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Preterm Birth among Infants Exposed to *in Utero* Ultrafine Particles from Aircraft Emissions

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Introduction: Ambient air pollution is a known risk factor for adverse birth outcomes, but the role of ultrafine particles (UFPs) is not well understood. Aircraft-origin UFPs adversely affect air quality over large residential areas downwind of airports, but their reproductive health burden remains uninvestigated.

Objectives: This analysis evaluated whether UFPs from jet aircraft emissions are associated with increased rates of preterm birth (PTB) among pregnant mothers living downwind of Los Angeles International Airport (LAX).

Methods: This population-based study used birth records, provided by the California Department of Public Health, to ascertain birth outcomes and a novel, validated geospatial UFP dispersion model approach to estimate *in utero* exposures. All mothers who gave birth from 2008 to 2016 while living within 15 km of LAX were included in this analysis ($N = 174{,}186$; including 15,134 PTBs).

Results: *In utero* exposure to aircraft-origin UFPs was positively associated with PTB. The odds ratio (OR) per interquartile range (IQR) increase [9,200 particles per cubic centimeter (cc)] relative UFP exposure was 1.04 [95% confidence interval (CI): 1.02, 1.06]. When comparing the fourth quartile of UFP exposure to the first quartile, the OR for PTB was 1.14 (95% CI: 1.08, 1.20), adjusting for maternal demographic characteristics, exposure to traffic-related air pollution, and airport-related noise.

Conclusion: Our results suggest that emissions from aircraft play an etiologic role in PTBs, independent of noise and traffic-related air pollution exposures. These findings are of public health concern because UFP exposures downwind of airfields are common and may affect large, densely populated residential areas. https://doi.org/10.1289/EHP5732

Introduction

Approximately 1 in 10 births in the United States are preterm (Martin et al. 2018), increasing the infant's risk for developing complications, such as respiratory problems, infections, developmental delays, and vision or hearing impairments (WHO 2018). Prematurity is also the leading cause of neonatal mortality (Harrison and Goldenberg 2016) and generates an annual economic burden in the United States of ~$26 billion [Institute of Medicine (U.S.) 2007].

Exposure to ambient air pollution during pregnancy has previously been identified as a risk factor for adverse birth outcomes, including preterm birth (PTB) (Maisonet et al. 2004; Ponce et al. 2005; Ritz et al. 2000, 2002; Ritz and Yu 1999; Šrám et al. 2005; Stillerman et al. 2008; Wilhelm and Ritz 2003, 2005). The effect of ambient air pollution from ground-transportation emissions on birth outcomes has been extensively studied, but the effects of aircraft emissions have not. During landing, takeoff, and taxiing, aircraft generate pollutant plumes that are blown downwind of airports, potentially adversely affecting the health of residents. The pollutants include particulate matter (PM), especially ultrafine particles (UFPs) from jet engines; volatile organic compounds; oxides of sulfur; and oxides of nitrogen (Carslaw et al. 2006; Ratliff et al. 2009; Valotto and Varin 2016; Yu et al. 2004). PM has traditionally been measured and regulated in terms of mass concentration of particles with aerodynamic diameter less than 10 μm (PM_{10}) or less than 2.5 μm ($PM_{2.5}$). Ultrafine or nanoparticles, which are less than 0.1 μm in diameter, are not routinely monitored or regulated. They account for little mass, but make up the majority of particles in terms of number and surface area (Hinds 1999). On an equal mass basis, UFPs may have more impact on health than do particulates with larger aerodynamic diameters, such as $PM_{2.5}$ (Hyder et al. 2014; Lamichhane et al. 2015; Lee et al. 2013) and PM_{10} (Ritz et al. 2000; Wilhelm and Ritz 2005), due to their greater mobility in the body and greater surface area.

Recent studies report adverse air quality impacts from landing jets over large areas downwind of major airports (Hudda et al. 2016, 2018, 2014; Keuken et al. 2015; Masiol et al. 2017b, 2017a; Riley et al. 2016). For example, jets approaching Los Angeles International Airport (LAX) in Los Angeles, California, produce ground-level UFP concentrations more than twice the nearby ambient levels at distances up to 16 km away from the airport (Hudda et al. 2014). Here, we evaluated whether UFPs from jet aircraft emissions increase rates of PTB near LAX based on an AERMOD dispersion model for UFPs that we built and validated with spatially extensive ground-level measurements.

Materials and Methods

Sample Population and Health Outcome

We identified all mothers who gave birth from 2008 through 2016 while living within 15 km of LAX using birth certificates obtained from the California Department of Public Health. Our health outcome, PTB, was defined as a live birth occurring before 37 wk gestation (yes/no). We excluded birth records with implausible gestational ages (<20 or >50 wk, $n = 686$), implausible birth weights (<500 g or >5,000 g, $n = 1{,}181$), nonsingleton pregnancies ($n = 6{,}407$), or missing data on any covariates ($n = 14{,}236$) leaving 174,186 births. This study was approved by the University

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of California Los Angeles Institutional Review Board and the California Health and Human Services Agency's Committee for the Protection of Human Subjects. This study used routinely collected administrative data only and thus required no contact with research participants. Therefore, a waiver of informed consent was granted because it would not affect the rights of the participant nor could this research be practicably carried out without the waiver. Privacy and confidentiality were assured by using an encrypted and secure, internet-disabled computer for all data storage and analysis.

Exposure Assessment—UFPs

The U.S. Environmental Protection Agency (U.S. EPA) AERMET model was used first to generate relevant meteorological parameters from surface measurements available at LAX. Hourly vector averages of 10-m wind speed and direction were compiled from raw 5-min average measured values. Figure S1 shows the hourly directional and speed frequency distributions (wind rose) during the modeling period. We then used U.S. EPA's AERMOD meteorological dispersion model to predict air quality impacts downwind of the airport, assuming two steady-state, volumetric line sources, $50\ \mathrm{m} \times 50\ \mathrm{m}$ in cross-section, to represent the emissions from descending aircraft approaching both runways. These two volume line sources were aligned in the same direction as the runways, which closely matched the predominant wind directions shown in Figure S1. One end of each source was placed at ground level on the eastern edge of each corresponding runway to account for the approximately 100-m induced downward plume travel from the interacting rotational energy of the vortices, which lowers the effective source positions relative to the actual position of the landing aircraft (Graham and Raper 2006). The other ends of the line sources were located at 1,000-m elevation to match the 3-degree approach angle as shown in Figure S2.

Due to the lack of regulation or standards for particle number, UFP emissions have not been well characterized historically and estimating UFP emission rates from jets involves high uncertainty (Durdina et al. 2017). For this reason, we initially assumed a nominal daily average total emission rate from both sources of $1\ \mathrm{g/s}$. These emissions were then allowed to vary on a relative basis by hour of the day, based on reported flight activity patterns, with nearly all flight activity occurring between 0700 and 2300 hours (7 A.M. and 11 P.M.), as shown in Figure S3 (LAWA 2014).

To determine and validate adjustments to this emission rate, we regressed the resulting AERMOD predictions against direct downwind measurements made along the transects shown in Figure S4 on seven days, five in summer and two in winter (Figure 1) (Hudda et al. 2014). The average values for all days along each transect were then compared with the volume line source model relative predictions, based on the nominal $1\ \mathrm{g/s}$ emissions rates and scaled to match observed values during the same hourly time periods using a simple linear regression model. We included an intercept in the model to account for any residual background not included in the prior adjustments. Predicted vs. measured values are shown in Figure S5. The model R^2 was 0.71 with an root mean square error (RMSE) of 2,300 particles per cc and a mean absolute percentage error of 6%. The intercept was statistically significant with a value of 13,900 [standard deviation (SD) = 4,800] particles per cc.

For sensitivity tests, we compared results from modeling UFP concentrations from an area source representing the ground-level emissions from the airport runway and tarmac. We also tested a 10-degree angle of ascent (Yim et al. 2013). Neither of these configurations predicted UFP concentrations that were significantly correlated with the observations.

The 3-degree, dual volume line source model was then run for the period January 2008 through December 2016. Average values were computed for each month during that period at the receptor locations shown in Figure S6. We assumed that the meteorology derived from the LAX data applied over the entire modeling region. The monthly activity patterns shown in Figure S7 relative to the overall average were then used to adjust the monthly average model predictions at each receptor location. Particle number concentrations reported here are based on an AERMOD conversion factor of 2.3×10^6.

Using the UFP dispersion model, we linked average per trimester and per pregnancy period UFP exposures within the 15-km buffer to geocoded maternal addresses reported on the birth certificate. Additionally, we evaluated noncircular, ellipsoid exposure buffers with semiminor axes of 10, 12, and 14 km and semimajor axes of 22.5, 18.8, and 16.1 km, respectively, to preserve the original exposure buffer area of $\sim 707\ \mathrm{km}^2$. These ellipses were aligned with the prevailing daytime wind direction of 263 degrees, the angle at which the runways are oriented.

Covariates

We controlled for NO_2 concentrations as a ground-level vehicle traffic surrogate for combustion emissions similar to methods used in previous studies (Ritz et al. 2009; Singer et al. 2004). Briefly, with a Land Use Regression (LUR) model we estimated annual NO_2 exposures for Los Angeles County using data collected over 2 wk from 201 passive air samplers (part number PS-100; Ogawa & Company USA). Final predicted concentration surfaces explained 85% of the variation of measured NO_2 concentrations. Mothers were assigned the annual average concentrations of the year during which the majority of their pregnancy occurred.

The analysis also included the known PTB risk factors (Campbell et al. 2017; Fuchs et al. 2018; Kyrklund-Blomberg and Cnattingius 1998; Luo et al. 2006; Ruiz et al. 2015) listed in the birth certificates, including parental age; mother's race/ethnicity [Hispanic (any race), non-Hispanic black, non-Hispanic white, and non-Hispanic Asian and non-Hispanic Other (including Native American and Hawaiian/Pacific Islander); maternal educational attainment; maternal nativity (U.S.- or foreign-born); and maternal smoking (ever/never during pregnancy)].

Thirty-nine noise monitors in the communities surrounding the airport routinely record noise from overhead flights and generate publicly reported community noise equivalent levels (CNELs). These monitors are deployed and managed by the airport authority and are certified by the California Department of Transportation, Division of Aeronautics. Monitors are located up to ~ 1 km north and south and 7 km east of the airport boundary, roughly following the usual approach pattern to LAX. Almost no monitoring occurs west of the airport because its western edge abuts the Pacific Ocean (LAWA 2015). Monitored data are the input into the Federal Aviation Administration's Integrated Noise Model to generate estimated annual noise impact areas due to aircraft activity. The areas affected above an annual average of 65 decibels (dB), the acceptable CNEL limit for individuals living near an airport, according to the California Department of Transportation (California Department of Transportation Division of Aeronautics) and the day–night average noise level threshold used by the Federal Aviation Administration (FAA) to make policy assessments (FAA 2018) are shown in Figure S8. We included CNEL values at each mother's residence as a dichotomous variable, either above or below 65 dB.

To further control for confounding by neighborhood socioeconomic status (nSES), we also adjusted for a composite score of nSES based on a principal component analysis selection of seven

indicator variables generated from United States census data. Mothers were assigned a quintile nSES index (5 = high, 1 = low), based on the ranking of their census tract's median household income, median rent, median house value, percent living 200% below poverty level, percent of blue-collar workers, percent unemployed, and education index (Yost et al. 2001).

Statistical Analysis

We assessed the association between quartiles of residential location-specific aircraft UFP concentrations during pregnancy and PTB using logistic regression (SAS version 9.3; SAS Institute, Inc.). Quartiles were defined by cut points at 5,300 particles/cc, 8,600 particles/cc, and 14,600 particles/cc. These cut points remained consistent across all models. In covariate-adjusted models, we estimated the odds ratio (OR) for PTB in each quartile of UFP exposure relative to the lowest quartile. To evaluate the role of maternal nativity and race/ethnicity, we conducted jointly stratified analyses because the health outcomes of some recent immigrant groups may differ from native-born individuals with the same race/ethnicity (Hoggatt et al. 2012; McDonald and Kennedy 2004). We also evaluated a continuous measure of UFP, examining a linear, per-IQR increase in relative UFP exposure and sensitivity analyses using a mixture of exposure quantiles. Additionally, we analyzed the association between quartiles of UFP exposure and very PTB (<32 wk gestation) using an adjusted logistic regression model.

Further sensitivity analyses included stratifying by nSES (quintiles) and educational attainment (high school education or less, some college to bachelor's degree, or more than a bachelor's degree) to estimate the association between UFP and PTB in population subgroups. Using monthly estimates of UFP exposure, per-trimester exposure estimates were generated. Per-trimester exposure models were modeled to assess potential periods of greater sensitivity to pollutants during gestation. Pearson correlations across trimesters and with other pollutants, nSES, and UFP exposures were also analyzed. To isolate aircraft movements at LAX from activities at a nearby municipal airport [Santa Monica Municipal Airport (SMO)], we additionally excluded in some sensitivity analyses residents living within a 2-km and 5-km buffer distance from the SMO airport. Subjects for whom any covariate data were missing were excluded from analyses.

Table 1. Maternal and infant demographics by gestational age.

Total $N = 174{,}186$	<37 wk ($n = 15{,}134$)	≥37 wk ($n = 159{,}052$)
Gestational age, mean weeks (SD), missing = 0	34.5 (2.8)	39.7 (1.4)
Birth weight, mean grams (SD), missing = 6	2,598 (752)	3,348 (444)
Parity, mean children (SD), missing = 0	2.3 (2.3)	2.1 (2.4)
Quintile of nSES Index,[a] mean (SD), missing = 0	1.9 (1.3)	2.2 (1.4)
Infant sex [*n* (%)]		
Male	8,282 (54.7)	80,774 (50.8)
Female	6,850 (45.3)	78,278 (49.2)
Missing (*n*)	2	0
Maternal age [*n* (%)]		
<20	1,322 (8.7)	11,658 (7.3)
20–24	2,980 (19.7)	30,731 (19.3)
25–29	3,440 (22.7)	38,339 (24.1)
30–34	3,702 (24.5)	43,372 (27.3)
35+	3,690 (24.4)	34,952 (22.0)
Missing (*n*)	1	2
Maternal Race [*n* (%)]		
White	1,842 (12.2)	29,749 (18.7)
Black	3,027 (20.0)	22,487 (14.1)
Hispanic	8,997 (59.5)	89,592 (56.3)
Asian	916 (6.1)	13,670 (8.6)
Others	352 (2.3)	3,554 (2.2)
Missing (*n*)	216	2,526
Maternal education [*n* (%)]		
High school graduate or less	8,909 (58.9)	81,542 (51.3)
Some college to bachelor's degree	4,928 (32.6)	57,883 (36.4)
More than a bachelor's degree	1,297 (8.6)	19,627 (12.3)
Missing (*n*)	435	4,584
Maternal nativity [*n* (%)]		
U.S.-born	10,802 (71.4)	111,087 (70.0)
Foreign-born	4,332 (28.6)	47,965 (30.2)
LUR modeled NO_2 exposure, mean ppb (SD), missing = 0	23.8 (2.6)	23.6 (2.7)
High noise at residence [*n* (%)]		
≥65 dB CNEL	779 (5.2)	6,685 (4.2)
<65 dB CNEL	14,355 (94.8)	152,367 (95.8)
Cigarette smoking [*n* (%)]		
Ever during pregnancy	157 (1.0)	923 (0.6)
Never during pregnancy	14,977 (99.0)	158,129 (99.4)
Missing	1,686	11,681

Note: Data are complete unless otherwise indicated. CNEL, community noise equivalent level; dB, decibels; LUR, land use regression.
[a]nSES measured as a composite index of seven indicator variables based on U.S. census data at the census tract level.

Results

Demographic factors by PTB status for the infants born within a 15-km radius of LAX between 2008 and 2016 are shown in Table 1. Most mothers were Hispanic with a high school degree or less. Mean age at delivery was 29 y (SD = 6.4 years). PTB occurred in 8.7% of all births and was more common in black and Hispanic mothers and mothers with less education and among male births. Demographic factors are also shown by quartile of UFP exposure in Table S1. In higher quartiles of exposure, mothers tended to be younger, more frequently Hispanic or black, and had less education than mothers in lower exposure quartiles. The mean UFP exposure concentration was 12,000 particles/cc (SD = 11,000 particles/cc), with a minimum of 2,500 particles/cc and maximum of 120,000 particles/cc. The IQR was 9,200 particles/cc.

In unadjusted logistic regression models, the highest quartile of pregnancy average UFP exposure was associated with a 1.32 OR of giving birth to a preterm baby in comparison with the lowest quartile. Controlling for demographic factors as well as traffic pollution and noise, the OR for PTB in the upper quartile of UFP exposure was 1.14 (95% CI: 1.08, 1.20) (Table 2), with the odds increasing monotonically with each increase in exposure quartile. When we stratified by maternal race/ethnicity and nativity when comparing the fourth quartile of UFP exposure to the first, we found the strongest associations among foreign-born women, particularly for Asian and Hispanic women (Table S2). By contrast, stronger associations were found in U.S.-born black women relative to foreign-born black women, though the sample size among black women was markedly smaller (Table S3). Exposure to the highest quartile of traffic-related NO_2 (>25.5 ppb) relative to the lowest (<21.8 ppb) was associated with an OR of 1.15 (95% CI: 1.09, 1.22). Additionally, exposure to noise >65 dB CNEL was associated with an OR of 1.10 (95% CI: 1.01, 1.19) (Table 2). Of note, maternal exposure with high airport noise was only moderately correlated with aircraft-origin UFPs (Pearson correlation coefficient $r = 0.56$) and weakly inversely correlated with traffic-related NO_2 ($r = -0.18$) (Table S4).

In additional sensitivity analyses using different quantiles of UFP exposure, the results remained consistent (Table S5). A monotonic dose–response of increasing risk of PTB with increasing exposure to UFP was evident for all exposure categorizations we examined. For UFPs using a continuous variable we estimated the OR of PTB to be 1.04 (95% CI: 1.02, 1.06) per IQR increase

Table 2. Adjusted odds ratios (ORs) [95% confidence intervals (CIs)] of preterm birth.[a]

Variable	95% CI			
	Unadjusted model	Adjusted model 1[b]	Adjusted model 2[c]	Adjusted model 3[d]
UFP				
Quartile 1 (<5,340 particles/cc)	Ref	Ref	Ref	Ref
Quartile 2 (5,340–8,600 particles/cc)	1.17 (1.11, 1.22)	1.01 (0.96, 1.07)	1.03 (0.98, 1.08)	1.03 (0.98, 1.08)
Quartile 3 (8,600–14,600 particles/cc)	1.27 (1.22, 1.33)	1.05 (1.00, 1.10)	1.08 (1.02, 1.13)	1.08 (1.02, 1.13)
Quartile 4 (>14,600 particles/cc)	1.32 (1.27, 1.39)	1.11 (1.05, 1.16)	1.16 (1.10, 1.22)	1.14 (1.08, 1.20)
NO_2				
Quartile 1 (<21.8 ppb)	—	—	Ref	Ref
Quartile 2 (21.8–23.8 ppb)	—	—	1.10 (1.05, 1.15)	1.10 (1.05, 1.16)
Quartile 3 (23.9–25.5 ppb)	—	—	1.10 (1.05, 1.16)	1.11 (1.05, 1.15)
Quartile 4 (>25.5 ppb)	—	—	1.15 (1.09, 1.21)	1.15 (1.09, 1.22)
Exposed to noise >65 dB CNEL	—	—	—	1.10 (1.01, 1.19)

Note: —, Data not available; CNEL, community noise equivalent level; dB, decibels; ppb, parts per billion; Ref, reference.
[a]PTB cases $n = 15{,}134$.
[b]Adjusted for maternal age, maternal educational attainment, SES, maternal race, and cigarette smoking. Educational attainment was recorded in 9 ordinal categories: No formal education, 8th grade or less, 9th grade through 12th grade with no diploma, high school graduate or GED, some college credit with no degree, associate's degree, bachelor's degree, master's degree, doctorate or professional degree.
[c]Adjusted for all variables in Adjusted Model 1 and NO_2.
[d]Adjusted for all variables in Adjusted Model 2 and airport noise.

in UFP. When we explored exposure to UFP at different times during pregnancy, we found that the per-trimester effect estimates were nearly identical to those for the entire pregnancy (Table S6). However, the UFP averages for trimesters and the whole pregnancy were highly correlated (Table S3); hence, our ability to detect differences between trimester-specific exposures was diminished. When we modified the aspect ratio of the exposure area, generating an ellipsoid buffer, we observed only minor changes in effect estimates (Table S7).

We also conducted stratified analyses to assess potential effect measure modifiers. When we stratified by quintile of nSES, we observed a modest increase in the odds of PTB associated with UFP exposure with decreasing nSES when comparing the fourth quartile of UFP exposure to the first, though estimates were not behaving strictly monotonically (Table S8). We also found nSES and UFP exposures to be negatively correlated [Pearson correlation coefficient: $-.27$, $p < .0001$ (Table S9)]; i.e., mothers living in areas with the lowest nSES tended to be exposed to higher levels of aircraft-origin UFPs relative to women living in areas with higher nSES. Stratifying by education suggested an increased risk of PTB due to UFP exposure in all quartiles of exposure among women with less than a high school education (OR 1.19, 95% CI: 1.10, 1.28). On the other hand, for those with some college education, the estimated effect sizes for UFP exposure were smaller (OR 1.10, 95% CI: 1.00, 1.21) (Table S10).

We also estimated the association between UFPs and very PTB ($n = 2{,}805$), and the OR for the highest quartile (1.13) of exposure was very similar to the overall estimate, but the CI was wider (95% CI: 0.98, 1.31) (Table S11). When excluding mothers living close to a nearby municipal airport (SMO), overall effect estimates changed only slightly. Specifically, after excluding mothers living within 2 km and 5 km of SMO, the ORs for the highest quartile of UFP exposure relative to the lowest quartile increased to 1.15 (95% CI: 1.09, 1.21) and 1.18 (95% CI: 1.11, 1.25), respectively (Table S12).

Discussion

We found *in utero* exposures to jet-specific UFP emissions, estimated using a spatially validated AERMOD dispersion model, to be associated with increased odds of PTB among mothers living within 15 km of LAX. This is the first study to report such associations for an adverse birth outcome among residents living in the incoming flight paths and downwind of a major airport. We also found associations between PTB and vehicular traffic-related air pollution NO_2, modeling with an LUR as reported previously in a study of births between 1997 and 2006 in Los Angeles (Wu et al. 2009), but the effect sizes were slightly weaker than those we estimated for LAX UFPs. These results suggest an association between traffic-related air pollution and PTB that has been previously reported for other population-based birth outcome studies (Ji et al. 2019; Ritz et al. 2007, 2000; Wilhelm et al. 2011) and was consistent across different categorizations of the UFP exposure variable.

Our results suggest that exposure to aircraft-origin UFP may be independently associated with PTB after accounting for coexposure to traffic-related air pollution and aircraft noise. Whether noise was included or excluded from models, the effect estimates for UFP exposure remained the same. Although previous research found some evidence for an etiological role of noise in PTB (Argys et al. 2019), other research has not consistently detected this link (Ristovska et al. 2014). In our cohort, although exposure to airport-related noise does appear to be associated with an increased risk for PTB for those living very close to the airport (Figure S8), aircraft-origin UFPs were associated with PTB in an area downwind of the LAX airfield that is much larger than the one affected by high noise levels. In fact, in 2010, more than 1.9 million residents lived within the 15-km buffer we studied (U.S. Census Bureau 2010). For comparison, aircraft activity at LAX has been previously estimated to generate an average particle number concentration equivalent to 280 km–790 km of freeway emissions, which represents emissions equivalent to 19%–53% of the total freeway length in all of Los Angeles County (Hudda et al. 2014).

An important aspect of this study is that it distinguishes aircraft-origin UFPs from traffic-origin UFPs. A previous study in California implicated vehicle traffic UFPs in PTBs from 2000 to 2008 (Laurent et al. 2016). However, the CALINE4 traffic model used to estimate exposures did not include the contributions of aircraft-origin UFP. In comparison with the sharp UFP gradients resulting from vehicle traffic that are limited to a few hundred meters from roadways, UFP emissions from jets, particularly landing planes, show unusually large impact areas with relatively little small-scale spatial variability (e.g., almost no change over hundreds of meters) (Hudda and Fruin 2016). This characteristic allowed for more accurate exposure estimates compared to with ground-source UFP concentrations from roadways, which typically have sharp downwind concentrations gradients (Kaur et al. 2006).

There is a relatively rapid downward transport of these aircraft-origin UFPs and thus very little time for physical aging of these UFP particles due to coagulation with larger particles. This downward transport is due to a combination of large-scale daytime, convective velocities of up to 1 m/s that are enhanced by local-scale jet wingtip vortices that can extend vertically downward for several hundred meters at similar, superimposed velocities (Graham and Raper 2006). This combination results in plumes from descending aircraft reaching ground level in approximately a few minutes near the airport and up to 15–20 min at 15 km downwind from the airport. At these plume transport times, 10–20 nm UFPs emitted by jet engines have a characteristic coagulation half-life of about an hour, assuming that they are emitted into a background aerosol with a number concentration of 1×10^4 particles per cubic centimeter and count mean diameter of 0.2 μm (Seinfeld and Pandis 2006). These half-lives depend on the number concentration and size of the surrounding background particles. However, the smaller UFPs that are transported downward from this elevated source spend even less time interacting with potentially higher concentrations of existing particles that occur at ground level, such as those found on or near major roadways. It is therefore not surprising that the typical size of these UFPs in the downwind footprint shown in Figure 2 are typically very small 10–30 nm, indicating minimal coagulation losses (Hudda and Fruin 2016; Hudda et al. 2014; Riley et al. 2016; Shirmohammadi et al. 2016). Furthermore, due to the consistency of daytime onshore breeze directions at LAX, the location of elevated, ground-level UFPs concentrations downwind and to the east of LAX is very stable (Hudda and Fruin 2016; Hudda et al. 2014), producing relatively large contrasts in concentrations between residences inside the area of impact in comparison with those located outside.

An interesting finding is that the effect estimates for UFPs and PTB were somewhat stronger among foreign-born Hispanic and Asian women, possibly because those women are less likely to be employed during pregnancy in comparison with U.S.-born mothers (von Ehrenstein et al. 2013, 2014); thus, they could have spent more time at their residences during pregnancy, which may have resulted in greater exposure and/or reduced exposure misclassification, which could possibly explain the stronger effect sizes we estimated. Alternatively, the foreign-born women may have been at increased risk for PTB due to decreased utilization of prenatal care (Heaman et al. 2013)—possibly driven by several barriers, including language comprehension (Edwards 1994) and access to health care (Gagnon 2004)—or working in physically demanding occupations that adversely affect birth outcomes (von Ehrenstein et al. 2013).

Several aspects of UFP could contribute to the estimated effects on PTB. Inhaled UFPs penetrate the lung mucosa and can translocate to other parts of the body because their size facilitates movement across cell barriers, entrance into the bloodstream, and relocation to distal tissues (Baldauf et al. 2016), including the placenta (Bové et al. 2019). Additionally, UFPs escape the usual clearance mechanisms by phagocytes, which remove larger particles like PM_{10} and $PM_{2.5}$ (Li et al. 2016). Murine cell–based experiments have linked UFP exposures with an increased oxidative stress response and inflammation (Li et al. 2003; Nel et al. 2001), mechanisms that have been implicated in PTB (Ferguson et al. 2015; Romero et al. 1991; Vadillo-Ortega et al. 2014). For example, at concentrations occurring in ambient Los Angeles air, one experiment found large increases in measures of oxidative stress, such as heme oxygenase expression, intracellular glutathione depletion, and reactive oxygen species generation (via dithiothreitol assay) in exposure to quasi-UFP size fractions (<0.15 μm) in comparison with fine or coarse PM fractions (Li et al. 2003). In humans, intrauterine inflammation is common in PTB (Üstün et al. 2001), and PTB is associated with an unusually large presence of proinflammatory immune cells and tumor necrosis factor-α (Romero et al. 1989).

Another important physiochemical property of UFPs that may increase their pathogenic potential is their large particle surface area. Depending on their sources, they may carry adsorbed or condensed air toxics, such as polycyclic aromatic hydrocarbons (PAHs) (Sioutas et al. 2005). In fact, UFPs are responsible for up to 30% of the PAHs deposited in the lung (Kawanaka et al. 2009). UFP plumes from aircraft emissions are highly enriched in particle-bound PAHs (Kinsey 2009) and an order of magnitude higher than background particle-bound PAH levels reported up to 6 km downwind of LAX (Hudda et al. 2014). Other research in the Los Angeles area has found that UFPs contain much

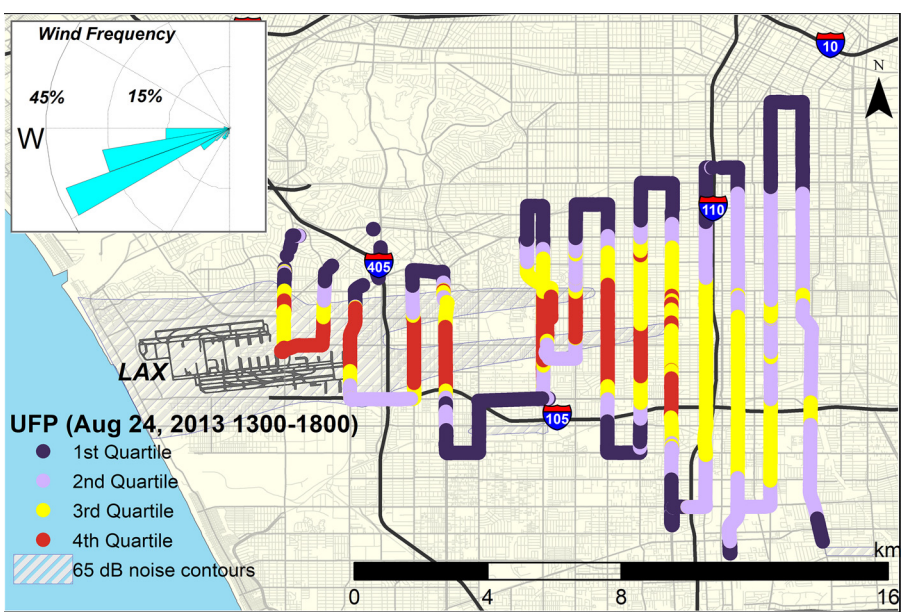

Figure 1. Measured ultrafine particles (UFP) concentrations downwind of Los Angeles International Airport (LAX) on 3 December 2013 with area above 65 decibels (dB) average noise in gray. Base layers obtained from USGS.gov (USGS 2019).

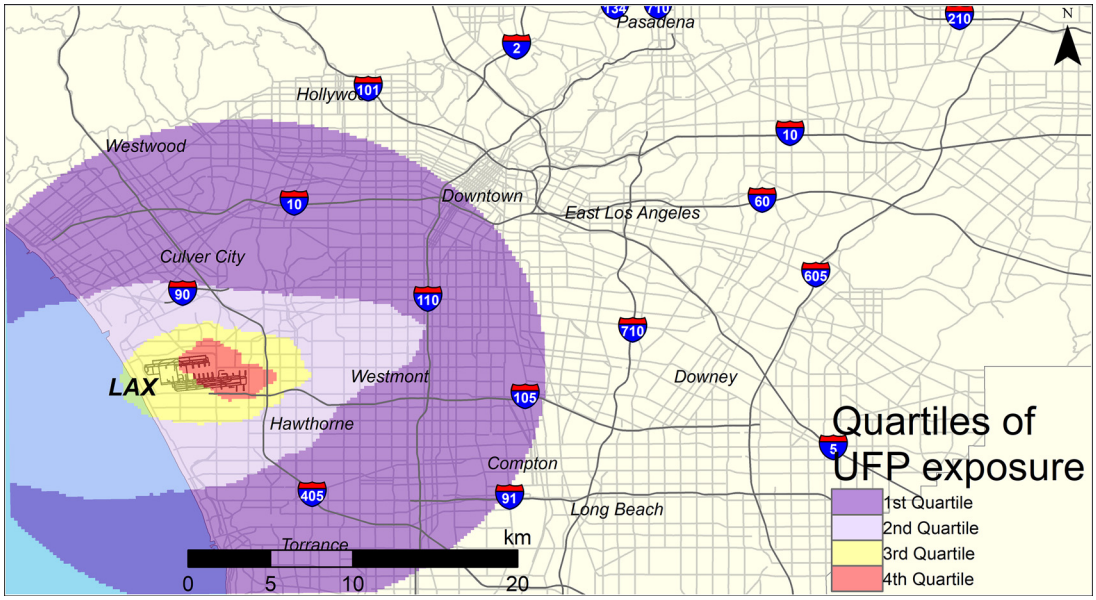

Figure 2. Estimated UFP exposure quartiles from AERMOD results. Base layers obtained from USGS.gov (USGS 2019).

higher PAH content than fine (<2.5-μm) particles and coarse (2.5–10-μm) particles (Li et al. 2003). With respect to aircraft-based PAHs, a study of emissions within the plane loading area of a major airport showed that the particle-bound PAHs were composed of ~80% high-molecular-weight compounds with high toxicity (Lai et al. 2013). Altogether, there is evidence suggesting that UFPs, especially those of aircraft-origin, carry pathogenic PAHs linked to inflammation (den Hartigh et al. 2010; Schober et al. 2007) and PTB (Wilhelm et al. 2011).

Another source of aviation emissions located in the study area is the general aviation airport SMO (~7.5 km north of LAX), but the aircraft using this airfield are smaller, using Avgas, which contains tetraethyl lead (ASTM International 2017). *In utero* lead exposure is a known cause of adverse birth outcomes (Andrews et al. 1994). To account for potential lead exposures in areas near this municipal airport, we excluded births within a 2- and 5-km distance from SMO, but this exclusion did not change our effect estimates for UFPs.

Our study has several strengths. The UFP dispersion model allowed us to assess exposure profiles in a large population encompassing tens of thousands of births. Due to the daytime wind directions at LAX being very consistent throughout the entire year, the locations at which UFP exposures occur downwind of LAX are quite stable (Hudda and Fruin 2016; Hudda et al. 2014). Such consistency allows for accurate exposure estimation at residences across the years due to improved AERMOD exposure model generalizability. Further, the outcome data were derived from birth records, reported and recorded in a uniform manner in California.

Another strength of our study is its public health importance. UFP exposures have received limited research attention, and this project addresses impacts of aircraft movements that could have profound public health impacts, given the ever-growing demand for air travel. In the United States, more than 40,000 daily flights (FAA 2017) service nearly 400 primary airports (FAA 2013). UFP emissions from these aircraft are spread across large residential areas. For example, in the United States, ~40 million people live near 89 major airports (i.e., in areas with ≥45 dB noise levels). Due to the noise from airports, many of the UFP affected areas are low nSES with especially vulnerable populations. In analyses by nSES, PTB was associated with higher levels of aircraft-origin UFP exposures only in low nSES areas (Table S8). Low nSES communities are overrepresented in housing stock located directly downwind of this highly trafficked airport. In addition, because lower household income has been shown to be inversely correlated with air conditioner use (Malig et al. 2010), the proximity might be magnifying air pollution exposures due to the opening of windows in homes lacking air conditioning, which can result in increased indoor UFP concentrations (Rim et al. 2013). Although we cannot confirm this hypothesis in our data, it is one possible explanation for this observation. Another explanation is increased susceptibility to PTB among low-nSES pregnant women, possibly due to differences in health care access.

This study has some limitations, including a semiecological exposure assessment because we are estimating UFP exposures only at the home address provided on the birth certificate, and we cannot account for time spent by mothers at work, in transit, or at other residences prior to birth. A previous study estimated that 9%–32% of mothers move during their pregnancy (Bell and Belanger 2012). We were not able to adjust for exposure to $PM_{2.5}$ in our analyses because only a single government-operated $PM_{2.5}$ monitor is located in the area of interest and does not provide spatial variation in measures. However, our adjustment for LUR modeled NO_2, a valid marker for traffic-related air pollution in the region (Su et al. 2009), helped control for spatially distinct traffic-related pollutants that may act as confounders on a fine spatial scale. Future studies of this type would benefit from greater temporal coverage of UFP measurements for dispersion model validation, perhaps via fixed monitors. Finally, our assumption of a constant per-aircraft UFP emission rate did not account for possible changes in relative emission factors over the study period. Unfortunately, adequate information to quantify historical trends for aircraft UFP emission factors is not available.

Conclusion

An increased risk of PTB was estimated with *in utero* exposure to higher concentrations of aircraft-origin UFPs in women living near LAX. Although *in utero* air pollution exposure from particulate matter—especially from traffic-related combustion sources—are known risk factors for PTB, our results suggest that emissions

from aircraft might play an independent etiological role in adverse birth outcomes. These findings are of great public health concern because UFP exposures downwind of airfields are common and may affect large densely populated residential areas.

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