Original Research

ENVIRONMENTAL EPIDEMIOLOGY

OPEN

Hazardous Air Pollutants and Adverse Birth Outcomes in Portland, OR

Mary Willis, Perry Hystad*

Background: The impact of multiple hazardous air pollutant (HAP) exposures during pregnancy on adverse birth outcomes is unknown. We examined associations between cumulative and individual HAP exposures and adverse birth outcomes in Portland, OR, a region that has exceeded HAP air quality guidelines for decades.

Methods: We used vital statistics records in the Portland Metropolitan Region from 2000 to 2014 (n = 279,051 births). Prenatal exposure to 19 HAPs was assessed using a dispersion model applied to maternal residential address at delivery. We used linear and logistic multivariate regression models to assess associations between individual and cumulative HAP exposures and preterm term (PTB), term birth weight (TBW), and small for gestational age (SGA), adjusting for several potential individual and neighborhood confounding factors.

Results: We observed no associations for composite HAP exposure metrics and adverse birth outcomes. Associations were observed in fully adjusted models comparing the highest to lowest quintiles of exposure for certain HAPs including chromium VI and TBW (–12.70; 95% confidence interval [CI]: –23.10, –2.31); 1,3-butadiene and TBW (–16.86; 95% CI: –29.66, –4.06) and SGA (1.18; 95% CI: 1.07, 1.30); and cadmium and TBW (–31.37; 95% CI: –56.20, –.54). For some HAP metrics, we observed higher HAP exposures for minority groups and large unadjusted associations between other HAPs and adverse birth outcomes, but most associations were attenuated in adjusted models.

Conclusions: Adverse birth outcomes were not consistently associated with most HAP exposures in Portland, OR, although some specific air toxic exposures warrant further attention.

Keywords: Adverse birth outcomes; Hazardous air pollutants; air toxics; preterm birth; small for gestational age; birth weight; chromium; cadmium; 1,3-butadiene

Background

Currently, the United States Environmental Protection Agency (EPA) regulates emission of 187 specific hazardous air pollutants (HAPs) via the Clean Air Act.[1] Unlike criteria air pollutants, HAPs are defined as air toxics with known or suspected serious health effects, usually focusing on cancer outcomes.[1] However, 105 of these 187 HAPs are known to be associated with health effects other than cancer, including adverse birth outcomes.[2] Many areas, such as Portland, OR, attain criteria air pollutant standards but fail to maintain HAP levels that are compliant.[3,4] There is no exposure threshold for HAPs that is considered safe for human health per the EPA,[1] but there is a dearth of epidemiological research linking HAP exposure to birth outcomes.

Most of the evidence for an association between HAP and adverse pregnancy outcomes come from studies of traffic-related air pollutants. For example, a meta-analysis of 62 studies observed a decrease in term birth weight of 28.1 g (95% confidence interval [CI]: –44.8, –11.5) per 20 ppb increase in nitrogen dioxide (NO_2).[5] NO_2 is a surrogate for the traffic-related air pollution mixture that contains numerous HAPs, such as diesel particulate matter (DPM), polycyclic aromatic hydrocarbons (PAHs), and benzene, toluene, ethylbenzene, and xylene (BTEX).[6,7] While there are fewer studies specifically examining nonvehicle air toxic exposures, some studies have observed associations between adverse birth outcomes and nonspecific ambient HAP exposures to PAHs, chromium, and nickel[8–10] as well as proximity to industrial sources such as oil and gas development,[11–14] coal power plants,[15–17] mining activity,[18,19] and metal smelters.[20] Overall, there are limited studies examining exposure to specific HAPs during pregnancy, especially HAP mixtures from multiple sources.[5,21,22]

What this study adds

Using a vital statistics cohort (n = 279,051 births), our study examined associations between adverse birth outcomes and hazardous air pollution (HAP) exposures in Portland, OR. Few studies have addressed the effects of HAP exposures during pregnancy, a major shortcoming to the literature that we address in a city with high HAP concentrations and extensive community concern. We documented exposure gradients by sociodemographic characteristics, highlighting a potential environmental inequity. However, we did not observe consistent associations between adverse birth outcomes and cumulative HAP exposures after accounting for sociodemographic characteristics. Some HAP-specific models (e.g., butadiene, cadmium, chromium) demonstrated elevated risks that should be investigated in more depth.

School of Biological & Population Health Sciences, College of Public Health & Human Sciences, Oregon State University, Corvallis, Oregon.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of the article.

The data used in this research are not publicly available but can be requested from the Oregon Vital Statistics program.

SDC *Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.environepidem.com).*

**Corresponding author. Address: 160 SW 26th St, Corvallis OR 97331. 541-737-4829. E-mail address: perry.hystad@oregonstate.edu (P. Hystad).*

Environmental Epidemiology (2018) 3:e034

Received: 24 July 2018; Accepted 12 November 2018

Published online 24 December 2018

DOI: 10.1097/EE9.0000000000000034

In this study, we examine associations between 19 HAP exposures and adverse birth outcomes (term birth weight, preterm birth, and small for gestational age) for 279,051 births in the Portland Metropolitan Region from 2000 to 2014. Portland, OR, has consistently exceeded hazardous air pollutant (HAP) regulations for decades. Although some studies have addressed community health concerns regarding these emissions,[4,23] the potential negative impacts on adverse birth outcomes is a major concern that has yet to be addressed. This analysis builds on a previous study to assess HAP concentrations in Portland and links these HAPs models to birth outcomes using a vital statistics cohort.[24] The results of this study will inform the potential impacts of different air toxics and mixtures to adverse birth outcomes, address community concerns, and highlight future research needs.

Methods

Birth cohort

We obtained vital statistics information from the Oregon Health Authority Center for Health Statistics for all births in the Portland Metropolitan Region with corresponding mothers residential addresses from 2000 to 2014 (n = 314,988 births). Sociodemographic characteristics for each mother, father, and infant were captured from birth certificate records. This analysis was restricted to births with a maternal residence within the city limits of Portland, OR (n = 289,651). We removed implausible observations based on maternal ages (<10 and >65 years old; n = 13), gestational ages (<12 and >45 weeks; n = 125), and birth weights (<100 and >6,500 g; n = 34). In addition, after considering our previous criteria, we removed stillbirths (n = 384) and multiple births (n = 10,044). Our final sample consists of 279,051 live singleton births in the Portland Metropolitan Region.

Air toxics exposure data

The Oregon Department of Environmental Quality (DEQ) created the Portland Air Toxics Solutions (PATS) dispersion model to better understand air toxic sources and concentrations in Portland. DEQ selected the 2005 inventory year as the base year for this project because it has the most air toxics monitoring data and good emissions inventory data.[4] The 2005 inventory estimates emissions based on the amount of specific air toxic generating activity occurring and the air toxics emission rate for that activity. The main emission inventory components included emission factors, activity data, and spatial allocation. Categories of emissions include nonpoint (area) sources, mobile road sources, mobile nonroad sources, and permitted point sources. A full description of the emission inventories has previously been published.[4]

Briefly, all emissions were spatially allocated within the PATS region for input into a CALPUFF dispersion model. Background concentrations were added to all modeled values to account for transport of regional emissions from outside the PATS study area as well as natural and unidentified emission sources. These background estimates were developed by EPA for the 2002 National-scale Air Toxics Assessment. A 2017 forecast was produced by applying growth factors to the 2005 emissions and then subtracting any emissions controlled by federal and state air toxics regulations. DEQ refined and improved emissions data between the 2005 and 2017 estimates and we use the updated estimates as our primary exposure measures. The locations used to estimate toxic concentrations in the PATS project are the geographic centers, or centroids, of the year 2000 census block groups in the study area. The PATS model yields a single projected estimate of exposure that is spatially varying, but not temporally varying, across the Portland Metropolitan Region.

The PATS dispersion model estimates 19 specific pollutants: 1,3-butadiene, 1,4-para-dichlorobenzene, polycyclic aromatic hydrocarbon (PAH) composite estimate, acetaldehyde, acrolein, arsenic, benzene, cadmium, chromium VI, DPM, ethylbenzene, formaldehyde, lead, manganese, methylene chloride, naphthalene, nickel, perchloroethylene, and trichloroethylene.[4] The PAH composite estimate takes into account 15 of the 16 PAHs identified by EPA for Toxic Release Inventory estimates excluding naphthalene, which is separate in the PATS model. For each maternal residence in our study we assign the corresponding PATS estimate for each of these pollutants as a log continuous estimate standardized by dividing the estimate by the interquartile range and as a categorical estimate by taking the geometric interval quintiles. The categorical estimates are derived from the spatial distribution of the PATS estimates across Portland, which allows us to examine specific hotspots of concern within the city that would otherwise be obscured.

In addition to examining each air toxic separately, we examined cumulative HAP exposures. We examined different cumulative metrics, including summing each air toxic, summing cancer potency factor weighted concentrations, as well as summing the highest exposure quintiles of each HAP. This set of composite metrics allows us to examine simultaneously spatial colocations of various HAPs. Because some areas of Portland have modeled concentrations that are statistical outliers, we leverage these multiple metrics to ensure that these hotspots and their potential health effects are not obscured in our models. We hypothesize that these composite metrics are a better representation of how HAPs exposure may affect infant health, so these composite exposures are the primary focus of our analysis.

Neighborhood socioeconomic status data

Neighborhood contextual characteristics were calculated for census tracts from the 2000 and 2010 census (whichever was closest to the infant's birth year), including percent of households below the poverty line; percent of population that is nonwhite; race; and median household income. We did not include other measures of air pollution exposures (e.g., distance to major roads, known industrial point sources) as these were included in the PATS dispersion model.

Outcome assessment

We used information in the vital statistics database to determine the outcome for each infant using birth weight and gestational age fields. For term birth weight, we excluded all births with a gestational age less than 37 weeks and evaluated this outcome as a continuous variable. For preterm birth, we included all births with a gestational age less than 37 weeks and examined this outcome as a binary variable. For SGA, we calculated the 10th percentile for birth weight by gestational age and infant sex across our sample and assessed this outcome as a binary variable.

Analysis methods

We examined associations between cumulative and individual PATS exposure measures with term birth weight, preterm birth, and SGA using linear and logistic models. For each exposure metric, we ran models with the exposure as a log continuous variable standardized by the IQR (to account for the skewed distributions of HAP levels) and as a categorical quintile metric by geometric intervals, comparing the highest to lowest quintiles. Fully adjusted models included infant sex, birth month, birth year, maternal and paternal age, maternal and paternal race, maternal and paternal education, insurance status, parity, maternal smoking and alcohol use during pregnancy, gestational and chronic hypertension, gestational and chronic diabetes, maternal weight gain during pregnancy, and Women, Infants, and Children (WIC) service eligibility.

The neighborhood socioeconomic measures described above were also included in the fully adjusted models. We coded missing covariates in as a separate category for categorical variables and excluded missing data for continuous variables. Exploratory stratified analyses were conducted to examine potentially important modifying variables, including maternal education, maternal race, maternal ethnicity, delivery payment mechanism (i.e., insurance status), and neighborhood poverty levels.

Results

Demographic characteristics

Table 1 summarizes the demographic characteristics of all births within the Portland city boundary by cumulative air toxics (lowest and highest quintiles of the sum of individual air toxics weighted by toxicity). Compared with babies born in the lowest quintile of cumulative air toxics, babies in the highest quintile experienced lower mean birth weights, higher percentage of SGA, lower maternal education at birth; were more likely to be non-white, Hispanic, and use Medicaid or the Oregon Health Plan; were less likely to be exposed to maternal tobacco smoke in utero, be eligible for WIC, and have gestational diabetes and hypertension; and had lower median household incomes in their neighborhood, higher percentage of people below the poverty line, and higher percentage of nonwhite population in their neighborhood.

Hazardous air pollution exposures

Figure 1 shows the spatial distribution of the composite risk metric as well as individual patterns for select HAP exposures in Portland, OR. Other HAP spatial patterns are included in eFigure 1 (http://links.lww.com/EE/A25). Individual HAPs demonstrate substantial spatial heterogeneity due to differences in major source contributions (e.g., traffic, industry, home heating). eTable 1 (http://links.lww.com/EE/A25) demonstrates the distribution of the individual HAP exposures.

We first examined multiple metrics of cumulative HAPs that were derived from the PATS models (Table 2). These metrics include sum of the HAPs concentrations, sum of HAPs risk weight by cancer toxicity, and sum of the HAPs exposure quintiles, all of which we examined in log continuous and quintile frameworks. Across all metrics, we found unadjusted results that demonstrate an increased risk of adverse birth outcomes, but these risks are fully attenuated after we adjust our models for confounding sociodemographic characteristics. For example, in the composite sum of the HAPs concentrations metric, we find a 36.99 (95% CI: −42.66, −31.32) decrease in unadjusted models, but this association trends toward null in adjusted models (−4.14; 95% CI: −9.64, 1.37). Similar attenuation was observed for the other composite metrics and birth outcomes.

Next, we investigated associations between each of the 19 hazardous air pollutants and birth outcomes. Table 3 summarizes fully adjusted models for the log of an IQR increase and the highest versus the lowest exposure quintiles. In unadjusted models, we observed elevated risks of all three adverse pregnancy outcomes (eTable 2; http://links.lww.com/EE/A25), but most of these associations were attenuated in the fully adjusted models (Table 3), similar to our cumulative HAP measures. In our adjusted models comparing the highest to the lowest quintile of exposures, we observed elevated risks for term birth weight and 1,3-butadiene (−16.86; 95% CI: −29.66, −4.06), cadmium (−31.37; 95% CI: −56.20, −6.54), and chromium VI (−12.70; 95% CI: −23.10, −2.31); and SGA and 1,3-butadiene (1.18; 95% CI: 1.07, 1.30). In our fully adjusted log IQR models, we observed elevated risks for term birth weight and manganese (−4.51; 95% CI: −6.88, −2.13), methylene chloride (−1.99; 95% CI: −3.93, −0.05), and trichloroethylene (−4.24; 95% CI: −8.02, −0.45); preterm birth and methylene chloride (1.02; 95% CI: 1.00, 1.04); and SGA and ethylbenzene (1.03; 95% CI: 1.00, 1.06). We also observed some protective associations for specific HAPs, including for PAH and term birth weight as well as acetaldehyde, benzene, diesel particulate matter, and ethylbenzene and preterm birth.

Table 1

Descriptive statistics of birth cohort

	All births	Composite air toxics[a] (lowest quintile)	Composite air toxics[a] (highest quintile)
Births	279,051	55,870	55,792
Birth weight, mean	3,410	3,426	3,404
Preterm (<37 weeks), (%)	6.0	5.9	6.0
SGA, (%)	10.6	9.8	11.0
Female sex, (%)	48.7	48.9	48.9
Nulliparous, (%)	34.1	33.6	34.7
Maternal age, mean	28.7	29.1	28.1
Maternal education (%)			
≤8th grade	5.8	4.2	7.9
9th grade to high school	33.0	31.5	35.4
College (<4 years)	22.7	23.2	22.8
College (≥4 years)	37.4	40.0	33.1
Maternal race (%)			
White non-Hispanic	82.4	86.2	83.2
African American	4.3	2.5	3.1
Asian and Pacific Islander	9.5	7.8	10.2
American Indian	0.9	0.8	0.8
Other	0.6	0.6	0.6
Maternal Hispanic (%)	19.03	15.6	26.5
Payment for delivery (%)			
Medicaid/Oregon Health Plan[b]	33.6	30.1	37.1
Private insurance	62.7	66.2	59.3
Self-pay	2.5	2.6	1.1
Mothers smoking during pregnancy (%)	8.4	8.6	7.3
Mothers drinking during pregnancy (%)	1.2	1.4	0.7
WIC (%)	32.3	29.0	36.0
Gestational diabetes (%)	5.6	5.2	6.0
Chronic diabetes (%)	0.6	0.6	0.7
Gestational hypertension (%)	5.2	4.9	5.6
Chronic hypertension (%)	1.1	1.1	1.2
Neighborhood characteristics[c]			
Median household income (USD)	55,803	58,174	52,994
Below poverty line (%)	13.5	12.0	14.0
Non-white (%)	22.4	16.5	25.6

[a]Composite risk quintiles are derived based on the entire population using the PATS composite cancer potency factor toxicity estimates.

[b]Oregon Health Plan is the state's Medicaid program.

[c]Derived from US Census data. For each birth before 2005, characteristics from the 2000 Census were used. For each birth including and after 2005, characteristics from the 2010 census were used.

To explore what covariates may be influencing the strong risk attenuations in our models, we implemented incremental models and note that the main decreases in point estimates are from adding socioeconomic, behavioral, clinical, and neighborhood covariates (Table 4). Covariate selection for the incremental models followed a logical progression of covariates determined a priori that we hypothesize would influence the results from most to least. We also considered what covariates have been commonly used in the existing literature on environmental exposures and birth outcomes.

Stratified analyses

Exploratory stratified models were conducted to determine if associations between HAP exposures and adverse birth outcomes were similar across sociodemographic and neighborhood characteristics using the log sum of continuous HAP concentrations. Within racial and ethnic groups, we observed some

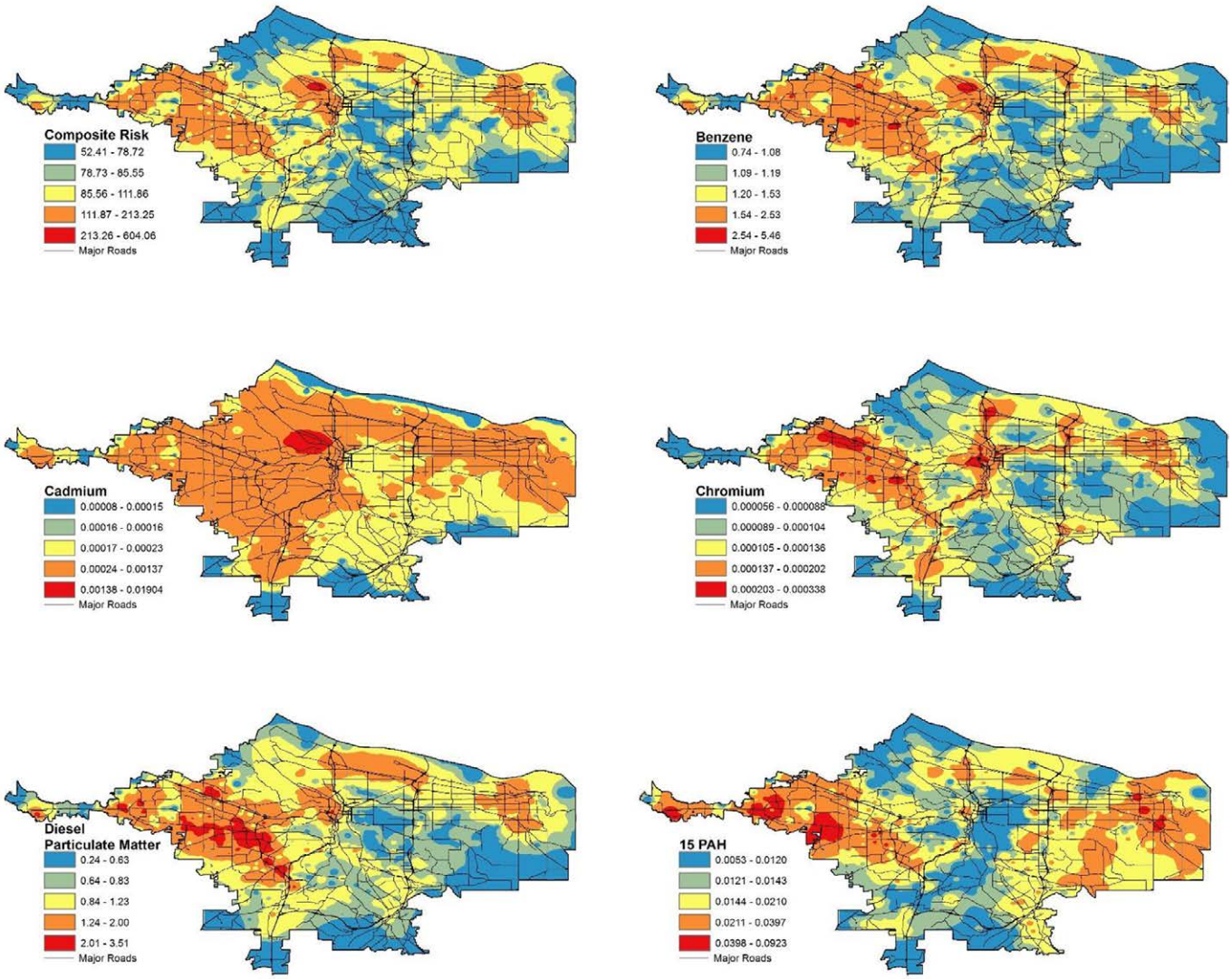

Figure 1. Portland Air Toxic CALPUFF model outputs for specific hazardous air pollutants by geometric intervals.

large differences for minority populations in terms of HAPs exposures (eTable 3; http://links.lww.com/EE/A25). For example, black mothers are exposed to more methylene chloride than other groups and infants born to Hispanic mothers appear to have higher exposures to 1,3-butadiene, acetaldehyde, benzene, DPM, ethylbenzene, formaldehyde, and methylene chloride. However, in our stratified models (eTable 4; http://links.lww.com/EE/A25), we observed no consistent pattern of associations between our cumulative HAP metrics and adverse birth outcomes for specific populations.

Discussion

The Environmental Protection Agency (EPA) National Air Toxics Assessment (NATA) shows that Portland's air exceeds regulatory levels of at least 66 HAPs, 49 of which are known carcinogens.[3] There is tremendous community concern regarding past and current air toxic exposure levels and their potential health impacts, especially since a 2016 study using tree moss identified previously unknown hot spots of metals in Portland.[25] We examined associations between HAP concentrations and adverse birth outcomes using a population-based birth cohort in Portland, OR, between 2000 and 2014. To accomplish this analysis, we took advantage of a unique city-wide HAP dispersion model that allows us to estimate multiple HAP exposures. Our results show that composite HAPs exposures, and most individual HAP exposures, were not associated with adverse birth outcomes. However, some specific air toxic exposures warrant further research, including 1,3-butadiene, cadmium, and chromium VI.

We did not observe associations between our metrics of combined HAP exposures and adverse birth outcomes, but we note that many of our estimates lack sufficient precision to rule out a small yet meaningful impact of infant health. We used three different methods to capture potential HAP mixtures, including summing individual HAP concentrations, summing cancer toxicity weighted measures, and summing the quintiles of each HAP concentration. Each toxicity metric allows us to capture different aspects of exposure mixtures that may be affecting perinatal health. By summing the individual HAP concentrations, we examined whether the total amount of HAP is a driving pathway toward adverse pregnancy outcomes. In our cancer toxicity-weighted measures, we included the differing toxicological impacts of each HAP (we did not use a developmental toxicity weighting as several of the HAPs do not have weights established[22]). Finally, the sum of each HAP quintile focused on capturing spatial hot-spots for each HAP, rather than absolute concentrations. For all three measures, we did not observe consistent associations with adverse pregnancy outcomes in fully adjusted models. Within our composite toxicity measures,

Table 2

Unadjusted and fully adjusted models for composite toxicity metrics of regional air toxics for term birth weight, preterm birth, and small for gestational age

Composite hazardous air pollutant measures	n[a]	Term birth weight β (95% CI)		Preterm birth β (95% CI)		SGA β (95% CI)	
		Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Sum HAP[b]							
Log continuous	279,051	−36.99 (−42.66, −31.32)	−4.14 (−9.64, 1.37)	1.13 (1.07, 1.18)	1.02 (0.97, 1.08)	1.17 (1.13, 1.22)	0.99 (0.95, 1.04)
Quintiles (Q5 vs. Q1)	55,797	−35.97 (−41.58, −30.36)	−3.36 (−8.81, 2.09)	1.13 (1.08, 1.19)	1.03 (0.97, 1.09)	1.17 (1.12, 1.21)	0.98 (0.94, 1.02)
Composite risk[c]							
Log continuous	279,051	−31.40 (−39.33, −23.47)	0.48 (−6.94, 7.90)	1.03 (0.96, 1.11)	0.94 (0.87, 1.01)	1.20 (1.14, 1.27)	1.04 (0.98, 1.10)
Population quintiles (Q5 vs. Q1)[d]	55,792	−22.36 (−27.96, −16.75)	0.76 (−4.46, 5.98)	1.01 (0.96, 1.06)	0.95 (0.90, 1.00)	1.14 (1.09, 1.18)	1.02 (0.98, 1.07)
Sum of quintiles[e]							
Log continuous	279,051	−19.02 (−24.66, −13.38)	3.30 (−1.93, 8.53)	1.04 (0.99, 1.09)	0.97 (0.92, 1.03)	1.13 (1.08, 1.17)	1.01 (0.97, 1.05)
Quintiles (Q5 vs. Q1)	55,797	−31.56 (−37.62, −25.50)	−1.94 (−7.72, 3.83)	1.06 (1.00, 1.12)	0.97 (0.91, 1.02)	1.19 (1.15, 1.24)	1.01 (0.97, 1.06)

[a]For continuous metrics, n is the entire sample for preterm birth and small-for-gestational age models. For quintile metrics, n is the number of births in the top quintile of exposure for preterm birth and small-for-gestational age models.

[b]Derived from summing the concentrations of each individual HAP.

[c]Derived from the PATS composite risk estimate using cancer potency factors.

[d]Derived from geometric intervals of the distribution of pollutant exposure among the population.

[e]Derived from summing the spatial quintile of exposure for each residential location.

Table 3

Adjusted models for individual air toxics for term birth weight, preterm birth, and small for gestational age

Hazardous air pollutant measures	Term birth weight β (95% CI)		Preterm birth β (95% CI)		SGA β (95% CI)	
	Q5 versus Q1	Log IQR	Q5 versus Q1	Log IQR	Q5 versus Q1	Log IQR
1,3-butadiene	−16.86 (−29.66, −4.06)	2.31 (−2.21, 6.83)	0.93 (0.81, 1.06)	0.95 (0.91, 1.00)	1.18 (1.07, 1.30)	1.02 (0.99, 1.06)
1,4-para-dichlorobenzene	4.56 (−3.02, 12.14)	2.41 (−2.34, 7.16)	0.96 (0.89, 1.03)	0.95 (0.91, 1.00)	1.00 (0.94, 1.06)	1.01 (0.98, 1.05)
15-polycyclic aromatic hydrocarbon	10.46 (2.30, 18.62)	6.44 (2.46, 10.43)	0.94 (0.86, 1.02)	0.96 (0.92, 1.00)	1.01 (0.95, 1.08)	1.02 (0.99, 1.05)
Acetaldehyde	2.20 (−7.68, 12.08)	5.91 (−26.72, 38.53)	0.87 (0.79, 0.96)	0.68 (0.49, 0.94)	1.05 (0.97, 1.13)	1.26 (0.98, 1.62)
Acrolein	−0.93 (−7.04, 5.19)	−2.58 (−8.08, 2.93)	1.04 (0.97, 1.10)	1.06 (1.00, 1.12)	0.98 (0.93, 1.03)	0.97 (0.93, 1.01)
Arsenic	−8.08 (−18.22, 2.05)	−3.32 (−10.16, 3.53)	0.99 (0.89, 1.09)	0.95 (0.88, 1.01)	1.03 (0.95, 1.11)	1.04 (0.99, 1.10)
Benzene	−1.38 (−6.91, 4.16)	−2.06 (−8.47, 4.35)	0.96 (0.90, 1.01)	0.93 (0.87, 0.99)	1.03 (0.99, 1.08)	1.05 (1.00, 1.10)
Cadmium	−31.37 (−56.20, −6.54)	−3.03 (−7.03, 0.96)	1.05 (0.81, 1.37)	0.98 (0.94, 1.02)	1.06 (0.87, 1.30)	1.01 (0.98, 1.04)
Chromium VI	−12.70 (−23.10, −2.31)	−2.99 (−9.02, 3.04)	1.00 (0.90, 1.11)	0.96 (0.90, 1.02)	1.06 (0.99, 1.15)	1.04 (1.00, 1.09)
Diesel particulate matter	4.16 (−3.89, 12.21)	−0.30 (−4.21, 3.62)	0.92 (0.84, 0.99)	0.96 (0.92, 1.00)	1.01 (0.95, 1.08)	1.02 (0.99, 1.05)
Ethylbenzene	4.55 (−2.37, 11.47)	−0.47 (−4.19, 3.24)	0.92 (0.86, 0.98)	0.95 (0.92, 0.99)	0.99 (0.94, 1.05)	1.03 (1.00, 1.06)
Formaldehyde	2.11 (−16.47, 20.70)	−1.12 (−23.70, 21.47)	0.93 (0.78, 1.12)	0.83 (0.66, 1.04)	0.95 (0.82, 1.09)	1.15 (0.97, 1.37)
Lead	−0.20 (−11.22, 10.83)	−0.10 (−4.05, 3.85)	0.98 (0.87, 1.09)	1.02 (0.98, 1.06)	0.98 (0.90, 1.07)	0.97 (0.94, 1.00)
Manganese	−12.63 (−45.82, 20.57)	−4.51 (−6.88, −2.13)	0.98 (0.69, 1.40)	1.01 (0.98, 1.03)	0.95 (0.72, 1.25)	1.00 (0.99, 1.02)
Methylene chloride	−4.27 (−9.69, 1.15)	−1.99 (−3.93, −0.05)	1.04 (0.98, 1.10)	1.02 (1.00, 1.04)	0.98 (0.94, 1.02)	0.99 (0.97, 1.00)
Naphthalene	−13.92 (−47.53, 19.70)	−1.65 (−5.73, 2.44)	0.94 (0.65, 1.34)	0.98 (0.94, 1.03)	0.94 (0.71, 1.24)	1.00 (0.97, 1.04)
Nickel	−18.63 (−51.32, 14.05)	−2.48 (−5.40, 0.44)	0.94 (0.66, 1.34)	1.01 (0.98, 1.04)	0.94 (0.72, 1.23)	1.01 (0.98, 1.03)
Perchloroethylene	7.37 (−2.55, 17.28)	2.38 (−1.89, 6.66)	0.92 (0.83, 1.02)	0.97 (0.93, 1.01)	0.99 (0.92, 1.07)	1.01 (0.98, 1.04)
Trichloroethylene	0.30 (−6.71, 7.31)	−4.24 (−8.02, −0.45)	0.95 (0.88, 1.02)	0.98 (0.94, 1.01)	0.99 (0.94, 1.05)	1.00 (0.98, 1.03)

Continuous air toxics measures are standardized via the log of the IQR. Term birth weight models exclude infants with gestational ages under 37 weeks. Adjustment covariates include birth year, birth month, infant sex, maternal and paternal race, maternal and paternal ethnicity, maternal and paternal education, payment mechanism, maternal alcohol and tobacco use during pregnancy, gestational or chronic diabetes, gestational or chronic hypertension, WIC status, maternal weight gain, census tract median household income, census tract percent population below poverty line, census tract percent racial minority, and PATS pollutants, and gestational age (birth weight only).

we examined what industry may be driving the highest exposures via the Toxic Release Inventory and observed a very high number of emission sources located in a small area emitting a wide range of pollutants, including chromium, lead, naphthalene, nickel, toluene, xylene, and zinc (eFigure 1; http://links.lww.com/EE/A25).[26] To fully understand the health impacts of local industrial emissions, future studies may need to incorporate mixture modeling techniques such as structural equation models to assess the distinct impacts of simultaneous exposure to multiple HAPs during pregnancy.

We observe some positive associations for individual HAP exposures, but the majority of our models indicate no associations. We present a graphical version of our results in Figure 2, where we demonstrate the relationships between our point estimates and their two-sided *P* values. Labeled HAPs reflect exposures that are statistically significant for at least one outcome. Although we find many point estimates suggestive of an association between HAP exposure and adverse infant health outcomes, Figure 2 shows that many of these associations do not demonstrate statistical significance and no clear pattern between HAP exposures and adverse birth outcomes emerge.

There is little existing literature for direct comparison to our results, however, some of our specific HAPs have been examined in other studies. One previous study[27] shows that increases in maternal blood manganese were associated with decreased birth weight, which was also observed in our study (4.51 g [95% CI: −6.88, −2.13] decrease per log IQR increase in manganese exposure). Another study shows that each μg/m^3 unit increase in maternal benzene exposure is associated with a birth weight decrease of 16.5 g (95% CI: 17.6, 15.4).[28] Although we did not find associations among benzene and birth weight, we do note an elevated risk of SGA among mothers with higher benzene exposure. In addition, a meta-analysis of traffic-related air pollution studies, using NO_2 as a surrogate marker, observed a decrease in term birth weight of 28.1 g (95% CI: −44.8, −11.5) per 20 ppb increase in nitrogen dioxide (NO_2).[5] We did not observe associations with DPM, although the resolution of the PATS model does not capture fine-scale spatial

Table 4

Full results of incremental models of composite hazardous air pollution exposure concentrations and term birth weight, preterm birth, and small for gestational age

	Term birth weight β (95% CI)		Preterm birth β (95% CI)		SGA β (95% CI)	
Covariate additions	**Q5 versus Q1**	**Log IQR**	**Q5 versus Q1**	**Log IQR**	**Q5 versus Q1**	**Log IQR**
Base model						
Unadjusted	−35.97 (−41.58, −30.36)	−36.99 (−42.66, −31.32)	1.13 (1.08, 1.19)	1.13 (1.07, 1.18)	1.17 (1.12, 1.21)	1.17 (1.13, 1.22)
Gestational age	−35.97 (−41.58, −30.36)	−34.34 (−39.66, −29.01)	-	-	-	-
Birth year	−33.09 (−38.35, −27.82)	−33.69 (−39.01, −28.37)	1.13 (1.08, 1.19)	1.13 (1.08, 1.19)	1.17 (1.12, 1.21)	1.17 (1.13, 1.22)
Birth month	−32.98 (−38.25, −27.72)	−33.59 (−38.91, −28.27)	1.13 (1.08, 1.19)	1.13 (1.08, 1.19)	1.17 (1.12, 1.21)	1.17 (1.13, 1.22)
Demographics						
Infant sex	−32.48 (−37.68, −27.27)	−33.17 (−38.44, −27.91)	1.13 (1.08, 1.19)	1.13 (1.09, 1.19)	1.17 (1.12, 1.21)	1.17 (1.13, 1.22)
Maternal age	−25.89 (−31.07, −20.70)	−25.18 (−30.43, −19.93)	1.13 (1.08, 1.19)	1.13 (1.07, 1.19)	1.14 (1.10, 1.19)	1.14 (1.10, 1.19)
Maternal race	−16.78 (−21.95, −11.61)	−18.03 (−23.26, −12.81)	1.10 (1.04, 1.15)	1.10 (1.04, 1.15)	1.08 (1.04, 1.12)	1.09 (1.050, 1.14)
Paternal race	−15.70 (−20.86, −10.54)	−17.38 (−22.60, −12.16)	1.09 (1.03, 1.14)	1.08 (1.03, 1.14)	1.07 (1.03, 1.11)	1.09 (1.04, 1.13)
Maternal ethnicity	−12.76 (−17.93, −7.589)	−13.90 (−19.13, −8.68)	1.08 (1.02, 1.13)	1.07 (1.02, 1.13)	1.06 (1.02, 1.10)	1.07 (1.03, 1.11)
Paternal ethnicity	−12.05 (−17.22, −6.881)	−13.05 (−18.28, −7.83)	1.07 (1.02, 1.13)	1.07 (1.02, 1.13)	1.05 (1.01, 1.10)	1.07 (1.03, 1.11)
Socioeconomic status						
Maternal education	−11.42 (−16.59, −6.24)	−12.46 (−17.70, −7.23)	1.06 (1.01, 1.11)	1.05 (1.00, 1.11)	1.05 (1.01, 1.09)	1.06 (1.02, 1.10)
Paternal education	−10.96 (−16.14, −5.79)	−12.00 (−17.24, −6.77)	1.05 (1.00, 1.10)	1.04 (0.99, 1.10)	1.04 (1.00, 1.08)	1.06 (1.02, 1.10)
Payment mechanism	−10.39 (−15.57, −5.21)	−11.35 (−16.59, −6.11)	1.05 (1.00, 1.10)	1.04 (0.99, 1.10)	1.04 (1.00, 1.08)	1.05 (1.01, 1.09)
WIC eligibility	−10.77 (−15.95, −5.59)	−11.79 (−17.03, −6.54)	1.05 (1.00, 1.11)	1.05 (1.00, 1.10)	1.04 (1.00, 1.08)	1.05 (1.01, 1.10)
Behavioral						
Maternal tobacco use	−10.00 (−15.16, −4.83)	−10.84 (−16.07, −5.62)	1.05 (1.00, 1.10)	1.04 (0.99, 1.10)	1.04 (1.00, 1.07)	1.05 (1.01, 1.09)
Maternal alcohol use	−9.90 (−15.07, −4.74)	−10.78 (−16.01, −5.55)	1.05 (1.00, 1.10)	1.04 (0.99, 1.10)	1.03 (0.99, 1.08)	1.05 (1.01, 1.09)
Clinical						
Maternal weight gain	−7.79 (−12.90, −2.68)	−8.57 (−13.74, −3.40)	1.04 (0.99, 1.09)	1.03 (0.98, 1.08)	1.02 (0.99, 1.07)	1.04 (1.00, 1.08)
Parity	−4.07 (−9.13, 1.00)	−4.31 (−9.44, 0.82)	1.03 (0.98, 1.08)	1.02 (0.97, 1.08)	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)
Gestational diabetes	−3.24 (−8.30, 1.82)	−3.30 (−8.42, 1.82)	1.03 (0.98, 1.09)	1.03 (0.98, 1.08)	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)
Prepregnancy diabetes	−3.46 (−8.51, 1.60)	−3.58 (−8.69, 1.54)	1.03 (0.98, 1.08)	1.02 (0.97, 1.08)	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)
Gestational hypertension	−3.45 (−8.50, 1.60)	−3.66 (−8.78, 1.45)	1.03 (0.98, 1.08)	1.02 (0.97, 1.08)	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)
Prepregnancy hypertension	−3.44 (−8.49, 1.61)	−3.64 (−8.75, 1.48)	1.03 (0.98, 1.08)	1.02 (0.97, 1.08)	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)
Neighborhood						
Neighborhood minority	−2.61 (−7.98, 2.77)	−2.84 (−8.23, 2.55)	1.03 (0.97, 1.09)	1.02 (0.97, 1.08)	0.98 (0.94, 1.02)	0.99 (0.95, 1.04)
Neighborhood income	−3.85 (−9.28, 1.59)	−4.60 (−10.09, 0.88)	1.03 (0.97, 1.08)	1.02 (0.97, 1.08)	0.98 (0.94, 1.02)	0.99 (0.95, 1.04)
Neighborhood poverty	−3.36 (−8.81, 2.09)	−4.14 (−9.64, 1.37)	1.03 (0.97, 1.09)	1.02 0.97, 1.08)	0.98 (0.94, 1.02)	0.99 (0.95, 1.04)

Term birth weight models exclude infants with gestational ages under 37 weeks.

variability of air toxics associated with the highest roadway gradients. We also observed protective associations with composite PAH exposure, which has been shown in a previous study.[29] We do not know what biological explanation may exist for these inverse results, though both results could be due to residual confounding.

For most HAPs, we observed consistently higher HAP exposures for lower socioeconomic and minority groups, and large unadjusted associations between HAPs and adverse birth outcomes, but no consistent increases in adverse birth outcomes in fully adjusted models. This attenuation was due primarily to the inclusion of clinical and neighborhood characteristics, as shown in the incremental models illustrated in Table 4. The large disparities in HAP exposures between ethnicity status highlight the well-recognized patterns of higher air toxic exposures for minority populations, but the distribution of HAPs appears to be less unequal than in other urban populations (eTable 3; http://links.lww.com/EE/A25).[2,30,31] In models restricted to these populations, we did not observe consistent adverse impacts of HAP exposures on adverse birth outcomes. Some of the attenuation observed in our adjusted models may also be due to the rapid gentrification of the Portland Metropolitan Region, which has been extensively documented.[32–35] Since 2000, 25.4% of census tracts in Portland have met criteria for undergoing gentrification.[36] These swift sociodemographic neighborhood changes may be altering longer-term exposure patterns as well as how traditional risk factors are affecting adverse pregnancy outcomes.

Several limitations of our study should be considered when interpreting our results. First, we rely on surrogate measures of HAP exposure during pregnancy that are based on models applied to mother's residential address at time of delivery. The PATS CALPUFF dispersion model is based on available emissions data in 2005 (and subsequently updated) and model accuracy is driven by the quality of these emissions data. In fact, the PATS estimates do not account for some previously unknown emissions sources, such as two artisan glass factories.[37] The PATS model also represents a snapshot of HAP in Portland and does not produce monthly or yearly estimates to match pregnancy periods. In addition, the PATS model does not capture fine-scale pollution gradients (e.g., 100s of meters around roadways or industrial sources) that may be important for HAP exposures. Nevertheless, the PATS model represents a unique resource to simultaneously examine multiple HAP exposures from different sources, with many of these sources being spatially stable over time. Second, we only had maternal address at time of delivery, and we do not necessarily know where the mother resided during pregnancy if they moved. Third, because we are exploring broad categories of HAPs and adverse birth outcomes, we ran over 200 models in our analyses, which puts us at a high probability of some results being due to chance instead of a true association. We interpret our models with caution due to a multiple comparisons issue, but we note that our conclusions are drawn from overall patterns of results and not individual associations. Fourth, many of our risk estimates yield wide confidence intervals that lack precision, thus we cannot dismiss the notion that some of our maternal exposures may have a meaningful, albeit small, impact on infant health. Fifth, residual confounding from unmeasured confounding factors cannot be ruled out in this analysis, similar to other birth cohort studies. However, we included a wide range of individual and geographic covariates to account for as much unmeasured variation as possible. We also control for secular

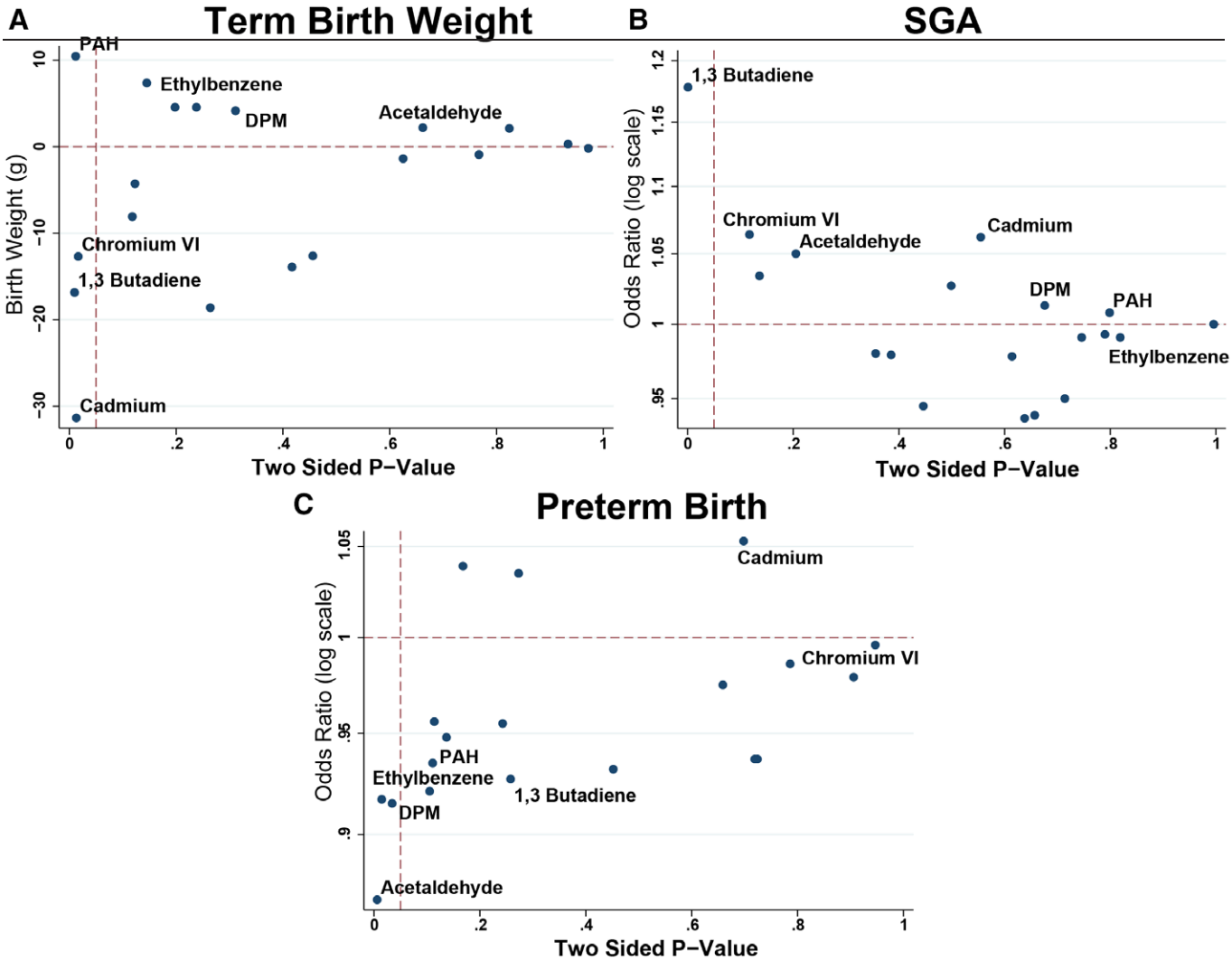

Figure 2. Association of infant health outcomes with air pollutant concentration, highest quintile versus lowest quintile by two-sided *P* values. This figure depicts point estimates associations from hazardous air pollutants by their two-sided *P* value for three specific infant health outcomes.

trends in birth outcomes via birth year and month covariates in all models.

Conclusions

Our analysis provides a broad examination of 19 HAPs and adverse birth outcomes in a large population-based birth cohort in Portland, OR, a city with consistently high HAP concentrations that result from a diverse set of emission sources. Our results show that cumulative HAPs exposures, and most individuals HAP exposures, were not associated with adverse birth outcomes, while some specific air toxic exposures warrant further research, including 1,3-butadiene, cadmium, and chromium VI.

Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

Acknowledgments

We thank Oregon Vital Statistics for providing the birth outcome data and the Oregon Department of Environmental Quality for providing the Portland Air Toxics Study (PATS) modeling data.

References

1. US EPA. *What are Hazardous Air Pollutants?* US EPA. Available at: https://www.epa.gov/haps/what-are-hazardous-air-pollutants. Published December 3, 2015. Accessed 21 April 2018.
2. US EPA. *Environments & Contaminants: Hazardous Air Pollutants*. Washington, D.C.: United States Environmental Protection Agency; 2016:50–57.
3. Koberstein P. *Study: Portland Air Among Worst in Nation*. The Portland Tribune. Available at: http://koin.com/2016/03/02/study-portland-air-among-worst-in-nation/. Published March 2, 2016. Accessed August 29, 2017.
4. Armitage S. *Portland Air Toxics Solutions Committee Report and Recommendations*. Portland, OR: State of Oregon Department of Environmental Quality; 2012.
5. Stieb DM, Chen L, Eshoul M, Judek S. Ambient air pollution, birth weight and preterm birth: a systematic review and meta-analysis. *Environ Res*. 2012;117(suppl C):100–111.
6. Kampa M, Castanas E. Human health effects of air pollution. *Environ Pollut*. 2008;151:362–367.
7. Richmond-Bryant J, Owen RC, Graham S, et al. Estimation of on-road NO_2 concentrations, NO_2/NO_X ratios, and related roadway gradients from near-road monitoring data. *Air Qual Atmosphere Health*. 2017;10:611–625.
8. Choi H, Jedrychowski W, Spengler J, et al. International studies of prenatal exposure to polycyclic aromatic hydrocarbons and fetal growth. *Environ Health Perspect*. 2006;114:1744–1750.

9. Laurent O, Hu J, Li L, et al. Sources and contents of air pollution affecting term low birth weight in Los Angeles County, California, 2001–2008. *Environ Res*. 2014;134:488–495.
10. McDermott S, Salzberg DC, Anderson AP, Shaw T, Lead J. Systematic review of chromium and nickel exposure during pregnancy and impact on child outcomes. *J Toxicol Environ Health A*. 2015;78:1348–1368.
11. McKenzie LM, Guo R, Witter RZ, Savitz DA, Newman LS, Adgate JL. Birth outcomes and maternal residential proximity to natural gas development in rural Colorado. *Environ Health Perspect*. 2014;122:412–417.
12. Casey JA, Savitz DA, Rasmussen SG, et al. Unconventional natural gas development and birth outcomes in Pennsylvania, USA. *Epidemiology*. 2016;27:163–172.
13. Whitworth K, Marshall A, Symanski E. Maternal residential proximity to unconventional gas development and perinatal outcomes among a diverse urban population in Texas. *PLoS One*. 2017;12:e0180966.
14. Hill EL. Shale gas development and infant health: evidence from Pennsylvania. *J Health Econ*. 2018;61:134–150.
15. Ha S, Hu H, Roth J, Kan H, Xu X. Associations between residential proximity to power plants and adverse birth outcomes. *Am J Epidemiol*. 2015;182:215–224.
16. Yang M, Bhatta RA, Chou S-Y, Hsieh C-I. The impact of prenatal exposure to power plant emissions on birth weight: evidence from a Pennsylvania power plant located upwind of New Jersey. *J Policy Anal Manag J Assoc Public Policy Anal Manag*. 2017;36:557–583.
17. Casey JA, Karasek D, Ogburn EL, et al. Retirements of coal and oil power plants in California: association with reduced preterm birth among populations nearby. *Am J Epidemiol*. 2018;187:1586–1594.
18. Ahern MM, Hendryx M, Conley J, Fedorko E, Ducatman A, Zullig KJ. The association between mountaintop mining and birth defects among live births in central Appalachia, 1996–2003. *Environ Res*. 2011;111:838–846.
19. Ahern M, Mullett M, Mackay K, Hamilton C. Residence in coal-mining areas and low-birth-weight outcomes. *Matern Child Health J*. 2011;15:974–979.
20. Berkowitz Z, Price-Green P, Bove FJ, Kaye WE. Lead exposure and birth outcomes in five communities in Shoshone County, Idaho. *Int J Hyg Environ Health*. 2006;209:123–132.
21. Ferguson KK, Chin HB. Environmental chemicals and preterm birth: biological mechanisms and the state of the science. *Curr Epidemiol Rep*. 2017;4:56–71.
22. Backes CH, Nelin T, Gorr MW, Wold LE. Early life exposure to air pollution: how bad is it? *Toxicol Lett*. 2013;216:47–53.
23. *Oregon Health Authority : New Soil, Cancer, Urine Test Data Show Low Risk for Portland Residents : External Relations Division : State of Oregon*. Available at: http://www.oregon.gov/oha/ERD/Pages/New-Soil-Cancer-Urine-Data-Shows-Low-Risk.aspx. Accessed March 2, 2018.
24. Tam BN, Neumann CM. A human health assessment of hazardous air pollutants in Portland, OR. *J Environ Manage*. 2004;73:131–145.
25. Donovan G, Jovan S, Gatziolis D, Burstyn I, Michael Y, Monleon V. Using an epiphytic moss to identify previously unknown sources of atmospheric cadmium pollution. *Sci Total Environ*. 559:84–93.
26. US EPA. *TRI Data and Tools*. US EPA. Available at: https://www.epa.gov/toxics-release-inventory-tri-program/tri-data-and-tools. Published March 3, 2013. Accessed May 24, 2018.
27. Zota AR, Ettinger AS, Bouchard M, et al. Maternal blood manganese levels and infant birth weight. *Epidemiology*. 2009;20:367.
28. Zahran S, Weiler S, Mielke HW, Pena AA. Maternal benzene exposure and low birth weight risk in the United States: a natural experiment in gasoline reformulation. *Environ Res*. 2012;112:139–146.
29. Padula AM, Noth EM, Hammond SK, et al. Exposure to airborne polycyclic aromatic hydrocarbons during pregnancy and risk of preterm birth. *Environ Res*. 2014;135:221–226.
30. Stewart JA, Mitchell MA, Edgerton VS, VanCott R. Environmental justice and health effects of urban air pollution. *J Natl Med Assoc*. 2015;107:50–58.
31. Vinikoor-Imler LC, Davis JA, Meyer RE, Messer LC, Luben TJ. Associations between prenatal exposure to air pollution, small for gestational age, and term low birthweight in a state-wide birth cohort. *Environ Res*. 2014;132:132–139.
32. Breyer B, Voss-Andreae A. Food mirages: geographic and economic barriers to healthful food access in Portland, Oregon. *Health Place*. 2013;24:131–139.
33. Goodling E, Green J, McClintock N. Uneven development of the sustainable city: shifting capital in Portland, Oregon. *Urban Stud Plan Fac Publ Present*. 2015;36:504–527.
34. Hagerman C. Shaping neighborhoods and nature: urban political ecologies of urban waterfront transformations in Portland, Oregon. *Cities*. 2007;24:285–297.
35. Monroe Sullivan D, Shaw SC. Retail gentrification and race: the case of Alberta Street in Portland, Oregon. *Urban Aff Rev*. 2011;47:413–432.
36. *Portland Gentrification Maps and Data*. Available at: http://www.governing.com/gov-data/portland-gentrification-maps-demographic-data.html. Accessed July 16, 2018.
37. Allen P. Bullseye Glass Monitoring Report. Available at: https://www.oregon.gov/deq/filterdocs/bullseyemodelingreview.pdf Published June 2017. Accessed September 2017.