051)	174,977
Mean NO_2, month of birth (p.p.b.)	0.018 (0.013, 0.025)	222,359
Mean CO, month of birth (p.p.m.)	0.58 (0.45, 0.78)	222,359

Table 2

Results of single-pollutant models of outdoor air pollutants with birth outcomes and neonatal health care utilization in 2000, 2003, and 2006 Kids Inpatient Database.

Exposure	*Outcome*	*OR/increment (95% CI)*
Mean $PM_{2.5}$, month of birth ($\mu g/m^3$)	Preterm birth	0.97 (0.96, 0.98)***
	Low birth weight	1.10 (1.06, 1.14)***
Mean NO_2, month of birth (p.p.b.)	Preterm birth	1.02 (1.01, 1.04)**
Mean PM_{10}, month of birth ($\mu g/m^3$)	Birth weight	+1.86 (+0.22, +3.50)*
Mean $PM_{2.5}$, month of birth ($\mu g/m^3$)	Very low birth weight	1.08 (1.05, 1.11)***
	Term-low birth weight	1.12 (1.08, 1.16)***
	Preterm-low birth weight	1.09 (1.04, 1.14)**
Mean NO_2, month of birth (p.p.b.)	Preterm-low birth weight	1.26 (1.06, 1.50)**
Mean PM_{10}, month of birth ($\mu g/m^3$)	Preterm-low birth weight	1.02 (1.006, 1.04)**
Mean CO, month of birth (p.p.m.)	Very low birth weight	1.35 (1.09, 1.65)**
	Term-low birth weight	2.07 (1.19, 3.59)**
	Preterm-low birth weight	1.48 (1.03, 2.14)*
Mean O_3, month of birth (p.p.m.)	Very low birth weight	2.60 (1.40, 4.82)**
Exposure	*Outcome*	*Increment (95% CI)*
Mean PM_{10}, month of birth ($\mu g/m^3$)	Length of stay	−0.008 (−0.01, −0.002)*
Mean NO_2, month of birth (p.p.b.)	Charges	+$310 (+$101, +526)**
	Length of stay	−0.04 (−0.07, −0.01)*
Mean CO, month of birth (p.p.m.)	Charges	+$2948 (+$1794, +$4179)***
	Length of stay	+0.18 (+0.06, +0.30)**
	Costs	+$1350 (+$616, +$2134)***
Mean O_3, month of birth (p.p.m.)	Charges	+$3632 (+$2080, +$5315)***

* $P < 0.05$,

** $P < 0.01$,

*** $P < 0.0001$.

All models control for race, primary expected payer, median income quartile for patient zip code, hospital region, admission month, teaching hospital status, and gender.

Table 3

Pearson correlation coefficients for outdoor air pollutants.

All births with available $PM_{2.5}$, NO_2, and CO data	**$PM_{2.5}$**	**PM_{10}**	**O_3**	**SO_2**	**NO_2**
$PM_{2.5}$					
PM_{10}	0.395				
O_3	−0.071	0.041			
SO_2	0.031	−0.157	−0.296		
NO_2	−0.090	−0.011	−0.023	−0.101	
CO	0.171	0.066	−0.297	0.035	0.123

Table 4

Three-pollutant models of outdoor air pollutants with birth outcomes in 2000, 2003, and 2006 Kids Inpatient Database.

	Increment in birth weight, grams (n=62,906)	*OR, low birth weight (n=82,379)*	*OR, very low birth weight (n=82,379)*
Mean $PM_{2.5}$, month of birth ($\mu g/m^3$)	+0.31 (−4.63, +4.01)	1.09 (1.05, 1.14)***	1.07 (1.04, 1.10)***
Mean NO_2, month of birth (p.p.b.)	−1.24 (−18.90, +16.42)	1.01 (0.86, 1.18)	1.01 (0.89, 1.16)
Mean CO, month of birth (p.p.m.)	+41.44 (−47.47, 130.35)	1.20 (0.81, 1.78)	1.19 (0.90, 1.56)
	OR, preterm birth (n=179,928)	*OR, preterm-low birth weight (n=67,545)*	*OR, term-low birth weight (n=67,545)*
Mean $PM_{2.5}$, month of birth ($\mu g/m^3$)	0.97 (0.96, 0.98)***	1.09 (1.04, 1.15)***	1.12 (1.07, 1.16)**
Mean NO_2, month of birth (p.p.b.)	1.03 (1.02, 1.05)***	1.06 (0.90, 1.24)	0.88 (0.62, 1.26)
Mean CO, month of birth (p.p.m.)	1.10 (0.99, 1.22)	1.32 (0.84, 2.07)	1.07 (0.56, 2.02)

Insignificant after Bonferroni[31] correction ($0.05>P>0.0167$);

* $P<0.0167$,

** $P<0.001$,

*** $P<0.0001$.

All models control for race, primary expected payer, median income quartile for patient zip code, hospital region, admission month, teaching hospital status, and gender.

Table 5

Four-pollutant models of outdoor air pollutants with neonatal health care utilization in 2000, 2003, and 2006 Kids Inpatient Database.

	Increment in LOS, days (n = 1,672,700)	Increment in total charges, 2005$ (n = 1,607,113)	Increment in total costs 2005$ (n = 596,591)
Mean $PM_{2.5}$, month of birth ($\mu g/m^3$)	+0.0001 (−0.02, +0.02)	−$115 (−$237, +$4)	+$77 (−$41, +$195)
Mean NO_2, month of birth (p.p.b.)	−0.05 (−0.08, −0.01)*	+$462 (+$219, +$704)**	−$111 (−$295, +$75)
Mean CO, month of birth (p.p.m.)	+0.13 (+0.004, +0.25)[a]	+$3677(+$2420, +$4983)***	+$1166 (+$542, +$1830)**
Mean O_3, month of birth (p.p.m.)	−0.06 (−0.26, +0.15)	+$4877(+$3422, +$6428)***	+$964 (+$21, +$2001)[a]

All models control for race, primary expected payer, median income quartile for patient zip code, hospital region, admission month, teaching hospital status, and gender. Missing category were added to model due to univariate significant associations but were insignificant at $P > 0.2$ in all models.

[a] Insignificant after Bonferroni correction ($0.05 > P > 0.0167$);

* $P < 0.0167$,

** $P < 0.001$,

*** $P < 0.0001$.