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Fine Particulate Matter Metal Composition, Oxidative Potential, and Adverse Birth Outcomes in Los Angeles

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Background: Although many studies have linked prenatal exposure to $PM_{2.5}$ to adverse birth outcomes, little is known about the effects of exposure to specific constituents of $PM_{2.5}$ or mechanisms that contribute to these outcomes.

Objectives: Our objective was to investigate effects of oxidative potential and $PM_{2.5}$ metal components from non-exhaust traffic emissions, such as brake and tire wear, on the risk of preterm birth (PTB) and term low birth weight (TLBW).

Methods: For a birth cohort of 285,614 singletons born in Los Angeles County, California, in the period 2017–2019, we estimated speciated $PM_{2.5}$ exposures modeled from land use regression with cokriging, including brake and tire wear related metals (barium and zinc), black carbon, and three markers of oxidative potential (OP), including modeled reactive oxygen species based on measured iron and copper (ROS), OH formation (OP^{OH}), and dithiothreitol (DTT) loss (OP^{DTT}). Using logistic regression, we estimated odds ratios (OR) and 95% confidence intervals (CI) for PTB and TLBW with speciated $PM_{2.5}$ exposures and $PM_{2.5}$ mass as continuous variables scaled by their interquartile range (IQR).

Results: For both metals and oxidative potential metrics, we estimated increased risks for PTB (ORs ranging from 1.01 to 1.03) and TLBW (ORs ranging from 1.02 to 1.05) per IQR exposure increment that were robust to adjustment for $PM_{2.5}$ mass. Associations for $PM_{2.5}$ mass, black carbon, metal components, and oxidative potential (especially ROS and OP^{OH}) with adverse birth outcomes were stronger in Hispanic, Black, and mixed-race or Native American women.

Discussion: Our results indicate that exposure to $PM_{2.5}$ metals from brake and tire wear and particle components that contribute to oxidative potential were associated with an increased risk of PTB and TLBW in Los Angeles County, particularly among Hispanic, Black, and mixed-race or Native American women. Thus, reduction of $PM_{2.5}$ mass only may not be sufficient to protect the most vulnerable pregnant women and children from adverse effects due to traffic source exposures. https://doi.org/10.1289/EHP12196

Introduction

Numerous studies have found that fine particulate matter with aerodynamic diameter <2.5 μm ($PM_{2.5}$) is associated with adverse birth outcomes, including preterm birth (PTB) and term low birth weight (TLBW).[1] According to the State of Global Air 2020 report,[2] particulate matter (PM) air pollution worldwide contributed to nearly 20% (500,000) of deaths among neonates, with most deaths related to complications of low birth weight (LBW) and preterm birth. $PM_{2.5}$ is a heterogeneous mixture of chemical species, including sulfate, nitrate, organic and inorganic carbon, metals, and toxic organic pollutants.[3–5] The specific composition of particulate air pollution varies by PM source, location, and chemical transformations during transport in the atmosphere.[6] PM toxicity depends partly on chemical composition.[7] In the past decades, traffic exhaust has been recognized as a significant contributor to adverse birth outcomes.[8,9] Although there has been a downward trend in outdoor $PM_{2.5}$ mass concentrations in Europe and the United States,[10,11] especially in urban areas, it is important to evaluate whether exposures from certain sources pose a health risk even at low levels.[12] Meanwhile, the exhibited risk to public health at a very low level of $PM_{2.5}$ may shed light on the relative importance of non-exhaust emission sources in metropolitan areas.

Brake and tire wear are one of the primary contributors to non-exhaust emissions but are rarely addressed by regulation and technology development.[6] Multiple studies have used barium, among other metals, as a tracer of brake wear, because barium is a component of brake lining in the form of barium sulfate and is highly correlated with other metals found in brake wear.[13–15] Zinc is added to tire rubber in the form of zinc oxide, and tire wear is an important source of zinc in the environment.[15–17] Furthermore, metal components are thought to play an important role in determining health effects of $PM_{2.5}$. Specifically, metals are known to contribute to the production of reactive oxygen species (ROS), such as the hydroxyl radical (OH), superoxide (O_2^-), the hydroperoxyl radical (HO_2), hydrogen peroxide (H_2O_2), and other reactive species in humans.[18–20] Acellular oxidative potential (OP) assays, such as the OH assay and the dithiothreitol (DTT) assay, provide an integrated metric for predicting PM-induced oxidative stress which has been linked to adverse health outcomes with trace metals as important drivers of their responses.[21] With the increasing shift toward electric and hydrogen vehicles, particles from brake and tire wear will become a relatively larger constituent of the urban air pollution mixture. Nascent evidence also suggests that in disadvantaged neighborhoods the oxidative potential of the particles might be higher, suggesting potentially synergistic effects between social disadvantage and effects from brake and tire wear particles.[21] Thus, understanding the health effects from this growing exposure is critically important in guiding future policy interventions aimed at protecting public health, particularly in disadvantaged communities.

Few birth outcome studies have focused on metal components or non-exhaust traffic sources of $PM_{2.5}$, except for some studies previously conducted in California targeting $PM_{2.5}$ sources and

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components,[7–9,22–25] which based their observed associations on $PM_{2.5}$ constituent models or measurements with limited spatial resolution or insufficient data. High spatial resolution, however, is necessary to estimate the risk of adverse birth outcomes caused by variations in exposures from noncombustion traffic sources. Specifically brake and tire wear particles near roadways exhibit a high degree of spatial heterogeneity, but have not been sufficiently captured by previous combustion-focused traffic models.

In the current study, we sought to address this research gap by developing fine-scale estimates of brake and tire wear particles as well as the oxidative potential of these constituents. Specifically, we used co-kriging models based on field-monitoring campaign data combined with data from a low-cost $PM_{2.5}$ network to estimate exposures to $PM_{2.5}$ metal constituents from brake wear (barium) and tire wear (zinc) and $PM_{2.5}$ oxidative potential metrics. These models resulted in much-improved spatial resolution for the targeted $PM_{2.5}$ constituents and were found to produce more accurate predictions than a land use regression (LUR) model.[26] With these novel measures in hand, we estimated effects on adverse birth outcomes (PTB, TLBW) in Los Angeles.

Methods

Study Population

Birth certificate records for all births occurring from 1 January 2017 through 31 December 2019 in Los Angeles (LA) County, California ($N = 334{,}059$) were obtained from the California Department of Public Health. We excluded births with missing data for maternal residential address ($n = 1{,}321$) or gestational length based on the date of the last reported menses ($n = 1{,}521$), with extreme or implausible gestational ages (<20 wk or >45 wk) ($n = 8{,}425$) or birth weights (<500 g or >6,800 g) ($n = 362$), with home addresses outside of California ($n = 47$), and those that failed geocoding ($n = 72$), as well as multiple births ($n = 10{,}524$). The remaining births included 25,674 preterm births, defined as having a gestational age <37 wk, and 283,005 term normal birth weight infants (2,500–6,800 g) born between 37 and 45 wk of gestation as the reference. To examine TLBW, we identified 6,727 term births with a birth weight of <2,500 g, indicating intrauterine growth restriction, and used the same reference group of term normal birth weight infants. After further restricting to those individuals residing at time of birth within the areas covered by the exposure surfaces that we generated for Los Angeles County, 23,131 PTBs, 6,102 infants with TLBW, and 256,381 term normal birth weight infants remained for analyses. The research protocol for this study was approved by the UCLA institutional review board (IRB#10-000617).

Air Pollution Estimation

$PM_{2.5}$ sample collection and $PM_{2.5}$ constituents' measurement. Details of $PM_{2.5}$ sample collection, measurements and modeling methods were described elsewhere.[15] In brief, PM samples were collected by Harvard cascade impactors (for collecting particles of different size ranges on different substrates, in this deployment $PM_{2.5}$ and $PM_{2.5\text{-}10}$ samples were collected),[27] and $PM_{2.5}$ impactors (H-PEM, BGI Inc.) over two seasons (one in summer 2019 and the other in winter 2020). In each season monitors simultaneously collected 2-wk samples, for a total of 46 different locations composed of a mix of individual homes and government regulatory air monitoring stations in the Greater Los Angeles region.[28]

Here, we focus on $PM_{2.5}$ mass and a total of six speciated $PM_{2.5}$ exposures: two $PM_{2.5}$ metals (barium and zinc as tracers for brake and tire wear, respectively), two measures of oxidative potential by $PM_{2.5}$ using assays that measure OH formation in simulated lung fluid (OP^{OH}) and loss of dithiothreitol (DTT) in phosphate buffer (OP^{DTT}), 2-h modeled ROS based on measured concentrations of $PM_{2.5}$ iron and $PM_{2.5}$ copper, both of which are metals associated with brake and tire wear and active in oxidative potential assays (ROS), as well as black carbon, which represents the vehicle exhaust emission from incomplete combustion of fossil fuels.[21]

Barium and zinc. The Harvard cascade impactor samples we collected from our sampling sites were sent to the University of Wisconsin-Madison State Laboratory of Hygiene (WLSH) (www.slh.wisc.edu) for $PM_{2.5}$ mass and metal analysis. The mass concentrations (ng/m^3) and PM mass-normalized concentrations of 50+ chemical elements, including barium (Ba), zinc (Zn), copper (Cu), and iron (Fe), were determined by Sector Field Inductively Coupled Plasma Mass Spectrometry (SF-ICP-MS).[15] See Oroumiyeh et al.[15] for details.

Black carbon and measures of oxidative potential (OP^{OH}, OP^{DTT}). Samples from the $PM_{2.5}$ impactors (H-PEM, BGI Inc.) were used for measurement of black carbon concentrations, as well as oxidative potential including OH formation (OP^{OH}) and DTT loss (OP^{DTT}). The black carbon concentration was estimated using a Magee Scientific Optical Transmissometer. Filters were then halved and used in the OH and DTT assays, respectively.[29,30] In the OH assay, samples were incubated in surrogate lung fluid containing the OH probe, disodium terephthalate, which reacts with OH and form 2-hydroxyterephthalic acid. OH formation rate was calculated for each sample for a 2-h incubation period. The DTT assay measured the decay of DTT in phosphate buffer over a 32-min filter incubation period. DTT was quantified by its reaction with dithiobisnitrobenzoic acid, forming 2-Nitro-5-thiobenzoic acid. More details about the black carbon and oxidative potential measurements can be found in Shen et al.[21]

Modeled ROS. ROS concentrations were estimated with the kinetic multilayer model of surface and bulk chemistry in the epithelial lining fluid (KM-SUB-ELF). In brief, this model estimates ROS concentrations (i.e., OH, O_2^-, HO_2, and H_2O_2) generated by $PM_{2.5}$ Cu and $PM_{2.5}$ Fe in the epithelial lining fluid (ELF) of the human respiratory tract, using a series of mathematical formulas to describe mass transport and chemical reactions involving redox-active pollutants, antioxidants, and surfactants in the lung. The concentration of Fe and Cu ions in the ELF was estimated based on the concentrations of Fe and Cu in $PM_{2.5}$ determined by SF-ICP-MS, as described above in the metal analysis, according to the following equation:

$$ELF\ concentration = \frac{Ambient\ concentration\ of\ Fe/Cu \times Breathing\ rate \times PM\ deposition\ rate \times Fractional\ solubility \times Accumulation\ time}{MW \times Total\ ELF\ volume},$$

where MW is the molecular weight of the species, breathing rate is $1.5\ m^3/h$,[31,32] PM deposition rate is 45%,[33] and total ELF volume is 20 mL.[34,35] The fractional solubilities of Fe and Cu were assumed to be 0.1 and 0.4, respectively.[36–38] The accumulation time was set to 2 h because inhaled particles can accumulate in the respiratory tract over several hours before they are removed by the immune system and related metabolic activity. The modeled 2-h ROS concentrations represent an average exposure to ROS at the place of residency over the time of pregnancy. For a detailed description see Lakey et al.[39]

$PM_{2.5}$ mass and $PM_{2.5}$ constituents modeling. The concentrations of $PM_{2.5}$ mass and speciated $PM_{2.5}$ exposures including barium, zinc, black carbon, ROS, OP^{OH}, and OP^{DTT} were modeled at a resolution of 30×30 m using a cokriging approach, which predicts the value of an outcome of interest at a spatial location

exploiting information from direct measurements of the primary variable and measurements of auxiliary variables or covariables by modeling the spatial correlation between the two, then interpolating the primary variable over the geographic area.[26] The external drift in each cokriging model, a linear combination of predictors, was calculated based on our measurements and land use data including the 2016 National Land Cover Database,[40] 2018 traffic volume,[41] road network and rail network information,[42] and location of brake and tire wear–related businesses, such as auto repair shops.[43] We also obtained ambient $PM_{2.5}$ concentrations data between March 2019 and February 2020 (overlapping with our filter collection and avoiding major traffic disruptions associated with the COVID-19 pandemic) from 294 PurpleAir sensors (https://www2.purpleair.com) in the Greater Los Angeles region that provided publicly available monitoring data. These data were used as a secondary or auxiliary variable in the cokriging models. As shown in Liu et al.,[26] we constructed and evaluated our exposure surfaces using repeated cross-fold validation with 1,000 iterations, assessing the mean square prediction error (MSE) for each iteration, ultimately obtaining a distribution of the mean and standard deviation (SD) of prediction errors. The model performance is presented in Table S1. See Liu et al.[26] for further details.

$PM_{2.5}$ mass and $PM_{2.5}$ constituents' assessments. After geocoding maternal address of residence as recorded on birth certificates, we estimated each mother's average exposures to $PM_{2.5}$ mass, black carbon, metals (barium, zinc), measures of oxidative potential (OP^{OH} and OP^{DTT}), and ROS by overlaying the cokriging surfaces onto the geocoded addresses. $PM_{2.5}$ mass was predicted as micrograms per cubic meter, and all of the speciated $PM_{2.5}$ components except for ROS were predicted as normalized concentrations according to $PM_{2.5}$ mass per volume (ng/m^3 for barium and zinc, $\mu g/m^3$ for black carbon, $pmol/min/m^3$ for OH formation and DTT loss). ROS were treated as continuous measures in nanomoles per liter. The surfaces for the six speciated $PM_{2.5}$ exposures as well as for $PM_{2.5}$ mass vary spatially only, i.e., we used the same surfaces in every year for the entire pregnancy periods in our study population (i.e., 2017–2019). The surfaces represent long-term spatial patterns and approximate annual average concentration distributions rather than specific concentration levels, which are expected to be maintained despite year-to-year changes in land use, meteorology, and other factors.[44,45] Thus, we are estimating exposure levels based on spatial contrasts only; therefore a birth in 2017 and a birth in 2019 would be assigned the same exposures if the mothers lived in the same spatially defined area.

Traffic exhaust–related air pollutant assessments. We also assessed the effect of traffic-related exposures of NO_2 concentrations on PTB and TLBW using an LUR model for combustion emissions. The modeling methods were described elsewhere.[46,47] In brief, 201 locations were selected using a location-allocation algorithm that considered variability in traffic pollution and the spatial distribution of the Los Angeles population. In two seasons during September 2006 and February 2007, samplers from Ogawa & Company USA, Inc. were placed at preselected sampling sites. In 2012 October and 2013 March, Ogawa monitors were redeployed to measure NO_2 at a total of 72 sites selected from the 201 locations across Los Angeles County. Routine government monitoring data from California Air Resources Board (CARB) for NO_2 were also included to provide a temporal dimension to the exposures derived from the LUR models. The LUR estimates for each address were predicted based on traffic volumes, truck routes, and road networks, as well as land use data for the relevant years. A machine-learning algorithm was used to select variables that optimally predicted out-of-sample measured values via a v-fold cross-validation technique. The LUR model for NO_2 had a cross-validation r-square of 0.78.

We applied the year specific LUR surfaces for 2019 to generate annual NO_2 estimates for each woman's pregnancy in this study by residence, in a process similar to that used to assign PM exposures.

Covariates

Potential confounders were selected based on previous literature.[7–9,22–25,48,49] We obtained information from the birth certificate records, including fetal sex (female, male), maternal age (<20, 20–24, 25–29, 30–35, >35), maternal race/ethnicity (non-Hispanic White, Hispanic or Latinx of any race, Black, Asian or Pacific Islander, multirace or other), maternal educational attainment (≤8th grade, 9th–12th grade, high school diploma, college credits but no degree or associate's degree, bachelor's degree or more), maternal birthplace (US-born, foreign-born), parity (1, 2, ≥3), maternal smoking during pregnancy (yes, no) and payment source for prenatal care (no prenatal care, private insurance, MediCal or government or self-pay, other), the latter as a proxy for family income.

Statistical Analyses

We calculated Pearson correlations for average $PM_{2.5}$ mass, speciated $PM_{2.5}$ exposures (metals, black carbon, and oxidative potential metrics), and LUR-NO_2 during pregnancy. For comparability across pollutants, we scaled each exposure concentration according to its interquartile range (IQR) among noncases, i.e., births with term normal birth weight. To further evaluate potential nonlinear exposure–outcome responses, we also fitted restricted cubic spline models with 4 knots equally spaced at the 5th, 35th, 65th, and 95th percentile of the speciated $PM_{2.5}$ exposures values on PTB or TLBW. We also allowed for higher flexibility (5 knots) in the spline models, but because results did not change substantially, we employed 4 knots to avoid overfitting.

We conducted unconditional logistic regression analyses to estimate odds for PTB and TLBW per IQR increase of entire pregnancy exposures of $PM_{2.5}$ mass, speciated $PM_{2.5}$ constituents, or modeled or measured oxidative potential, respectively. We adjusted for fetal sex, parity, maternal age, maternal race/ethnicity, maternal birthplace, payment source for prenatal care, maternal education, and maternal smoking (for the definitions of the categories, see above). Furthermore, we also estimated effects while adjusting for combustion-related traffic emissions, relying on the traffic-related NO_2 LUR model for Los Angeles County. Given the profound racial disparities found in adverse birth outcomes[50] and no consensus on whether maternal race/ethnicity or socioeconomic status (SES) factors modify the association between PM exposure during pregnancy and birth outcomes,[51] we conducted analyses stratified by maternal race/ethnicity and maternal education as one of the proxies for SES to evaluate potential effect measure modification. Tests for heterogeneity (multiplicative scale) were performed by assessing the p-value of the interaction term for the exposure and the potential effect modifier. In addition, we also conducted stratified analyses by fetal sex considering differences in PTB and TLBW by fetal sex as shown in Table 1.

In sensitivity analyses we categorized births according to gestational week beyond term/preterm and estimated the odds for very PTB (<32 gestational weeks). Meanwhile, to better control for the role of gestational age beyond term, we also evaluated the association between continuous birth weight (g) and air pollutants among the term births while adjusting for gestational age (days). We also conducted a sensitivity analysis restricting to 2019 births only, i.e., the births after pregnancies covered best by our monitoring campaign. Considering the collinearity between $PM_{2.5}$ mass and the metal tracers for brake and tire wear, we also compared volume-normalized vs. $PM_{2.5}$ mass–normalized results. In addition, to further control for any unmeasured confounders

Table 1. Characteristics of the cases of PTB, TLBW, and term normal birth weight infants born in Los Angeles County, California, 2017–2019.

Characteristics	PTB ($n = 23,131$) *n* (%)	TLBW ($n = 6,102$) *n* (%)	Term normal birth weight ($n = 256,381$) *n* (%)
Infant sex			
Male	12,818 (55.4)	2,585 (42.4)	131,290 (51.2)
Female	10,313 (44.6)	3,517 (57.6)	125,091 (48.8)
Year of birth			
2017	7,886 (34.1)	2,132 (34.9)	91,068 (35.5)
2018	7,194 (31.1)	2,014 (33.0)	84,177 (32.8)
2019	8,051 (34.8)	1,956 (32.1)	81,136 (31.7)
Maternal age (y)			
<20	954 (4.1)	299 (4.9)	9,395 (3.7)
20–24	3,304 (14.3)	985 (16.1)	37,971 (14.8)
25–29	5,228 (22.6)	1,442 (23.6)	63,736 (24.9)
30–35	6,604 (28.6)	1,763 (28.9)	78,352 (30.6)
>35	7,041 (30.4)	1,613 (26.4)	66,927 (26.1)
Maternal education			
≤8th grade	1,261 (5.6)	264 (4.4)	10,027 (4.0)
9th–12th grade	3,189 (14.1)	697 (11.7)	27,086 (10.8)
High school diploma	6,104 (27.1)	1,601 (26.8)	60,794 (24.2)
College credits but no degree or associate's degree	6,006 (26.6)	1,528 (25.6)	64,257 (25.6)
Bachelor's degree or more	5,993 (26.6)	1,874 (31.4)	88,767 (35.4)
Missing	578	138	5,450
Maternal race/ethnicity			
White, non-Hispanic	2,863 (12.5)	762 (12.7)	45,503 (18.0)
Hispanic/Latinx of any race	14,314 (62.7)	3,265 (54.3)	141,002 (55.7)
Black	1,920 (8.4)	636 (10.6)	15,094 (6.0)
Asian/Pacific islander	2,464 (10.8)	870 (14.5)	34,548 (13.7)
Other[a]/multirace, non-Hispanic status	1,267 (5.6)	484 (8.0)	16,839 (6.7)
Not stated or unknown	303	85	3,395
Parity			
1	9,005 (39.0)	3,164 (51.9)	106,389 (41.5)
2	6,560 (28.4)	1,562 (25.6)	83,683 (32.7)
3 or more	7,548 (32.7)	1,371 (22.5)	66,210 (25.8)
Missing	18	5	99
Payment type of prenatal care			
No prenatal care	362 (1.6)	55 (0.9)	810 (0.3)
MediCal/Government/self-pay	12,938 (56.1)	3,319 (54.5)	132,747 (51.9)
Private	9,344 (40.5)	2,591 (42.6)	117,304 (45.8)
Other	419 (1.8)	125 (2.1)	5,146 (2.0)
Missing	68	12	374
Maternal birthplace			
U.S. born	13,629 (58.9)	3,692 (60.5)	149,462 (58.3)
Foreign born	9,496 (41.1)	2,409 (39.5)	106,894 (41.7)
Missing	6	1	25
Smoking during pregnancy			
Yes	175 (0.8)	50 (0.8)	930 (0.4)
No	22,432 (99.2)	5,922 (99.2)	251,589 (99.6)
Missing	524	130	3,862

Note: Data source: birth certificate records for all births occurring from 1 January 2017 through 31 December 2019 in Los Angeles (LA) County, California, which were obtained from the California Department of Public Health. Preterm birth was defined as having a gestational age <37 wk, and term normal birth weight was defined as infants born between 37 and 45 wk of gestation with a birth weight of 2,500–6,800 g. TLBW was defined as infants born between 37 and 45 wk of gestation with a birth weight of <2,500 g. PTB, preterm birth; TLBW, term low birth weight.

[a]"Other" included American Indian, Asian Indian, Eskimo, Aleut, and all that reported their race/ethnicity as "Other".

related to the spatial clusters, we conducted a hierarchical logistic regression model by adding a random intercept for Service Planning Area[52] as a spatial cluster indicator variable.

Considering the low percentage of missing values for all covariates used for confounder adjustment in our models, we conducted complete-case analyses. Statistical significance was determined based on 2-tailed *p*-values with a significance level of 0.05. Analyses were performed using SAS (version 9.4; SAS Institute Inc.) and STATA (version 14; StataCorp).

Results

Characteristics of Study Population

Study population characteristics are summarized in Table 1. More than half (55%, $n = 157,125$) of the mothers were 25–35 y of age, and almost 60% ($n = 168,425$) had more than a high school education; more than half (55%, $n = 158,581$) identified as Hispanic/Latinx, and ~40% ($n = 118,799$) were born in foreign countries; 45% ($n = 129,239$) were covered by private insurance and the remaining mostly by government programs providing medical care to low-income populations. Very few (<1%, $n = 1,155$) mothers included reported smoking during pregnancy. Demographics for the mothers whom we excluded due to missing residential address and/or gestational length data are shown in Table S2. In addition to the dichotomous PTB, we also showed demographics distributions for births according to gestational weeks in Table S3.

Pregnancy Exposures

Summary statistics, including mean, SD, and quartiles for all exposures included in our study, are presented in Table 2. For

Table 2. Distributions of air pollution exposures among 285,614 singleton births in Los Angeles County, California, 2017–2019.

Air pollutants	Unit	PTB ($n = 23,131$)						TLBW ($n = 6,102$)						Term normal birth weight ($n = 256,381$)					
		No. of births	Mean ± SD	25th percentile	75th percentile	Min	Max	No. of births	Mean ± SD	25th percentile	75th percentile	Min	Max	No. of Births	Mean ± SD	25th percentile	75th percentile	Min	Max
$PM_{2.5}$ mass	$\mu g/m^3$	22,944	10.1 ± 1.0	9.4	10.9	3.1	15.5	6,053	10.0 ± 1.1	9.4	10.9	3.3	15.0	254,594	10.0 ± 1.1	9.3	10.8	2.7	15.7
Black carbon	$\mu g/m^3$	23,131	0.4 ± 0.1	0.4	0.5	0.0	1.0	6,102	0.4 ± 0.1	0.4	0.5	0.0	1.0	256,381	0.4 ± 0.1	0.4	0.5	0.0	1.1
Barium	ng/m^3	23,131	17.3 ± 3.9	14.7	20.1	0.0	34.4	6,102	17.4 ± 4.0	14.7	20.2	0.0	33.7	256,381	17.1 ± 3.9	14.5	19.8	0.0	35.2
Zinc	ng/m^3	23,131	9.8 ± 1.8	8.8	11.1	0.0	16.9	6,102	9.8 ± 1.7	8.7	11.1	0.0	16.2	256,381	9.7 ± 1.7	8.7	11.0	0.0	16.9
ROS	nmol/L	23,131	1,13.7 ± 11.8	105.7	121.3	49.8	164.3	6,102	114.0 ± 12.2	105.7	121.7	53.2	162.7	256,381	113.5 ± 12.1	105.1	121.3	44.3	169.7
OP^{OH}	$pmol/min/m^3$	23,131	5.6 ± 1.2	4.9	6.5	0.8	10.0	6,102	5.6 ± 1.2	4.9	6.5	0.8	10.1	256,381	5.5 ± 1.2	4.8	6.4	0.5	10.2
OP^{DTT}	$pmol/min/m^3$	23,131	613.0 ± 115.4	536.0	681.0	163.6	1,333.2	6,102	615.2 ± 119.3	533.9	684.6	208.8	1,210.6	256,381	609.1 ± 1,16.4	527.5	677.2	138.4	1,497.8
LUR-NO_2	ppb	23,131	17.2 ± 4.6	14.2	20.1	1.4	44.1	6,102	17.0 ± 4.6	14.1	19.8	1.3	41.0	256,381	16.8 ± 4.6	13.8	19.6	1.4	43.0

Note: PTB was defined as having a gestational age <37 wk, and term normal birth weight was defined as infants born between 37 and 45 wk of gestation with a birth weight of 2,500–6,800 g. TLBW was defined as infants born between 37 and 45 wk of gestation with a birth weight of <2,500 g. CI, confidence interval; DTT, dithiothreitol; IQR, interquartile range; LUR, land use regression Max, maximum; Min, minimum; No., number; OH, hydroxyl radical; OP, oxidative potential; OP^{DTT}, DTT loss; OP^{OH}, OH formation; OR, odds ratio; ppb, parts per billion; PTB, preterm birth; Ref, reference; ROS, modeled reactive oxygen species based on measured iron and copper; SD, standard deviation; TLBW, term low birth weight.

most of the exposures, the means among cases (PTB or TLBW) were slightly higher than among noncases. The exposure estimates for $PM_{2.5}$ mass were moderately to highly correlated with speciated $PM_{2.5}$ exposures (Pearson $r = 0.3$–0.9) as expected, and the correlations were similar among cases and noncases (Figure S1). Specifically, among the noncases, the Pearson correlation coefficients for $PM_{2.5}$ mass with black carbon were the highest ($r = 0.9$) followed by the brake and tire wear tracer metals (barium and zinc with $r = 0.7$ and $r = 0.8$, respectively). In contrast, the correlations of oxidative potential metrics and $PM_{2.5}$ mass were lower than for the $PM_{2.5}$ metal constituents (ROS and OP^{DTT} with $r = 0.3$ and $r = 0.4$, respectively) except for OP^{OH} ($r = 0.7$). The markers of brake and tire wear, barium, and zinc were highly correlated with each other as expected and correlated moderately to highly with oxidative potential metrics and black carbon. The oxidative potential metrics were also highly correlated with each other (ranging from 0.6 to 0.8). Correlations of black carbon and oxidative potential metrics were weak except for OP^{OH}. The correlation coefficients for NO_2 with $PM_{2.5}$ mass or speciated $PM_{2.5}$ exposures were weak to moderate (Pearson $r = 0.2$–0.5).

Association between pregnancy exposures and PTB/TLBW. We estimated increases in the odds with almost all speciated $PM_{2.5}$ exposures for PTB (ORs ranging from 1.01 to 1.03) and TLBW (ORs ranging from 1.02 to 1.05) per IQR exposure increment (Figure 1; Table S4). The effect estimates for $PM_{2.5}$ mass and PTB (OR = 1.04; 95% CI: 1.02, 1.06) were not very different from those for the speciated $PM_{2.5}$ and oxidative potential metrics. The effect estimates for most of the speciated $PM_{2.5}$ exposures as well as $PM_{2.5}$ mass and very PTB were stronger than PTB (Table S5). For TLBW, the OR of $PM_{2.5}$ mass (OR = 1.01; 95% CI: 0.98, 1.05) was weaker than the speciated $PM_{2.5}$ and oxidative potential metrics per IQR increment (Table S4). When evaluating birth weight as a continuous variable, we found each IQR exposure increment was associated with a reduction in birth weight ranging from 1.87 g to 6.86 g; the associations were stronger when additionally adjusting for gestational age in days, with a decrease in birth weight ranging from 3.71 g to 8.30 g per IQR increase in exposure (Table S6).

When adjusting each of the speciated $PM_{2.5}$ exposure regression models for $PM_{2.5}$ mass exposure (Model B in Table S4), the ORs for PTB and most of the speciated $PM_{2.5}$ exposures moved toward the null or became null, but we still observed small positive associations for barium, zinc, ROS, and OP^{OH} [ORs 1.02 (95% CI: 0.99, 1.04); 1.01 (95% CI: 0.98, 1.05); 1.01 (95% CI: 0.99, 1.03) and 1.02 (95% CI: 0.99, 1.04), respectively]. Associations for black carbon and PTB were null with $PM_{2.5}$ mass adjustment, which may partly reflect the high correlations between the two measures. For TLBW, ORs associated with each IQR increment of the speciated $PM_{2.5}$ exposures were slightly higher after adjusting for the modeled $PM_{2.5}$ mass exposures. Specifically, associations were stronger for speciated $PM_{2.5}$ exposures with ORs ranging from 1.04 to 1.09. LUR-NO_2 reflecting combustion-related traffic exposures during pregnancy were associated with both PTB (OR = 1.03; 95% CI: 1.01, 1.05) and TLBW (OR = 1.02; 95% CI: 0.98, 1.06) per IQR increment, albeit the latter was not statistically significant (Table S4). When adjusting each model for speciated $PM_{2.5}$ exposures for LUR-NO_2, effect estimates changed little or only decreased slightly. In addition, the effect estimates for NO_2 exposure during pregnancy were stable when additionally adjusted for $PM_{2.5}$ or each of the speciated $PM_{2.5}$ exposures (Table S7).

The spline models suggested generally a monotonic exposure response for most exposures, with some minor nonlinearities detected (Figure 2; Figure S2). The estimated odds for PTB (Figure 2) were not increasing for $PM_{2.5}$ mass, black carbon, and

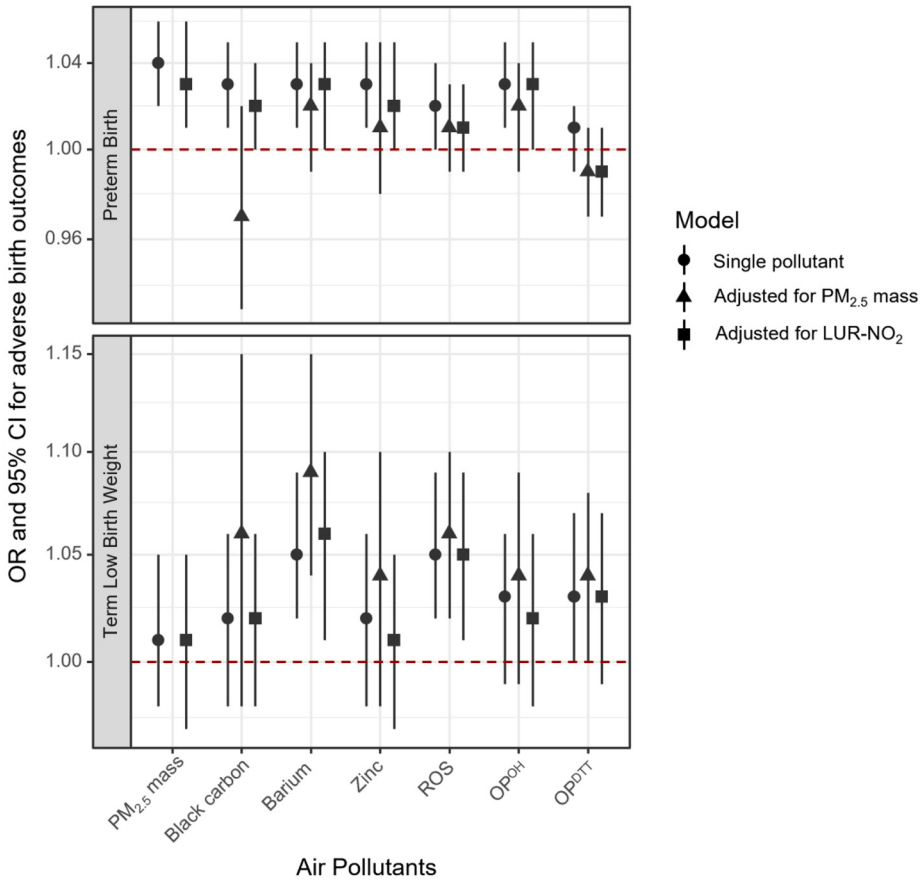

Figure 1. ORs and 95% CIs from unconditional logistic regression models for adverse birth outcomes according to per- IQR increase in exposure to air pollutants during pregnancy among 285,614 singleton births in Los Angeles County, California, 2017–2019. Model adjusted for fetal sex, parity, maternal age, maternal race/ethnicity, maternal birthplace, payment source for prenatal care, maternal education, and maternal smoking. The points show the ORs for PTB and TLBW per IQR increase in exposures to air pollutants during pregnancy. Error bars represent the lower and upper bound of the 95% CIs for each point estimate. Different shapes of the points represent the different models as shown in the legend. The dashed lines represent the reference of the null effect (OR = 1.00). Data are provided in Table S4. Note: CI, confidence interval; DTT, dithiothreitol; IQR, interquartile range; LUR, land use regression; OP^{DTT}, DTT loss; OP^{OH}, hydroxyl radical (OH) formation; OR, odds ratio; TLBW, term low birth weight; PTB, preterm birth; ROS, modeled reactive oxygen species based on measured iron and copper.

tracer metals (barium and zinc) before we reached the mid-exposure ranges; however, for the $PM_{2.5}$ oxidative potential metrics (ROS, OP^{OH}) elevated OR point estimates for PTB were estimated already at the lower exposure range and were relatively constant at higher ranges. The effect estimates of PTB with OP^{DTT} showed a fairly flat pattern throughout the exposure range. Similar patterns were also found for TLBW except for OP^{OH} and OP^{DTT}, for which increasing odds only appeared in the higher exposure range (Figure S2).

In the sensitivity analysis for 2019 births only, the ORs for $PM_{2.5}$ mass and speciated exposures on PTB and TLBW among 2019 births are very similar (slightly higher) than the ones for 2017–2019 births, and the effect estimates were consistent after coadjusting for $PM_{2.5}$ mass or NO_2 for each of the pollutants modeled (Table S8). We compared volume-normalized vs. $PM_{2.5}$ mass–normalized results, and although the effect estimates for $PM_{2.5}$ mass-normalized metals were null for PTB and TLBW, except for zinc and TLBW, the oxidative potential metrics still showed robust effects for both PTB and TLBW, as we might have expected due to the low correlations (Table S9). The effect estimates of air pollutants on both PTB and TLBW also changed minimally after adding a random intercept for a spatial cluster indicator[52] (Table S10).

Stratification by maternal education, race/ethnicity, and fetal sex. In analyses stratified by maternal education, the PTB/TLBW effect estimates for each of the speciated exposures did not differ much by higher levels of maternal education (high school graduate or higher level) (Table S11). Although most of the interaction *p*-values were large (>0.05), we did, however, estimate stronger effects for these outcomes and most of the speciated exposures among mothers with lower education (9th–12th grade), although these associations were weak for PTB and null for TLBW among mothers with an 8th-grade or less education.

Depending on the outcome, analyses stratified by maternal race/ethnicity suggested stronger effects per IQR increase for most of the speciated $PM_{2.5}$ exposures for mothers with Hispanic, Black, Asian/Pacific Islander race/ethnicity; for non-Hispanic White women we estimated null effects for most of the speciated $PM_{2.5}$ exposures and both outcomes, PTB and TLBW (Tables 3 and 4). This difference may be due to the lower levels of speciated $PM_{2.5}$ exposures among non-Hispanic White women (Table S12). However, interaction term *p*-values for race/ethnicity and most of the speciated exposure measures were relatively large (>0.05), suggesting that these differences might be due to random fluctuation and limited sample size, given the small estimated effect sizes for air pollutants and adverse birth outcomes. In Hispanic mothers, the effect estimates were increased for both outcomes, whereas for Black mothers, the increased odds were mainly seen for preterm birth, and in Asian/Pacific Islander mothers for TLBW. For Asian/Pacific islanders and other or multiple race groups, the highest odds increases were estimated for TLBW with exposures to $PM_{2.5}$

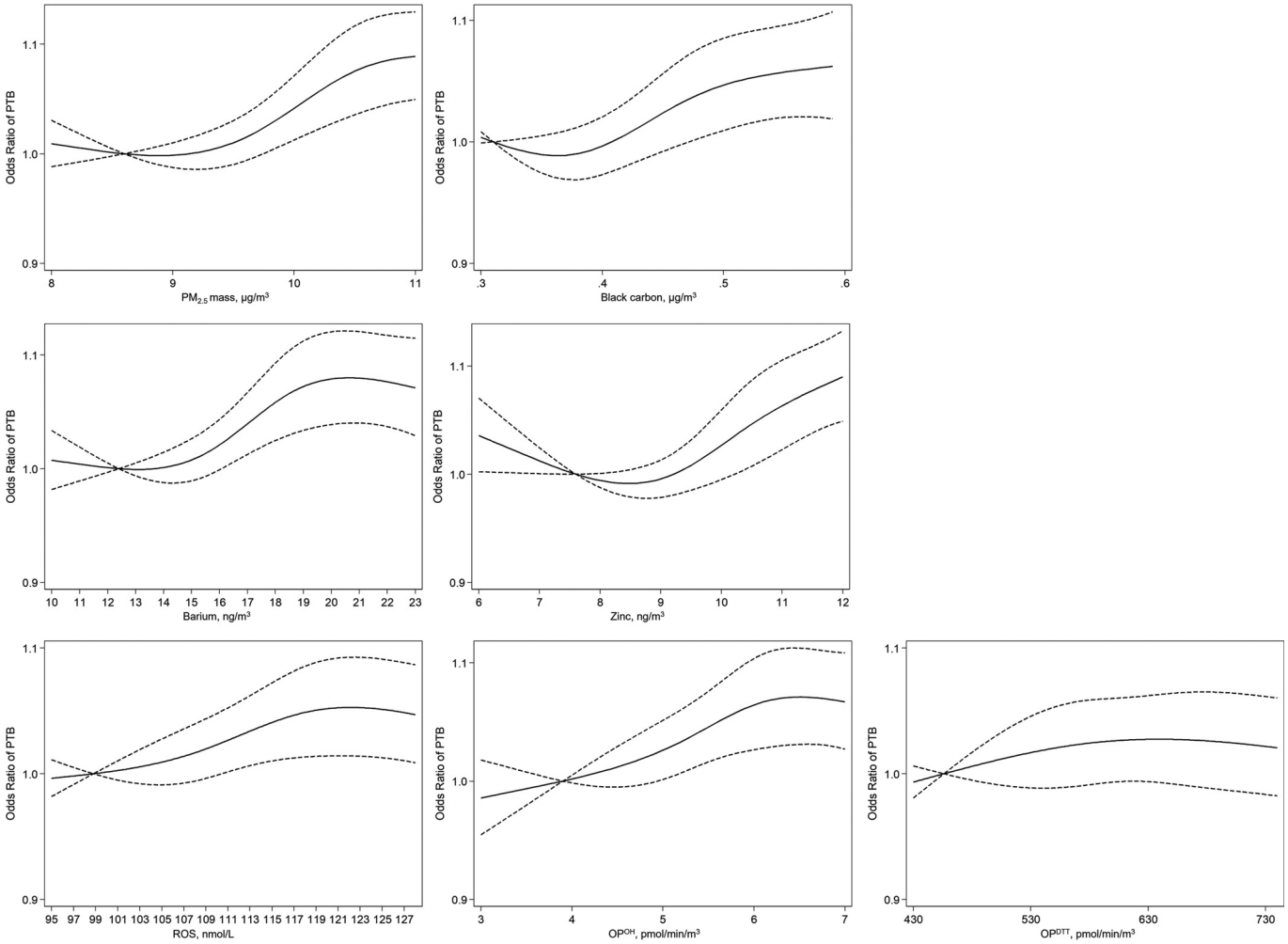

Figure 2. OR and 95% CIs for PTB among 279,512 singleton births in Los Angeles County, California, 2017–2019, according to continuous air pollution exposures values using a restricted cubic spline regression model with 4 knots at the fifth, 35th, 65th, and 95th percentiles. Model adjusted for fetal sex, parity, maternal age, maternal race/ethnicity, maternal birthplace, payment source for prenatal care, maternal education, and maternal smoking. The solid lines represent the ORs for PTB, and the dashed lines represent 95% CIs for the spline model (reference is the 10th percentile of each air pollutant level). Data are provided in Table S14. Note: CI, confidence interval; DTT, dithiothreitol; OP, oxidative potential; OP^{DTT}, DTT loss; OP^{OH}, hydroxyl radical (OH) formation; OR, odds ratio; PTB, preterm birth; ROS, modeled reactive oxygen species based on measured iron and copper.

oxidative potentials (ROS, OP^{OH}, and OP^{DTT}), although for some of the effect estimates the 95% CIs included the null.

When stratifying by fetal sex, stronger effects were estimated for the modeled air pollutants on TLBW among boys, whereas slightly stronger effect estimates were observed in girls for PTB, but interaction term *p*-values were large (Table S13).

Discussion

We observed positive associations between two adverse birth outcomes, PTB and TLBW, and markers of metals from brake wear (barium) and tire wear (zinc) and oxidative potential metrics for fine PM. For TLBW most of these estimated effects were not affected by coadjustment for $PM_{2.5}$ mass exposure measures, suggesting that these PM components and the oxidative potential of the mixture is associated with fetal growth independently of other components represented by mass. In addition, we observed stronger effect estimates for tracer metals and markers of oxidative potential in Hispanic, Black, Asian, and other non-White populations when stratifying by maternal race/ethnicity. In fact, we found no associations between exposures and birth outcomes in White mothers.

Speciated $PM_{2.5}$ exposures (barium and zinc) and black carbon were most strongly correlated with $PM_{2.5}$ mass, which may explain why some of the effect estimates for PTB decreased or became null after adjustment. We still, however, observed the associations between $PM_{2.5}$ metals/oxidative potential metrics and TLBW after adjusting for the $PM_{2.5}$ mass exposure measure. Given that the correlations among the different $PM_{2.5}$ exposures do not differ by outcome, the decreased or null effect estimates for PTB might suggest stronger effects of metals and OP that are independent from $PM_{2.5}$ mass on TLBW than PTB. Barium and zinc are good tracers for brake and tire-wear particle mixtures, respectively, but generally these metals are not redox-active metals and would not be expected to be active in OP assays.[53,54] Iron and copper, which are active in OP assays, are also common tracers for brake wear and are associated with oxidative stress.[15] Thus, barium and zinc may act indirectly or simply be indicators of the action of other metals, such as iron and copper, from brake and tire wear. Furthermore, the robust effect estimates for volume-normalized and $PM_{2.5}$ mass–normalized OP exposures were as would be expected due to the low correlations with $PM_{2.5}$ mass.

Oxidative stress, which can cause or be a consequence of increased inflammation, is one of the main hypothesized mechanisms through which air pollution such as $PM_{2.5}$ may cause adverse pregnancy outcomes.[55,56] Maternal air pollution exposure may

Table 3. ORs and 95% CIs from unconditional logistic regression models for PTB according to air pollution exposures during pregnancy, stratified by maternal race/ethnicity, among 275,814 singleton births in Los Angeles County, California, 2017–2019.

		Preterm birth									
		White, non-Hispanic ($n = 48,366$)		Hispanic/Latinx of any race ($n = 155,316$)		Black ($n = 17,014$)		Asian/Pacific Islander ($n = 37,012$)		Other[a] ($n = 18,106$)	
Air pollutants	Unit (IQR)	OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]
$PM_{2.5}$ mass	1.5 $\mu g/m^3$	0.98 (0.93, 1.03)	Ref	1.06 (1.03, 1.09)	0.01	1.08 (0.98, 1.18)	0.03	0.99 (0.94, 1.04)	0.96	1.07 (1.00, 1.16)	0.06
Black carbon	0.1 $\mu g/m^3$	0.96 (0.90, 1.01)	Ref	1.05 (1.02, 1.07)	0.01	1.07 (0.98, 1.17)	0.02	0.98 (0.92, 1.03)	0.84	1.07 (0.98, 1.17)	0.06
Barium	5.3 ng/m^3	0.99 (0.94, 1.04)	Ref	1.04 (1.01, 1.07)	0.23	1.01 (0.94, 1.09)	0.81	1.02 (0.95, 1.08)	0.94	1.07 (0.99, 1.16)	0.21
Zinc	2.3 ng/m^3	0.99 (0.94, 1.04)	Ref	1.04 (1.02, 1.07)	0.14	1.08 (1.00, 1.16)	0.07	0.99 (0.93, 1.05)	0.34	1.06 (0.98, 1.15)	0.22
ROS	16.2 nmol/L	0.98 (0.94, 1.03)	Ref	1.03 (1.00, 1.05)	0.21	0.97 (0.90, 1.04)	0.47	1.02 (0.96, 1.08)	0.54	1.05 (0.97, 1.13)	0.17
OP^{OH}	1.6 $pmol/min/m^3$	0.99 (0.94, 1.04)	Ref	1.04 (1.01, 1.06)	0.17	1.05 (0.98, 1.13)	0.21	1.01 (0.95, 1.07)	0.93	1.06 (0.99, 1.15)	0.17
OP^{DTT}	149.7 $pmol/min/m^3$	0.99 (0.94, 1.04)	Ref	1.01 (0.98, 1.03)	0.68	0.99 (0.92, 1.06)	0.75	1.01 (0.95, 1.07)	0.73	1.00 (0.93, 1.07)	0.92

Note: Preterm birth was defined as having a gestational age <37 wk, term normal birth weight was defined as infants born between 37 and 45 wk of gestation with a birth weight of 2,500–6,800 g. The IQR were based on the 75th and 25th percentiles of each air pollutant among births with term normal birth weight. CI, confidence interval; DTT, dithiothreitol; IQR, interquartile range; LUR, land use regression; Max, maximum; Min, minimum; OH, hydroxyl radical; OP, oxidative potential; OP^{DTT}, DTT loss; OP^{OH}, OH formation; OR, odds ratio; PTB, preterm birth; Ref, reference; ROS, modeled reactive oxygen species based on measured iron and copper.

[a]"Other" included American Indian, Asian Indian, Eskimo, Aleut, and mothers who reported their race/ethnicity as "Other", as well as multirace/ethnicities.

[b]Adjusted for fetal sex, parity, maternal age, maternal birthplace, payment source for prenatal care, maternal education, and maternal smoking. Tests of heterogeneity were conducted based on 2-tailed p-values with a significance level of 0.05 for the product term of the continuous exposure variable and each of the binary potential effect modifier in the regression model.

affect pregnancy by inducing oxidative stress and systemic inflammation, in turn causing suboptimal placentation or placental inflammation.[57] In addition, redox-active metals from $PM_{2.5}$ have been reported to induce excessive production of ROS, which leads to an increased level of oxidative stress and proinflammatory effects.[58] Furthermore, air pollution exposures have also been associated with pregnancy complications such as preeclampsia,[59] which is a major contributor to PTB and thought to have its origin largely in abnormal early placentation. Specifically, the impaired trophoblastic invasion is theorized to cause maladaptation of uteroplacental arteries and reduced uteroplacental perfusion leading to maternal and fetal complications.[60]

As shown in Table S1, among the births we excluded due to missing residential address and/or gestational length data, there were more women with race/ethnicity of Black, lacking prenatal care, and smoking during pregnancy. In addition, the mean birth weight for excluded births is lower (3,150.8 g vs. 3,290.7 g for all births we included). Assuming excluded women are at higher risk for adverse birth outcomes—at least in terms of birth weight—and are also of lower SES (according to payment method of prenatal care and higher percentage without prenatal care), this exclusion would likely induce bias toward the null for the effect estimates if these women also experienced higher levels of air pollution.

When stratifying by maternal education, we estimated somewhat stronger effects for most of the speciated exposures and PTB and TLBW among mothers with 9th–12th grade education, but weaker and null associations for PTB and TLBW among mothers with an 8th-grade or lower education, even though the interaction p-value is not formally statistically significant. The null association may be explained by the healthy immigrant effects.[61] Specifically, it may represent better health status, better nutrition, lower rates of smoking and alcohol consumption, or a more supportive social environment among low-acculturated foreign-born immigrants mostly from Mexico, because mostly Mexican women (90%, $n = 10,660$) with little formal education make up this group of immigrants.[62]

When stratifying by maternal race/ethnicity, stronger associations were generally observed for both outcomes among Hispanic women, who made up the majority of births, as well as among women in the heterogenous group of other races and mixed race/ethnicity. We saw stronger associations with measures of brake and tire wear and oxidative potential only for PTB in Black women and only for TLBW in Asian American/Pacific Islander women. Many of the positive effect estimates, however, had wide 95% CIs because these subgroup analyses had reduced statistical power. Thus, our results suggest either greater vulnerability of these women or higher exposures, including the possibility that indoor air quality is more strongly affected by housing characteristics such as a lack of air filtration or air conditioning and higher infiltration of pollutants indoors in lower income neighborhoods with a higher proportion of minorities.[63] The spatial clustering of women by race/ethnicity in Los Angeles is depicted in Figure S3. Furthermore, stronger clustering in just one area, such as observed for Black women, reduces exposure contrasts and our ability to estimate effects, even if exposures are larger on average as shown by the highest means and lowest SDs that we observed among Black women for most $PM_{2.5}$ component exposures (Table S12). In support of this argument, we estimated increased risks for both outcomes in the much smaller group of "Other" races that included multiracial parents whose residences were generally quite dispersed throughout Los Angeles County, with exposures contrasts similar to those in Hispanic and White women. Finally, it has been suggested that Black women have a higher baseline risk for adverse birth outcomes due to limited social support,[64] which may result in

Table 4. ORs and 95% CIs from unconditional logistic regression models for TLBW according to air pollution exposures during pregnancy, stratified by maternal race/ethnicity, among 259,003 singleton births in Los Angeles County, California, 2017–2019.

Air pollutants	Unit (IQR)	White, non-Hispanic ($n=46,265$)		Hispanic of any race ($n=144,267$)		Black ($n=15,730$)		Asian/Pacific Islander ($n=35,418$)		Others[a] ($n=17,323$)	
		OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]	OR (95% CI)[b]	Interaction p-value[b]
$PM_{2.5}$ mass	1.5 μg/m^3	0.94 (0.86, 1.03)	Ref	1.04 (0.99, 1.10)	0.07	1.04 (0.90, 1.21)	0.09	0.95 (0.87, 1.04)	0.87	1.02 (0.91, 1.15)	0.38
Black carbon	0.1 μg/m^3	0.91 (0.81, 1.02)	Ref	1.05 (1.00, 1.11)	0.03	0.99 (0.86, 1.13)	0.27	0.96 (0.87, 1.05)	0.68	1.14 (0.99, 1.32)	0.02
Barium	5.3 ng/m^3	1.01 (0.92, 1.12)	Ref	1.06 (1.01, 1.12)	0.50	0.93 (0.83, 1.05)	0.22	1.06 (0.96, 1.17)	0.73	1.11 (0.98, 1.25)	0.44
Zinc	2.3 ng/m^3	0.99 (0.91, 1.09)	Ref	1.03 (0.98, 1.08)	0.59	1.02 (0.90, 1.15)	0.62	0.94 (0.85, 1.03)	0.17	1.05 (0.92, 1.19)	0.62
ROS	16.2 nmol/L	1.06 (0.98, 1.16)	Ref	1.05 (1.00, 1.10)	0.62	0.91 (0.81, 1.03)	0.01	1.07 (0.97, 1.17)	1.00	1.09 (0.97, 1.22)	0.86
OP^{OH}	1.6 pmol/min/m^3	0.96 (0.88, 1.05)	Ref	1.02 (0.97, 1.07)	0.30	1.01 (0.90, 1.14)	0.51	1.04 (0.94, 1.14)	0.34	1.10 (0.98, 1.24)	0.13
OP^{DTT}	149.7 pmol/min/m^3	0.99 (0.90, 1.09)	Ref	1.01 (0.96, 1.05)	0.86	0.99 (0.89, 1.11)	0.82	1.12 (1.03, 1.23)	0.07	1.14 (1.02, 1.28)	0.08

Note: Term normal birth weight was defined as infants born between 37 and 45 wk of gestation with a birth weight of 2,500–6,800 g. TLBW was defined as infants born between 37 and 45 wk of gestation with a birth weight <2,500 g. The IQRs were based on the 75th and 25th percentiles of each air pollutant among births with term normal birth weight. CI, confidence interval; DTT, dithiothreitol; IQR, interquartile range; LUR, land use regression; OH, hydroxyl radical; OP^{DTT}, DTT loss; OP^{OH}, OH formation; OR, odds ratio; Ref, reference; ROS, modeled reactive oxygen species based on measured iron and copper; TLBW, term low birth weight.

[a]"Other" included American Indian, Asian Indian, Eskimo, Aleut, and mothers who reported their race/ethnicity as "Other", as well as multirace/ethnicities.

[b]Adjusted for fetal sex, parity, maternal age, maternal birthplace, payment source for prenatal care, maternal education, and maternal smoking. Tests of heterogeneity was conducted based on 2-tailed p-values with a significance level of 0.05 for the product term of the continuous exposure variable and each of the binary potential effect modifier in the regression model.

an observed lower risk attributable to air pollution; nevertheless, we did observe some of the strongest associations for particle mass and our toxicity measures and PTB in Black mothers.

To the best of our knowledge, this is the first study to assess the effects of speciated $PM_{2.5}$ constituents with OP and adverse birth outcomes. We investigated both effects of metals from brake and tire wear as well as the OP of the entire particle mixture, with the aim of identifying $PM_{2.5}$ sources and components with adverse effects on birth outcomes. We considered confounding by exhaust emissions from traffic for the speciated $PM_{2.5}$ exposures using an LUR model that predicts NO_2 exposures as markers of tailpipe emissions. The positive associations between metals and markers of OP metrics and PTB/TLBW remained when we added exhaust emission markers into our regression models. Finally, it is important to note that using birth certificate data in our study also allowed us to eliminate the possibility of self-selection of participants and its related biases.

Our study has several limitations. We could only estimate air pollution exposures at home addresses provided on the birth certificates, and we are not able to assess time spent by mothers at work, in transit, or at other residences prior to birth, which is a problem common to most air pollution health effects studies. In addition, we had no information on whether the mother moved during pregnancy, which could have substantially changed the exposure profiles for those who moved. This lack of relocation information would cause exposure misclassification bias that most likely is nondifferential and, thus, biases the effect estimates toward the null. We cannot completely negate the possibility of differential exposure misclassification in the unlikely event that mothers of preterm infants systematically moved to more- (or less-) exposed homes. A previous study estimated that 9%–32% of all mothers move during pregnancy.[65] Our model only predicted spatial exposures for the whole 3-y period, and 2-wk integrated period measurements, one in winter and one in summer, were used to build the model and were the only temporal influences that contributed to our model building. Therefore, we were not able to assess exposures specific to each trimester of pregnancy or the actual pregnancy period, nor were we able to investigate a critical window for the effect of speciated $PM_{2.5}$ exposures on adverse birth outcomes.

Although there is some seasonality in exposure levels, the novel cokriging modeling framework used to estimate exposures did not allow for extension to different temporal periods. Therefore, we were unable to assess exposures by trimester of pregnancy or critical windows. The modeling did, however, produce high-resolution estimates for exposure assignment of the novel indicators we used in this study. We therefore made the decision to favor the spatial contrasts over the temporal ones, given that spatial exposure contrasts are expected to be maintained despite some year-to-year changes in land use, meteorology, and other factors.[44,45] When restricting to 2019 births only, the results for $PM_{2.5}$ mass and speciated exposures on PTB and TLBW were stable with slightly higher ORs than for the 2017–2019 births. Thus, there may be some bias toward the null for results including births in 2017 and 2018 using the surfaces based on the 2019–early 2020 monitoring data. Moreover, the lack of the air pollution samplers or low-cost sensors in low-income communities might increase uncertainty of exposure estimates and induce greater measurement error. Low-income communities often have higher levels of air pollution,[21] but spatial contrasts are less well characterized in our model and exposure extremes (hot spots) missed. Thus, the effect estimates may be biased toward the null.[66] Furthermore, adverse pregnancy outcomes can be affected by live birth biases—i.e., a fetus has to survive to be born alive to contribute to TLBW or preterm births. It is conceivable that the mostly highly exposed fetuses who would have been born low weight or preterm if

they had survived are in fact lost due to early spontaneous abortions or fetal deaths among the most vulnerable and highly exposed, which may lead to a lower rate of TLBW or preterm births with higher exposure.

With the high correlations among the various elements, it is difficult to ascribe specific health effects to each element. In addition, disadvantaged communities typically face numerous burdens from other pollutants and conditions. People living in areas with high air pollution also are more likely to have chronic health conditions that would make them more susceptible to the adverse effects of environmental stressors. For example, they are more likely to experience adverse social conditions that increase stress in the family. A previous study among participants drawn from the Los Angeles Family and Neighborhood Survey (L.A.FANS) reported statistically significant synergism between selected psychosocial stressors and air pollution on the lung functions of adolescents.[67] This is known as the double-jeopardy hypothesis, whereby people living in disadvantaged communities are exposed to higher levels of environmental stressors and they have higher susceptibility to these exposures.[68] Such double jeopardy may also affect our epidemiological results. Another example is the coexposure to noise. Previously, we found that coexposure to both traffic-related air pollution and noise from aircraft increased the risk of adverse birth outcomes more than each exposure alone.[69] Combined with finding of positive associations between oxidative potential and lower socioeconomic position reported by Shen et al.,[21] these findings cast a new light on the issue because people in disadvantaged communities face not only higher levels of exposure on average, but the pollutants that are emitted locally are also more toxic on a per-unit basis.[21] Moving forward we recommend that further research should be undertaken to understand social gradients in OP and their potential impact on adverse birth outcomes.

Conclusion

Our results indicate that exposures to $PM_{2.5}$ metals from brake and tire wear and fine particles with higher OP are associated with higher risks of PTB and TLBW in Los Angeles County and that infants born to mothers with Hispanic, Black, Asian/Pacific Islander, or multiracial/mixed-race origin were most affected. Thus, it is important to consider not only mass but type of particles when assessing health effects, because this may affect vulnerable subgroups of pregnant women differently depending on their exposure levels and vulnerability.

Acknowledgments

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