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Comparing exposure assessment methods for traffic-related air pollution in an adverse pregnancy outcome study

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Abstract

Background—Previous studies reported adverse impacts of traffic-related air pollution exposure on pregnancy outcomes. Yet, little information exists on how effect estimates are impacted by the different exposure assessment methods employed in these studies.

Objectives—To compare effect estimates for traffic-related air pollution exposure and preeclampsia, preterm birth (gestational age less than 37 weeks), and very preterm birth (gestational age less than 30 weeks) based on four commonly-used exposure assessment methods.

Methods—We identified 81,186 singleton births during 1997–2006 at four hospitals in Los Angeles and Orange Counties, California. Exposures were assigned to individual subjects based on residential address at delivery using the nearest ambient monitoring station data [carbon monoxide (CO), nitrogen dioxide (NO_2), nitric oxide (NO), nitrogen oxides (NO_x), ozone (O_3), and particulate matter less than 2.5 ($PM_{2.5}$) or less than 10 (PM_{10}) μm in aerodynamic diameter], both unadjusted and temporally-adjusted land-use regression (LUR) model estimates (NO, NO_2, and NO_x), CALINE4 line-source air dispersion model estimates (NO_x and $PM_{2.5}$), and a simple traffic-density measure. We employed unconditional logistic regression to analyze preeclampsia in our birth cohort, while for gestational age-matched risk sets with preterm and very preterm birth we employed conditional logistic regression.

Results—We observed elevated risks for preeclampsia, preterm birth, and very preterm birth from maternal exposures to traffic air pollutants measured at ambient stations (CO, NO, NO_2, and NO_x) and modeled through CALINE4 (NO_x and $PM_{2.5}$) and LUR (NO_2 and NO_x). Increased risk of preterm birth and very preterm birth were also positively associated with PM_{10} and $PM_{2.5}$ air pollution measured at ambient stations. For LUR-modeled NO_2 and NO_x exposures, elevated risks for all the outcomes were observed in Los Angeles only – the region for which the LUR models were initially developed. Unadjusted LUR models often produced odds ratios somewhat larger in size than temporally-adjusted models. The size of effect estimates was smaller for exposures based on simpler traffic density measures than the other exposure assessment methods.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

Conclusion—We generally confirmed that traffic-related air pollution was associated with adverse reproductive outcomes regardless of the exposure assessment method employed, yet the size of the estimated effect depended on how both temporal and spatial variations were incorporated into exposure assessment. The LUR model was not transferable even between two contiguous areas within the same large metropolitan area in Southern California.

Keywords

Air monitoring; CALINE4; land-use regression; preeclampsia; preterm birth

INTRODUCTION

Adverse pregnancy outcomes are an emotional and financial burden on families both in the short and long term, and are a major public health concern (Stillerman et al. 2008). More than half a million infants are born prematurely each year in the United States (CDC 2005). Preterm birth is a primary cause of infant mortality and morbidity and is potentially associated with learning disabilities and other chronic conditions in adulthood (Cano et al. 2001; Dik et al. 2004; Stillerman et al. 2008). Preeclampsia, characterized by elevated blood pressure, edema, and protein in the urine, is a multisystem disorder affecting 2–8% of pregnant women. Since the only cure is delivery of the fetus and placenta, preeclampsia is the most frequent primary reason for elective, non-spontaneous preterm birth, accounting for 30–35% of total preterm deliveries (Goldenberg et al. 2008; Meis et al. 1998).

Numerous epidemiologic studies have documented adverse effects of air pollution on pregnancy outcomes (Lacasana et al. 2005; Sram et al. 2005; Stillerman et al. 2008; Woodruff et al. 2009). Motor vehicle emissions are the principal source of ambient air pollution in most urban areas and are a significant contributor to the adverse effects of air pollution on health (Samet 2007). Traffic emits a complex mixture of hundreds of toxic components including ultrafine particles and polycyclic aromatic hydrocarbons that have the potential to induce oxidative stress and other mechanisms leading to adverse impacts on the pregnancy and fetal development. Our prior studies in Southern California have linked traffic-related air pollution with preeclampsia (Wu et al. 2009a) and preterm birth (Ritz et al. 2000; Ritz et al. 2007; Wilhelm and Ritz 2005; Wu et al. 2009a).

In the current literature there are four major approaches to measure pregnant women's exposures to traffic-related air pollutants. The most widely used method relies on measurements from existing ambient monitoring stations, and some studies restrict the study population to those living within a specified distance to a monitoring station (Darrow et al. 2009; Ritz et al. 2000; Wilhelm and Ritz 2005). In general, measurements of concentrations of pollutants at air monitoring stations have the highest temporal resolution, especially for certain gaseous pollutants such as carbon monoxide (CO) and nitrogen oxides (NO_x) that are usually measured on a continuous, hourly basis. However, due to the high cost of establishing and operating monitoring stations, the routine monitoring network for criteria pollutants is generally poor in spatial coverage and unlikely to adequately capture the high spatial heterogeneity of air pollutants directly emitted from traffic such as ultrafine particles (Hitchins et al. 2000; Zhu et al. 2002). In addition, CO may no longer be a good marker for traffic in Southern California because levels of this pollutant continue to decline, due to gasoline reformulation, and are reaching the minimum detection threshold of the routine monitoring system (Kirchstetter et al. 1999; South Coast Air Management District 2007).

Recently, geographic information system (GIS)-based methods have been developed to better estimate exposures to traffic-specific pollutants. Some research has employed GIS tools to account for the high spatial heterogeneity of local traffic emissions with simple

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exposure surrogates such as distance-weighted traffic density (Wilhelm and Ritz 2003). Other studies have either spatially-interpolated measured concentrations from a small number of ambient monitoring stations (Leem et al. 2006) or developed more sophisticated land-use regression (LUR) models using data on pollutants collected in short-term intensive monitoring campaigns and supplemental GIS information for pollution sources and meteorology (Aguilera et al. 2009; Ballester et al. 2010; Brauer et al. 2008; Hoek et al. 2008; Slama et al. 2007). The GIS-based methods provide high spatial resolution in estimated concentrations, but have no or limited capabilities in characterizing temporal variability. For instance, most existing LUR models were developed using one to four 7- or 14-day measurement periods to characterize temporal variation in pollution over a year; temporal trends derived from measures taken at ambient monitoring stations were then applied to the modeled values based on the assumption that ambient monitoring site measures and LUR-modeled concentrations co-vary over space.

Another approach is to assign exposure based on air dispersion models that take into account the spatial relationship of sources and receptors, source emission strength, and meteorology parameters that influence dispersion (e.g. atmospheric stability and wind) (Wu et al. 2009a). These models output concentrations at high spatial but only moderate temporal variability because of a general lack of real-time inputs (e.g. hourly traffic counts), and a simplified treatment of meteorology, atmospheric chemistry, transport, and diffusion. More sophisticated air pollution models account for not only dispersion but also atmospheric chemistry and physical dynamics (Vutukuru et al. 2006; Zhang et al. 2006); however, these models are usually developed to simulate air quality at a relatively coarse spatial resolution (e.g. 5 km * 5 km) and are computer-intensive, making them unsuitable for health studies that require both high spatial and temporal resolution. A combination of the above approaches has also been used in exposure assessment, such as integrating dispersion modeling results into LUR (Wilton et al. 2008) or developing two-stage geostatistical models that incorporate measured concentrations and information on temporally or spatially varying covariates (Fanshawe et al. 2008).

Reliable estimation of exposure to traffic-related air pollution is a complex and challenging issue, and different exposure assessment methods may account for differences in published findings (Woodruff et al. 2009). To date, only one Canadian study examined the implications of three different exposure assessment methods on the size of effect estimates for adverse birth outcomes and traffic-related air pollution exposure (Brauer et al. 2008). Compared to exposures derived from ambient monitoring stations, temporally-adjusted LUR exposures were associated with somewhat more precise effect estimates [i.e., smaller confidence intervals (CIs)], but not necessarily larger effect estimates (Brauer et al. 2008).

In our study, we employed four commonly-used exposure assessment methods: ambient monitor-based measurements, land-use regression modeling, CALINE4 line-source dispersion modeling, and traffic-density estimates to further examine whether traffic can be considered an important source of air pollution contributing to adverse pregnancy outcomes and to assess the impact of different exposure assessment methods on the size of effect estimates.

METHODS

Study Subjects

The study subjects resided in southern Los Angeles County and Orange County in the South Coast Air Basin of California. This area is heavily impacted by several major commuter freeways (e.g. I-405 and I-5) and main trucking routes (e.g. Interstate 710) for goods leading out of the Ports of Los Angeles and Long Beach. The study subjects were identified from a hospital-based birth database that included residential address at delivery, birth hospital, estimated date of conception (based on last menstrual period and ultrasound dating), prenatal care insurance, maternal age and race-ethnicity, maternal medical history (heart disease, chronic hypertension, previous preterm birth), preeclampsia and other maternal complications during pregnancy (diabetes, pyelonephritis), parity (first birth vs. second or subsequent birth), gestational age, and the neonate's sex (Wu et al. 2009a). Diagnosis dates for the onset of preeclampsia were not available. Out of 105,092 neonatal records from the birth database, we obtained 81,186 singleton birth records after excluding multiple gestations, incomplete records including those without full residential address or missing covariate information, unsuccessfully geocoded residential addresses, and addresses outside the study region (Wu et al. 2009a).

Study Design

We defined preeclampsia as the occurrence of preeclampsia (blood pressure > 140/90 and proteinuria) or hemolysis, elevated liver enzyme levels, and low platelet count (HELLP) syndrome at any time during pregnancy. As HELLP is on the continuum of preeclampsia severity and is relatively uncommon, we chose to combine this diagnosis with preeclampsia. Preterm birth was defined as births at less than 37 completed gestational weeks, and very preterm birth as births at less than 30 gestational weeks.

We examined associations between ambient air pollution and preeclampsia in our birth cohort using unconditional logistic regression. For preterm birth, we employed a risk set design, which allowed us to estimate effects for gestational age-matched exposure windows. For each preterm case, we randomly selected five controls from among those who were born one year before or after the birth date of the case and who were still *in utero* at the gestational age when the case was delivered. Exposure periods for preterm cases and controls were based on the gestational age of the case infant at birth. For example, for a preterm birth occurring at 34 weeks gestation, controls were selected randomly from all infants still *in utero* at age 34 weeks. Thus the "one month before birth" exposure period covered the same developmental period for cases and controls (weeks 30 to 34 of gestation). This matching approach provided a similar length of exposure for both cases and controls while retaining both temporal and spatial variability in air pollution exposures.

We geocoded residential addresses with exact matches to house number using the TeleAtlas Geocoding Service (http://www.geocode.com). All exposure measures were based on estimated outdoor air pollution concentrations at individual residential locations, without considering time-activity patterns and potential exposures in other microenvironments. Time-resolved exposures were estimated for the 1st trimester (1–13 gestational weeks), 2nd trimester (14–26 gestational weeks), last month before delivery, and for the entire pregnancy period. Exposure periods for preterm cases and controls were based on the gestational age of the case infant at birth.

Air Pollution Exposure Assessment

Ambient monitoring data—We obtained from the California Air Resources Board (http://www.arb.ca.gov/aqd/aqdpage.htm) measurements of concentrations of CO, NO_x, nitric oxide (NO), nitrogen dioxide (NO_2), ozone (O_3), particulate matter (PM) less than 10 μm in aerodynamic diameter (PM_{10}) and less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) from 1997 to 2006 ($PM_{2.5}$ data started in 1998). Hourly measurements of CO, NO, NO_2, and NO_x, and O_3 (10 AM-6 PM) were converted to daily means using a criterion of 75% data completeness (i.e. > 18 hours of valid data in a day was required for a daily average to be generated). Monthly averages for gaseous pollutants were calculated for stations with >22 days of valid data in a month. Since real-time PM measurements accounted for less than 6%

of the total data, we only included filter-based PM measurements that were collected every 3rd or 6th day. Monthly averages for PM_{10} and $PM_{2.5}$ were calculated if three or more daily measures per month were available. Final exposures were calculated for each individual subject by weighting monthly average concentrations by the number of days in each month for specific exposure periods (1st trimester, 2nd trimester, last month before delivery, and entire pregnancy period). The number of active monitoring stations varied by pollutant and by year. There were 14–19 stations with valid measurement data for CO, 17–21 stations for $NO/NO_2/NO_x$ and O_3, and 10–11 stations for PM_{10} during 1997 to 2006 in the study area. $PM_{2.5}$ sites started at only 2 in September, 1998 and increased to 10 in February 1999; thus we only included subjects who delivered in 2000 and after in the $PM_{2.5}$ analyses.

Exposure measures were derived using the nearest station approach, i.e. we assigned to each residential location daily concentrations for each specific pollutant measured at the closest operational monitoring station. The median distance from the residence to the nearest monitoring station was 6.1 km for CO and O_3, 7.1 km for $NO/NO_2/NO_x$, 7.0 km for PM_{10}, and 6.5 km for $PM_{2.5}$, and the 95th percentile of the distance was 14.0 km for CO and O_3, 27.8 km for $NO/NO_2/NO_x$, 17.6 km for PM_{10}, and 18.2 km for $PM_{2.5}$, respectively (Supplemental Materials Table S1). Subjects in Los Angeles resided closer to monitoring stations because of a higher density of monitors in Los Angeles than in Orange County (Supplemental Materials Table S1).

Land use regression models—LUR models were developed for NO, NO_2, and NO_x based on simultaneous two-week measurements using Ogawa passive diffusion samplers at 181 sites in Los Angeles during September 2006 and February 2007 in a separate study (Su et al. 2009). The LUR model included the following variables: traffic volumes, truck routes and road network, land use data, coordinates of the sampling sites, and satellite-derived soil brightness. The final regression models explained 81%, 86% and 85% of the variance in measured NO, NO_2 and NO_x concentrations, respectively.

NO_x measurement data from the two seasons were averaged to derive an annual average pollution surface for the Los Angeles Basin, which was then used to assign exposures to all subjects, without considering year-to-year and seasonal differences in the spatial surface (unadjusted LUR). We also derived temporally-adjusted LUR estimates based on the relative temporal profiles of yearly and monthly concentrations of pollutants measured at government-operated monitoring stations. Yearly and monthly scaling factors at the nearest monitoring station were assigned to each residence and the distances between the residences and the closest stations were recorded. Temporally-adjusted monthly LUR concentrations at each residence were calculated by multiplying the unadjusted LUR estimates by the yearly and monthly scaling factors, and then averaging over specific pregnancy periods. Since the LUR models were originally developed and validated based on measurements in Los Angeles but not Orange County, we estimated effects separately for the two regions.

Traffic density—A comprehensive database with annual average daily traffic counts was constructed for the study region based on data from the California Department of Transportation and other sources (Wu et al. 2009b). Traffic count data were available for all freeways and highways, most major arterial streets, and a small portion of local streets. Previous measurement studies indicate ultrafine particles and CO drop to near-background levels at 200 m during daytime hours (10 AM – 6 PM) (Zhu et al. 2002) and up to 2000 m during pre-sunrise hours (4:00 – 7:30 AM) (Hu et al. 2009) downwind from major roadways. A recent summary of 41 roadside monitoring studies conducted worldwide concluded that most traffic-related pollutants (e.g. ultrafine particles, CO, NO_x, and elemental carbon) decay to background concentrations at 570 m from the edge of the road (Karner et al. 2010). While the area of traffic influence varies according to a number of factors, we decided to calculate traffic densities within a 300 m buffer, as this is the size commonly employed in previous studies of traffic-related air pollution (Chang et al. 2009; Kan et al. 2008). Traffic densities were calculated on a 10×10 m grid using the kernel density plotting feature of Spatial Analyst in ArcInfo GIS 9.1 (ESRI, Redlands, CA), which effectively caused the densities to decrease from volume-dependent values at roadway edges to zero at 300 m perpendicular distance from roadways.

Air dispersion model—A modified CALINE4 dispersion model was used to model local traffic emissions within 3 km of each residence for five traffic-related pollutants (CO, NO_2, NO_x, PM_{10}, and $PM_{2.5}$) (Benson 1989; Wu et al. 2005; Wu et al. 2009a; Wu et al. 2009b). Vehicle emission factors were obtained from the California Air Resources Board's EMFAC2007 model (http://www.arb.ca.gov/msei/onroad/latest_version.htm). Paved road-dust emissions for $PM_{2.5}$ were based on in-roadway measurements (Fitz and Bufalino 2002). Hourly wind speed, direction, and temperature were obtained from the National Weather Service. Average mixing heights by season and hour were obtained from the 1997 Southern California Ozone Study (Croes and Fujita 2003) and assigned to each modeled day based on season and hour. More details about the CALINE4 model and the evaluation of the model can be found in Wu et al. (2009a).

Statistical Analysis

The statistical package R (version 2.6.1; The R Foundation for Statistical Computing 2008) was used for analyses. For preeclampsia, we performed multiple logistic regression and excluded women who had preexisting chronic conditions such as hypertension and heart disease prior to pregnancy. Conditional logistic regression was used for the preterm outcomes to account for our risk set approach, which matched on gestational age. Confounders for both logistic regression models were selected based on *a priori* knowledge and included maternal age, maternal race/ethnicity, parity, prenatal care insurance type (private, non-private: government-sponsored or self pay, and unknown), season of conception, pyelonephritis (preterm analyses only), diabetes (preeclampsia analyses only), and poverty (the percent of the population living below the poverty level from U.S. Census 2000 block group data). We adjusted for maternal age as a continuous variable using a quadratic polynomial function. No interaction terms for confounding variables were included in the regression models. We separately calculated odds ratios (ORs) and 95% CIs for the inter-quartile range (IQR) increase and for a specified unit increase in each exposure metric (0.1 ppm for CO, 5 ppb for NO, NO_2, NO_x, and O_3, 5 $\mu g/m^3$ for PM_{10}, and 1 $\mu g/m^3$ for $PM_{2.5}$). The IQR-scaled ORs were used to compare effect estimates across different pollutants using the same exposure assessment method, while the ORs for a standardized increase in exposure were used to compare effect estimates across the four exposure assessment methods for a specific pollutant. We also examined the outcomes by exposure window (1^{st} trimester, 2^{nd} trimester, last month before delivery) for ambient monitor-based and CALINE4-modeled exposures. We additionally examined effect measure modification of air pollution and preeclampsia associations by socio-demographic variables (e.g. maternal age, infant sex, insurance type, parity, poverty, and race) using stratified analyses.

RESULTS

Preeclampsia, preterm birth (less than 37 weeks), and very preterm birth (less than 30 weeks) occurred in 3.0%, 8.3%, and 1.0% of the singleton births in our study population, respectively (Table 1). Compared to the entire study population, the prevalence of preeclampsia, preterm birth, and very preterm birth was in general greater for women younger than 20 years of age or older than 39 years of age at delivery, were primiparous, had government-sponsored or self-pay health insurance, were of African American race, or

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were living in areas of higher poverty. Women in Los Angeles accounted for 48% of the total study population, contributed disproportionately to the number of cases for preeclampsia (53.4%), preterm birth (58.5%), and very preterm birth (70.5%), were on average two years younger, were less likely to have private health insurance, were more often of African American race or Hispanic ethnicity, and resided in areas with higher poverty rates compared to women from Orange County.

Table 2 lists mean values and Pearson's correlation coefficients for exposure measures for the entire pregnancy based on the four methods of exposure assessment. For ambient monitoring data, concentrations of traffic-related gaseous air pollutants (CO, NO, NO_2, and NO_x) were highly correlated, but they were only moderately correlated with monitor-measured $PM_{2.5}$ and PM_{10}, and negatively correlated with O_3. LUR-modeled exposures for NO, NO_2 and NO_x were moderately to highly correlated with each other. The traffic density measure was moderately correlated with CALINE4-modeled exposures, less correlated with LUR measures, and poorly correlated with all ambient monitor-based measures. CALINE4-modeled exposures of CO, NO_2, NO_x, PM_{10}, and $PM_{2.5}$ were highly correlated (r ranged from 0.75 to 1.00; data not shown), most likely because CALINE4 was only used to estimate concentrations of pollutants from a single emission source – local traffic within 3 km of a residence – which is also why CALINE4-modeled concentrations were only about 13% and 11% of the ambient monitor-based NO_x and $PM_{2.5}$ levels, respectively. Therefore, we only report CALINE4-modeled NO_x and $PM_{2.5}$ exposures and corresponding effect estimates. Compared to women in Orange County, we found that, on average, all monitor-measured pollutants except O_3 were higher for women residing in Los Angeles (46%–73% higher for CO, NO, NO_2, and NO_x, 11–18% higher for PM_{10} and $PM_{2.5}$, but 35% lower for O_3) (Supplemental Materials Table S2).

Table 3 presents effect estimates for preeclampsia with inter-quartile range increases in exposures for the entire pregnancy by study region (the effect estimates per standard increase in exposures are listed in Supplemental Materials Table S3). We present our results by region for two reasons. First, our study populations in Los Angeles and Orange County were remarkably different in socio-demographic characteristics. In addition, our LUR models were originally developed based on measurements in Los Angeles County only. For subjects in Los Angeles, we observed increased risks of preeclampsia (2–16%) with each inter-quartile range increase in exposure to residential traffic density, ambient CO, NO, NO_2, NO_x, LUR-modeled NO, NO_2 and NO_x, and CALINE4-modeled NO_x and $PM_{2.5}$. In Orange County, no increased risk of preeclampsia was found for monitor measured pollutants except NO_x and O_3 or for temporally-adjusted LUR measures; estimated risks from unadjusted LUR models were much lower than for subjects residing in Los Angeles. On the other hand, effect estimates for CALINE4-modeled exposures and traffic density estimates were of similar size in both regions (3–10% increases in risk per inter-quartile range).

We estimated 3–14% risk increases for preterm birth and 26–76% risk increases for very preterm birth per inter-quartile increase in monitor-measured CO, NO, NO_2 and NO_x; effect estimates were similar in magnitude for subjects in LA and Orange County for both outcomes (Tables 4 and 5). Risks of preterm and very preterm birth increased by approximately 9% and 30%, respectively, with increases in ambient PM_{10} and $PM_{2.5}$ for subjects residing in Orange County, but we observed only small risk increases for particles in Los Angeles. For unadjusted LUR-modeled NO_2 and NO_x, inter-quartile range increases in exposure were associated with 5–7% and 27–42% increases in risk for preterm and very preterm birth, respectively, in Los Angeles, but no associations were apparent for preterm and very preterm births in Orange County. Additionally, effect estimates were greater for unadjusted versus temporally-adjusted LUR-modeled NO_2 and NO_x in Los Angeles. Inter-

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quartile range increases in entire pregnancy CALINE-model NO_x and $PM_{2.5}$ exposures were associated with 4% increases in risk of preterm birth in Los Angeles but not Orange County, and about 16% increases in risk of very preterm birth in both regions. Inter-quartile range increases in traffic density were associated with slightly increased risks of both preterm and very preterm birth (2–3%) in Los Angeles County but not Orange County.

We did not observe consistent differences in patterns of effect estimates for specific periods of pregnancy using either monitor-based exposure measures (Supplemental Materials Table S4) or CALINE4-modeled exposures (results not shown). In general, risk of preeclampsia, preterm birth, and very preterm birth increased with increasing quartiles of exposure (data not shown). No consistent patterns or differences in risk estimates were observed in analyses stratified by socio-demographic parameters such as maternal age, infant sex, insurance type, parity, poverty, and race (data not shown); some of these comparisons however were limited by the small number of cases, particularly for preeclampsia and very preterm birth.

DISCUSSION

In the past decade, interest in effects of air pollution on fetal and perinatal development has increased since the growing fetus may be particularly susceptible to the toxic effects of environmental contaminants (Maisonet et al. 2004; Mone et al. 2004; Pinkerton and Joad 2006). Traffic is an important source of ambient air pollution in urban areas. Here, we addressed how exposure assessment influences the size of estimated effects for adverse pregnancy outcomes when traffic-related air pollution is modeled by four commonly-used methods. Based on these four measures, results were consistent in suggesting that pregnant women who experience higher exposure to traffic-related pollutants were more likely to develop preeclampsia during pregnancy or to give birth to preterm and very preterm infants. For preeclampsia, gaseous air pollutants (CO, NO, NO_2 and NO_x) were most important, while for preterm birth both gases (CO, NO, NO_2 and NO_x) and particulate matter (PM_{10} and $PM_{2.5}$) pollution contributed to adverse effects. Importantly, the LUR model we developed based on monitoring in one region (Los Angeles) was not applicable to a neighboring region (Orange County) in the same metropolitan area. Finally, temporal adjustment of LUR pollution surfaces by scaling using data from ambient monitoring stations may not be an improvement over unadjusted (annual average) LUR data possibly because of the un-validated and potentially incorrect assumption that measures from ambient monitoring sites and LUR-modeled concentrations co-vary over space.

The exposure metrics we employed capture different aspects of traffic-related air pollution, such as emission sources (local vs. regional) and spatio-temporal variability, and may result in differences in measurement error and effect estimates (Brauer et al. 2008). Monitor-based measures provide the greatest temporal variability and reflect mostly regional emission sources, and to a lesser extent, local sources in areas with denser monitoring networks (e.g. Los Angeles). The CALINE4 model was developed to capture local traffic emissions and resulting estimates have limited temporal variability since some model inputs were not derived from real-time measurements but averages based on data for limited time periods (e.g. mixing height by season and time of day, traffic volume by day of week and time of day, and emission factor by season). Unadjusted LUR measures have no temporal variability and capture largely local traffic emissions, local land use characteristics, as well as regional traffic emissions up to 11 km (Su et al. 2009). Thus, even though monitor-based measures capture temporal variability best and CALINE4- and LUR-modeled exposures are more spatially defined (Brauer et al. 2008; Marshall et al. 2008), they are not mutually exclusive in terms of emission sources and spatio-temporal variability. This may explain why we found associations with all, even though the measures were only moderately to poorly correlated.

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For preeclampsia, we observed similar increases in magnitude of risk for women in Los Angeles for all measures of traffic-related pollution except monitor-based PM_{10} and $PM_{2.5}$, suggesting that both temporal and spatial variability may contribute to risk. In addition, local emissions better represented by CALINE4- and LUR-modeled exposures may contribute somewhat more strongly to the risk of preeclampsia than regional sources better captured by monitor-based $PM_{2.5}$ (Gomiscek et al. 2004; Russell et al. 2004). Both temporal and spatial variability in concentrations of pollutants seemed to also contribute to the risk of delivering a preterm and very preterm infant. Although the 95% CIs overlapped, risk estimates for very preterm births were higher for monitor-based and LUR-modeled (Los Angeles only) NO_x than for CALINE4-modeled NO_x, indicating the importance of a regional component of exposure, in addition to local traffic emissions. In Supplemental Materials Table S5 we present results from two-pollutant models for monitor-based and CALINE4-modeled exposures and monitor- and LUR-based exposure estimates. Results from the two-pollutant models suggest somewhat stronger contributions from local traffic for preeclampsia and from regional sources for preterm and very preterm births, but both spatial and temporal variations in concentrations of traffic-related pollutants seem to contribute to both outcomes.

Since preeclampsia is one of the major reasons for elective non-spontaneous preterm birth, there is overlap between this outcome and preterm delivery. Data were not available to separate the impacts of air pollution on spontaneous versus non-spontaneous preterm births. However, no appreciable differences in air pollution effect estimates for preterm birth were observed for women with and without a diagnosis of preeclampsia (data not shown).

We consistently estimated larger effects for preeclampsia, preterm birth and very preterm birth in Los Angeles than in Orange County for LUR-modeled exposures. Los Angeles and Orange Counties seem to be different enough in land use characteristics, emission sources, topography, and meteorology such that the LUR model developed from measurements taken in Los Angeles resulted in larger measurement error when applied to residences in Orange County. Higher risks of preeclampsia were observed in Los Angeles than in Orange County for ambient monitor-based traffic-related pollutants (CO, NO, NO_2, NO_x), which may be partly explained by the denser monitoring network and presumably better measures of local traffic emissions at Los Angeles monitoring stations (see residential distances to monitoring stations in Supplemental Materials Table S1). On the other hand, the magnitudes of effect estimates for each region were similar for CALINE4-modeled and traffic density exposure measures, suggesting that these two measures are of comparable quality in both regions.

Contrary to what we expected, effect estimates were often greater for unadjusted versus temporally-adjusted LUR exposures for preterm and very preterm births in both regions and for preeclampsia in Orange County. This indicates that the assumption of a stable spatial surface used to temporally adjust the LUR – as is commonly done for most existing LUR models – may have been inappropriate. Thus, temporally-adjusted LUR models may not necessarily be better surrogates for traffic pollution than simpler metrics like distance to roadways and may suffer from potentially larger exposure misclassification, as suggested previously by Brauer et al. (2008).

We did not find specific exposure windows of greater relevance for any of the outcomes. However, our ability to assess the impact of exposures during specific windows of pregnancy was limited since ambient monitor-based and CALINE4-modeled exposures were moderately to highly correlated across pregnancy periods (data not shown). Also, the exposure window of one month before birth may be irrelevant for preeclampsia since time of onset was not available. One the other hand, since even an entire pregnancy is a relatively short period of time, our results based on temporally-resolved exposures may not be directly applicable to chronic health outcomes for which longer-term rather than shorter-term exposures are more important.

Our study had several limitations. We estimated exposures for the mother's residential address at birth, possibly resulting in exposure misclassification since about 12% to 35% of pregnant women may move during pregnancy (Brauer et al. 2008; Fell et al. 2004). In addition, we lacked time-activity data and time spent in non-residential locations (e.g. workplace, commuting). For example, we previously reported associations between preterm birth and monitor-based air pollution exposure to be greater for women who did not work (and for whom a residence-based measure of exposure presumably is more accurate) than for women who worked outside their homes (Ritz et al. 2007).

Another potential source of bias is residual confounding due to risk factors we could not control for in our analyses (e.g., maternal smoking, environmental tobacco smoke, stress). In a previous study, we found that for short-term (pregnancy months or trimesters) exposures that change seasonally, behavioral factors that do not change seasonally were not strong confounders of air pollution and preterm birth associations (Ritz et al. 2007). Therefore, we expect less residual confounding of exposure-outcome associations with temporally-based exposures from ambient monitoring stations than for the primarily spatially-based CALINE4, LUR and traffic density measures.

CONCLUSIONS

Elevated risks of preeclampsia, preterm birth, and very preterm birth were associated with all measures of traffic-related air pollution exposure in Southern California women living in our Los Angeles and Orange County study region. Preeclampsia was more strongly associated with local traffic-related air pollution, while preterm birth and very preterm birth were associated with both local and regional air pollution. The size of effect estimates was generally smaller for exposures based on traffic density measures compared to more refined exposure assessment methods. We found that LUR models developed in one region (Los Angeles) may not be readily transferred and applied to a neighboring region (Orange County) in the same metropolitan area. In addition, a simple scaling of annual average LUR pollution surfaces using existing monitoring station data may be inappropriate and may introduce larger exposure misclassification than unadjusted (annual average) LUR estimates. These results provide further evidence that traffic-related air pollution is associated with adverse reproductive outcomes. While this study underscores the importance of improving exposure assessment in air pollution and reproductive health research, it nevertheless suggests that simple measures (e.g. concentrations of pollutants measured at ambient monitoring stations or traffic density measures) can still be useful.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

CI	95% confidence interval
CO	carbon monoxide
GIS	geographic information system
IQR	inter-quartile range
LUR	land-use regression
NO	nitric oxide
NO_2	nitrogen dioxide
NO_x	nitrogen oxides
O_3	ozone
PM_{10}	particulate matter less than 10μm
$PM_{2.5}$	particulate matter less than 2.5μm
OR	odds ratio

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Table 1

Characteristics of pregnant women delivering during 1997–2006 within the Memorial Health Care System in Los Angeles and Orange Counties.

Variable	All subjects			Preeclampsia				Preterm birth (less than37 weeks)				Very preterm birth (less than30 weeks)			
				Cases		Non-cases		Cases		Controls		Cases		Controls	
	All	Los Angeles	Orange County	Los Angeles	Orange County	Los Angeles	Orange County	Los Angeles	Orange County	Los Angeles	Orange County	Los Angeles	Orange County	Los Angeles	Orange County
N	81186	38709	42477	1303	1139	37406	41338	3928	2784	19640	13920	546	229	2730	1145
Maternal age (%)															
<20	6.2	8.6	4.1	10.6	5.9	8.5	4.0	9.2	4.7	8.8	4.0	9.7	5.7	8.8	3.9
20–29	41.6	47.2	36.6	41.6	38.4	47.4	36.5	45.4	34.1	46.9	36.5	44.9	33.6	47.9	35.9
30–39	47.4	40.0	54.1	40.8	49.2	40.0	54.2	40.1	53.1	40.2	54.2	39.7	51.5	39.0	55.6
≥40	4.8	4.2	5.3	7.0	6.5	4.1	5.3	5.2	8.1	4.2	5.3	5.7	9.2	4.4	4.6
First birth (%)	81.5	82.4	80.7	90.9	88.5	82.1	80.5	85.5	85.7	82.6	80.3	87.7	93.0	84.3	80.3
Insurance (%)															
Private	67.6	56.3	78.0	53.8	74.3	56.4	78.1	48.1	75.5	57.2	78.5	45.2	70.7	57.9	77.4
Non-private[a]	28.4	43.1	14.9	45.6	16.1	43.1	14.8	51.4	16.6	42.4	14.4	54.8	22.3	41.7	14.0
Unknown	4.0	0.5	7.2	0.6	9.6	0.5	7.1	0.5	7.9	0.5	7.1	0.0	7.0	0.4	8.7
Race (%)															
African American	8.8	16.9	1.4	19.3	2.5	16.9	1.4	21.3	1.9	16.9	1.4	25.3	3.1	18.6	1.3
Hispanic	32.1	38.3	26.5	41.2	29.1	38.2	26.4	40.5	27.8	38.0	26.4	40.8	30.6	37.2	26.6
Asian	9.9	9.8	9.9	7.9	9.0	9.9	10.0	8.8	10.8	9.4	9.9	6.4	10.9	10.3	7.7
White	40.3	26.0	53.4	22.9	52.9	26.1	53.4	20.0	50.0	26.6	54.0	9.5	45.8	25.1	56.5
Other	8.9	9.0	8.8	8.8	6.6	9.0	8.8	9.4	9.5	9.2	8.3	18.0	9.6	8.9	8.0
Poverty[b] (%)	14.2	20.6	8.4	20.1	9.1	20.6	8.3	21.9	8.8	20.4	8.2	22.5	10.0	20.5	7.9

[a]Government sponsored or self-pay

[b]The percent of the population living below the poverty level based on U.S. Census block group data for the year 2000.

Table 2

Means, inter-quartile ranges and Pearson's correlation coefficients for different exposure measures for the entire pregnancy.

	Pollutant	n	Mean±SD[a]	IQR[a, b]	Pearson r															
					Measured pollutant[c]							LUR (unadjusted)			LUR (adjusted)			CALINE4		Traffic density
					CO	NO	NO_2	NO_x	O_3	PM_{10}	$PM_{2.5}$	NO	NO_2	NO_x	NO	NO_2	NO_x	NO_x	$PM_{2.5}$	
Measured pollutant[c]	CO	81186	0.7+0.4	0.5	1.00															
	NO	81186	30.9+15.7	18.3	0.85	1.00														
	NO_2	81186	24.9+7.4	11.7	0.83	0.83	1.00													
	NO_x	81186	55.8+22.2	28.2	0.88	0.98	0.92	1.00												
	O_3	81186	35.6+7.5	11.5	−0.74	−0.80	−0.81	−0.84	1.00											
	PM_{10}	81186	32.7+5.7	6.8	0.60	0.51	0.70	0.59	−0.49	1.00										
	$PM_{2.5}$	68055	17.3+3.5	5.1	0.77	0.65	0.77	0.72	−0.61	0.86	1.00									
LUR (unadjusted)	NO	81186	25.2+10.9	8.2	0.03	0.03	0.01	0.02	0.02	0.06	0.05	1.00								
	NO_2	81186	22.4+3.6	4.3	0.09	0.06	0.06	0.06	0.05	0.05	0.06	0.39	1.00							
	NO_x	81186	48.6+10.8	12.1	0.05	0.04	0.01	0.03	0.06	0.05	0.05	0.72	0.87	1.00						
LUR (adjusted)	NO	81186	30.9+18.1	11.6	0.24	0.35	0.20	0.32	−0.24	0.23	0.25	0.76	0.26	0.53	1.00					
	NO_2	81186	28.0+7.0	5.1	0.43	0.42	0.57	0.49	−0.39	0.52	0.52	0.25	0.63	0.55	0.48	1.00				
	NO_x	81186	59.9+20.3	15.6	0.36	0.48	0.38	0.46	−0.35	0.37	0.39	0.47	0.53	0.64	0.80	0.84	1.00			
CALINE4	NO_x	79629	7.2+5.2	5.6	0.43	0.41	0.50	0.45	−0.37	0.41	0.43	0.24	0.56	0.51	0.25	0.63	0.49	1.00		
	$PM_{2.5}$	79629	1.8+1.3	1.4	0.22	0.21	0.25	0.23	−0.15	0.19	0.21	0.29	0.63	0.58	0.16	0.44	0.34	0.89	1.00	
Traffic density		81186	73.8+116.3	76.6	0.07	0.06	0.09	0.07	−0.05	0.09	0.09	0.28	0.37	0.43	0.19	0.27	0.27	0.58	0.61	1.00

[a] The units of exposure are parts per million (ppm) for CO, parts per billion (ppb) for NO, NO_2, NO_X, and O_3, and μg m^{-3} for PM_{10} and $PM_{2.5}$. The unit for traffic density is vehicle number per day*meter/meter^2.

[b] Inter-quartile range

[c] Exposure was assigned based on residential distance to the nearest air quality monitoring station with valid measurement data. All exposures were averaged over 24 hours except O_3, which was averaged over 8 hours from 10 AM to 6 PM. $PM_{2.5}$ data were first collected in 2000 while data for the other pollutants were available starting in 1997.

Table 3

Crude odds ratios and adjusted odds ratios for preeclampsia per inter-quartile range[a] increase in air pollution exposures for the entire pregnancy.

	Los Angeles			Orange County		
	Cases (n)	**Crude OR (95% CI)**	**Adjusted OR[b] (95% CI)**	**Cases (n)**	**Crude OR (95% CI)**	**Adjusted OR[b] (95% CI)**
CO	1303	1.14 (1.07–1.21)	1.11 (1.03–1.19)	1139	1.13 (1.02–1.25)	0.97 (0.87–1.09)
NO	1303	1.10 (1.04–1.17)	1.09 (1.02–1.17)	1139	1.09 (0.98–1.22)	0.97 (0.84–1.11)
NO_2	1303	1.16 (1.03–1.31)	1.13 (0.99–1.29)	1139	1.25 (1.11–1.40)	1.08 (0.95–1.23)
NO_x	1303	1.12 (1.04–1.21)	1.11 (1.02–1.20)	1139	1.15 (1.03–1.29)	1.01 (0.88–1.16)
O_3	1303	0.99 (0.86–1.13)	1.00 (0.86–1.16)	1139	1.07 (0.95–1.20)	1.21 (1.06–1.38)
PM_{10}	1303	1.01 (0.92–1.10)	0.97 (0.89–1.07)	1139	1.07 (1.00–1.14)	0.98 (0.91–1.05)
$PM_{2.5}$	1025	0.96 (0.86–1.07)	0.90 (0.79–1.01)	995	1.09 (0.99–1.20)	0.98 (0.88–1.09)
NO LUR (unadjusted)	1303	1.03 (0.99–1.08)	1.02 (0.98–1.07)	1139	1.02 (0.98–1.06)	1.01 (0.96–1.05)
NO_2 LUR (unadjusted)	1303	1.18 (1.09–1.28)	1.16 (1.07–1.26)	1139	1.09 (1.02–1.16)	1.04 (0.97–1.12)
NO_x LUR (unadjusted)	1303	1.16 (1.07–1.25)	1.13 (1.04–1.22)	1139	1.06 (1.00–1.12)	1.03 (0.96–1.09)
NO LUR (adjusted)	1303	1.06 (1.00–1.12)	1.05 (0.99–1.13)	1139	0.98 (0.93–1.03)	0.96 (0.90–1.02)
NO_2 LUR (adjusted)	1303	1.12 (1.03–1.23)	1.12 (1.02–1.23)	1139	1.10 (1.02–1.18)	1.01 (0.93–1.10)
NO_x LUR (adjusted)	1303	1.15 (1.05–1.25)	1.16 (1.05–1.28)	1139	1.02 (0.96–1.09)	0.96 (0.89–1.04)
NO_x CALINE4	1303	1.10 (1.04–1.17)	1.08 (1.02–1.15)	1106	1.15 (1.08–1.22)	1.08 (1.01–1.16)
$PM_{2.5}$ CALINE4	1303	1.09 (1.02–1.16)	1.08 (1.02–1.15)	1106	1.13 (1.08–1.19)	1.10 (1.04–1.17)
Traffic density	1303	1.03 (1.00–1.07)	1.03 (0.99–1.06)	1139	1.05 (1.01–1.08)	1.03 (1.00–1.07)

[a] To compare results between regions, we used the inter-quartile range values for the entire region (see Table 2).

[b] Adjusted for maternal age, maternal race/ethnicity, parity, diabetes, prenatal care insurance type, poverty, and season of conception.

Table 4

Crude odds ratios and adjusted odds ratio for preterm birth (less than 37 weeks) per inter-quartile range[a] increase in air pollution exposures for the entire pregnancy.

	Los Angeles			Orange County		
	Cases (n)	**Crude OR (95% CI)**	**Adjusted OR[b] (95% CI)**	**Cases (n)**	**Crude OR (95% CI)**	**Adjusted OR[b] (95% CI)**
CO	3928	1.13 (1.09–1.18)	1.13 (1.08–1.19)	2784	1.11 (1.02–1.20)	1.14 (1.04–1.26)
NO	3928	1.08 (1.05–1.12)	1.11 (1.06–1.16)	2784	0.97 (0.91–1.04)	1.03 (0.94–1.13)
NO_2	3928	1.06 (0.97–1.15)	1.06 (0.95–1.18)	2784	1.07 (0.99–1.16)	1.13 (1.02–1.25)
NO_x	3928	1.09 (1.05–1.14)	1.13 (1.07–1.19)	2784	1.00 (0.93–1.07)	1.07 (0.97–1.18)
O_3	3928	0.99 (0.92–1.07)	1.00 (0.90–1.10)	2784	1.09 (1.01–1.18)	1.04 (0.93–1.16)
PM_{10}	3928	1.05 (0.98–1.12)	1.06 (0.98–1.14)	2784	1.10 (1.05–1.16)	1.09 (1.02–1.15)
$PM_{2.5}$	3174	1.02 (0.95–1.10)	1.04 (0.94–1.15)	2333	1.08 (1.00–1.17)	1.09 (1.00–1.20)
NO LUR (unadjusted)	3928	1.01 (0.98–1.04)	1.01 (0.98–1.04)	2784	1.02 (0.99–1.04)	1.01 (0.98–1.04)
NO_2 LUR (unadjusted)	3928	1.13 (1.07–1.18)	1.07 (1.02–1.13)	2784	1.00 (0.96–1.04)	0.97 (0.92–1.01)
NO_x LUR (unadjusted)	3928	1.09 (1.04–1.15)	1.05 (1.00–1.10)	2784	1.01 (0.97–1.05)	0.98 (0.94–1.03)
NO LUR (adjusted)	3928	1.00 (0.99–1.02)	1.02 (0.98–1.07)	2784	0.98 (0.97–1.00)	0.98 (0.94–1.02)
NO_2 LUR (adjusted)	3928	0.98 (0.95–1.00)	0.92 (0.85–0.98)	2784	0.98 (0.96–1.00)	0.95 (0.89–1.01)
NO_x LUR (adjusted)	3928	1.01 (0.99–1.03)	1.02 (0.95–1.08)	2784	0.97 (0.95–0.99)	0.95 (0.90–1.00)
NO_x CALINE4	3928	1.05 (1.01–1.10)	1.04 (0.99–1.08)	2677	1.05 (1.00–1.09)	1.01 (0.96–1.07)
$PM_{2.5}$ CALINE4	3928	1.06 (1.02–1.10)	1.04 (1.00–1.08)	2677	1.04 (1.00–1.09)	1.02 (0.97–1.07)
Traffic density	3928	1.03 (1.00–1.05)	1.02 (1.00–1.04)	2784	1.01 (0.99–1.04)	1.00 (0.98–1.03)

[a]To compare results between regions, we used the inter-quartile range values for the entire region (see Table 2).

[b]Adjusted for maternal age, maternal race/ethnicity, parity, pyelonephritis, prenatal care insurance type, poverty, and season of conception.

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Table 5

Crude odds ratios and adjusted odds ratios for very preterm birth (less than 30 weeks) per inter-quartile range[a] increase in air pollution exposures for the entire pregnancy.

	Los Angeles			Orange County		
	Cases (n)	Crude OR (95% CI)	Adjusted OR[b] (95% CI)	Cases (n)	Crude OR (95% CI)	Adjusted OR[b] (95% CI)
CO	546	1.25 (1.14–1.37)	1.34 (1.20–1.49)	229	1.49 (1.18–1.88)	1.76 (1.27–2.44)
NO	546	1.13 (1.05–1.21)	1.27 (1.15–1.40)	229	1.12 (0.95–1.33)	1.26 (0.95–1.68)
NO_2	546	1.21 (1.00–1.46)	1.46 (1.11–1.92)	229	1.31 (1.02–1.67)	1.43 (1.02–2.01)
NO_x	546	1.16 (1.06–1.27)	1.34 (1.18–1.53)	229	1.17 (0.97–1.42)	1.35 (0.98–1.84)
O_3	546	0.99 (0.85–1.16)	0.97 (0.77–1.24)	229	1.05 (0.84–1.31)	1.20 (0.85–1.69)
PM_{10}	546	1.03 (0.89–1.20)	1.10 (0.92–1.32)	229	1.35 (1.13–1.62)	1.34 (1.09–1.66)
$PM_{2.5}$	410	0.98 (0.83–1.16)	1.03 (0.81–1.30)	190	1.23 (0.98–1.53)	1.33 (0.99–1.77)
NO LUR (unadjusted)	546	1.05 (0.97–1.13)	1.06 (0.98–1.15)	229	1.09 (1.00–1.18)	1.06 (0.97–1.16)
NO_2 LUR (unadjusted)	546	1.47 (1.29–1.67)	1.42 (1.24–1.62)	229	1.09 (0.94–1.27)	1.01 (0.85–1.20)
NO_x LUR (unadjusted)	546	1.33 (1.17–1.50)	1.27 (1.12–1.45)	229	1.14 (0.99–1.30)	1.05 (0.91–1.22)
NO LUR (adjusted)	546	1.01 (0.97–1.05)	1.06 (0.96–1.18)	229	1.00 (0.96–1.04)	0.98 (0.88–1.10)
NO_2 LUR (adjusted)	546	1.01 (0.95–1.07)	1.04 (0.87–1.24)	229	1.03 (0.96–1.10)	1.03 (0.84–1.26)
NO_x LUR (adjusted)	546	1.03 (0.98–1.08)	1.18 (1.01–1.39)	229	1.00 (0.95–1.06)	0.97 (0.82–1.15)
NO_x CALINE4	546	1.17 (1.06–1.29)	1.16 (1.04–1.28)	217	1.21 (1.05–1.40)	1.17 (0.99–1.38)
$PM_{2.5}$ CALINE4	546	1.18 (1.07–1.30)	1.17 (1.06–1.29)	217	1.20 (1.06–1.35)	1.16 (1.01–1.34)
Traffic density	546	1.05 (0.99–1.11)	1.03 (0.97–1.09)	229	1.01 (0.93–1.10)	0.99 (0.90–1.08)

[a]To compare results between regions, we used the inter-quartile range values for the entire region (see Table 2).

[b]Adjusted for maternal age, maternal race/ethnicity, parity, pyelonephritis, prenatal care insurance type, poverty, and season of conception.