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Residential Proximity to Oil and Gas Development and Birth Outcomes in California: A Retrospective Cohort Study of 2006–2015 Births

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BACKGROUND: Studies suggest associations between oil and gas development (OGD) and adverse birth outcomes, but few epidemiological studies of oil wells or inactive wells exist, and none in California.

OBJECTIVE: Our study aimed to investigate the relationship between residential proximity to OGD and birth outcomes in California.

METHODS: We conducted a retrospective cohort study of 2,918,089 births to mothers living within 10 km of at least one production well between January 1, 2006 and December 31, 2015. We estimated exposure during pregnancy to inactive wells count (no inactive wells, 1 well, 2–5 wells, 6+ wells) and production volume from active wells in barrels of oil equivalent (BOE) (no BOE, 1–100 BOE/day, >100 BOE/day). We used generalized estimating equations to examine associations between overall and trimester-specific OGD exposures and term birth weight (tBW), low birth weight (LBW), preterm birth (PTB), and small for gestational age birth (SGA). We assessed effect modification by urban/rural community type.

RESULTS: Adjusted models showed exposure to active OGD was associated with adverse birth outcomes in rural areas; effect estimates in urban areas were close to null. In rural areas, increasing production volume was associated with stronger adverse effect estimates. High (>100 BOE/day) vs. no production throughout pregnancy was associated with increased odds of LBW [odds ratio (OR) = 1.40, 95% confidence interval (CI): 1.14, 1.71] and SGA (OR = 1.22, 95% CI: 1.02, 1.45), and decreased tBW (mean difference = −36 grams, 95% CI: −54, −17), but not with PTB (OR = 1.03, 95% CI: 0.91, 1.18).

CONCLUSION: Proximity to higher production OGD in California was associated with adverse birth outcomes among mothers residing in rural areas. Future studies are needed to confirm our findings in other populations and improve exposure assessment measures. https://doi.org/10.1289/EHP5842

Introduction

Oil and gas development (OGD) by the U.S. petroleum industry spans decades in many states but concern about its potential health and equity impacts did not gain traction among researchers until the recent rapid increase in hydraulic fracturing (HF) (Finkel and Law 2011; Kovats et al. 2014; Mitka 2012). As of 2017, California (CA) was one of the top five producers of crude oil in the country (U.S. EIA 2018a, 2018b). Four of the 10 largest U.S. oil fields are in CA's San Joaquin and Los Angeles Basins (Long et al. 2015a), and unlike newer shale gas plays, most of CA's natural gas is extracted from reservoirs also producing oil (Long et al. 2015b). Given the long history of OGD in CA, stimulation techniques, such as water and steam injection and HF, are primarily used at established sites rather than newly drilled wells. Oil recovered via water flooding and steam injection (conventional enhanced oil recovery methods) accounted for 76% of the state's oil production in 2009 (Long et al. 2015b), whereas HF, an unconventional stimulation technique, accounted for 20% of CA's oil production in the last decade. Due to types of geological formations, HF practices in CA differ from other states, potentially resulting in differing environmental hazards (Long et al. 2015b). OGD production in CA also occurs in both rural and urban settings in comparison with other states, such as rural Pennsylvania and Colorado, where many epidemiological studies have been conducted (Casey et al. 2015; Currie et al. 2017; Hill 2018; McKenzie et al. 2014; Rasmussen SG et al. 2016; Tustin et al. 2017). Therefore, an epidemiological study of the relationship between adverse birth outcomes and OGD in CA, a state with a diverse population and the most annual births of any U.S. state, can provide insights about the potential health impacts of OGD exposure in both rural and urban areas.

Characterizing exposures related to OGD poses significant measurement challenges because multiple environmental hazards are associated with different stages of extraction and production. OGD involves the development of oil and gas sites and wells (production and injection for enhanced recovery), transport of materials to and from well sites, drilling, operation of equipment to recover oil and gas, and collection and disposal of chemicals and waste separated from the raw oil and gas (Long et al. 2015a). These activities are associated with diverse environmental hazards, including air and water pollutants, noise, odors, excessive and inappropriate lighting, and undesired land use changes (Adgate et al. 2014; Long et al. 2015a). The application of unconventional techniques presumably enhances the environmental burdens because the additional toxic chemicals that are used can potentially be released into air, water, and soil (Adgate et al. 2014; Long et al. 2015a; Macey et al. 2014; Roy et al. 2014; Vengosh et al. 2014).

Air pollutants associated with OGD include particulate matter (PM) with an aerodynamic diameter of $<2.5\ \mu m$ ($PM_{2.5}$), diesel PM, nitrogen oxides (NO_x), secondary ozone formation, mercury, and volatile organic compounds (VOCs) like benzene, toluene, ethylbenzene and xylene (BTEX) from truck traffic, drilling, hydraulic fracturing, production, and flaring (Allshouse et al. 2019; Brantley et al. 2015; Colborn et al. 2014; Eapi et al. 2014; Esswein et al. 2014; Franklin et al. 2019; Goetz et al. 2015; Koss et al. 2017; Lan et al. 2015; Macey et al. 2014; Marrero et al. 2016; Maskrey et al. 2016; Mellqvist et al. 2017; Roy et al. 2014; Warneke et al. 2014). Additionally, fugitive toxic air contaminants can escape at the wellhead (Garcia-Gonzales et al. 2019; Warneke et al. 2014) that might affect health near the points of release. Water contaminants

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associated with OGD include gas-phase hydrocarbons, chemicals mixed in drilling fluids, and naturally occurring salts, metals, and radioactive elements within shale that surface with wastewater along with recovered oil and gas and that can contaminate potable water via leaks and spills or evaporate (Adgate et al. 2014; Hildenbrand et al. 2015; Long et al. 2015a; Vengosh et al. 2014). Noise pollution is associated with well pad construction, truck traffic, drilling, pumps, flaring of gases, and other processes (Allshouse et al. 2019; Blair et al. 2018; Ebisu and Bell 2012; U.S. BLM 2006). Drilling and production activities occur both during the daytime and nighttime, and light pollution has been previously reported as a nuisance in communities undergoing unconventional OGD (Long et al. 2015a), suggesting OGD may affect the health of nearby communities via increased psychosocial stress.

Several OGD-related environmental exposures have been linked to reduced birth weight and gestational age: air pollution, e.g., $PM_{2.5}$, NOx, SOx (Basu et al. 2014; Dadvand et al. 2013, 2014; Ebisu and Bell 2012; Long et al. 2015a; Morello-Frosch et al. 2010; Ponce et al. 2005; Ritz et al. 2007); noise pollution (Arroyo et al. 2016; Gehring et al. 2014); some of the chemical compounds found in OGD wastewater (Long et al. 2015a; Valero de Bernabé et al. 2004); and psychosocial distress (Dominguez et al. 2008; Goldenberg et al. 2008; Rondó et al. 2003; Valero de Bernabé et al. 2004). Previous studies examining the relationship between unconventional OGD and birth outcomes provide suggestive evidence of adverse effects. Although study designs vary, most have characterized OGD exposure based on the density and distance of HF shale gas wells near the maternal residence in urban and rural Colorado (McKenzie et al. 2014, 2019), Pennsylvania (Casey et al. 2015; Currie et al. 2017; Hill 2018; Ma 2016; Stacy et al. 2015), Oklahoma (Janitz et al. 2019), and urban Texas (Walker Whitworth et al. 2018, 2017). Among the 10 studies, 8 evaluated our outcomes of interest. Some studies found greater exposure to OGD was associated with reductions in term birth weight (tBW) (Hill 2018; Stacy et al. 2015) and increased odds or incidence of low birth weight (LBW) (Currie et al. 2017; Hill 2018), preterm birth (PTB) (Casey et al. 2015; Walker Whitworth et al. 2018, 2017), and small for gestational age births (SGA) (Hill 2018; Stacy et al. 2015). However, those studies also reported statistically insignificant (Casey et al. 2015; Whitworth et al. 2017) or inverse associations (McKenzie et al. 2014; Stacy et al. 2015) for some birth outcomes.

Building on this research, our study focused on OGD in CA. We conducted our analysis in regions where OGD is concentrated: the Sacramento Valley, San Joaquin Valley, South Central Coast, and South Coast air basins. To our knowledge, our retrospective cohort study with births from 2006–2015 is the first to evaluate prenatal OGD exposure from oil as well as gas wells, inactive as well as active wells, and non-HF and HF wells in rural and urban settings of CA.

Methods

Study Population

Birth records for 1 January 2006 to 31 December 2015 were obtained from the California Department of Public Health (CDPH). CDPH collects statewide birth records that include mother's residential address at the time of birth, which we geocoded to assign exposure to OGD exposure and area-level covariates using ArcGIS (ESRI). Births with missing street-level addresses or that could not be successfully geocoded after a manual cleaning of the address fields for spelling and punctuation errors were excluded (5%). We selected the Sacramento Valley, San Joaquin Valley, South Central Coast, and South Coast air basins because they had the highest well densities in CA between 2005 and 2015 (Figure S1). We illustrate the construction of the study population in Figure 1. Exclusion criteria included missing last menstrual period (LMP) date, which was approximated as the date of conception and used to estimate gestational age (3%); congenital anomalies or abnormal birth conditions such as cleft lip and Down's syndrome (4%); plural births, e.g., twins, triplets (4%); implausible birth weights of less than 500 g or greater than 5,500 g (4%) (Alexander et al. 1996; Padula et al. 2014; Ponce et al. 2005; Talge et al. 2014); and implausible gestational ages of less than 22 or greater than 44 wk (4%) (Alexander et al. 1996; Talge et al. 2014). To limit unmeasured confounding and enhance comparability of exposed and unexposed populations, we also excluded births to mothers who did not live within 10 km of at least one oil/gas production well (3%). Finally, we excluded observations with any missing covariates or outcomes (2%) to arrive at a final study population of 2,918,089 births ($N = 2,718,629$ term births). All study protocols were approved by the Institutional Review Board of the CA Department of Public Health (#13-05-z) and the University of California, Berkeley (# 2013-10-5,693).

Birth Outcomes

We assessed the relationship between OGD and four outcomes: *a*) continuous birth weight (grams) among tBW (≥37 completed weeks); *b*) LBW (<2,500 g); *c*) PTB (<37 wk); and *d*) SGA (birth weight less than the U.S. sex-specific 10th percentile of weight for each week of gestation (Talge et al. 2014). Gestational age was estimated by subtracting the LMP date from the date of birth.

Exposure Assessment

Active and inactive oil and gas well records including monthly production data were downloaded from the CA Division of Oil, Gas and

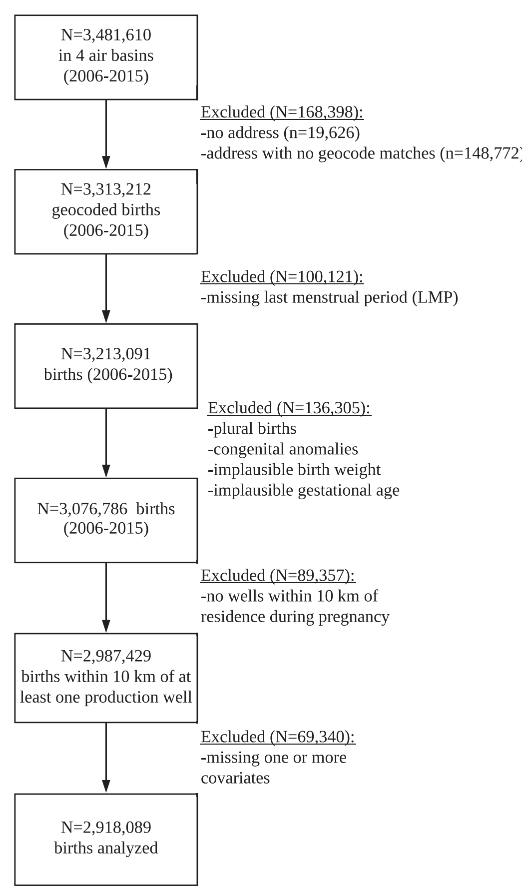


Figure 1. Flow diagram of study population development and exclusion criteria applied.

Geothermal Resources website (CA DOGGR) in December 2015 (the division has been renamed to the CA Geologic Energy Management Division, CalGEM, as of January 2020). We assessed exposure to inactive wells because previous studies have found fugitive methane emissions from abandoned production wells that have not been plugged or were improperly plugged (Boothroyd et al. 2016; U.S. EPA 2018; Kang et al. 2016). VOCs, such as BTEX and toxic air contaminants, are likely coemitted with methane (LACDPH 2018; SCAQMD 2019), and exposure to VOCs, including BTEX and formaldehyde, are associated with adverse birth outcomes (Bolden et al. 2015; Chang et al. 2017; Maroziene and Grazuleviciene 2002). Some of the 224,695 wells in the data set began producing as far back as 1900. The DOGGR data included well latitude/longitude and monthly production volume (barrels of oil and/or cubic meters of natural gas). We defined a production well as active if it produced at least one unit of oil or gas in a given month; production wells could transition between active and inactive status across the study period. We combined these well data with mothers' residential addresses at the time of delivery, date of conception (defined as LMP), and date of delivery to assign prenatal exposure to oil and gas wells.

Study participants lived within 10 km of at least one active or inactive well at the time of delivery. We classified women who had at least one active or inactive well within 1 km of their residential address as exposed (Figure 2); prior literature suggests highest exposure to OGD-related hazards within this radius (Boyle et al. 2017; McKenzie et al. 2012; Meng 2015; Walker Whitworth et al. 2018, 2017). We selected the 1-km buffer presuming that localized air pollution is likely the greatest contributor to OGD-related exposure in CA. We used the short distance to minimize the impact of dispersion and the contribution of exposure from other sources of air pollution. We calculated exposure across the entire pregnancy and by trimester to examine potential critical windows of prenatal exposure.

Exposure to active wells was characterized by oil and gas production volume during pregnancy and exposure to inactive wells by well count. Total production volume exposure from active wells within 1 km was derived by summing monthly barrels of oil and

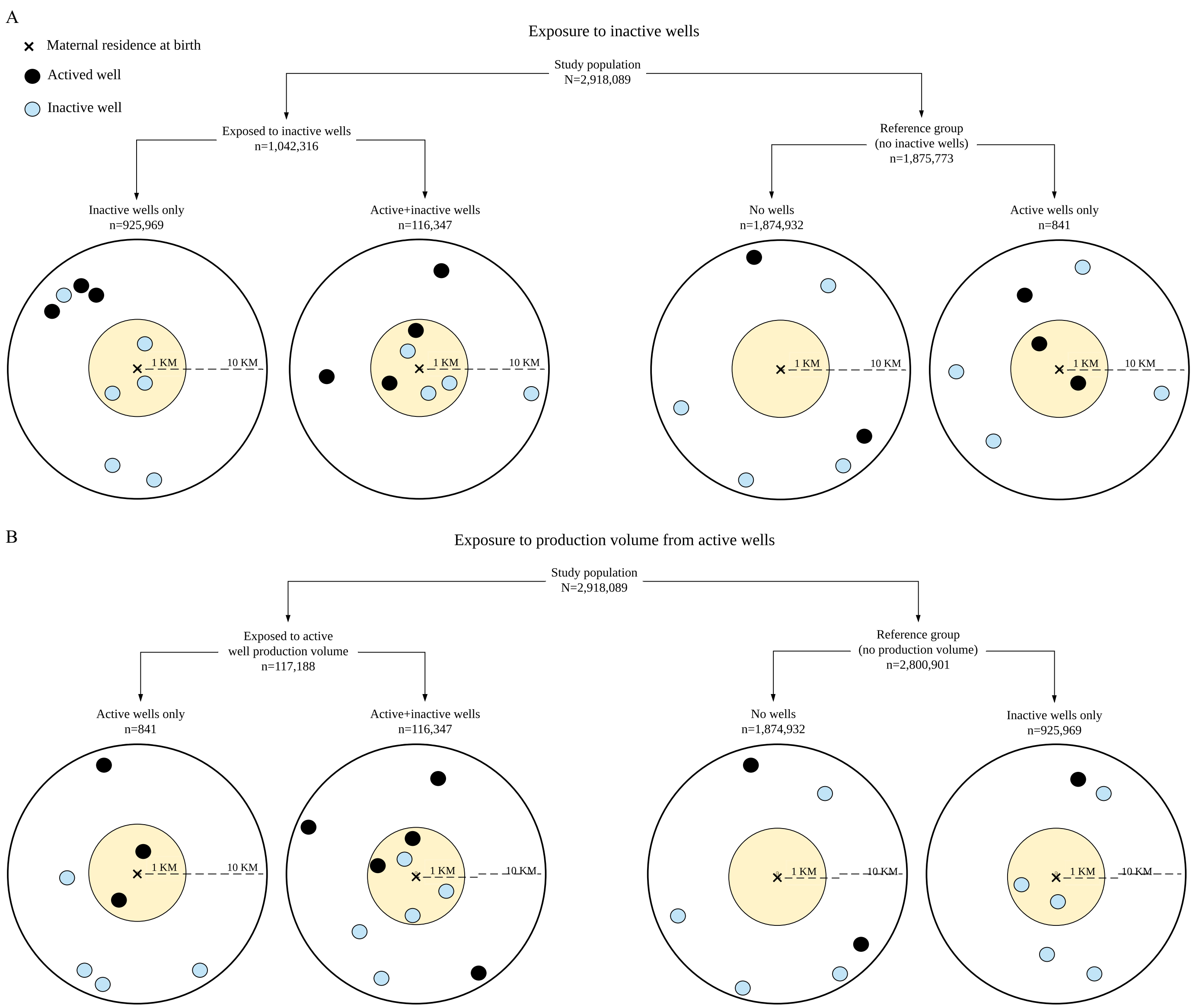


Figure 2. Schematic of definition of exposure and reference groups for inactive well count (A) and active well production volume (B). For each exposure metric, exposure was based on the presence of inactive or active wells within the 1 km buffer. Observations without the specific well type for each metric were assigned into the reference category.

barrels of oil equivalent (BOE) of natural gas. Production volume from oil and gas wells were summed because 95% of gas wells also produced oil (i.e., wet gas) and gas-only wells did not produce significant amounts of gas. Production volume was summed as shown in Equation 1:

$$\text{Total production volume}_j = \sum_{i=1}^{n}\sum_{k=k}^{l}\text{Prod(oil)}_{ik} + \sum_{i=1}^{n}\sum_{k=k}^{l}\text{Prod(gas)}_{ik}/6,$$

where Prod(oil)_{ik} was the production volume of oil (in barrels), and Prod(gas)_{ik} was the production volume of gas (in thousand cubic feet, mcf) at well i during month and year k of mother j's entire pregnancy or trimester. K is the month and year of conception or beginning of a trimester, and l is the month and year of delivery or end of a trimester. K has a minimum value of 1 equal to January 2005, and l has a maximum of 124 or December 2015. Gas production volume was converted from the original units to BOE by dividing by 6 because 6,000 cubic feet $(\text{mcf}) = 1$ BOE (Bonavista Energy Corporation 2018; Schmoker and Klett 2005). The total production volume for the first and last month of the entire pregnancy or trimester was also weighted by the proportion of the month the mother was pregnant.

We calculated the number of inactive wells within 1 km of a mother's residence during her pregnancy by subtracting the number of active wells from the total number of wells within 1 km. For analysis, we first normalized production volume by the number of days of the entire pregnancy or within each trimester by dividing production volume by the total number of days and then categorized exposure to production volume of active wells based on the exposure distribution as: *a*) no active wells, *b*) 1–100 BOE/d (moderate), and *c*) more than 100 BOE/d (high). We similarly categorized exposure to inactive wells as: *a*) no inactive wells, *b*) 1 inactive well, *c*) 2–5 inactive wells, and *d*) 6 or more inactive wells. The production volume was normalized to prevent bias from neonates born later because their exposure period was longer. Given a lack of *a priori* knowledge about the production volume or inactive well count that might constitute a harmful exposure, we selected these categories based on the distribution of each exposure metric across cases and noncases to ensure sufficient overall sample size and number of cases in each exposure group. The exposure variables were not modeled as continuous because the distribution was right skewed (Table S2). Both active and inactive well exposure variables were included in all regression models. The exposure variables were generated in R version 3.3.1 (R Development Core Team).

Covariates

Individual-level covariates that were identified *a priori* as significant predictors of our outcomes and potential confounders based on prior studies were derived from the CDPH birth records. Infant covariates included sex, month (categorical) of birth, and year of birth (categorical) to control for seasonal and secular trends. Maternal covariates included age in years (<20, 20–24, 25–29, 30–34, 35+), race/ethnicity (non-Hispanic white, black, American Indian, Asian-Pacific Islander, unknown or other, and Hispanic), educational attainment (<high school, high school graduate/GED, some college, college+), Kotelchuk index of prenatal care (inadequate, intermediate, adequate, adequate+) (Alexander and Kotelchuck 1996; Kotelchuck 1994), and parity (nulliparous vs. multiparous). For maternal race/ethnicity, American Indian, unknown, and other were combined into one category due to the small number of women in each group. We included mean-centered and mean-centered squared variables for gestational age in the tBW model to allow for nonlinearity.

We also integrated area-level variables, including indicators for air basin and census tract-based urban/rural status, modeled nitrogen dioxide (NO_2) concentrations, and a measure of income concentration. These covariates accounted for neighborhood and regional differences in air quality, economic activity, and emission sources (Arruti et al. 2011; Finkelstein et al. 2003; O'Neill et al. 2003; Wunderli and Gehrig 1990; Zhao et al. 2009). We used 2014 air basin boundaries designated by the California Air Resources Board (CARB 2014), which coincide with county boundaries and roughly delineate areas with similar air quality, meteorology, and geography. We used U.S. Census urban areas [defined as a densely developed territory consisting of urbanized areas of 50,000 or more and urbanized clusters with between 2,500 and 50,000 people (U.S. Census Bureau 2010)] to designate census tracts as urban or rural. Using 2010 boundaries, we categorized census tracts as urban if 60% or more of the tract overlapped with an urban area. We assigned, based on LMP year, tract-level annual ambient NO_2 concentration as a proxy for traffic-related air pollution (Kim et al. 2018). Last, we used the Index of Concentration at the Extremes (ICE) for income as a measure of neighborhood relative deprivation or affluence based on household income by census tract (Massey 1996). ICE provides information about concentration of privilege and deprivation of communities and has previously been associated with infant mortality (Krieger et al. 2016). ICE ranges from -1 to 1, where negative values indicate a concentration of household incomes in the lower 20th percentile of area median household income, whereas positive values indicate a concentration of household incomes in the higher 80th percentile. We calculated ICE using 2006–2010 ACS and 2011–2015 ACS metropolitan area median household income to establish percentile cutoff values that account for regional differences in the cost of living. These values were then used in combination with census tract median household income from the ACS data of the vintage of the birth year to assign a tract-level ICE value to each birth. For tracts that were not within metropolitan areas, county-level household income cutoffs were used. ICE was categorized by quartile and this categorical variable was included in adjusted models.

Statistical Analyses

Statistical analyses were conducted in SAS 9.4 (SAS Institute Inc.). All models were adjusted for individual-level and community-level covariates selected *a priori*: neonate sex, gestational age (tBW model only), month and year of birth, maternal age, race/ethnicity, educational attainment, Kotelchuck index, urban indicator, air basin, NO_2, and ICE for income. Generalized estimating equations were used to account for clustering of mothers within census tracts (Hubbard et al. 2010). Observations with any missing covariate were removed from analyses.

Initial analyses assessed exposure across the entire pregnancy and then during each trimester for the entire study population across the four air basins. Statistical significance was assessed at $\alpha = 0.05$. Effect modification (EM) of exposure to active wells by urban/rural status (primary), maternal race/ethnicity, and air basin (both secondary) was evaluated via stratification. We report the strata-specific effect estimates and confidence intervals derived from this methodology. To test the heterogeneity between strata-specific estimates, we modeled interaction terms to derive Bonferroni adjusted p-values for two-sample z-tests using model-estimated beta coefficients and variances (Buckley et al. 2017; UCLA: Statistical Consulting Group). These EM p-values indicate whether the strata-specific associations are statistically significantly different from each other or the referent group. Non-Hispanic whites were used as the referent in heterogeneity tests for the other racial/ethnic groups because higher rates of adverse birth outcomes have been observed among people of color in

Table 1. Neonate, maternal, and area-level characteristics of births by oil and gas well production volume category, California 2006–2015. Prepregnancy BMI and smoking during pregnancy were available for 2007–2015 births (2006 births excluded from the missing category).

Variable	*n* (%)	No BOE ($n=2,866,735$)	Production volume 1–100 BOE/day ($n=70,615$)	GT 100 BOE/day ($n=50,079$)	*p*-Value[a]
Neonate characteristics					
Mean birth weight [g (mean ± SD)]	2,987,429 (100)	3,327 ± 528	3,318 ± 527	3,316 ± 527	<0.0001
Mean gestational age [weeks (mean ± SD)]	2,987,429 (100)	39 ± 2	39 ± 2	39 ± 2	<0.0001
Sex					
Female	1,456,548 (49)	49	48	49	0.2879
Male	1,530,866 (51)	51	52	51	—
Missing[b]	15 (<1)	100	0	0	—
Birth month					
January	244,433 (8)	8	8	8	0.3261
February	224,691 (8)	8	8	8	—
March	245,683 (8)	8	8	8	—
April	233,297 (8)	8	8	8	—
May	242,652 (8)	8	8	8	—
June	241,962 (8)	8	8	8	—
July	260,028 (9)	9	9	9	—
August	269,714 (9)	9	9	9	—
September	266,586 (9)	9	9	9	—
October	261,399 (9)	9	9	9	—
November	245,566 (8)	8	8	8	—
December	251,418 (8)	8	8	8	—
Birth year					
2006	320,330 (11)	11	10	12	<0.0001
2007	320,698 (11)	11	11	12	—
2008	312,732 (10)	10	10	11	—
2009	300,201 (10)	10	10	10	—
2010	290,469 (10)	10	10	10	—
2011	288,006 (10)	9	10	9	—
2012	288,855 (9)	10	10	9	—
2013	287,425 (10)	10	10	9	—
2014	293,637 (10)	10	10	9	—
2015	285,076 (10)	9	9	9	—
Maternal Characteristics (%)					
Education					
<High school	764,090 (26)	26	31	21	<0.0001
High school diploma/GED	764,206 (26)	26	23	21	—
Some college	724,574 (25)	25	22	23	—
College+	665,993 (23)	23	24	35	—
Missing[b]	68,566 (2)	95	3	2	—
Age at delivery					
<20	252,857 (8)	9	9	6	<0.0001
20–24	651,062 (22)	22	21	18	—
25–29	809,072 (27)	27	27	25	—
30–34	754,714 (25)	25	26	29	—
35+	519,700 (17)	17	17	22	—
Missing[b]	24 (<1)	92	8	0	—
Race/ethnicity					
Asian/Pacific Islander	356,603 (12)	12	11	13	<0.0001
Black	154,047 (5)	5	6	9	—
Hispanic	1,673,517 (56)	56	59	47	—
Other	84,384 (3)	3	2	4	—
White	718,878 (24)	24	22	27	—
Kotelchuck index					
Inadequate	351,729 (12)	12	13	12	<0.0001
Intermediate	349,946 (12)	12	12	9	—
Adequate+	905,545 (30)	30	29	34	—
Adequate	1,380,209 (46)	46	46	45	—
Parity					<0.0001
Nulliparous	1,154,875 (39)	39	40	44	—
Multiparous	1,831,556 (61)	61	60	56	—
Missing[b]	998 (<1)	93	4	3	—
Mean pre-pregnancy BMI[c] (SD)	2,472,066 (93)	26 ± 6	26 ± 6	25 ± 6	<0.0001
Missing[b]	195,033 (7)	94	4	2	—
Smoking during pregnancy[c]					<0.0001
Smoked	49,461 (2)	2	1	1	—
Did not smoke	257,7903 (97)	98	99	99	—
Missing[b]	39,735 (1)	92	5	3	—
TRI facility: 1+within 1 km	48,189 (2)	2	4	3	<0.0001

Table 1. (*Continued.*)

Variable	n (%)	No BOE ($n=2,866,735$)	Production volume 1–100 BOE/day ($n=70,615$)	GT 100 BOE/day ($n=50,079$)	p-Value[a]
Area-level characteristics (%)					
Mean NO_2 [ppb (mean ± SD)]	2,987,408 (99)	16 ± 7	18 ± 7	19 ± 5	<0.0001
Missing[b]	21 (<1)	95	0	5	—
Urban	2,651,066 (89)	89	87	97	—
Air Basin					
Sacramento Valley	296,668 (10)	10	1	0.5	<0.0001
San Joaquin Valley	563,276 (19)	19	21	4	—
South Central Coast	178,647 (6)	6	6	1	—
South Coast	1,948,838 (65)	65	72	94	—
ICE					
Quartile 1–poverty	731,431 (25)	25	31	27	<0.0001
Quartile 2	731,403 (25)	25	23	19	—
Quartile 3	730,283 (25)	25	19	23	—
Quartile 4–wealth	724,972 (25)	25	27	31	—
Missing[b]	217 (<1)	76	9	15	—
Oil/gas wells					
Mean inactive well count (mean ± SD)	2,987,429 (100)	0	89 ± 111	160 ± 191	<0.0001
Mean active well count	2,987,429 (100)	0	4 ± 4	32 ± 27	<0.0001
Mean production volume (BOE)/d (mean ± SD)	2,987,429 (100)	0	26 ± 26	599 ± 711	<0.0001

Note: —, No data; BOE, barrels of oil equivalent; ICE, Index of Concentration at the Extremes.
[a]ANOVA or chi-square test.
[b]Distribution of missingness across categories of production volume rather than percent missing in each production volume category.
[c]No covariate data available for 2006 (not included as missing), $n=2,667,099$ births between 2007 and 2015.

comparison with whites (Bryant et al. 2010; Teitler et al. 2007). Sacramento Valley was the referent in heterogeneity tests for the other air basins because exposures to active wells were limited to rural areas of that basin, where there were also fewer births. For the effect modification analyses with race/ethnicity and air basin, only exposure across the entire pregnancy was evaluated because trimester-specific estimates were similar to those for the entire pregnancy.

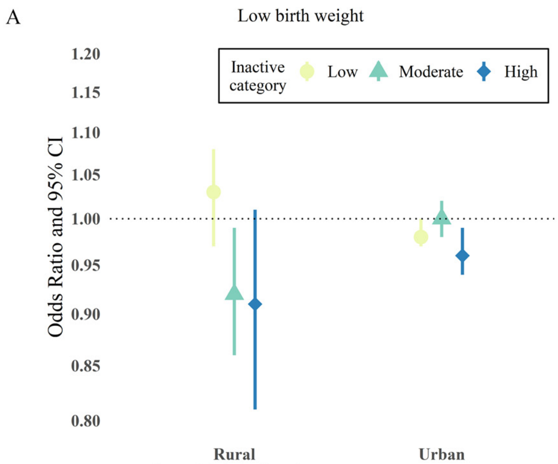
We conducted two sensitivity analyses with exposure variables across the entire pregnancy only. Mothers' smoking status during pregnancy and prepregnancy body mass index (BMI) were not collected by CDPH in 2006, so we conducted sensitivity analyses with both of these variables in one model for 2007–2015. Only 2% of mothers smoked during pregnancy among our study population within our study period (prevalence of smoking during pregnancy in CA was 2.5% in 2015) (CDPH 2015). Additionally, we considered potential confounding from other industrial sources of air pollution and included a binary variable for exposure to air pollution from other facilities (e.g., refineries, power plants, metal mining facilities) monitored for emissions, including air toxics by the CARB (CARB 2017) within 1 km (referred to as TRI facilities). Only $\sim 2\%$ of mothers resided within proximity to TRI facilities during our study period.

We tested for multicollinearity between all model variables by calculating the variance inflation factors (Schreiber-Gregory 2012), none of which were high (i.e., >10). To assess residual spatial dependence, we generated semivariograms of regression residuals plotted against distance between mothers' residential addresses (Le Rest et al. 2013; SAS) (Figure S3). The residuals appeared randomly distributed, suggesting spatial autocorrelation was likely controlled for by the study design and inclusion of spatial covariates (e.g., NO_2) in regression models.

Results

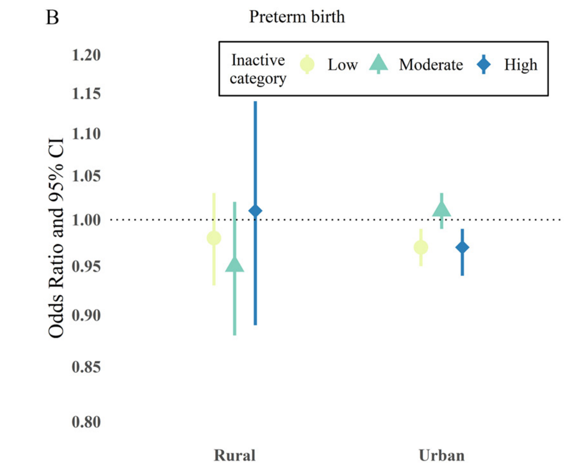
Our study included 2,918,089 births in CA between January 2006 and December 2015 located in four air basins: the Sacramento Valley, San Joaquin Valley, South Central Coast, and South Coast. The overall mean birth weight was 3,327 g [standard deviation (SD) = 528] (Table 1). Five percent ($n=148,100$) of births were LBW, 7% ($n=199,460$) preterm, and 12% SGA ($n=337,943$). A maximum of 1,189 inactive wells and 441 active wells were located within 1 km of mothers' residences during pregnancy. On average, mothers exposed to moderate production volume (1–100 BOE/d) had 89 inactive and 4 active wells within 1 km of their home during pregnancy, whereas mothers exposed to high production volume (>100 BOE/d) had an average of 160 inactive wells and 32 active wells within a 1-km buffer. The average moderate total production volume from active wells producing oil and gas during pregnancy was 26 BOE/d, and the average high total production volume was 599 BOE/d. Temporal trends of mean annual production volume and annual rates of the binary birth outcomes showed no distinct patterns in either rural or urban areas (Figure S4A,B). Plots of temporal trends in mean annual production volume and mean annual tBW also did not reveal consistent patterns in either rural or urban areas (Figure S4C,D). The reference (no BOE) and exposed populations were relatively similar in terms of demographic and socioeconomic factors (Table 1). Compared to the reference and moderate production volume groups, mothers in the high production volume category were slightly more educated (35% vs. 23.5%, on average, college or more educated), older (22% vs. 17%, on average, aged 35 or more), more often non-Hispanic (53% vs. 42.5%, on average, non-Hispanic races), more likely to have no previous pregnancies (44% vs. 39.5%, on average, nulliparous), and to reside in urban areas (97% vs. 88%, on average), in the South Coast air basin (94% vs. 68.5%, on average) and in areas with greater wealth (31% vs. 26%, on average, in ICE quartile 4). Finally, babies born to mothers exposed to high production volume weighed on average 2 and 11 grams less than those born to mothers exposed to moderate production volume and reference group, respectively.

Adjusted models generally found no associations between inactive well count and adverse birth outcomes in both rural and urban areas (Figure 3, Tables S1–S2). All statistically significant associations indicated modestly decreased odds of LBW and PTB (0.96–0.97) (Figure 3A,B; Table S1) or minimally increased birth weight (4–5 g) (Figure 3D; Table S2) related to increased inactive OGD well exposure. Models based on trimester-specific exposures yielded similar estimates across trimesters for all four birth outcomes (Table S1–S2).



Number of births by inactive count category

	Rural	Urban
Low	36,357	380,234
Moderate	26,387	319,349
High	21,573	258,416



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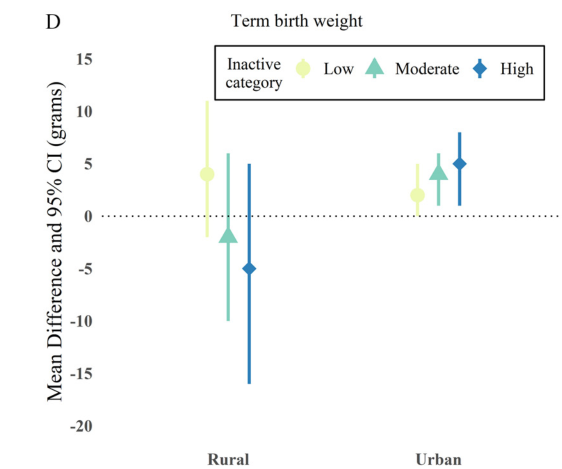
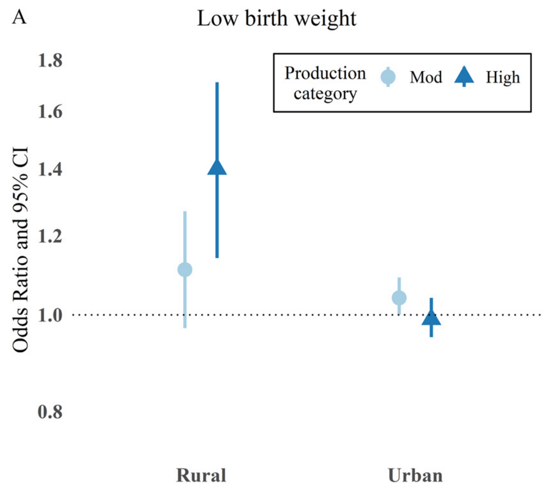


Number of births by inactive count category

	Rural	Urban
Low	34,056	354,859
Moderate	24,818	297,511
High	20,203	241,377

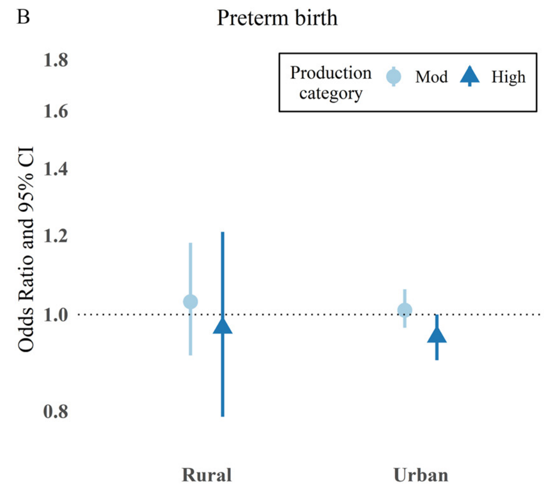
Figure 3. Plots of rural vs. urban odds ratios or mean difference in birth weight (grams) and 95% confidence interval (CI) for associations between exposure to low, moderate, and high counts of inactive wells across the entire pregnancy and low birth weight (A), preterm birth (B), small for gestational age (C), and continuous term birth weight (D). Logistic regression models adjust for inactive well count, child's sex, birth month and birth year, and maternal education, age, race/ethnicity, Kotelchuck prenatal care index, parity, air basin, NO_2 and ICE for income. In addition to the covariates adjusted for in the logistic regression models, the linear regression models also adjusted for gestational age. All y-axes are on the logarithmic scale except for on the term birth weight plot. Numerical values plotted here can be found along with estimates for the three trimesters and p-values for statistical tests for effect modification in Tables S1–S2.

For exposures to production volume from active wells in unstratified models, we observed significant associations between production volume and LBW and SGA (Table S3). When we stratified models by the urban indicator, we observed significant effect modification with stronger associations between high production volume and LBW ($p = 0.01$, Table S4) and tBW ($p = 0.001$, Table S7) in rural areas (Figure 4). Compared to the reference group, the odds ratio for LBW was 1.11 [95% confidence interval (CI): 0.97, 1.27] (Table S4) and the OR for SGA was 1.07 (95% CI: 0.97, 1.19) (Table S6) with exposure to moderate production volume across the entire pregnancy in rural areas vs. ORs of 1.04 (95% CI: 1.00, 1.09) and 1.03 (95% CI: 1.00, 1.07), respectively, in urban areas (Figure 4A,C). Exposure to high production volume was associated with an OR of 1.40 (95% CI: 1.14, 1.71) for LBW and an OR of 1.22 (95% CI: 1.02, 1.45) for SGA in rural areas vs. ORs of 0.99 (95% CI: 0.95, 1.04) and 1.04 (95% CI: 1.01, 1.07), respectively, in urban areas (Figure 4A,C; Tables S4, S6). Exposure to high production volume was also associated with decreased tBW (mean difference $= -36$ g; 95% CI: -54, -17) for the rural stratum in comparison with the urban stratum (mean difference $= 1$ g, 95% CI: -5, 8) (Figure 4D; Table S7). For LBW, SGA, and tBW, the strength of the associations increased with higher production volume among the rural, but not the urban, population. In general, exposure to production volume throughout pregnancy was not associated with PTB within rural or urban populations (Figure 4B; Table S5). Models based on trimester-specific exposures yielded similar estimates and EM p-values for all birth outcomes (Tables S4–S7), except the third trimester for PTB, where exposure to moderate production volume was associated with increased odds of PTB (OR $= 1.06$; 95% CI: 1.02, 1.11) and high production volume was associated



Number of births by production category

	Rural	Urban
Moderate	8,957	59,685
High	1,689	46,857



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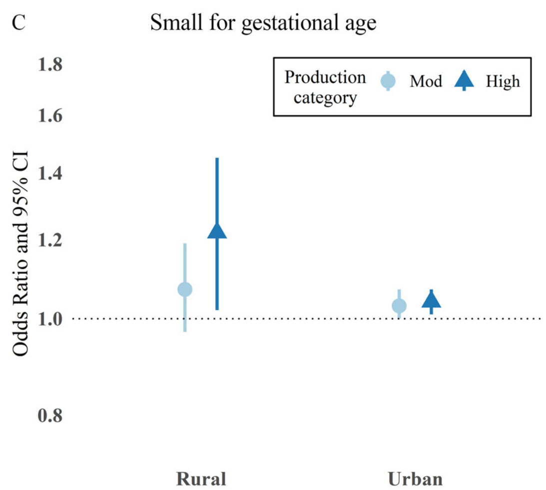

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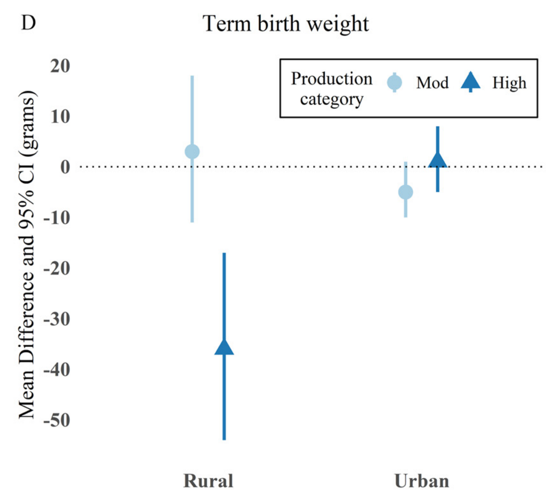

Number of births by production category

	Rural	Urban
Moderate	8,339	55,565
High	1,590	43,770

Figure 4. Plots of rural vs. urban odds ratios or mean difference in birth weight (grams) and 95% confidence interval (CI) for associations between exposure to moderate and high production volume across the entire pregnancy and low birth weight (A), preterm birth (B), small for gestational age (C), and continuous term birth weight (D). Logistic regression models adjust for inactive well count, child's sex, birth month and birth year, and maternal education, age, race/ethnicity, Kotelchuck prenatal care index, parity, air basin, NO_2 and ICE for income. In addition to the covariates adjusted for in the logistic regression models, the linear regression models also adjusted for gestational age. All *y*-axes are on the logarithmic scale except for on the term birth weight plot. Numerical values plotted here can be found along with estimates for the three trimesters and *p*-values for statistical tests for effect modification in Tables S4–S7.

with decreased odds of PTB in urban areas (OR = 0.82; 95% CI: 0.77, 0.88) (Table S5).

Maternal race/ethnicity (Tables S8–S9) and air basin (Tables S10–S11) did not significantly modify associations between exposure to active well production volume and birth outcomes. Heterogeneity tests were only conducted on the rural population because the effect sizes across outcomes were greater than those of the urban population. Nearly all strata-specific effect estimates included the null and all EM *p*-values from heterogeneity tests were insignificant across all outcomes.

Sensitivity analyses that included: *a*) prepregnancy BMI and smoking during pregnancy for 2007–2015 births (Table S12) and *b*) exposure to TRI facilities (Table S13) did not change effect estimates by more than 10%.

Discussion

CA's OGD primarily uses conventional drilling and enhancement methods and, to a much lesser degree, HF. To our knowledge, our study is the first to quantify prenatal exposures to both inactive wells and cumulative oil and gas production volume from active wells in proximity to pregnant women and to evaluate differences in associations by rural vs. urban areas in CA. In rural areas, we found that exposure to high production volume was significantly associated with increased odds of LBW and SGA and decreased tBW in comparison with the nonexposed group. In urban areas, exposure within 1 km of high production volume relative to no exposure was only significantly associated with increased odds of SGA; effect estimates for exposure to moderate production volume in rural and urban areas were all insignificant.

One prior study, by McKenzie et al. (2019), evaluated urban/rural residential status as an effect modifier. Although that study examined birth defects, the authors found significantly increased odds for four congenital heart defects in the medium and highest exposure groups (based on an intensity-adjusted inverse-distance weighted well-count metric) relative to the lowest group in rural areas (McKenzie et al. 2019); no significant associations were observed for birth defects in urban areas. These rural vs. urban differences in effect estimates align with the stronger effect estimates we observed in rural areas in CA for LBW and tBW. McKenzie et al. (2019) also discovered a potential additive effect from other sources of air pollution besides OGD in their analysis. Here, we considered residual confounding from TRI facilities within 1 km, but inclusion of this covariate did not change the rural/urban strata-specific effect estimates. Nevertheless, there may be residual confounding from other sources of air or drinking water pollution that we could not account for in our analysis. For example, the ratio of produced water from OGD (which can contain naturally occurring or injected organic/inorganic chemicals, chemicals that are reaction byproducts, and radioactive materials) to oil and gas extracted increases with well age (Veil et al. 2004). Certain chemicals from produced water could evaporate into the air or percolate into groundwater sources, depending on disposal methods (Long et al. 2015a). Air and water pollution concentrations could differ regionally based on dispersion and hydrological transport patterns. Additionally, individual factors that we could not measure in our study, such as maternal occupation, housing quality, indoor air quality, dependence on groundwater sources for drinking water, and underlying population sensitivity to OGD-related pollutants may have contributed to observed differences in effect estimates between rural and urban settings. In the air pollution literature, the exposure–response relationship between cardiovascular disease mortality and $PM_{2.5}$ is relatively steep at low levels of exposure but flattens out at higher levels (Pope et al. 2009; Smith and Peel 2010). Such exposure–response relationships could apply to the OGD setting where urban dwellers may be less affected by OGD-specific pollutants because OGD as an emission source contributes a relatively small percentage to ambient air pollution levels in urban areas, which tend have higher pollutant concentrations overall from diverse mobile and stationary sources. Indeed, average NO_2 levels among urban areas in our study were double that of rural areas.

Results from our analysis align with prior studies that observed decreased birth weight associated with maternal exposure to OGD activities (Currie et al. 2017; Hill 2018; Stacy et al. 2015). However, associations between exposure to OGD and LBW and SGA from other studies have been mixed, with increased odds (Stacy et al. 2015) or incidence probability (Currie et al. 2017; Hill 2018) as well as decreased odds (McKenzie et al. 2014) or no associations (Casey et al. 2015; Whitworth et al. 2017). Although the mechanisms by which OGD may adversely affect birth weight outcomes remain uncertain, air pollution and noise may be possible pathways that affect maternal health during pregnancy. During production, operation of various ancillary equipment (e.g., wellhead compressors, pneumatic devices, separators, and dehydrators) to collect and process oil and gas generate air pollutants (Garcia-Gonzales et al. 2019). Multiple VOCs have been measured at oil and gas wellheads and off-site, including BTEX and formaldehyde. At ambient levels, BTEX and formaldehyde have been linked to significant decreases in birth weight (Bolden et al. 2015; Chang et al. 2017; Maroziene and Grazuleviciene 2002). Flaring also occurs with oil-producing and horizontally drilled wells (Franklin et al. 2019) and can contribute to spikes in $PM_{2.5}$, black carbon, and VOCs during production (Allshouse et al. 2019; Franklin et al. 2019). Relative to other phases of OGD, excessive noise is minimized during production (Allshouse et al. 2019; Hays et al. 2017). However, noise from compressor stations often exceed the World Health Organization's recommended 55 dBA at night (Hays et al. 2017) and noise above 65 dBA was measured 20% of the time between 1900 hours and 0700 hours (7:00 P.M. and 7:00 A.M.) in one study (Allshouse et al. 2019). Excessive noise can lead to annoyance and impaired sleep quality (Hays et al. 2017), which have been linked to LBW (Abeysena et al. 2010; Owusu et al. 2013) and PTB (Li et al. 2017).

Unlike previous studies, we found no significant association between exposure to active wells and PTB except in the third trimester in urban areas where moderate exposure appeared harmful and high exposure protective. Exposure to OGD was associated with modestly decreased odds for PTB (Stacy et al. 2015) and increased odds (Casey et al. 2015) in Pennsylvania and increased odds in Texas (Walker Whitworth et al. 2018; Whitworth et al. 2017). The two Pennsylvania studies were conducted in different regions of Pennsylvania and among different populations [general for Stacy et al. (2015) and patients served by one health-care provider for Casey et al. (2015)]. The inverse association in the Stacy et al. (2015) analysis was only observed for the second quartile of exposure in comparison with the lowest quartile, whereas the association increased with greater exposure (quartiled) in the Casey et al. (2015) study. In Texas, the association was only significant with the highest level of exposure within 10 miles (Walker Whitworth et al. 2018) and the first and second trimesters with exposure within half a mile (Whitworth et al. 2017). Associations for PTB appear to vary by level of exposure as well as trimester. We only observed significant associations—increased odds with moderate exposure and decreased odds with high exposure—in urban areas in the third trimester. Previous studies on air pollution and birth outcomes have suggested that the first and third trimesters are critical windows of exposure for LBW and PTB (Ritz and Wilhelm 2008; Woodruff et al. 2009). Additionally, the significant inverse association between high OGD exposure and PTB in urban areas may reflect residual confounding or live-birth bias. Other socioeconomic status characteristics that were not controlled for in our models could have led to underlying differences among urban dwellers or their exposure patterns. Moreover, if more highly exposed or more vulnerable mothers were less likely to become pregnant or more likely to experience fetal loss, a so-called "depletion of susceptibles" could have occurred (Raz et al. 2018), and a seemingly protective effect would then be observed. Although we could not evaluate fertility patterns or spontaneous abortion in our analysis, a study in Ecuador observed greater odds of spontaneous abortion among women who lived within 5 km downstream of an oil field in comparison with those who lived at least 30 km upstream of an oil field (San Sebastian et al. 2002).

The inconsistent results across studies may reflect differences in statistical and exposure assessment methods, study population demographics, and OGD infrastructure. First, to limit unmeasured confounding, our analyses restricted the study population to those individuals living within 10 km of at least one active or inactive well at the time of delivery. Similar to Whitworth et al. (2017), we specified the unexposed group as those pregnancies with some well activity, but no well activity within 1 km. Besides their exposure, the control and exposed groups are likely more similar to each other on other characteristics (e.g., unmeasured socioeconomic factors) than a control group selected from greater distances or other regions. Second, we applied a 1-km buffer for our exposure metric without weighting, i.e., without up-weighting wells at a shorter distance from maternal residences. Previous studies used inverse distance weighting (McKenzie et al. 2014; Stacy et al. 2015) or inverse distance squared weighting (Casey et al. 2015; Walker Whitworth et al. 2018, 2017) but often included wells beyond our 1-km buffer.

Inverse distance weighting has been applied in many air pollution studies (de Mesnard 2013). Although air pollution may be a large contributor to OGD-related exposure, we did not assume that it is the only OGD-related hazard, and within such a short distance (1 km), dispersion patterns of OGD pollutants may be relatively uniform. Therefore, we weighted all wells equally within the 1-km buffer. Third, we examined separate effects of inactive wells and active well production volume, whereas prior studies have not considered inactive wells separately and often only examined the density of (McKenzie et al. 2014; Stacy et al. 2015; Whitworth et al. 2017) or total production volume from unconventional wells (Casey et al. 2015; Walker Whitworth et al. 2018). Including both inactive and active wells allowed us to distinguish possible differential effects by well type. Fourth, our CA study population was more racially and ethnically diverse than those in other studies conducted in Colorado and Pennsylvania, which may contribute to differences in analytical results. Finally, California's OGD infrastructure is older than infrastructure in other states and utilizes less HF in comparison with OGD in Pennsylvania, Colorado, and other states where production infrastructure is newly established (Long et al. 2015b). These regional differences in OGD infrastructure may affect the type of hazards associated with them and their implications for maternal health and birth outcomes.

Our study is the first to highlight differences in potential health impacts of exposure to active OGD based on total production volume from both oil and gas wells and inactive wells. We did not, however, directly measure OGD environmental impacts via, for example, air or drinking water monitoring near active or inactive wells. Several OGD-related hazards—air toxics, water pollutants, noise, excessive lighting—may elicit a variety of biological responses, but our exposure measure precluded identification of specific pathways through which OGD may affect birth outcomes. Further, the cumulative exposure–response curve of all of the potential hazards and health outcomes may differ than that for each individual hazard separately. For example, living in proximity to oil and gas fields and seeing the active rigs daily might induce stress, worry, and lack of sleep (Ferrar et al. 2013; Hirsch et al. 2018; Long et al. 2015a; Palagini et al. 2014). However, individuals may habituate, leading to biological responses that may peak and level off (Basner et al. 2011), whereas we might expect a linear exposure–response related to air pollution exposures.

We observed some modest inverse associations between inactive wells and birth outcomes, primarily in urban areas. Inactive wells can pose risks in several ways. To date, excessive fugitive methane emissions have been measured at abandoned (unplugged) well sites, with higher concentrations detected at sites with compromised wells (Boothroyd et al. 2016; Kang et al. 2016). Residual off-gassing of air contaminants such as BTEX could also occur, which has prompted the South Coast air district and DOGGR to begin to collect air toxics and VOCs emissions data (LACDPH 2018; SCAQMD 2019; California AB1328). Of greater concern is contamination of potable water sources from subsurface leakage and migration of contaminants through abandoned or idle wells (Long et al. 2015a). In an assessment of groundwater contamination from OGD in Ohio and Texas over more than a decade, abandoned wells accounted for 22% (Ohio) and 14% (Texas) of contamination incidents (Ground Water Protection Council 2011). In CA, idle wells may be repurposed for wastewater disposal or later revitalized with new technologies (Walker 2011). Wells operating with old infrastructure pose greater risks of leakages through the well casing and cement barriers (Ingraffea et al. 2014). HF could also increase the risk of surface or groundwater contamination via abandoned wells due to hydrological pressure changes; in one rare incident, an abandoned well in Pennsylvania produced a 30-foot geyser of brine and gas for more than a week after a nearby gas well underwent HF (EPA 2016). We may not have observed any consistent or significant associations between exposure to inactive wells and adverse birth outcomes because we were not able to capture these nuanced exposure pathways with well count alone, leading to potential exposure misclassification.

Other limitations include our inability to adjust for several individual-level factors. Due to lack of data linkage, we could not control for the correlation between siblings (though we do include parity in all models) or maternal mobility during pregnancy. Birth records did not include a linking variable for siblings and only documented the residential address at time of birth. Previous studies on impacts of residential mobility during pregnancy suggest that ignoring residential mobility may lead to modest bias in associations toward the null or result in nondifferential exposure misclassification (Chen et al. 2010; Hodgson et al. 2015; Lupo et al. 2010; Pennington et al. 2017). However, exposure estimates based on addresses captured at birth vs. conception have been highly correlated (Chen et al. 2010; Lupo et al. 2010; Pennington et al. 2017). Across studies, $\leq 30\%$ of mothers moved during pregnancy and moving distances were relatively short and within the same county (Bell and Belanger 2012; Chen et al. 2010; Hodgson et al. 2015; Lupo et al. 2010; Miller et al. 2010; Pennington et al. 2017). The extent of misclassification error depends on the spatial variability in the exposure (Hodgson et al. 2015). Additionally, exposure misclassification may be less prominent in the third trimester. Across environmental epidemiological studies that evaluated the impact of residential mobility on effect estimates by trimester, the highest rates of mobility occurred in the second trimester (Bell et al. 2018; Bell and Belanger 2012). Lowest residential mobility was observed in the first trimester among three studies and in the third trimester among two studies (Bell et al. 2018; Bell and Belanger 2012). Exposure misclassification due to mobility in the third trimester is less likely to be an issue, due to its proximity to the time of delivery, when the maternal residential address is collected and listed on the birth certificate. In addition to residential mobility, maternal occupational mobility should also be considered. One study that evaluated the impact of occupational mobility on air pollution exposure misclassification among Parisian women in the two first trimesters found that mode of transport increased NO_2 exposure in the first trimester (Blanchard et al. 2018). Our study results yielded similar effect estimates across trimesters, suggesting that any bias resulting from maternal residential and occupational mobility is likely nondifferential across trimesters.

In summary, this study expands the current literature on the health implications of OGD. We observed that prenatal exposure to active oil/gas production from both conventional and unconventional wells in CA was associated with adverse birth outcomes, and these associations varied by rural and urban areas. We observed the strongest associations with exposure to high production volume in rural areas. Future studies should consider inactive wells and conduct exposure assessments that collect environmental samples of OGD-related hazards. Such data would greatly improve exposure assignment and advance our understanding of underlying exposure sources and pathways. Additional evaluations of the relationship between oil/gas operator size, pollutant emissions, and frequency and type of violations and health outcomes would also elucidate which types of wells may be of greatest concern. Such data can inform regulatory decisions in terms of prioritizing inspection and pollution monitoring as well as emissions reduction requirements and community exposure reduction strategies.

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