Final Report

for

Pennsylvania Department of Health,
Bureau of Epidemiology

Hydraulic Fracturing Epidemiology Research Studies: Birth Outcomes

Prepared by:
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Background

Over the last 25 years, the American energy landscape has undergone an evolution, perhaps most notably with the expansion of hydraulic fracturing operations[1]. From 2000 to 2015, the number of hydraulically fractured wells in the United States increased from 23,000 to approximately 300,000. This rapid growth has corresponded to a range of economic benefits, including decreased energy costs and greatly increased production of both oil and natural gas[2]. However, mounting evidence suggests that hydraulic fracturing may have adverse impacts on public health and the environment[3-24].

Hydraulic fracturing – also known as fracking – is a process of unconventional natural gas development (UNGD) done by injecting large amounts of fluid at high pressure into dense rock in order to free trapped oil and natural gas[25]. The fluid used for injection typically consists of a mixture of water, sand (or other proppants), and various chemical additives. These wells, which are typically deeper than conventional wells, access previously unavailable reservoirs of oil and natural gas trapped in shale. The Marcellus Shale formation encompasses approximately half of Pennsylvania and is a large reservoir of natural gas.

Studies examining the associations between UNGD and birth outcomes, including small for gestational age (SGA), preterm birth, and lower term birthweight, have found inconsistent results. Table 1 summarizes results from studies examining associations between birth outcomes and exposure to UNGD (additional details can be found in Appendix Table 1). Five of the fourteen studies included in Table 1 were conducted using births in Pennsylvania (PA), which was the most commonly represented state. Other states included were California (n=2), Colorado (n=2), Oklahoma (n=1) and Texas (n=4).

Six studies examined associations with SGA[5,6,10,18,26,27]. Of these, three found associations and three did not. Among those that found associations, estimates of increased risk ranged from 18%[26] to 34%[5]. Two of the three studies conducted in PA bracketed the range of associations (Hill[26], with an increase of 18% over the mean rate, and Stacy[5], with an odds ratio of 1.34 comparing most to least exposed) and the third found no association (Casey[6]).

Nine of the fourteen studies examined preterm birth[5,6,10,12,17,23,26,28,29]. Of those, five of the nine studies did not find an association[5,17,23,26,29] while the remaining four reported an association[6,10,12]. Increased risk of preterm birth ranged from 14%[10] to 40%[6]. Of the three studies that examined preterm births in PA, two found no association (Stacy[5] and Hill[26]) while Casey[6] found the highest increased risk of any of the studies (40%), associated with the highest tertile of exposure.

Nine studies also investigated the association between birthweight and UNGD[5,6,10,18,22,23,26,27,30]. Of those, six[5,18,22,26,27,30] of the studies found associations, ranging from 19 grams[30] to 50 grams[26] reduced birthweight, while three[6,10,23] did not. Of the four studies examining birthweight conducted in PA, three[5,22,26] found associations, ranging from reductions in birthweight from 21 grams[5] to 50 grams[26], and one did not (Casey et al.[6]).

Table 1. Summation of Literature Examining Associations Between UNGD and Birth Outcomes

Year	First Author	State	SGA	Preterm Birth	Reduced Birthweight	Birth Defects
2014	McKenzie[23]	CO	--	N	N	Y/N[1]
2015	Stacy[5]	PA	Y	N	Y	--
2016	Casey[6]	PA	N	Y	N	--
2016	Ma[7]	PA	--	--	--	N
2017	Currie[22]	PA	--	--	Y	--
2017	Whitworth[10]	TX	N	Y	N	--
2018	Hill[26]	PA	Y	N	Y	--
2018	Whitworth[12]	TX	--	Y	--	--
2019	Janitz[31]	OK	--	--	--	Y/N[2]
2019	McKenzie[24]	CO	--	--	--	Y[3]
2020	Cushing[28]	TX	--	Y	Y	--
2020	Gonzalez[17]	CA	--	N/Y[4]	--	--
2020	Tran[29]	CA	Y[5]	N	Y[5]	--
2021	Willis[18]	TX	N	--	Y	--

1 – Association observed with congenital heart defects and neural tube defects but not oral clefts
2 – Association observed with neural tube defects but not congenital heart defects or oral clefts
3 – Association observed with congenital heart defects
4 – Association only observed in very preterm births (<31 weeks)
5 – Association only observed in rural and not urban areas

The study conducted by Casey et al.[6] in Eastern Pennsylvania had many strengths. They formed their cohort using electronic health record data on 10,946 infants born between January 2009 and January 2013. They estimated cumulative exposure to UNGD activity using an inverse-distance squared model that incorporated distance to maternal residence and information about four phases of well activity: well pad development, drilling, and hydraulic fracturing; and production during pregnancy. However, their time period is relatively short and early in the development of UNGD activity in PA. They also included all wells in the state in their metric as opposed to enforcing any buffer distances from residences to wells. They examined associations between well activity and four birth outcomes: small for gestational age, preterm birth, term birthweight, and low 5-minute Apgar score. As noted in Table 1, Casey et al. found evidence of an association with preterm birth, with an odds ratio of 1.4 (95% CI 1.0-1.9) in the highest quartile of well activity. They did not find any associations with term birthweight, small for gestational age, or low Apgar score.

This retrospective cohort study of birth outcomes had three specific aims: 1) to replicate earlier studies conducted in Eastern PA using a population in Southwestern PA, where UNGD has proliferated in the past 15 years; 2) to enhance and improve upon previous UNGD exposure characterizations by assessing the associations between the most studied birth outcomes and each the four phases of UNGD; and 3) to enhance and improve upon previous UNGD exposure characterizations by assessing whether associations varied by multiple buffer distances to individuals' residences.

Methods

Birth Record Data

Birth data were retrieved from the Bureau of Health Statistics and Research, Department of Health, Pennsylvania for years 2010 to 2020 following Institutional Review Board (IRB) and Protected Access approvals.

Inclusion and Exclusion Criteria

We included live births between January 1, 2010, and December 31, 2020 to mothers residing in the eight-county study area (Allegheny, Armstrong, Beaver, Butler, Fayette, Greene, Washington, and Westmoreland counties).

Exclusion criteria for the study were: Serious birth defects identified at birth; Multiple (non-singleton) birth; Unknown gestational age; Gestational age <22 weeks (pre-viability); Gestational age >41 weeks (post-term); Birth weight <500 g; and Maternal residence located outside the eight-county study area or within the City of Pittsburgh (see Appendix Table 2).

Outcome Measures

Of *a priori* interest were four birth outcomes:

1. **Low 5-minute Apgar score -** A standardized method for assessing the status of a newborn 5 minutes after birth based on five criteria, including heart rate, respiratory effort, reflex irritability, muscle tone, and color [32,33]. Each criterion is given a score of 0, 1, or 2. These scores are summed for an overall score, ranging from 0-10. A low 5-minute Apgar score was defined as a score less than 7.
2. **Small for gestational age -** Neonates with birthweights less than the 10^{th} percentile for their gestational age[34]. Small for gestational age was defined as less than the sex-specific 10^{th} percentile of weight for each week of gestation using United States birth weight reference data from Talge et al. [35].
3. **Preterm birth -** Births occurring between 22- and 36-weeks gestation. Moderate-to-late preterm births were defined as those occurring between 32-36 weeks gestation.
4. **Term birthweight -** Birthweight in grams for birth occurring between 37- and 41-weeks gestation.

Covariate Definitions

Each birth was assigned to a community based on the latitude and longitude of the birth residence associated with the record. Mothers with multiple births could have been assigned to different communities if they changed addresses between births. Community was defined as townships, boroughs, municipalities, or tracts within cities (i.e., Minor Civil Division (MCD) or component Census tract of city MCDs; Schwartz et al., 2011).

Clinical and demographic features of the neonate and mother were included as covariates to control for potential confounding, as shown in Table 2.

Table 2. Clinical and demographic covariates from birth records

Covariate	Definition
Neonate sex	Neonate sex (male, female, unknown)
Gestational age (weeks)	Obstetric estimate of gestation from the birth certificate
Maternal age (years)	Mother's age at delivery
Maternal single race (self-designated)	White Black or African American All other races Unknown or refused
Maternal Education	Less than High School: 8th grade or less, 9th-12th grade but no diploma High School or GED: High School graduate or GED completed Some college: Some college credit but not a degree, Associate's degree Bachelor's or Graduate degree: Bachelor's degree, Master's degree, doctorate or professional degree Unknown: Unknown
Smoking during the three months before or during pregnancy	Yes No Unknown
Pre-pregnancy body mass index (BMI; kg/m^2)	BMI calculated based on the mother's pre-pregnancy weight in pounds and height in feet and inches[36] (Appendix Table 3). Categorized as underweight, normal, overweight, obese, or unknown based on CDC cutoffs.
Parity	Nulliparous: 0 previous births Multiparous: $\geq$ 1 previous births
Gestational diabetes	Yes No Unknown
Adequacy of Prenatal Care Utilization (APNCU) Index[37]	**Inadequate/Unknown:** beginning care after the fourth month of pregnancy (16 weeks gestation) OR receiving less than 50% of expected prenatal care visits OR Unknown **Intermediate:** beginning care by the fourth month of pregnancy AND receiving 50-79% of expected visits **Adequate:** beginning care by the fourth month of pregnancy AND receiving 80-109% of expected visits **Adequate plus:** beginning care by the fourth month of pregnancy AND receiving 110% or more of expected visits. Adequate plus may indicate a problem in the pregnancy and is not necessarily indicative of good prenatal care.
Receipt of maternal WIC services	Yes No Unknown
Community socioeconomic deprivation (quartiles)	Quartiles (Q)1 – Q4 divided equally by the total number of communities in our study area Higher values of the index reflect greater community socioeconomic deprivation (Appendix Table 4 for details)

Exposure measures

Unconventional natural gas development activity

The primary exposure measure was an inverse distance-weighted index of UNGD activity[6,8,11,13,15] up to 10 miles (or 16,093.4 m) of maternal residence. We considered five buffer distances: 0.5 miles, 1 mile, 2 miles, 5 miles, and 10 miles. We included cumulative well count as a secondary measure of exposure.

There are four phases of UNGD: well pad preparation, drilling, hydraulic fracturing, and production. These phases vary in terms of duration and potential exposures. Information required to calculate the UNGD activity metric was obtained from the Pennsylvania Department of Environmental Protection (PA DEP) and Pennsylvania Department of Conservation and Natural Resources (PA DCNR).

1. **Well pad preparation -** the process of preparing a site where one or more wells are located. It is defined as the period 30 days before the first well on the pad is spudded (i.e., the day drilling begins).

2. **Drilling -** the creation of the wellbore. This phase begins on the well's spud (first drilling) date and ends on the drilling completion date.

3. **Hydraulic fracturing** (fracking, stimulation) **-** the process of injecting large volumes of water at high pressure into the wellbore to fracture the shale layer. This period is defined as beginning on the stimulation commencement date and ending on the stimulation completion date. Hydraulic fracturing may be repeated over time for a given well.

4. **Production -** the process of collecting natural gas or oil that, following hydraulic fracturing, travels through the wellbore to the surface. Production durations are variable; produced gas volume was represented as an average daily gas volume. A well was defined as being in production for reporting periods when production is indicated and reported production volume is non-zero.

The later phases of hydraulic fracturing and early stages of production can also be characterized by the generation of large amounts of spent fracking fluid and water term flowback fluid and produced water, respectively. All stages, but especially hydraulic fracturing, are also characterized by large amount truck traffic and heavy equipment that can also produce various air pollutants.

Phase-specific UNGD metrics were calculated for each birth using the following equations (Table 3).

Table 3. Definition of UNGD activity metric phase durations

Phase	Phase Name	Calculation of Phase-Specific Activity Metric
1	Well pad preparation	$\text{Phase 1 metric for birth } j = \sum_{i=1}^{n} \sum_{k=1}^{l} \frac{I_A(K)}{d_{ij}^2}$ Where: • n is the number of well pads within 0.5, 1, 2, 5, or 10 miles of maternal residence j • k is equal to the date of the beginning of gestation and l is equal to the birth date for birth j • $I_A(K)$ is equal to 1 when $d_{ij} \leq$ buffer distance (miles) and the phase overlaps with gestation, and is equal to 0 otherwise • d^2_{ij} is the squared distance (m^2) between well pad i and maternal residence j
2	Drilling	$\text{Phase 2 metric for birth } j = \sum_{i=1}^{n} \sum_{k=1}^{l} \frac{I_A(K)}{d_{ij}^2}$ Where: • n is the number of wells within 0.5, 1, 2, 5, or 10 miles of maternal residence j • k is equal to the date of the beginning of gestation and l is equal to the birth date for birth j • $I_A(K)$ is equal to 1 when $d_{ij} \leq$ buffer distance (miles) and the phase overlaps with gestation, and is equal to 0 otherwise • d^2_{ij} is the squared distance (m^2) between well i and maternal residence j
3	Hydraulic fracturing	$\text{Phase 3 metric for birth } j = \sum_{i=1}^{n} \sum_{k=1}^{l} \frac{w_i \times I_A(K)}{d_{ij}^2}$ Where: • n is the number of wells within 0.5, 1, 2, 5, or 10 miles of maternal residence j • k is equal to the date of the beginning of gestation and l is equal to the birth date for birth j • w_i is the depth (m) of well i • $I_A(K)$ is equal to 1 when $d_{ij} \leq$ buffer distance (miles) and the phase overlaps with gestation, and is equal to 0 otherwise • d^2_{ij} is the squared distance (m^2) between well i and maternal residence j
4	Production	$\text{Phase 4 metric for birth } j = \sum_{i=1}^{n} \sum_{k=1}^{l} \frac{v_i \times I_A(K)}{d_{ij}^2}$ Where: • n is the number of wells within 0.5, 1, 2, 5, or 10 miles of maternal residence j

		• k is equal to the date of the beginning of gestation and l is equal to the birth date for birth j • v_i is the produced gas volume (m^3) of well i • $I_A(K)$ is equal to 1 when $d_{ij} \leq$ buffer distance (miles) and the phase overlaps with gestation, and is equal to 0 otherwise • d^2_{ij} is the squared distance (m^2) between well i and maternal residence j

Figure 1 illustrates the calculation of the phase-specific and buffer-specific metrics.

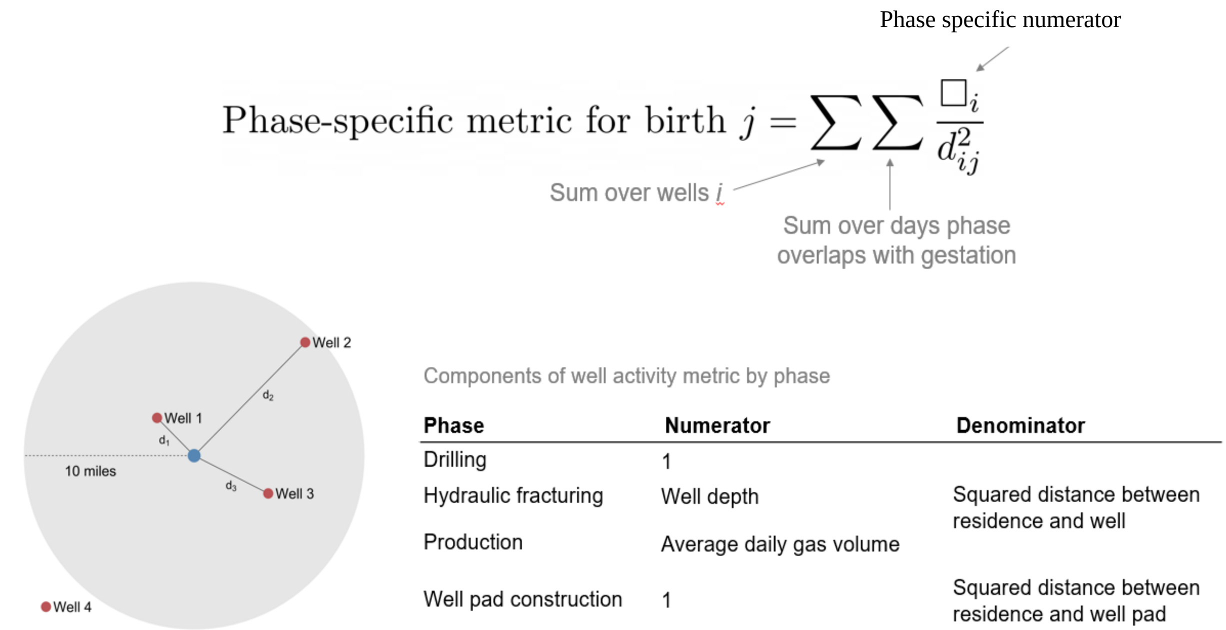

Figure 1. Well Phase Metric Calculation

We calculated both a cumulative well count and a phase-specific activity metric for each buffer distance.

Cumulative well counts represent the number of unconventional wells spudded on or before the child's date of birth within the specified distance of the maternal residence. These counts are irrespective of time (e.g., trimester or overall gestation) and phase of unconventional well development. The counts are not inverse distance-weighted but are the total number of wells within a given buffer distance.

We defined tertiles for each exposure metric (cumulative well count, and the well pad preparation, drilling, hydraulic fracturing, and production phases) within each buffer distance (0.5, 1, 2, 5, 10 mi):

- **Unexposed**: metric = 0
- **Exposed, low**: metric >0 and metric <33.3% of non-zero values among the entire cohort
- **Exposed, moderate**: metric >0 and metric ≥ 33.3% of non-zero values and metric <66.7% of non-zero values among the entire cohort
- **Exposed, high**: metric >0 and metric ≥ 66.7% of non-zero values among the entire cohort

Births further than 10 miles from any well were considered the unexposed group for all comparisons.

Other environmental exposures
In addition to the UNGD activity index, we also considered additional sources of environmental exposures in the study area during the study period. These include additional five additional sources: three associated with oil and gas-related activity (e.g., impoundment ponds, compressor stations, facilities accepting oil and gas waste), two with other industrial activities (e.g., Toxic Release Inventory sites, Superfund National Priorities List sites), and an air quality measure.

Compressor stations. The data for compressor stations came from the PA DEP's Air Emissions Report. These data give the location of oil and gas compressor stations, pollutant types, and emissions amounts. We included the proximity of the compressor stations to residences. [PA DEP Air Quality] [PA DEP Air Emissions]

Impoundment ponds. SkyTruth is a nonprofit that uses satellite imagery and data to illustrate environmental issues. Through a multi-step review process, SkyTruth produced a map of the locations of impoundment ponds that are used to store water and other fluids from the hydraulic fracturing process. We included the proximity of the impoundment ponds to residences as a method to measure exposure. [SkyTruth]

TRI sites. The US EPA Toxics Release Inventory (TRI) tracks the management of over 650 toxic chemicals that are manufactured, processed, or otherwise used by US facilities and pose a threat to human health and the environment. Available data include reports on releases, transfers, and waste managed by each reporting facility. We included the proximity of TRI sites to residences as a method to measure exposure to general industrial activities. [TRI] [TRI Release Reports] [TRI Search]

Superfund sites. Superfund was established to allow for cleanup of hazardous waste sites, either by the US EPA or the parties responsible for the waste. Thus, proximity to Superfund sites may pose an increased risk of exposure to water, soil, or air that has been contaminated by these hazardous sites. This is particularly important in Pennsylvania as the state has the third most Superfund sites in the country. We included the proximity of Superfund sites to residences as a method to measure exposure. [Superfund] [Superfund Map] [Superfund Data and Reports] [Superfund Site Search]

Facilities accepting oil and gas waste. Waste such as drill cuttings, flowback from hydraulic fracturing, and produced water are generated during the lifecycle of a well. The disposal of these wastes may represent another potential pathway of exposure to residents, through the air, water, or soil. The PA DEP collects information from well operators about facilities where oil and gas wastes are disposed. These data include the locations of the well that generated the waste and the waste facility, the method of disposal, and the type and quantity of waste. We included proximity to facilities accepting oil and gas waste as a method to measure exposure. [PA DEP Oil and Gas] [PA DEP Waste Report] [PA DEP Waste Facilities]

We used inverse distance-weighting to quantify exposure to these five additional sources as detailed for UNGD.

Satellite imagery-based air quality monitoring. The Atmospheric Composition Analysis Group at Washington University in St. Louis satellite imagery database provides measurements of average annual and monthly particulate matter (PM) 2.5 concentrations across the US at a resolution of 1 square kilometer. PM2.5 are the fine particles that are inhalable and are regulated via ambient air quality standards for criteria pollutants. These data were used to characterize ambient exposure levels to PM 2.5 across the study area using data available from 2009 to 2017. The monthly PM2.5 values for the parcel containing the maternal residential address for 12 months prior to the month of birth were averaged to form the metric. Only births from 2010-2018 were included to align with the data availability; February – December 2018 births had less than one full year of data available in their metrics. [Atmospheric Composition Analysis Group at Washington University at St Louis]

Data Analysis

Geocoding

Geocodes (latitude and longitude) for maternal residences were provided in the birth record, along with addresses. We chose to confirm these data by geocoding all maternal residential addresses in ArcGIS (Desktop version 10.8.1.14362) using the following parameters: minimum candidate score = 70, minimum match score = 75, match if candidates tie.

If the address was not matched at least to street level, *or* if we had previously determined that the address only contained a PO box number, we used the latitude and longitude corresponding to the centroid of the intersection of the zip code tabulation area (ZCTA) and county of residence. We jittered these points by retaining the centroid latitude and longitude only to the second decimal place digits, and randomly assigning third decimal place digits (which corresponds to a distance of 111 meters) that were validated to ensure the resulting point was located within the boundaries of the ZCTA-county intersection.

Data cleaning

We examined all datasets for missing data. We computed the proportion of missing data for each variable contributing to the calculation of the UNGD activity metric, the outcome variables, and the covariates. We stratified these calculations by year to examine patterns of missingness over time.

We compared demographics of participants missing and not missing data to examine if participants missing data differ from those not missing data. Participants missing address and/or birth date information were excluded because it precluded the assignment of exposure estimates. If a participant was missing data for one or more outcomes but not all, they were included in the analysis for the non-missing outcome(s).

For the UNGD activity metric, we imputed missing well data using other available data. Missing well depths were imputed using the median value among wells with non-missing values. Missing spud dates, drilling completion dates, and stimulation dates were extrapolated using other available dates for each well and median phase durations among wells without missing dates.

We used a series of graphical analysis and descriptive statistics to identify outlying observations, implausible values, and other inconsistencies. These were handled on a case-by-case basis.

Statistical analysis

We first examined each of the four phases of the UNGD activity metric for correlation. We found no evidence that the phases were collinear (Figure 2); all phases were included in the models simultaneously.

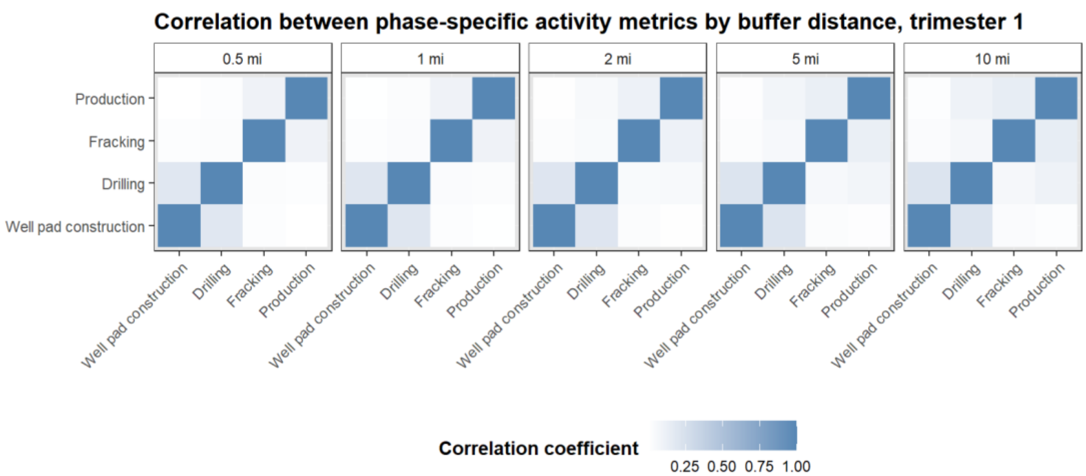

Figure 2. UNGD Phase Correlation Matrix by Buffer Distance

Phase-specific metrics were divided into tertiles among the exposed births, representing low, moderate, and high UNGD activity, respectively.

We computed descriptive statistics (for continuous variables: mean and standard deviation or median and interquartile range (IQR); for categorical variables: frequency) for outcome variables and covariates. Descriptive statistics were calculated for the entire sample as well as stratified by UNGD activity metric tertiles and, for covariates, birth outcome.

Our primary analyses assessed the association of UNGD activity metric (tertiles of exposure) with each of the four birth outcomes. We fit a series of linear (term birth weight) and logistic (preterm birth, small for gestational age, low Apgar score) regression models with clustered errors, obtained using a sandwich estimator, to account for nesting of births within mothers and of mothers within communities.

Each base model contained the four UNGD activity metrics. Our full set of covariates included neonate sex, season of birth, facility of birth, maternal age at delivery, race, ethnicity, education, smoking status three months before and during pregnancy, pre-pregnancy BMI, parity, gestational diabetes, adequacy of prenatal care, receipt of WIC services, distance to nearest roadway, community socioeconomic deprivation, greenness, and household water source.

Due to a lack of variability among our cohort in terms of ethnicity and birth facility (greater than 98% were non-Hispanic ethnicity and had hospital as the facility of birth), those two variables were not included in the models. During our checks for model fit, we identified a high proportion of records with high residuals and high leverage points and issues with model convergence, due to the inclusion of some of our environmental covariates. Additional evaluation led us to include a reduced set of covariates in all final models: neonate sex, maternal age at delivery, race, education, smoking status during pregnancy, pre-pregnancy BMI, parity, gestational diabetes, adequacy of prenatal care, receipt of WIC services, and community socioeconomic deprivation. The analysis of term birth weight was also adjusted for gestational age.

Our secondary analyses replicated the primary but included each of the five other environmental exposures (singularly) in the models.

We evaluated covariates for conditional significance using Wald or likelihood ratio tests. We assessed multicollinearity among model covariates by calculating variance inflation factors (VIF).

Associations were reported as a difference in term birth weight, or as odds ratios for preterm birth and small for gestational age. The odds ratio is used to determine whether a particular exposure (e.g., UNGD activity) is a risk factor for a particular birth outcome, and to compare the magnitude of various risk factors for that outcome. Odds ratios (OR) can be interpreted as:

OR=1 Exposure (e.g., UNGD activity) does not affect odds of the birth outcome
OR>1 Exposure (e.g., UNGD activity) is associated with higher odds of having the birth outcome
OR<1 Exposure (e.g., UNGD activity) is associated with lower odds of having the birth outcome

We compared the unexposed (reference level) to the exposed first, second, and third tertiles of the UNGD activity metric(s) with 95% confidence intervals. We used a two-sided type I error rate of 0.05 for significance testing. No adjustments were made for multiple comparisons. All analyses were performed using R version 4.1.2 (2021-11-01) and Stata 17 (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC).

Results

Total Cohort Descriptive Results

The file we received from PA DOH included data for n = 257,447 births to 171,431 mothers from 2010 to 2020. Table 4 displays the numbers of births dropped for meeting each of the exclusion criteria. Births which met criteria for serious birth defects were excluded by PA DOH Vital Statistics prior to file transfer and thus the number of births meeting this criterion is unknown.

Table 4. Final Cohort Size

Exclusion Reason	No. Meeting Exclusion	Cohort Size
Serious birth defects	Unknown	257,447
Multiple birth	8,771	248,676
Missing gestational age	1,950	246,726
Pre-viability (before 22 weeks gestation)	289	246,437
Post-term (after 41 weeks gestation)	979	245,458
Birth weight <500 g	185	245,273
Residence outside of study area*	59,424	185,849

*Includes within the City of Pittsburgh

Dropping births meeting one or more exclusion criteria resulted in a final cohort of **n = 185,849 births** to 128,155 mothers.

Residence geocoding results

Most births were able to be matched to the point address (81.4%), street address (10.7%) or sub-address (which includes apartment number, suite, etc.; 6.69%) (Figure 3). Among mothers with > 1 child, the majority (n = 28,497) lived in the same community for all births. Including in the mothers with 1 child (n = 82,605), a total of 111,084 (or 86.68% of all mothers) are nested within one community. A total of 17,053 mothers with two or more children lived in at least two different communities during the study period.

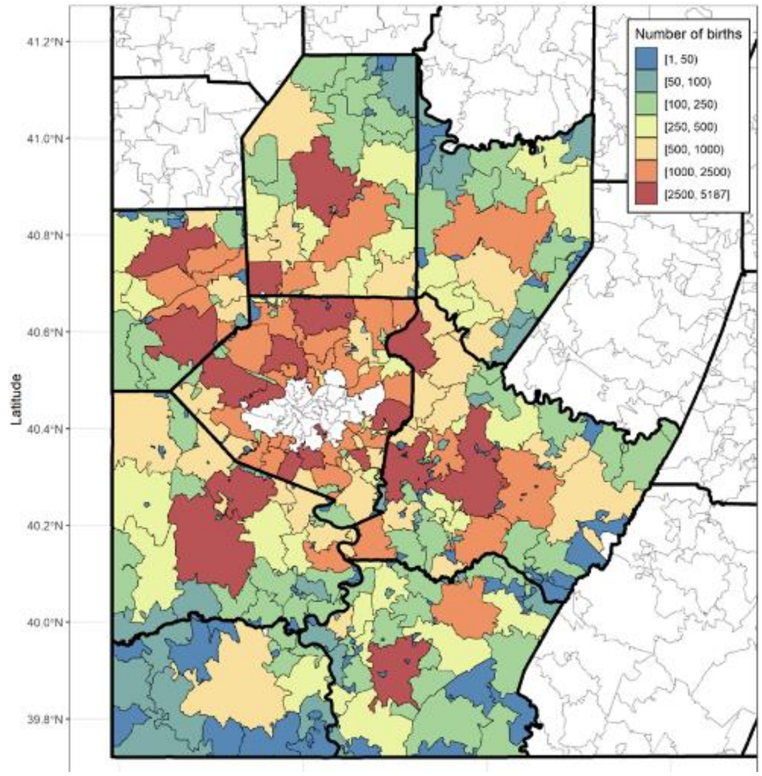

Figure 3. Map of Birth Residences by Community

Table 5 shows the count by county of number of births. Even excluding the City of Pittsburgh, Allegheny County had the highest number of births in the cohort (n=76,569, 42%), followed by Washington and Westmoreland Counties. Greene County only contributed 1% of the births to the cohort (n=2519).

Table 5. Number and Percent of Births by County

County	Number	Percent
Allegheny	76,569	42.1
Armstrong	6579	3.54
Beaver	17,322	9.32
Butler	18,185	9.78
Fayette	12,412	6.68
Greene	2519	1.36
Westmoreland	20,192	10.86
Washington	32,071	17.26

Birth outcomes

Figure 4 shows the distribution of birth weight (in grams) among term births (those with gestational age 37-41 weeks, inclusive), excluding those missing a value for birth weight.

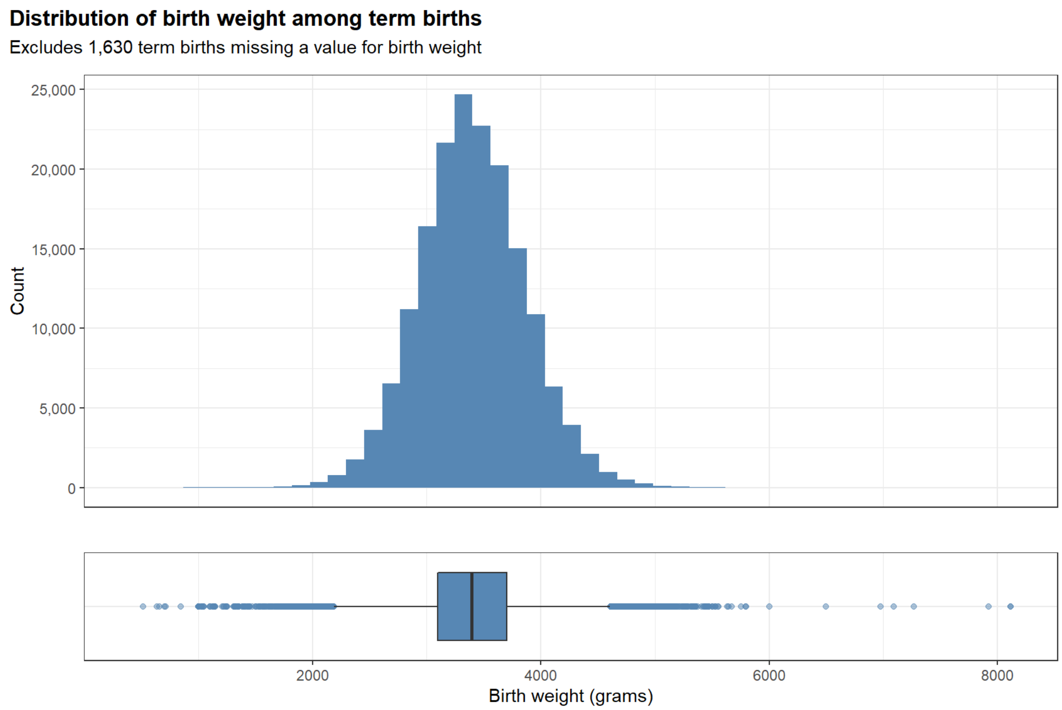

Figure 4. Histogram of Term Birthweights

	Mean	SD	Median	Min	Max
Term birthweight (g)	3402.29	463.75	3395	516	8115

Table 6 summarizes the birth outcomes in our cohort.

Table 6. Birth Outcomes in Cohort

Outcome	**N = 185,849 (%)**
Preterm (22-36 weeks gestation)	13,672 (7.4%)
Low 5-minute Apgar score	2,021 (1.1%)
Small for gestational age (SGA)	16,837 (9.2%)
Outcome	**N = 172,109 (Median; IQR[1])**
Term birth weight (grams) (37-41 weeks gestation)	3,395 (3,095, 3,700)

1- Interquartile range

Clinical and demographic covariates

There were 509 communities represented among the participants (Figure 5). The communities were divided into quartiles to form the cut points (approximately 127 communities in each quartile). Communities in Quartile 1 are those with the least deprivation and communities in Quartile 4 are those with the most deprivation. The figure shows the SDI quartile for each county, township, or census tract in the study area; those in blue (Q1) have the least deprivation while those in orange (Q4) have the highest deprivation.

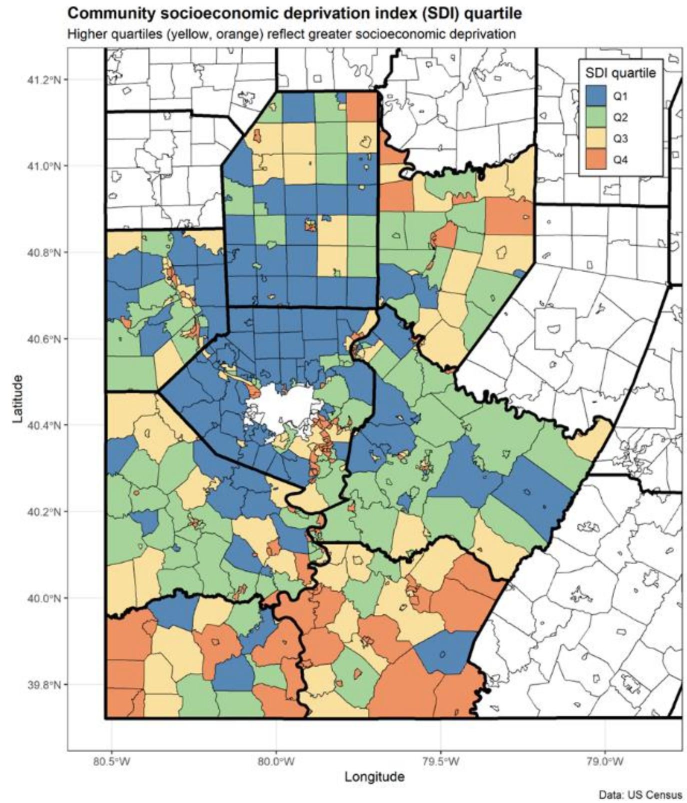

Figure 5. Map of Socioeconomic Deprivation Index by Community

Table 7 displays the number and percent of births per community socioeconomic deprivation index quartile.

Table 7. Quartiles of Socioeconomic Deprivation Index (SDI)

Community Socioeconomic Deprivation Index Quartile	Number	Percent
Quartile 1: -8.9 to <-2.77	79,409	42.8
Quartile 2: -2.77 to <-0.09	40,651	21.9
Quartile 3: -0.09 to <2.99	31,727	17.1
Quartile 4: 2.99 to <18.78	33,817	18.2

About 18% of the cohort resided in a community in the highest quartile of the SDI (Q4, most deprivation), while 43% lived in a community in the lowest quartile (Q1, least deprivation).

UNGD exposure

There were 5,799 wells included in our study from 2000 to 2020 (Figure 6). Through 2020, Washington County had the highest number of wells (n=1974), and Beaver County had the lowest number (n=141).

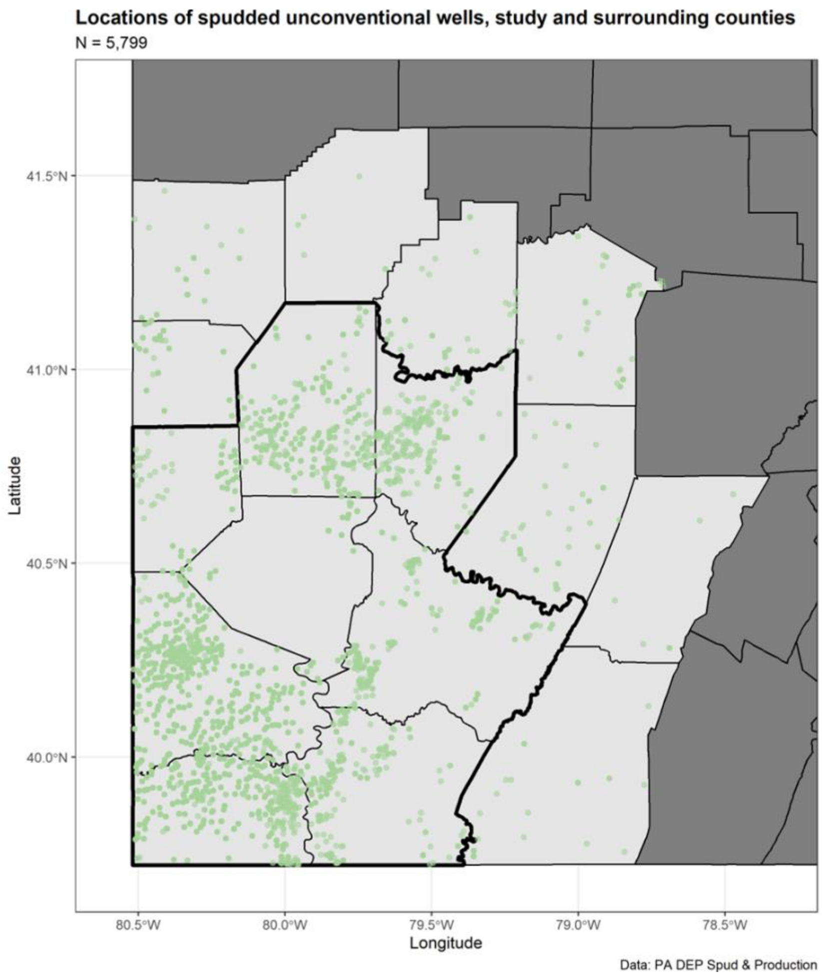

Figure 6. Map of UNGD Well Locations

There were fewer than 20 wells spudded in Southwestern Pennsylvania until 2007-2008, when production began increasing rapidly. The number of wells spudded peaked in 2014, with 765 as shown in Figure 7.

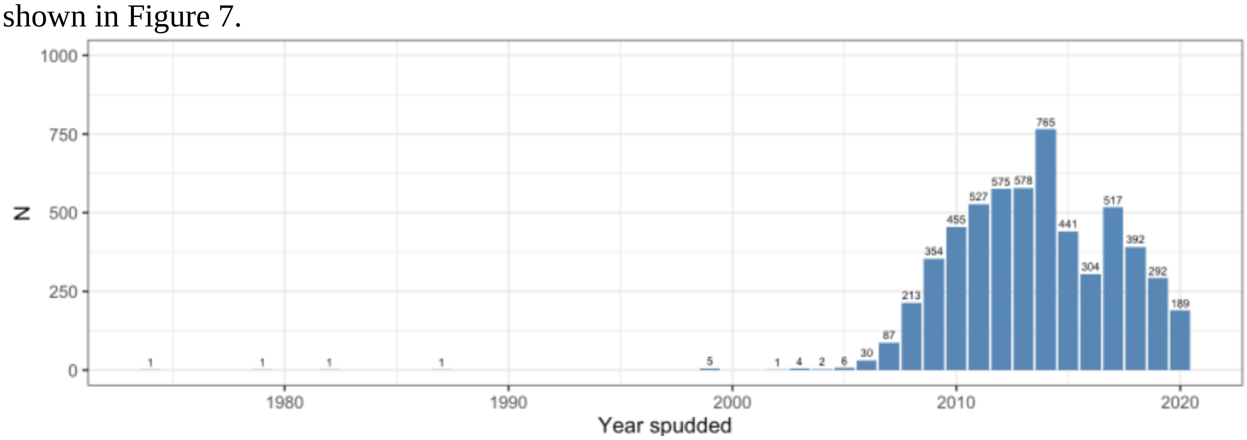

Figure 7. Histogram of UNGD Well Spud Dates by Year

Table 8 shows the median phase duration for each of the four UNGD activity metrics.

Table 8. UNGD activity metric phase durations

Phase	Phase Name	Phase Length
1	Well pad preparation	Minimum (spud date among wells on the pad) + 30 days 30 days
2	Drilling	Number of days between the spud and drilling completion dates Median: 104 days
3	Hydraulic fracturing	Number of days between stimulation commencement and stimulation completion Median: 12 days
4	Production	Duration of reporting period during which well reported production Mean: 2239 days (range 30-8769 days) Median: 2193 days

The cumulative well counts for the non-zero well counts for each buffer distance and their corresponding tertile cut points (33.3% and 66.7%) are shown in Table 9. Tertiles could not be formed for the 0.5 mi buffer because both the minimum and the 33.3% were 1.

Table 9. Cumulative Well Count Cutpoints

Exposure metric	Buffer (mi)	Min	33.3%	Median	66.7%	Max
Cumulative well count	0.5	1	1	2	3	22
	1.0	1	2	3	5	40
	2.0	1	4	7	11	114
	5.0	1	10	19	37	501
	10.0	1	39	69	111	1277

Phase- and buffer distance-specific tertile cut points (33.3% and 66.7%) for categorizing non-zero activity metrics for each buffer distance are shown in Table 10.

Table 10. Phase- and Buffer-Specific Cutpoints

Phase	Buffer (mi)	Min	33.3%	Median	66.7%	Max
Well pad preparation	0.5	0.0000016	0.0000585	0.0000714	0.0001010	3.486600e-03
	1.0	0.0000004	0.0000149	0.0000194	0.0000288	3.486600e-03
	2.0	0.0000001	0.0000041	0.0000059	0.0000093	3.497600e-03
	5.0	0.0000000	0.0000009	0.0000016	0.0000027	3.499400e-03
	10.0	0.0000000	0.0000004	0.0000007	0.0000013	3.499900e-03
Drilling	0.5	0.0000019	0.0001875	0.0003621	0.0006989	1.736130e-02
	1.0	0.0000004	0.0000471	0.0000982	0.0001985	1.736130e-02
	2.0	0.0000001	0.0000190	0.0000372	0.0000671	1.736130e-02
	5.0	0.0000000	0.0000067	0.0000136	0.0000258	1.737240e-02
	10.0	0.0000000	0.0000036	0.0000074	0.0000157	1.738150e-02
	0.5	0.0032741	0.0832197	0.1718940	0.3412145	1.353869e+01

Hydraulic fracturing	1.0	0.0005700	0.0220003	0.0473579	0.0923359	1.353869e+01
	2.0	0.0001473	0.0093184	0.0180530	0.0320462	1.353869e+01
	5.0	0.0000253	0.0032377	0.0062683	0.0119615	1.355166e+01
	10.0	0.0000063	0.0015206	0.0030728	0.0064455	1.355581e+01
Production	0.5	0.0000189	3.7609243	19.5167675	56.8160431	1.304742e+04
	1.0	0.0000074	3.4094035	12.1514347	29.8827560	1.304742e+04
	2.0	0.0000002	3.1194859	8.6408191	19.8056843	1.304742e+04
	5.0	0.0000000	1.6757591	5.1504258	13.5079528	1.308903e+04
	10.0	0.0000000	1.8369363	4.5370076	10.8305981	1.311022e+04

Table 11 shows the percentage of the birth cohort that was exposed at each buffer distance. Only about 3% of the cohort had wells within 0.5 miles of their residences. The production phase, which lasts the longest amount of time, had the highest percent exposed at each buffer distance from 2.4% at 0.5 miles to 89.4% at 10 miles. Less than 2% were exposed to the well pad preparation, drilling, or hydraulic fracturing phases at 1 mile. More than 90% of the cohort had at least one well within 10 miles of their residences.

Table 11. Percent of Cohort Exposed to UNGD Activity at Each Buffer Distance

	Buffer (miles)				
Well Metric	0.5	1	2	5	10
Cumulative well count	2.8	10.3	27.5	64.2	94.1
Well pad preparation phase	0.3	1.3	5.4	25.8	64.9
Drilling phase	0.3	1.8	8.1	35.3	76.3
Hydraulic fracturing phase	0.3	1.6	7.2	31.4	71.8
Production phase	2.4	8.9	23.8	57.9	89.4

Non-Well Exposures
We investigated modeling associations for five additional non-well exposures.

Compressor stations. We assigned inverse distance weighted activity metrics to stations that were active based on whether the facility had reported emissions during any given year (Figure 8).

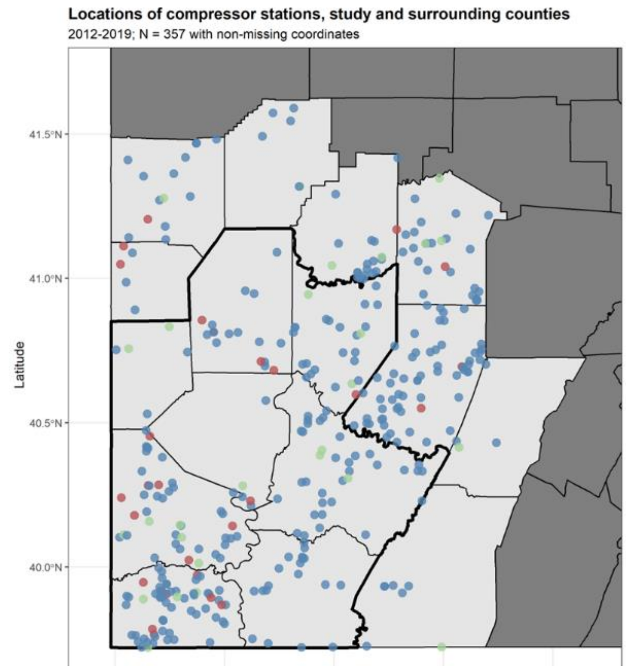

Figure 8. Locations of Study Area Compressor Stations

Impoundment ponds. We assigned inverse distance weighted activity metrics to ponds that were active based on whether the pond was visible by satellite monitoring during any given year (Figure 9).

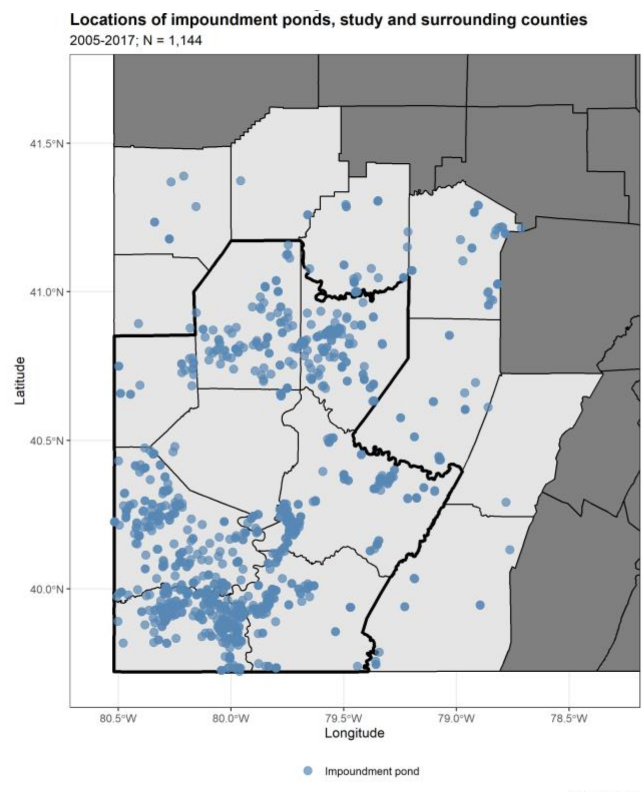

Figure 9. Locations of Study Area Impoundment Ponds

TRI sites. We assigned inverse distance weighted activity metrics to stations that were active based on whether the facility had reported emissions during any given year (Figure 10).

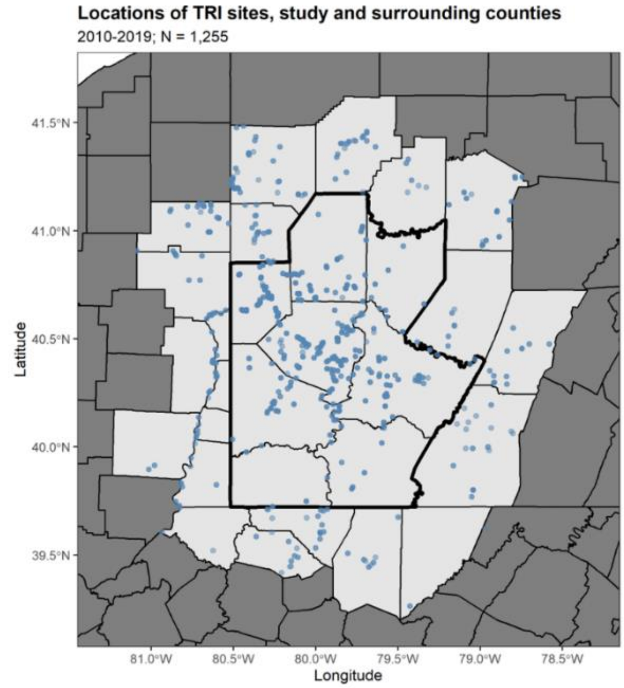

Figure 10. Locations of Study Area Toxics Release Inventory Sites

Data: US EPA

Facilities accepting oil and gas waste. We assigned inverse distance weighted activity metrics to stations that were active based on whether the facility reported accepting waste during any given year (Figure 11).

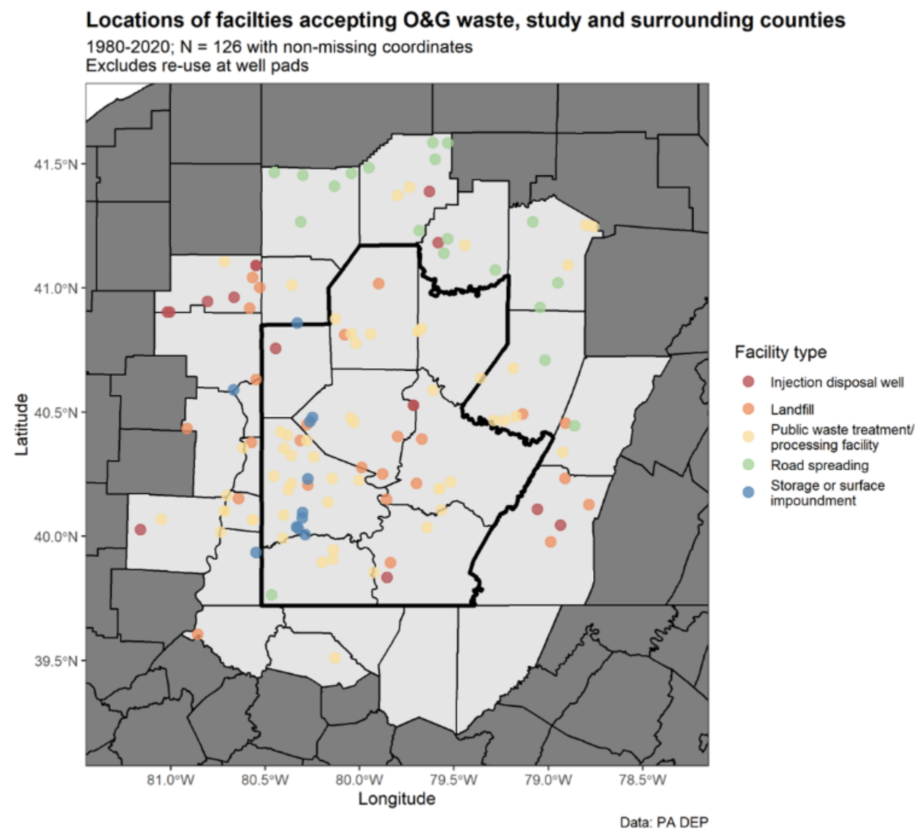

Figure 11. Locations of Study Area Facilities Accepting Oil & Gas Waste

The number of births by source within each buffer are shown in Table 12. Due to the very small number of births located within our buffer distances to Superfund sites, no additional analyses were performed using that source. Additionally, due to the high proportion of births with TRI sites within 10 miles (and correspondingly low proportion outside of 10 miles), no additional models are included due to the small baseline comparison group.

Table 12. Number of Births (Total Cohort) Within Each Buffer Distance for Non-Well Exposures

Buffer (miles)	Compressor Stations		Impoundment Ponds		Superfund Sites		TRI Sites		Facilities accepting oil & gas waste	
	Number	%	Number	%	Number	%	Number	%	Number	%
0.5	682	0.4	506	0.3	0	--	17,779	9.6	633	0.3
1	2,692	1.4	2,810	1.5	0	--	52,065	28.1	3,953	2.1
2	11,154	6.0	11,199	6.0	3	0.002	103,510	55.8	19,279	10.4
5	59,121	31.8	40,698	21.9	175	0.09	164,582	88.7	78,823	42.5
10	119,147	64.2	90,379	48.7	571	0.3	179,648	96.8	150,619	81.1

Apgar

The characteristics by low 5-minute Apgar score are shown in Table 13. Low Apgar score occurred more frequently among Black/African American mothers, those with a high school education or less, and to nulliparous and smoking mothers. A low Apgar score also occurred more frequently among those in communities with the most socioeconomic deprivation (Q4).

Table 13. Cohort Characteristics by Apgar Score Category

Characteristic	**Low 5-minute Apgar Score**		
	Yes, N = 2,189[1]	**No**, N = 181,731[1]	**Unknown**, N = 1,929[1]
Neonate sex			
Female	936 (42.8%)	88,874 (48.9%)	940 (48.7%)
Male	1,253 (57.2%)	92,857 (51.1%)	989 (51.3%)
Maternal age (years)[2]	29 (24, 33)	29 (25, 33)	30 (26, 33)
Gestational age (weeks)[2]	38 (34, 39)	39 (38, 40)	39 (37, 40)
Adequacy of prenatal care utilization (APNCU) index			
Inadequate	324 (14.8%)	18,919 (10.4%)	135 (7.0%)
Intermediate	207 (9.5%)	19,938 (11.0%)	96 (5.0%)
Adequate	858 (39.2%)	104,406 (57.5%)	1,350 (70.0%)
Adequate plus	600 (27.4%)	31,345 (17.2%)	208 (10.8%)
Unknown	200 (9.1%)	7123 (3.9%)	140 (7.3%)
Maternal race			
White	1,801 (82.3%)	158494 (87.2%)	1,554 (80.6%)
Black/African American	295 (13.5%)	14,585 (8.0%)	250 (13.0%)
All other races	70 (3.2%)	7,235 (4.0%)	110 (5.7%)
Unknown/refused	23 (1.1%)	1,417 (0.8%)	15 (0.8%)
Maternal education level			
Less than high school	226 (10.3%)	12,743 (7.0%)	156 (8.1%)
High school/GED	551 (25.2%)	39,261 (21.6%)	398 (20.6%)
Some college	609 (27.8%)	49,707 (27.4%)	416 (21.6%)
Bachelor's degree	480 (21.9%)	47,898 (26.4%)	571 (29.6%)
Graduate degree	290 (13.2%)	31,152 (17.1%)	357 (18.5%)
Unknown	33 (1.5%)	970 (0.5%)	31 (1.6%)
Maternal pre-pregnancy BMI			
Underweight	54 (2.5%)	4743 (2.6%)	42 (2.2%)
Normal	708 (32.3%)	69,404 (38.2%)	459 (23.8%)
Overweight	398 (18.2%)	33,685 (18.5%)	182 (9.4%)
Obese	505 (23.1%)	33,921 (18.7%)	159 (8.2%)
Unknown	524 (23.9%)	39,978 (22.0%)	1,087 (56.4%)
Gestational diabetes	149 (6.8%)	9,394 (5.2%)	59 (3.1%)
Nulliparous	1,221 (55.8%)	75,584 (41.6%)	747 (38.7%)
Mother received WIC	671 (30.7%)	50,074 (27.6%)	458 (23.7%)
Maternal smoking	545 (24.9%)	35,923 (19.8%)	305 (15.8%)
Community socioeconomic deprivation index			
Quartile 1 (least)	779 (35.6%)	77,813 (42.8%)	891 (46.2%)
Quartile 2	492 (22.5%)	39,849 (21.9%)	369 (19.1%)
Quartile 3	398 (18.2%)	31,088 (17.1%)	294 (15.2%)
Quartile 4 (most)	520 (23.8%)	32,981 (18.1%)	375 (19.4%)

[1] n (%); [2]Median (Interquartile Range (IQR))

Because low Apgar score occurred so infrequently among the births in our cohort, no additional modeling was performed.

Small for Gestational Age (SGA)

The cohort characteristics by SGA are shown in Table 14. SGA occurred more frequently among those with inadequate prenatal care, among Black/African American mothers, those with a high school education or less, and to nulliparous and smoking mothers. It also occurred more frequently among those in the highest quartile of socioeconomic deprivation.

Table 14. Cohort Characteristics by Small for Gestational Age Category

Characteristic	Small for gestational age (SGA)		
	Yes, N = 16,872[1]	**No**, N = 166,765[1]	**Unknown**, N = 2,212[1]
Neonate sex			
Female	8,273 (49.0%)	81,467 (48.9%)	1,010 (45.7%)
Male	8,599 (51.0%)	85,298 (51.1%)	1,202 (54.3%)
Gestational age (wks)	39 (38, 40)	39 (38, 40)	39 (37, 39)
Maternal age (years)	28 (24, 32)	29 (25, 33)	30 (26, 33)
Adequacy of prenatal care utilization (APNCU) index			
Inadequate	2,404 (14.2%)	16,925 (10.1%)	49 (2.2%)
Intermediate	1,815 (10.8%)	18,320 (11.0%)	106 (4.8%)
Adequate	9,157 (54.3%)	95,789 (57.4%)	1,668 (75.4%)
Adequate plus	2,779 (16.5%)	29,109 (17.5%)	265 (12.0%)
Unknown	717 (4.2%)	6,622 (4.0%)	124 (5.6%)
Maternal race			
White	13,393 (79.4%)	146,651 (87.9%)	1,805 (81.6%)
Black or African American	2,420 (14.3%)	12,431 (7.5%)	279 (12.6%)
All other races	913 (5.4%)	6,380 (3.8%)	122 (5.5%)
Unknown or refused	146 (0.9%)	1,303 (0.8%)	6 (0.3%)
Maternal education level			
Less than high school	2,131 (12.6%)	10,881 (6.5%)	113 (5.1%)
High school or GED	5,044 (29.9%)	34,778 (20.9%)	388 (17.5%)
Some college	4,609 (27.3%)	45,588 (27.3%)	535 (24.2%)
Bachelor's degree	3,043 (18.0%)	45,241 (27.1%)	665 (30.1%)
Graduate degree	1,951 (11.6%)	29,386 (17.6%)	462 (20.9%)
Unknown	94 (0.6%)	891 (0.5%)	49 (2.2%)
Maternal pre-pregnancy BMI			
Underweight	935 (5.5%)	3,873 (2.3%)	31 (1.4%)
Normal	6,999 (41.5%)	63,240 (37.9%)	332 (15.0%)
Overweight	2,627 (15.6%)	31,509 (18.9%)	129 (5.8%)
Obese	2,594 (15.4%)	31,860 (19.1%)	131 (5.9%)
Unknown	3,717 (22.0%)	36,283 (21.8%)	1,589 (71.8%)
Gestational diabetes	735 (4.4%)	8,829 (5.3%)	38 (1.7%)
Nulliparous	8,447 (50.1%)	68,133 (40.9%)	972 (43.9%)
Mother received WIC	6,481 (38.4%)	44,247 (26.5%)	475 (21.5%)
Maternal smoking	6,217 (36.8%)	30,306 (18.2%)	250 (11.3%)
Community socioeconomic deprivation index			
Quartile 1 (least)	5,503 (32.6%)	72,886 (43.7%)	1,094 (49.5%)
Quartile 2	3,787 (22.4%)	36,503 (21.9%)	420 (19.0%)
Quartile 3	3,151 (18.7%)	28,308 (17.0%)	321 (14.5%)
Quartile 4 (most)	4,431 (26.3%)	29,068 (17.4%)	377 (17.0%)

[1] n (%); Median (IQR)

Well Cumulative Count Models

The model results for the cumulative well count are shown in Table 15. There were no associations between cumulative well count and SGA for any of the buffer distances examined.

Table 15. SGA Birth Model Results – Well Cumulative Count Metric

Tertile Split	Adjusted OR[1] (95% CI)
0.5 miles[2]	
1 mile	
Unexposed	--
Low	0.97 (0.85, 1.10)
Moderate	0.95 (0.85, 1.06)
High	1.01 (0.90, 1.13)
Global p-value	0.23
Trend p-value	0.20
2 miles	
Unexposed	--
Low	1.07 (0.98, 1.16)
Moderate	1.02 (0.93, 1.11)
High	1.02 (0.93, 1.11)
Global p-value	0.50
Trend p-value	0.96
5 miles	
Unexposed	--
Low	1.03 (0.95, 1.11)
Moderate	1.04 (0.96, 1.12)
High	1.03 (0.95, 1.12)
Global p-value	0.91
Trend p-value	0.44
10 miles	
Unexposed	--
Low	1.02 (0.95, 1.09)
Moderate	1.01 (0.94, 1.09)
High	1.06 (0.98, 1.14)
Global p-value	0.19
Trend p-value	0.09

1- Models adjusted for neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during gestation and three months prior, and SDI

2- We could not use the tertile split among the exposed group for the 0.5-mile buffer because the cut points for the “exposed, low” category were [1, 1).

* p<0.05; ** p<0.001

Well Phase Activity Metric Models

Adjusted models by phase and buffer are shown in Table 16. Most of the odds ratios were at or near 1, with some exceptions. There were some statistically significantly reduced odds ratios in some metrics; the only consistent reductions were in the 10-mile buffer for well pad preparation. In the 2-to-10-mile buffers for the production phase, we found consistent, in most cases statistically significant, excesses of 10%.

Table 16. SGA Birth Model Results – Well Phase Activity Metrics

Phase	Adjusted OR[1] (95% CI)				
	0.5 miles	1 mile	2 miles	5 miles	10 miles
Well Pad Preparation					
Unexposed	--	--	--	--	--
Low	1.26 (0.59, 2.72)	0.97 (0.71, 1.32)	1.11 (0.95, 1.28)	0.95 (0.88, 1.03)	0.99 (0.94, 1.06)
Moderate	1.16 (0.56, 2.39)	1.19 (0.87, 1.64)	1.05 (0.91, 1.21)	0.96 (0.88, 1.05)	0.95 (0.89, 1.00)*
High	0.84 (0.39, 1.80)	0.91 (0.61, 1.36)	1.09 (0.94, 1.27)	0.94 (0.86, 1.02)	0.93 (0.87, 0.99)*
Global p-value	0.68	0.47	0.23	0.63	0.05
Trend p-value	0.18	0.37	0.95	0.18	0.03
Drilling					
Unexposed	--	--	--	--	--
Low	0.86 (0.43, 1.72)	1.12 (0.80, 1.55)	1.03 (0.89, 1.20)	1.00 (0.91, 1.09)	0.98 (0.92, 1.04)
Moderate	0.94 (0.47, 1.85)	0.91 (0.66, 1.25)	1.02 (0.88, 1.18)	1.03 (0.93, 1.14)	1.04 (0.96, 1.11)
High	1.39 (0.65, 2.94)	1.19 (0.87, 1.63)	1.05 (0.88, 1.24)	1.04 (0.93, 1.17)	1.03 (0.94, 1.13)
Global p-value	0.67	0.62	0.98	0.85	0.20
Trend p-value	0.45	0.29	0.28	0.49	0.39
Hydraulic Fracturing					
Unexposed	--	--	--	--	--
Low	0.76 (0.41, 1.40)	0.85 (0.63, 1.16)	0.73 (0.63, 0.84)**	0.95 (0.88, 1.03)	0.97 (0.92, 1.03)
Moderate	1.48 (0.92, 2.41)	0.72 (0.54, 0.97)*	0.87 (0.76, 1.01)	0.91 (0.83, 1.00)*	0.96 (0.90, 1.03)
High	0.88 (0.47, 1.65)	0.97 (0.73, 1.28)	0.87 (0.74, 1.01)	0.95 (0.87, 1.05)	0.97 (0.89, 1.05)
Global p-value	0.17	0.23	<0.001	0.36	0.68
Trend p-value	0.29	0.13	0.01	0.11	0.22
Production					
Unexposed	--	--	--	--	--
Low	1.05 (0.85, 1.28)	1.06 (0.94, 1.19)	1.12 (1.02, 1.22)*	1.11 (1.02, 1.20)*	1.08 (1.01, 1.16)*
Moderate	0.99 (0.80, 1.21)	0.95 (0.85, 1.07)	1.08 (0.99, 1.18)	1.11 (1.02, 1.20)*	1.09 (1.01, 1.17)*
High	1.06 (0.85, 1.32)	1.03 (0.90, 1.17)	1.08 (0.98, 1.19)	1.10 (1.01, 1.20)*	1.09 (1.01, 1.19)*
Global p-value	0.13	0.004	0.13	0.11	0.11
Trend p-value	0.24	0.38	0.43	0.04	0.03

1- Models adjusted for neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during gestation and three months prior, and SDI

* $p<0.05$; ** $p<0.001$

The SGA forest plots by buffer distance for each phase are shown in Figure 12. The vertical line at 1 represents a null relationship; dots below 1 indicate reduced risk and dots above 1 indicate increased risk.

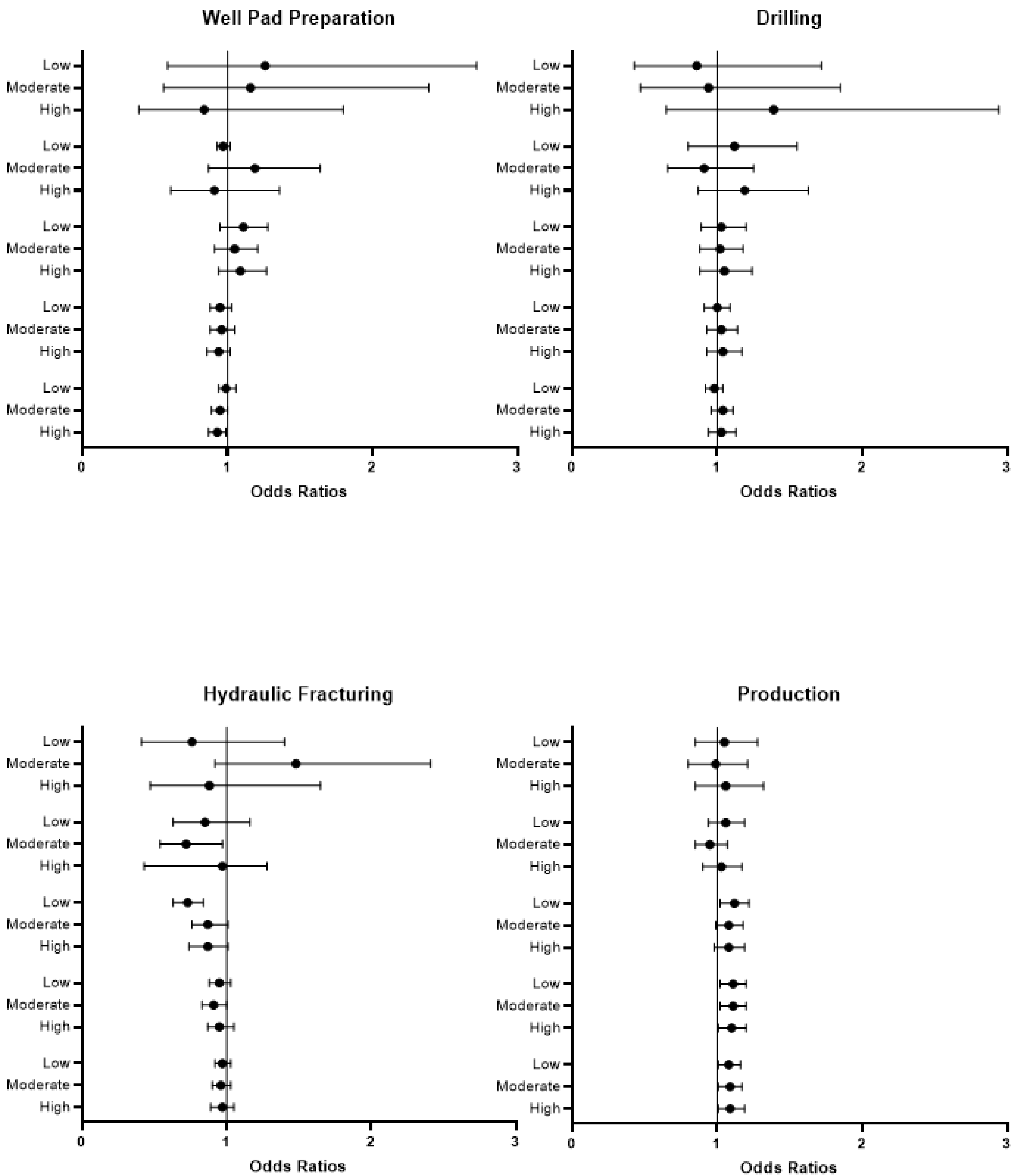

Figure 12. Forest Plots for Small for Gestational Age Well Phase Models

Non-Well Exposure Models

Table 17 shows results by buffer for compressor stations, impoundment ponds, and facilities accepting oil and gas waste. There were statistically significant elevations in the 2-, 5-, and 10-mile buffers for compressor stations, with statistically significant global tests at 2 and 5 miles. There were no consistent associations between SGA and impoundment ponds. For exposure to facilities accepting oil and gas waste, there were statistically significantly elevated odds ratios and trend tests in most of the buffer distances. The 1-mile buffer did not have any statistically significant odds ratios but was globally statistically significant.

Table 17. SGA Birth Model Results – Other Exposures

Buffer	Adjusted OR[1] (95% CI)		
	Compressor Stations	Impoundment Ponds	Facilities accepting oil & gas waste
0.5 miles			
Unexposed	--	--	--
Low	0.72 (0.42, 1.24)	1.23 (0.84, 1.82)	0.92 (0.60, 1.43)
Moderate	0.85 (0.59, 1.24)	0.89 (0.48, 1.65)	1.59 (1.05, 2.41)*
High	1.41 (1.03, 1.95)*	1.18 (0.73, 1.90)	1.28 (0.82, 2.00)
Global p-value	0.02	0.83	0.07
Trend p-value	0.01	0.96	0.01
1 mile			
Unexposed	--	--	--
Low	1.14 (0.91, 1.42)	1.01 (0.81, 1.25)	1.15 (0.96, 1.39)
Moderate	1.04 (0.84, 1.30)	0.94 (0.75, 1.18)	1.13 (0.95, 1.33)
High	0.99 (0.81, 1.22)	0.91 (0.75, 1.11)	1.21 (0.99, 1.49)
Global p-value	0.11	0.92	0.05
Trend p-value	0.02	0.58	0.003
2 miles			
Unexposed	--	--	--
Low	1.13 (1.01, 1.27)*	1.04 (0.92, 1.18)	1.01 (0.92, 1.12)
Moderate	1.13 (1.01, 1.26)*	0.91 (0.81, 1.02)	1.04 (0.96, 1.13)
High	1.08 (0.95, 1.23)	0.99 (0.88, 1.11)	1.12 (1.01, 1.23)*
Global p-value	0.02	0.56	0.07
Trend p-value	0.002	0.49	0.04
5 miles			
Unexposed	--	--	--
Low	1.02 (0.95, 1.08)	1.00 (0.93, 1.08)	1.06 (1.00, 1.12)*

Buffer	Adjusted OR[1] (95% CI)		
	Compressor Stations	Impoundment Ponds	Facilities accepting oil & gas waste
Moderate	1.01 (0.96, 1.07)	1.01 (0.94, 1.08)	1.08 (1.02, 1.14)*
High	1.09 (1.02, 1.16)*	0.99 (0.92, 1.06)	1.03 (0.98, 1.09)
Global p-value	0.03	0.99	0.12
Trend p-value	0.04	0.89	0.11
10 miles			
Unexposed	--	--	--
Low	1.05 (1.01, 1.10)*	0.99 (0.95, 1.04)	1.04 (0.99, 1.09)
Moderate	1.04 (0.99, 1.10)	1.01 (0.97, 1.06)	1.05 (1.00, 1.11)
High	1.05 (1.00, 1.10)*	0.99 (0.94, 1.04)	1.06 (1.01, 1.12)*
Global p-value	0.08	0.86	0.09
Trend p-value	0.02	0.79	0.01

1- Models adjusted for neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during pregnancy and three months prior, and SDI

* p<0.05; ** p<0.001

Figure 13 shows the corresponding forest plots for the associations of non-well exposures with SGA.

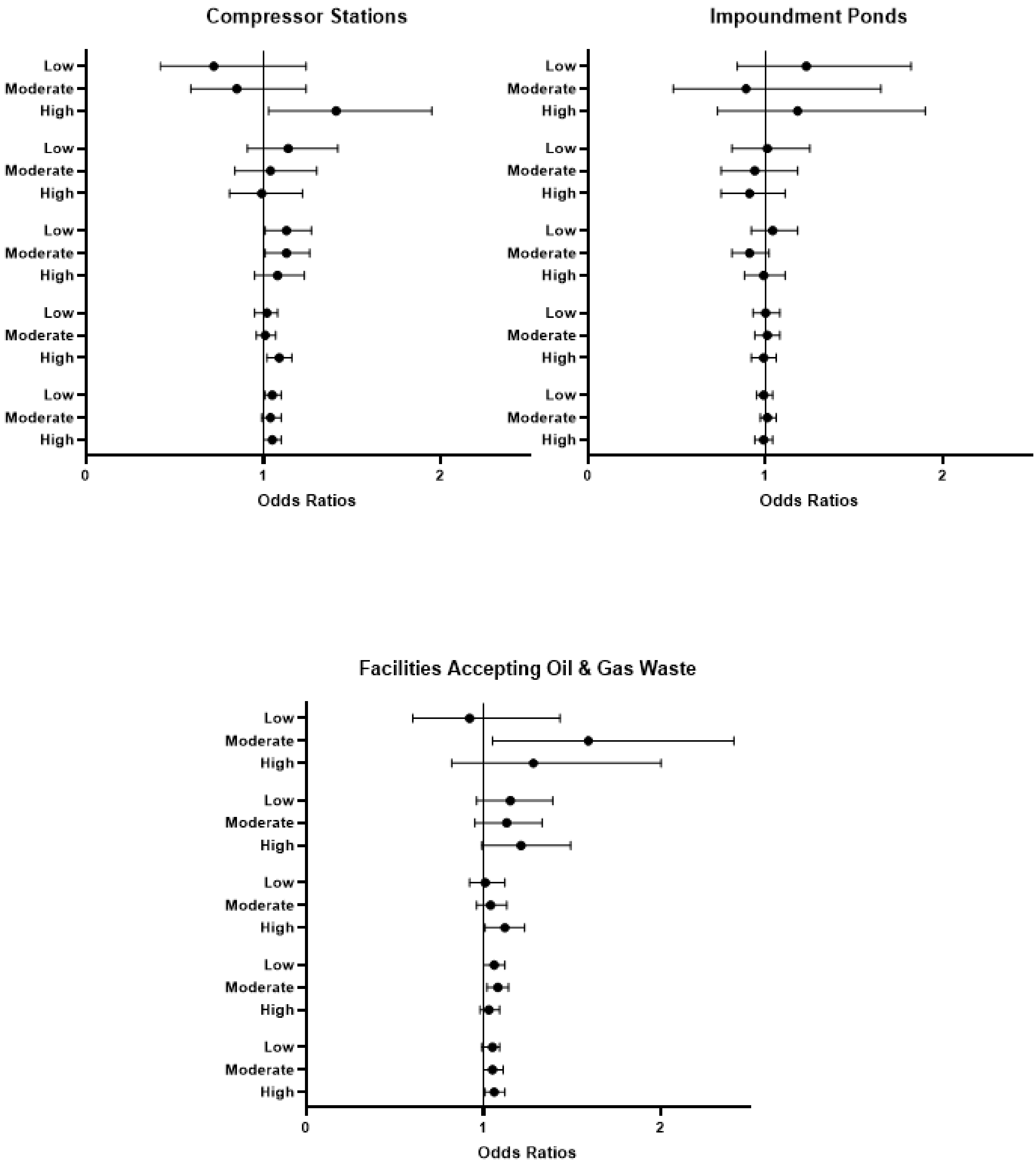

Figure 13. Forest Plots for Small for Gestational Age Non-Well Exposure Models

Preterm Birth

Preterm birth (Table 18) occurred more frequently among male neonates, those with adequate plus or unknown prenatal care, among Black/African American mothers, those with a high school education or less, and to smoking mothers. It also occurred more frequently among those in the highest quartile of socioeconomic deprivation.

Table 18. Cohort Characteristics by Preterm Birth Category

Characteristic	Preterm	
	Yes, N = 13,672[1]	**No**, N = 172,177[1]
Neonate sex		
Female	6,179 (45.2%)	84,571 (49.1%)
Male	7,493 (54.8%)	87,606 (50.9%)
Gestational age (weeks)	35 (34, 36)	39 (39, 40)
Maternal age (years)	29 (25, 33)	29 (25, 33)
Adequacy of prenatal care utilization (APNCU) index		
Inadequate	1,660 (12.1%)	17,718 (10.3%)
Intermediate	1,114 (8.1%)	19,127 (11.1%)
Adequate	4,213 (30.8%)	102,401 (59.5%)
Adequate plus	5,546 (40.6%)	26,607 (15.5%)
Unknown	1,139 (8.3%)	6,324 (3.7%)
Maternal race		
White	11,365 (83.1%)	150,484 (87.4%)
Black or African American	1,638 (12.0%)	13,492 (7.8%)
All other races	548 (4.0%)	6,867 (4.0%)
Unknown or refused	121 (0.9%)	1,334 (0.8%)
Maternal education level		
Less than high school	1,365 (10.0%)	11,760 (6.8%)
High school or GED	3,511 (25.7%)	36,699 (21.3%)
Some college	3,995 (29.2%)	46,737 (27.1%)
Bachelor's degree	2,813 (20.6%)	46,136 (26.8%)
Graduate degree	1,851 (13.5%)	29,948 (17.4%)
Unknown	137 (1.0%)	897 (0.5%)
Maternal pre-pregnancy BMI		
Underweight	483 (3.5%)	4,356 (2.5%)
Normal	4,535 (33.2%)	66,036 (38.4%)
Overweight	2,207 (16.1%)	32,058 (18.6%)
Obese	2,534 (18.5%)	32,051 (18.6%)
Unknown	3,913 (28.6%)	37,676 (21.9%)
Gestational diabetes	918 (6.7%)	8,684 (5.0%)
Nulliparous	5,970 (43.7%)	71,582 (41.6%)
Mother received WIC	4,210 (30.8%)	46,993 (27.3%)
Maternal smoking	3,528 (25.8%)	33,245 (19.3%)
Community socioeconomic deprivation index		
Quartile 1 (lowest deprivation)	4,884 (35.7%)	74,599 (43.3%)
Quartile 2	3,050 (22.3%)	37,660 (21.9%)
Quartile 3	2,472 (18.1%)	29,308 (17.0%)
Quartile 4 (highest deprivation)	3,266 (23.9%)	30,610 (17.8%)

[1] n (%); Median (IQR)

Well Cumulative Count Models

The adjusted model results for the cumulative well count are shown in Table 19. All of the odds ratios were less than 1 and most were statistically significant, including all those in the 2-, 5- and 10-mile buffers. All global and the 10-mile trend test were statistically significant.

Table 19. Preterm Birth Model Results – Well Cumulative Count Metric

Tertile Split	Adjusted OR[1] (95% CI)
0.5 miles[2]	
1 mile	
Unexposed	--
Low	0.95 (0.85, 1.06)
Moderate	0.85 (0.76, 0.96)*
High	0.92 (0.82, 1.03)
Global p-value	<0.001
Trend p-value	0.82
2 miles	
Unexposed	--
Low	0.83 (0.76, 0.91)**
Moderate	0.90 (0.82, 0.99)*
High	0.91 (0.83, 0.98)*
Global p-value	<0.001
Trend p-value	0.81
5 miles	
Unexposed	--
Low	0.85 (0.79, 0.92)**
Moderate	0.85 (0.79, 0.92)**
High	0.90 (0.83, 0.98)*
Global p-value	<0.001
Trend p-value	0.64
10 miles	
Unexposed	--
Low	0.88 (0.82, 0.94)**
Moderate	0.86 (0.80, 0.92)**
High	0.87 (0.80, 0.93)**
Global p-value	<0.001
Trend p-value	0.02

1- Models adjusted for neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during gestation and three months prior, and SDI

2- We could not use the tertile split among the exposed group for the 0.5-mile buffer because the cut points for the “exposed, low” category were [1, 1).

* p<0.05; ** p<0.001

Well Phase Activity Metric Models

Adjusted models by phase and buffer are shown in Table 20. There was no evidence of increased risk for the well pad preparation and hydraulic fracturing phases. There were statistically significant elevations in risk for the drilling phase in the 2- and 10-mile buffers that increased with increased exposure; however, the odds ratios in the 5-mile buffer were elevated but not statistically significant. Most of the odds ratios for the production phase were at or near 1, although there were some statistically significantly reduced odds ratios in the 5- and 10-mile buffers with statistically significant global and trend tests.

Table 20. Preterm Birth Model Results – Well Phase Activity Metrics

Phase	Adjusted OR[1] (95% CI)				
	0.5 miles	1 mile	2 miles	5 miles	10 miles
Well Pad Preparation					
Unexposed	--	--	--	--	--
Low	0.52 (0.17, 1.66)	1.04 (0.73, 1.51)	1.00 (0.85, 1.18)	0.94 (0.85, 1.03)	0.95 (0.89, 1.01)
Moderate	0.89 (0.41, 1.92)	1.08 (0.75, 1.57)	0.94 (0.78, 1.12)	0.92 (0.83, 1.03)	0.90 (0.83, 0.97)*
High	0.56 (0.20, 1.59)	0.74 (0.50, 1.09)	0.86 (0.70, 1.05)	0.95 (0.85, 1.07)	0.96 (0.88, 1.05)
Global p-value	0.54	0.34	0.37	0.55	0.03
Trend p-value	0.31	0.33	0.18	0.67	0.46
Drilling					
Unexposed	--	--	--	--	--
Low	1.09 (0.39, 3.03)	0.99 (0.72, 1.38)	1.13 (0.93, 1.36)	1.05 (0.94, 1.18)	1.05 (0.97, 1.14)
Moderate	1.08 (0.55, 2.13)	1.12 (0.79, 1.59)	1.25 (1.04, 1.50)*	1.08 (0.96, 1.22)	1.10 (1.01, 1.21)*
High	1.03 (0.51, 2.11)	0.93 (0.65, 1.32)	1.22 (1.00, 1.47)*	1.14 (0.99, 1.31)	1.12 (1.00, 1.26)*
Global p-value	0.99	0.84	0.15	0.42	0.18
Trend p-value	0.99	0.88	0.02	0.13	0.17
Hydraulic Fracturing					
Unexposed	--	--	--	--	--
Low	1.33 (0.60, 2.95)	1.02 (0.69, 1.49)	0.99 (0.83, 1.17)	1.06 (0.96, 1.17)	1.02 (0.96, 1.09)
Moderate	0.46 (0.22, 0.97)*	1.04 (0.79, 1.37)	0.89 (0.74, 1.07)	0.95 (0.86, 1.05)	0.99 (0.92, 1.07)
High	0.72 (0.36, 1.42)	0.82 (0.60, 1.12)	0.87 (0.74, 1.03)	0.98 (0.88, 1.10)	1.02 (0.93, 1.12)
Global p-value	0.19	0.76	0.47	0.22	0.66
Trend p-value	0.50	0.48	0.08	0.49	0.87
Production					
Unexposed	--	--	--	--	--
Low	1.01 (0.85, 1.20)	1.03 (0.89, 1.19)	0.96 (0.88, 1.05)	0.96 (0.88, 1.03)	1.00 (0.92, 1.07)
Moderate	0.96 (0.79, 1.17)	0.94 (0.83, 1.06)	0.91 (0.82, 1.01)	0.88 (0.81, 0.96)*	0.82 (0.76, 0.89)**

Phase	Adjusted OR[1] (95% CI)				
	0.5 miles	1 mile	2 miles	5 miles	10 miles
High	1.05 (0.84, 1.32)	0.84 (0.73, 0.97)*	0.86 (0.77, 0.95)*	0.82 (0.75, 0.90)**	0.79 (0.72, 0.86)**
Global p-value	0.01	0.004	0.01	<0.001	<0.001
Trend p-value	0.43	0.21	0.10	<0.001	<0.001

1- Models adjusted for neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during gestation and three months prior, and SDI

* p<0.05; ** p<0.001

The preterm birth forest plots by buffer distance for each phase are shown in Figure 14. The vertical line at 1 represents a null relationship; dots below 1 indicate reduced risk and dots above 1 indicate increased risk.

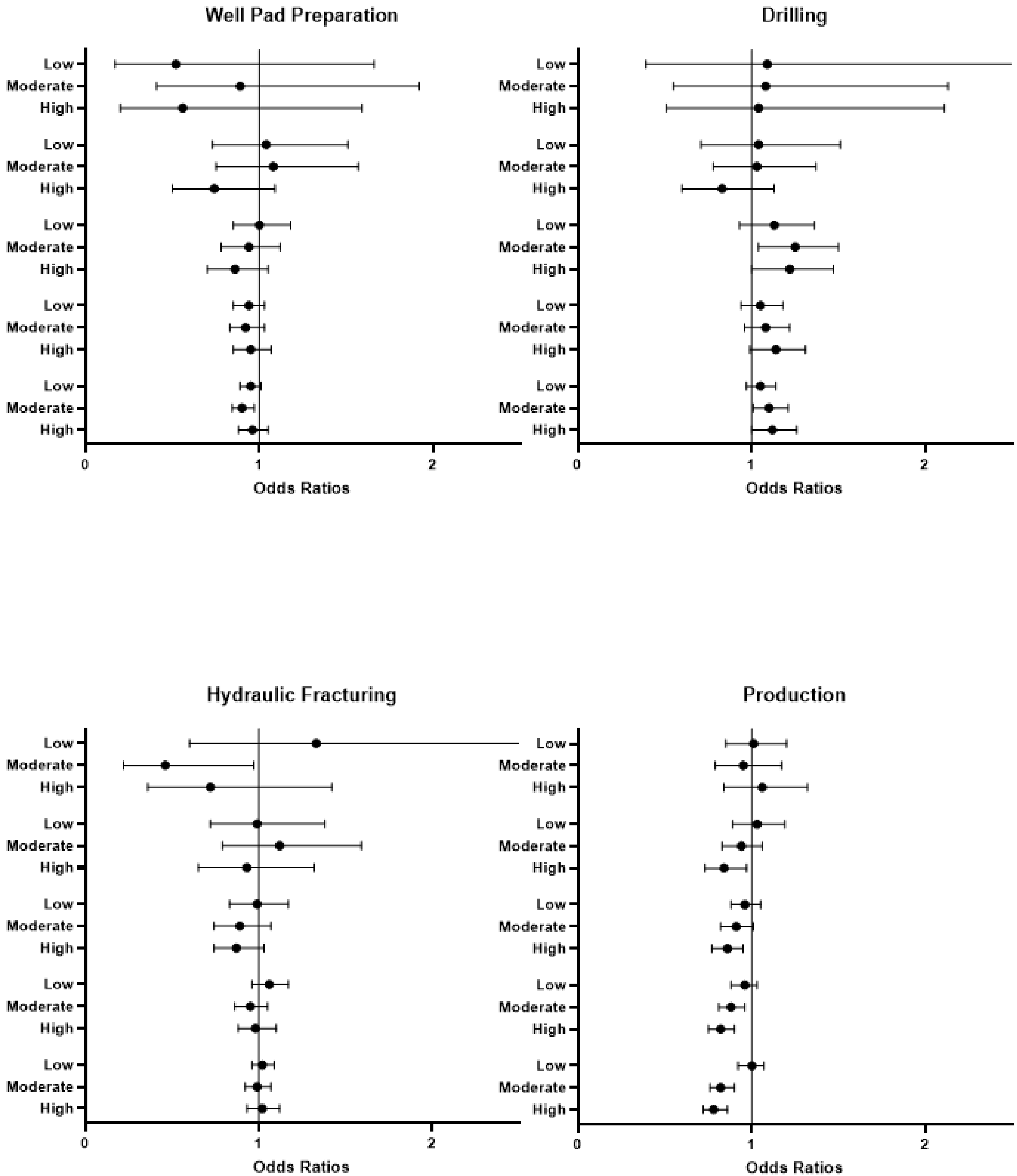

Figure 14. Forest Plots for Preterm Birth Models

Non-Well Exposure Models

Table 21 shows results by buffer for compressor stations, impoundment ponds, and facilities accepting oil and gas waste. There was no indication of increased risk of preterm birth for any of the facilities; many of odds ratios were at 1 or reduced, and many were statistically significant with significant global and trend tests.

Table 21. Preterm Birth Model Results – Other Exposures

Buffer	Adjusted OR[1] (95% CI)		
	Compressor Stations	Impoundment Ponds	Facilities accepting oil & gas waste
0.5 miles			
Unexposed	--	--	--
Low	0.78 (0.50, 1.21)	0.81 (0.47, 1.38)	1.14 (0.70, 1.87)
Moderate	0.56 (0.33, 0.95)*	1.41 (0.77, 2.58)	1.04 (0.63, 1.72)
High	0.78 (0.45, 1.37)	0.80 (0.39, 1.64)	0.68 (0.37, 1.25)
Global p-value	<0.001	0.50	<0.001
Trend p-value	<0.001	0.48	<0.001
1 mile			
Unexposed	--	--	--
Low	0.99 (0.74, 1.33)	1.17 (0.89, 1.53)	0.87 (0.69, 1.10)
Moderate	0.80 (0.59, 1.10)	0.96 (0.74, 1.24)	0.88 (0.71, 1.09)
High	0.79 (0.60, 1.04))	1.07 (0.82, 1.39)	0.89 (0.73, 1.08)
Global p-value	<0.001	0.73	<0.001
Trend p-value	<0.001	0.40	<0.001
2 miles			
Unexposed	--	--	--
Low	0.89 (0.78, 1.02)	1.03 (0.88, 1.21)	0.86 (0.77, 0.96)*
Moderate	0.82 (0.70, 0.95)*	1.05 (0.92, 1.21)	0.84 (0.76, 0.94)*
High	0.90 (0.77, 1.06)	1.12 (0.99, 1.27)	0.88 (0.79, 0.98)*
Global p-value	<0.001	0.49	<0.001
Trend p-value	<0.001	0.12	0.003
5 miles			
U.9nexposed	--	--	--
Low	0.91 (0.83, 0.98)*	1.00 (0.93, 1.08)	0.87 (0.81, 0.93)**
Moderate	0.89 (0.83, 0.96)*	1.09 (1.00, 1.18)*	0.81 (0.76, 0.87)**
High	0.88 (0.82, 0.95)**	1.09 (1.00, 1.19)*	0.85 (0.78, 0.91)**
Global p-value	<0.001	0.08	<0.001
Trend p-value	0.001	0.02	<0.001
10 miles			
Unexposed	--	--	--

Buffer	Adjusted OR[1] (95% CI)		
	Compressor Stations	Impoundment Ponds	Facilities accepting oil & gas waste
Low	0.94 (0.88, 1.00)	0.95 (0.90, 1.01)	0.89 (0.84, 0.94)**
Moderate	0.87 (0.82, 0.92)**	1.01 (0.95, 1.06)	0.85 (0.80, 0.90)**
High	0.89 (0.83, 0.95)**	1.09 (1.03, 1.16)*	0.81 (0.76, 0.86)**
Global p-value	<0.001	0.01	<0.001
Trend p-value	<0.001	0.04	<0.001

1- Models adjusted for neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during pregnancy and three months prior, and SDI

* p<0.05; ** p<0.001

The preterm birth forest plots for the non-well exposures are shown in Figure 15.

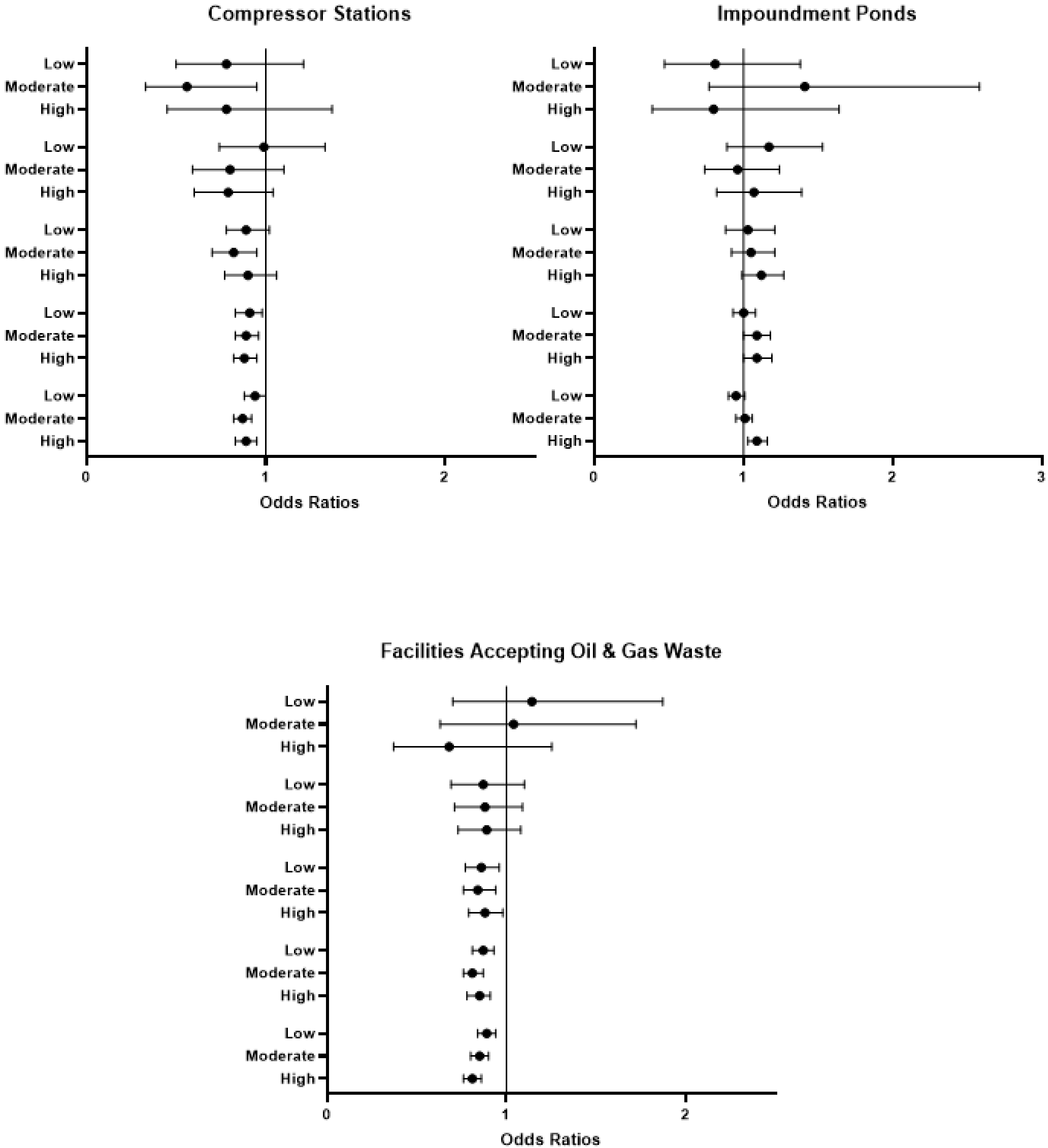

Figure 15. Forest Plots for Preterm Birth Non-Well Exposure Models

Term Birthweight

Term births were defined as those with gestational age between 37-41 weeks, inclusive. There were 170,479 births (37-41 weeks gestational age) with birthweight information available.

Well Cumulative Count Models

Table 22 below shows adjusted models for changes in term birthweight by buffer. In general, there were small, not statistically significant differences in birthweight using the cumulative count metric, although the Exposed, moderate metric had a statistically significantly elevated weight in the 1-mile buffer. The 10-mile buffer was statistically significant globally and the Exposed, high metric had a statistically significantly reduced weight.

Table 22. Term Birthweight (grams) Model Results – Well Cumulative Count Metric

Buffer	Adjusted Term Birthweight (grams)[1] (95% CI)
0.5 miles[2]	
1 mile	
Unexposed	--
Low	-6.29 (-23.61, 11.03)
Moderate	4.10 (-10.30, 18.50)
High	-14.12 (-31.80, 3.55)
Global p-value	0.12
Trend p-value	0.58
2 miles	
Unexposed	--
Low	-5.07 (-18.39, 8.25)
Moderate	-2.06 (-15.64, 11.52)
High	-11.70 (-25.49, 2.09)
Global p-value	0.27
Trend p-value	0.42
5 miles	
Unexposed	--
Low	-6.44 (-18.82, 5.94)
Moderate	-8.20 (-20.42, 4.03)
High	-8.49 (-20.87, 3.89)
Global p-value	0.65
Trend p-value	0.14
10 miles	
Unexposed	--
Low	-0.68 (-12.14, 10.78)
Moderate	-8.02 (-20.15, 4.10)
High	-12.40 (-24.47, -0.32)*
Global p-value	0.002
Trend p-value	0.002

1- Models adjusted for gestational age, neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during gestation and three months prior, and SDI

2- We could not use the tertile split among the exposed group for the 0.5-mile buffer because the cut points for the "exposed, low" category were [1, 1).

* p<0.05; ** p<0.001

Well Phase Activity Metric Models

Adjusted phase and buffer-specific model results for term birthweight are shown in Table 23. Across all buffers, there were consistent, statistically significant reductions in birthweight for the production phase. For well pad preparation, there were increases in birthweight which were statistically significant at the 5- and 10-mile buffers. There were no consistent relationships for the drilling and hydraulic fracturing phases.

Table 23. Term Birthweight (grams) Model Results – Well Phase Activity Metrics

Phase	Adjusted[1] Term Birthweight (grams) (95% CI)				
	0.5 miles	1 mile	2 miles	5 miles	10 miles
Well Pad Preparation					
Unexposed	--	--	--	--	--
Low	-18.27 (-103.00, 66.46)	23.80 (-15.77, 63.36)	15.14 (-4.96, 35.24)	17.97 (8.26, 27.68)**	7.92 (0.52, 15.31)*
Moderate	-44.23 (-135.75, 47.30)	1.40 (-36.20, 39.00)	3.11 (-16.13, 22.35)	19.74 (8.43, 31.05)**	13.97 (6.82, 21.12)**
High	3.30 (-74.36, 80.96)	25.35 (-12.69, 63.38)	5.36 (-14.70, 25.43)	23.16 (11.47, 34.84)**	27.28 (18.22, 36.35)**
Global p-value	0.002	<0.001	0.002	<0.001	<0.001
Trend p-value	<0.001	<0.001	0.004	<0.001	<0.001
Drilling					
Unexposed	--	--	--	--	--
Low	14.63 (-70.91, 100.17)	-13.00 (-55.59, 29.60)	-2.53 (-21.68, 16.62)	-4.02 (-15.77, 7.74)	2.91 (-4.99, 10.82)
Moderate	-11.97 (-79.66, 55.71)	-18.24 (-51.92, 15.44)	-4.54 (-23.52, 14.45)	-0.93 (-14.44, 12.58)	-5.80 (-15.34, 3.74)
High	-13.54 (-101.24, 74.16)	-28.45 (-70.58, 13.69)	-17.71 (-37.54, 2.11)	-5.05 (-19.28, 9.18)	-8.22 (-20.78, 4.35)
Global p-value	0.93	0.73	0.46	0.85	0.06
Trend p-value	0.17	0.03	0.02	0.73	0.10
Hydraulic Fracturing					
Unexposed	--	--	--	--	--
Low	43.99 (-29.25, 117.23)	15.83 (-17.52, 49.18)	32.23 (15.63, 48.83)**	5.17 (-3.90, 14.25)	5.05 (-1.29, 11.39)
Moderate	12.64 (-52.09, 77.38)	17.22 (-10.41, 44.85)	3.42 (-11.56, 18.40)	5.79 (-3.99, 15.57)	0.68 (-6.53, 7.88)
High	-0.36 (-73.51, 72.79)	5.04 (-26.74, 36.82)	19.48 (3.02, 35.94)*	0.75 (-9.48, 10.98)	1.49 (-7.39, 10.36)
Global p-value	0.69	0.67	<0.001	0.62	0.34
Trend p-value	0.31	0.19	0.004	0.63	0.64
Production					
Unexposed	--	--	--	--	--
Low	-24.71 (-51.60, 2.19)	-16.65 (-32.29, -1.02)*	-14.74 (-27.55, -1.93)*	-19.61 (-30.13, -9.09)**	-13.49 (-23.17, -3.82)*
Moderate	-16.55 (-43.97, 10.87)	-4.30 (-18.68, 10.09)	-18.13 (-30.71, -5.55)*	-19.89 (-30.93, -8.84)**	-17.47 (-27.82, -7.13)**
High	-16.54 (-46.77, 13.69)	-19.67 (-36.03, -3.31)*	-23.37 (-35.83, -10.91)**	-26.50 (-37.94, -15.07)**	-21.47 (-32.58, -10.37)**

Phase	Adjusted[1] Term Birthweight (grams) (95% CI)				
	0.5 miles	1 mile	2 miles	5 miles	10 miles
Global p-value	0.01	<0.001	0.004	<0.001	0.002
Trend p-value	0.01	0.22	0.02	<0.001	<0.001

1- Models adjusted for gestational age, neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during gestation and three months prior, and SDI

* p<0.05; ** p<0.001

The term birthweight forest plots by buffer distance for each phase are shown in Figure 16. The vertical line at 0 represents no change in term birthweight (grams); dots below 0 indicate reduced term birthweight and dots above 0 indicate increased term birthweight.

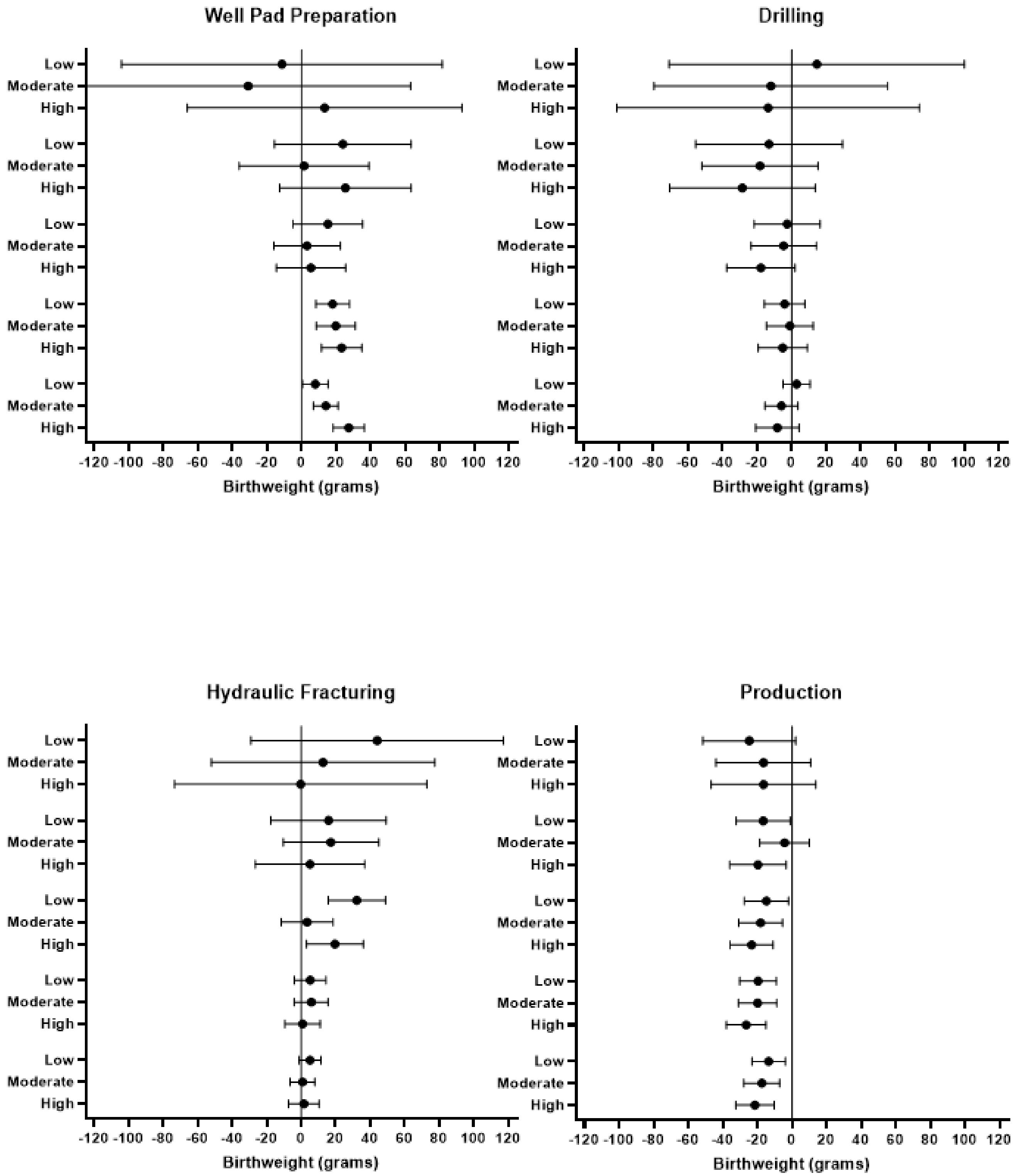

Figure 16. Forest Plots for Term Birthweight Models

Non-Well Exposure Models

Table 24 shows results by buffer for the non-well exposures. For compressor stations, we found reduced birthweights for nearly all tertiles in all buffers, many of which were statistically significant, with corresponding statistically significant global and trend tests. We found no consistent association with exposure to impoundment ponds. There were statistically significant reductions in birthweight for facilities accepting oil and gas waste in each buffer, many of which were statistically significant, with corresponding statistically significant global and trend tests.

Table 24. Term Birthweight (grams) Model Results – Other Exposures

Buffer	Adjusted[1] Term Birthweight (grams) (95% CI)		
	Compressor Stations	Impoundment Ponds	Facilities accepting oil & gas waste
0.5 miles			
Unexposed	--	--	--
Low	-21.68 (-87.11, 43.76)	-33.86 (-102.31, 34.60)	5.61 (-62.79, 74.01)
Moderate	-89.38 (-133.63, -45.12)**	5.78 (-59.22, 70.78)	-71.44 (-116.11, -26.76)*
High	-15.24 (-71.84, 41.36)	-10.52 (-59.32, 38.29)	-6.70 (-70.66, 57.25)
Global p-value	<0.001	0.46	<0.001
Trend p-value	<0.001	0.23	<0.001
1 mile			
Unexposed	--	--	--
Low	-23.10 (-52.04, 5.84)	-14.62 (-39.63, 10.39)	-51.35 (-75.10, -27.60)**
Moderate	-7.29 (-32.40, 17.82)	27.84 (-0.41, 56.09)	-41.42 (-66.90, -15.94)**
High	-36.98 (-63.60, -10.37)*	8.08 (-15.69, 31.85)	-33.08 (-55.80, -10.37)*
Global p-value	<0.001	0.17	<0.001
Trend p-value	<0.001	0.11	<0.001
2 miles			
Unexposed	--	--	--
Low	-20.52 (-35.43, -5.61)*	2.21 (-11.65, 16.07)	-14.72 (-28.44, -1.00)*
Moderate	-26.22 (-44.01, -8.43)*	20.06 (4.88, 35.24)*	-7.03 (-19.15, 5.09)
High	-28.56 (-46.12, -11.00)*	2.32 (-11.70, 16.34)	-37.37 (-50.34, -24.39)**
Global p-value	<0.001	0.12	<0.001
Trend p-value	<0.001	0.08	<0.001
5 miles			
Unexposed	--	--	--
Low	-12.22 (-19.24, -5.20)**	1.74 (-7.30, 10.77)	-21.76 (-28.89, -14.63)**

Buffer	Adjusted[1] Term Birthweight (grams) (95% CI)		
	Compressor Stations	Impoundment Ponds	Facilities accepting oil & gas waste
Moderate	-9.45 (-17.81, -1.10)*	4.39 (-3.98, 12.76)	-17.23 (-24.91, -9.55)**
High	-22.76 (-31.90, -13.62)**	5.01 (-4.00, 14.03)	-20.51 (-28.67, -12.35)**
Global p-value	<0.001	0.66	<0.001
Trend p-value	<0.001	0.16	<0.001
10 miles			
Unexposed	--	--	--
Low	-13.42 (-20.08, -6.76)**	-0.09 (-6.03, 5.86)	-12.85 (-18.88, -6.82)**
Moderate	-16.34 (-23.39, -9.29)**	3.41 (-3.00, 9.81)	-20.78 (-27.39, -14.17)**
High	-16.92 (-23.94, -9.89)**	5.87 (-0.27, 12.00)	-21.76 (-28.55, -14.98)**
Global p-value	<0.001	0.24	<0.001
Trend p-value	<0.001	0.07	<0.001

1- Models adjusted for neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, receipt of WIC services, gestational diabetes, parity, smoking during pregnancy and three months prior, and SDI

* p<0.05; ** p<0.001

The forest plots for term birthweight non-well exposures are shown in Figure 17.

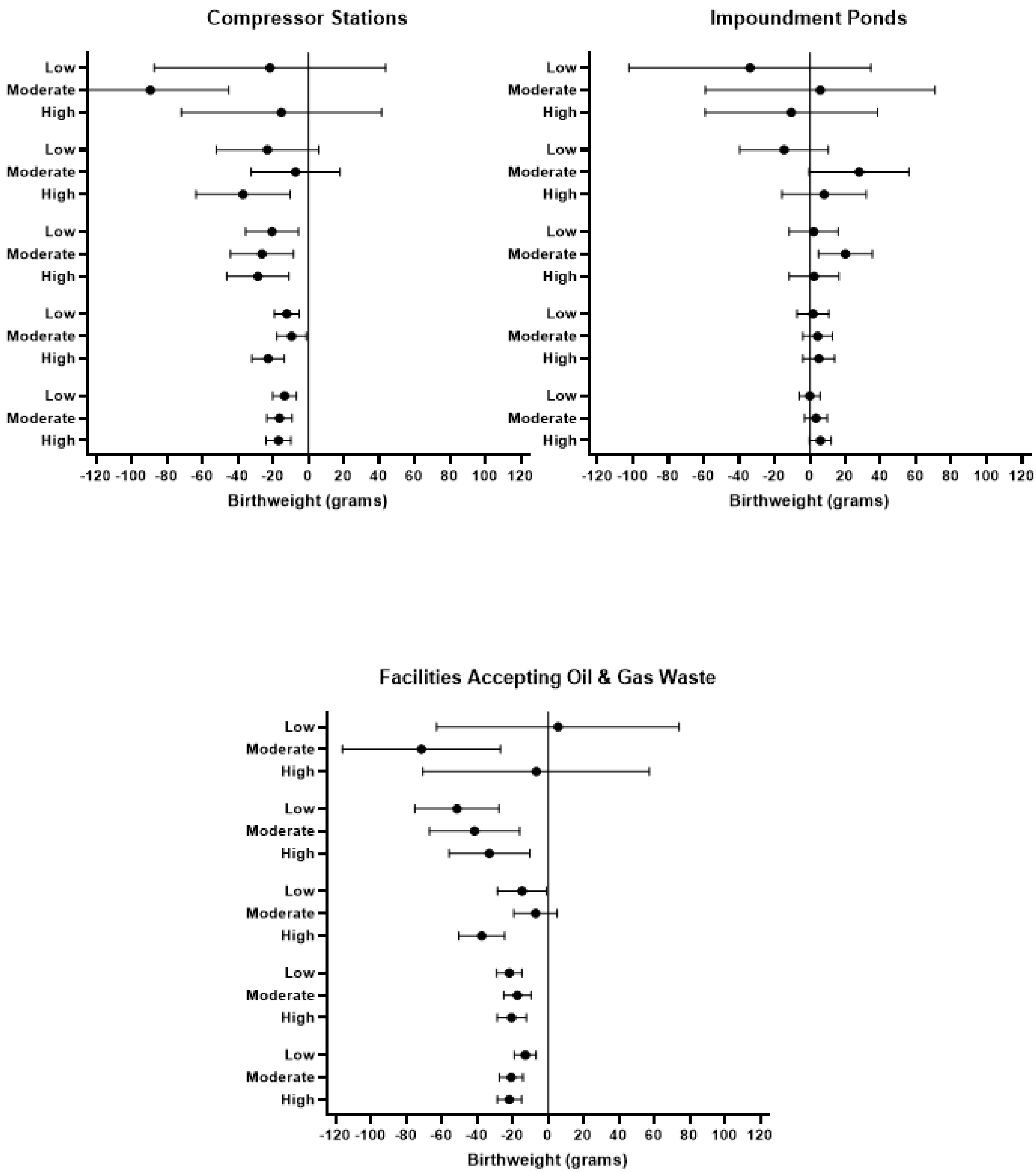

Figure 17. Forest Plots for Term Birthweight (grams) Non-Well Exposure Models

Exposure to PM2.5

As shown in Table 25 and in Figure 18, fine particulate matter, or PM 2.5 concentrations, have gradually declined over the course of the 2010-2018 period available for these data.

In December 2012, the EPA changed the primary annual fine particle standard from 15µg/m^3 to 12µg/m^3; areas are considered to meet this standard if their 3-year average annual PM 2.5 concentrations are equal to or less than 12µg/m^3 [38]. In 2010, both Allegheny and Westmoreland were above 12µg/m^3, but by the following year all counties were below that level and sustained it throughout the study period. It is likely that reductions in PM 2.5 pollution as shown by our data are due, in part, to the necessity of meeting this improved pollution standard. In 2021, the American Thoracic Society[39] recommend the standard for long-term exposure to PM2.5 be lowered to 8µg/m^3. County averages in 2016-2018 trend closer to this value; however, Allegheny County in 2018 was higher than 8µg/m^3. While the county averages are often below the 12µg/m^3 and close to the 8µg/m^3 benchmark in later years, geographic variability exists throughout each county, resulting in a significant portion of the population residing in areas below the respective benchmarks.

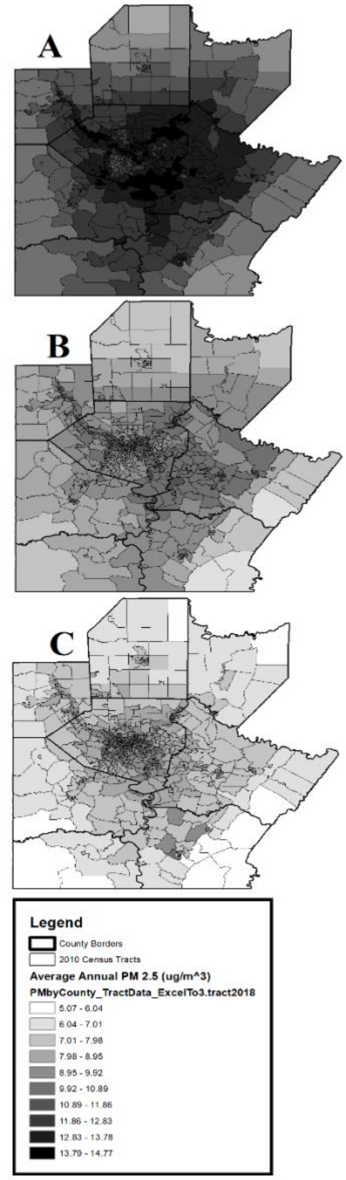

Figure: Average annual PM 2.5 concentrations in 2010 (A), 2014 (B), and 2018 (C) aggregated to the 2010 census tract level for southwestern Pennsylvania.

Figure 18. Study Area Maps of PM2.5 Values

Table 25. Average Annual PM2.5 (µg/m^3) by County for Study Region

County	2010	2011	2012	2013	2014	2015	2016	2017	2018
Allegheny	13.13	10.99	10.32	10.03	9.87	10.09	9.48	9.75	8.68
Armstrong	11.07	10.24	9.14	9.13	8.65	8.45	8.24	8.48	6.51
Beaver	11.24	10.15	8.93	9.72	9.00	8.91	8.39	8.42	7.23
Butler	10.39	9.63	8.40	8.86	8.09	8.13	7.79	8.33	6.82
Fayette	11.04	10.09	9.11	8.31	8.17	8.77	7.47	7.84	6.33
Greene	11.29	9.61	8.89	8.11	8.22	8.37	7.06	7.32	6.24
Washington	11.65	9.83	9.02	9.07	8.76	9.00	7.78	8.02	6.97
Westmoreland	12.17	10.88	9.94	9.52	9.25	9.30	8.65	8.92	7.23

Table 26 shows, for each of the three birth outcomes, the adjusted models for exposure to PM2.5 as a continuous term (no cut points were used) for the 153,339 births with PM2.5 measures. There was a statistically significantly elevated odds ratio for preterm birth (22-36 weeks gestation), indicating an increase in odds of preterm birth of 7% for each increase of 10μg/m³ of PM2.5. We did not find evidence of increased risk with exposure to PM2.5 for either SGA or decreased term birthweight (37-41 weeks gestation).

Table 26. Association Between Exposure to PM2.5 (μg/m³, continuous) and Birth Outcomes

Outcome	Adjusted OR[1] (95%CI) (per 10μg/m³ PM2.5)
SGA	0.98 (0.97, 1.00)*
Preterm birth	1.07 (1.05, 1.10)*
Outcome	Adjusted Term Birthweight (grams)[1] (95%CI) (per 10μg/m³ PM2.5)
Term birthweight (grams)	3.8 (2.0, 5.6)*

1- Models adjusted for county, neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, gestational diabetes, parity, smoking during pregnancy and three months prior, and SDI. Term birthweight model additionally adjusted for gestational age.

* p<0.05; ** p<0.001

PM2.5 was then dichotomized at 8μg/m³, as recommended by the American Thoracic Society[39] and recently implemented by Goobie et al.[40], as shown in Table 28. PM2.5 was also split at 8μg/m³ and 12μg/m³.

Only 5% of our cohort with exposure to PM2.5 were exposed to levels at or below 8μg/m³. The counties with lower PM2.5 had fewer births and exposure was an average of the year prior to birth, which reduced the number of births with PM2.5 exposure levels at or below 8μg/m³.

In our cohort, 8,189 births had PM2.5 exposure at or below 8μg/m³. Ten percent of births (n=15,840) had PM2.5 exposure greater than 12μg/m³.

In the model using the >=8μg/m³ cutoff, there was a statistically significant 8% increased risk of preterm birth compared to those below 8μg/m³. In the model splitting exposure at 8μg/m³ and 12μg/m³, the odds ratios increased with increasing PM2.5 exposure, with those exposed to greater than 12μg/m³ having a statistically significant 30% excess for preterm birth.

Table 27. Association Between Exposure to PM2.5 (μg/m³, categorized) and Preterm Birth

PM2.5 (μg/m³) Characterization	Adjusted OR[1] (95%CI)
Cutoff at >=8μg/m³	
<8μg/m³	--
>=8μg/m³	1.11 (1.01, 1.23)*
Cutoffs at >=8μg/m³ and >12μg/m³	
<8μg/m³	--
>=8 μg/m³ and <=12μg/m³	1.11 (1.00, 1.22)*
>12μg/m³	1.30 (1.15, 1.46)**

1- Models adjusted for county, neonate sex, APNCU index, maternal age (centered at the mean), maternal race, maternal education level, maternal BMI, gestational diabetes, parity, smoking during pregnancy and three months prior, SDI

* p<0.05; ** p<0.001

Discussion

This population-based study of birth records from 2010-2020 in eight Southwestern Pennsylvania counties assessed associations between UNGD activity and three birth outcomes: small for gestational age, preterm birth (22-36 weeks gestation), and term (37-41 weeks gestation) birthweight. Similar to other studies on UNGD and birth outcomes, we found mixed results. To help frame the study conclusions, we are using the following classifying terms and criteria:

1. There are no data to suggest/support an increased risk:
   a. No statistically significantly elevated odds ratios
   b. Odds ratios at or near 1
   c. Odds ratios below 1 (with or without statistical significance)

2. There are limited data to suggest/support an increased risk:
   a. Statistically significantly elevated odds ratios in a low or moderate tertile
   b. Not statistically significant elevated odds ratios in multiple tertiles

3. There are moderate data to suggest/support an increased risk:
   a. Statistically significantly elevated odds ratios in multiple low or moderate tertiles
   b. Statistically significantly elevated odds ratios in a high tertile

4. There are strong data to suggest/support an increased risk:
   a. Statistically significantly elevated odds ratios in multiple tertiles
   b. Statistically significantly elevated odds ratios that increase across low, moderate, and high tertiles

For our primary exposure of interest, UNGD activity, our results are summarized below.

Small for gestational age (SGA): In this study, we found no data to support an increased risk of SGA and well phase activity in the well pad preparation, drilling, or hydraulic fracturing phases, nor with cumulative well count. There were consistently statistically significantly reduced odds ratios in the 10-mile buffer for well pad preparation. There were moderate to strong data to suggest an increased risk with the production phase. Odds ratios in the 2-, 5-, and 10-mile buffers were statistically significantly elevated 8-12%, with limited evidence of increasing risk with increasing intensity.

Preterm (22-36 weeks gestation): In this study, we found no data to support an increased risk of preterm birth and cumulative well count, nor with well phase activity in the well pad preparation, hydraulic fracturing, or production phases. There were statistically significantly reduced odds ratios for cumulative well count in all buffers and the trend test was statistically significant in the 10-mile buffer. Odds ratios for the production phase were statistically significantly reduced in the 5- and 10-mile buffers. There were limited data to suggest an increased risk with the drilling phase.

Term (37-41 weeks gestation) birthweight: In this study, we found no data to support an increased risk of term birthweight and well phase activity in the well pad preparation or hydraulic fracturing phases. Term birthweights in the 5- and 10-mile buffers were statistically significantly elevated. There were limited data to suggest an increased risk with the drilling phase, moderate data to suggest an increased risk with cumulative well count, and strong data to suggest an increased risk with the production phase, with statistically significant reductions in birthweight with increasing intensity of exposure.

Table 28 shows the results of the previous literature in comparison with this study (last row). Previous studies have had mixed results for these three outcomes, as shown. Our study replicated the methods of Casey et al.[6] in Northeastern PA and is also similar to the study performed by Whitworth et al.[10] in Texas. Stacy et al.[5], also with a focus in Southwestern Pennsylvania, identified an association between SGA and UNGD activity, as did Hill[26] and Tran[27]. Neither Casey et al[6] nor Whitworth et al[10] found a similar association. Casey et al. [6] and Whitworth et al.[10,12] both found statistically significant odds ratios in the third tertile (T3) of UNGD activity and preterm birth.

This study did not find statistically significant excesses for preterm birth in cumulative well count, a cumulative measure of UNGD activity or in the phase specific metrics with the exception of a limited association in the drilling phase. The association with preterm birth identified in Whitworth[10] was stronger than the association found here. The current study found a strong association between reduced term birthweight and the production phase, a moderate association with cumulative well count, and a limited association with the drilling phase. Casey et al[6] identified a not statistically significant 20 gram reduction with the highest quartile (Q4) of UNGD exposure and Whitworth et al.[41] found similar not statistically significant reduced birthweights. Stacy et al[5] found a statistically significant 21 gram reduction in birthweight associated with Q4 of inverse-distance weighted well count.

The varying exposure characterizations make direct comparisons difficult between many studies. Phase-specific analyses help pinpoint the timing and degree of risk associated with UNGD activity. One possible difference between this and other studies that could explain some of the mixed associations is that our cohort contains a significant number of births occurring in more recent times. If UNGD activities have changed over time to result in less environmental impact, then that could attenuate some of the effect sizes seen here relative to previous work.

Table 28. Summary of UNGD Model Results from Peer-Reviewed Literature and Current Study

Year	First Author	State	SGA	Preterm Birth	Term Birthweight
2014	McKenzie[23]	CO	--	N	N
2015	Stacy[5]	PA	Y Q[1]4 IDW well count OR[2]=1.34 (1.10, 1.63)	N	Y Q4 IDW well count BW[3] = -21 (-30, -12)
2016	Casey[6]	PA	N	Y Q4 UNGD OR=1.4 (1.0, 1.9)	N
2017	Currie[22]	PA	--	Y	Y BW = -39g
2017	Whitworth[10]	TX	N	Y T[4]3 UNGD 0.5-mile buffer OR= 1.14 (1.03, 1.25)	N

				2-mile buffer OR = 1.14 (1.07, 1.22) 10-mile buffer OR=1.15 (1.08, 1.22)	
2018	Hill[26]	PA	Y	N	Y
2018	Whitworth[12]	TX	--	Y T3 UNGD Drilling OR=1.20 (1.06, 1.37) Production OR=1.15 (1.05, 1.26)	--
2020	Cushing[28]	TX	--	Y Q4 well count OR=1.31 (1.14, 1.49)	Y Q4 well count BW=−19.4 (−36.7, −2.0)
2020	Gonzalez[17]	CA	--	N[5]	--
2020	Tran[29]	CA	Y[6] High vs no production OR=1.22 (1.02,1.45)	N	Y[6] High vs no production BW=−36g (−54, −17)
2021	Willis[18]	TX	N	--	Y 0-1 v 3-10km BW= –7.3g (–11.6, –3.0)
2022	Pitt SPH	PA	Moderate/strong Production phase	Limited Drilling phase	Limited Drilling phase Moderate Cumulative well count Strong Production phase

1– Q=quartile
2 – OR=odds ratio
3 – BW=birthweight
4 – T=tertile
5- Association only observed in very preterm births (<31 weeks)
6 – Association only observed in rural and not urban areas

Non-Well Exposures

We examined non-UNGD activity exposures as secondary sources in this study. Table 29 summarizes the findings between our birth outcomes and non-UNGD well phase exposures.

Table 29. Summary of Increased Risk of Adverse Birth Outcomes in Non-Well Exposure Model Results

Type of Exposure	SGA	Preterm birth	Term birthweight (grams)
Compressor stations	Limited	None	Moderate
Impoundment ponds	None	None	None
Facilities accepting oil and gas waste	Limited	None	Moderate
PM2.5 (µg/m^3)	None	Moderate	None

We found limited data to support an association for small for gestational age and proximity to facilities accepting oil and gas waste, particularly within 1 mile. Industrial air pollution has previously been shown to be associated with SGA, especially during the first two trimesters[42]. Maternal exposure to PM10 has also shown to be associated[43]. Future work should examine gestational exposure windows as well as the amount and type of waste accepted by the facilities.

There were moderate data to support that reductions in term birthweight were associated with proximity to both compressor stations and facilities accepting oil and gas waste. Previous studies have identified associations between birthweight and UNGD[5,18,22,26,28,29], but few have investigated UNGD infrastructure. These results indicate that non-well activities may also have impacts on birth outcomes. Additional studies should confirm and explore the relationship further.

We also found a moderate association between preterm birth and PM2.5. This association has been shown previously in multiple studies in the United States and internationally[46-49]. Liu et al[47] identified a statistically significant 4% excess for preterm birth with each 10 $\mu g/m^3$ increase in PM2.5 in the first and third trimesters, very similar to the 5% excess identified here. Future work with the PM2.5 data should also include sensitivity analyses evaluating other time windows of exposure, various lengths of exposure, constituent analysis, and other characterizations of the metric.

UNGD activities also have the potential to produce a variety of air pollutants, including PM2.5 to varying degrees. Beginning with the 2012 reporting year, the PA DEP has collected self-reported emissions data from the UNGD industry We noted these self-reported emissions for UNGD wells can vary several orders of magnitude between individual sites and over different years for the same site (http://cedatareporting.pa.gov/reports/powerbi/Public/DEP/AQ/PBI/Air_Emissions_Report). Our exposure metrics applied here essentially weight the behavior of all wells equally varying only be density and stage of activity, which does not allow discrimination of high emission wells from low emission wells. Thus, it is possible that a subset of wells with high polluting potential could negatively impact nearby residents, especially given the robust effect seen with region wide PM2.5 levels.

We evaluated multiple buffer distances in this study. A 2018 Delphi study evaluated setback distances for UNGD[14]. After three rounds of discussion with 18 panelists, consensus was reached that setbacks less than 0.25 mile should not be recommended and additional setbacks should be recommended for vulnerable groups. However, the panel did not reach consensus on setback distances between 0.25 and 2 miles. A review by Deziel et al.[16] of the association of UNGD and various health outcomes, including births, advocated for policy changes, including assessing setbacks. We found some evidence of associations for increased risk of small for gestational age during the well pad preparation and drilling phases and for preterm birth during the production phase at the smallest buffer, 0.5 miles. However, even with our population-based cohort of births, the small sample size led to wide confidence intervals. Future analyses of these results should include examining different functional forms of the exposure metric and considering the contaminants and exposures occurring during each phase.

Strengths and Limitations

This study had considerable strengths, including a very large population and assessing multiple characterizations of the exposure metrics at multiple buffer distances. These phase-by-buffer analyses provide new and important information about the associations of UNGD with our three birth outcomes. However, our analyses were proximity and density-based and not associated with any specific exposure or pathway. Future studies should include defined exposure pathways with the collection of biospecimens to help elucidate potential paths. Additionally, we did not evaluate heterogeneity in well conditions or techniques by operator. It is feasible that different conditions may exist by operator, well, or well pad leading to differing levels of exposure.

Epidemiologic studies address risk at the population level and not for any specific individual. Even in our large population-based cohort study, we had small sample sizes in some analyses, especially those within our smallest buffer distances and during shorter well activity phases (e.g., hydraulic fracturing). This included an inability to examine low Apgar score as an outcome, similar to Casey et al.[6] An analysis encompassing the entire state of PA, or several states, may be necessary to get an adequately powered study for this outcome. We used obstetric estimate of gestational age from the birth certificate. While research has shown excellent specificity, positive predictive value, and negative predictive value[50], it could introduce error when calculating preterm and small for gestational age statuses. The rates of SGA (9.2%) and preterm births (22-36 weeks, 7.4%) found in this study are slightly below the US averages of 10%[35] and 8.5% for singleton births[51], respectively. This could indicate better maternal and fetal care in our study area, although the rate of adequate and adequate plus prenatal care in this study (74.7%) is very similar to that in the US (77.6%)[51]. Additionally, we did not adjust for multiple comparisons. Some of the relationships between outcome and exposure may indicate evidence of a threshold effect, which was not assessed in the functional forms of the exposures examined here. Future studies should examine non-linear and other functional forms. There were some statistically significantly increased risks (both odds ratios and reduced birthweight) that lacked a "dose-response" relationship (i.e., risk did not increase with increasing intensity of exposure) often in terms of buffer zone and intensity metric. These could be due to small sample sizes in certain subgroups, to multiple comparisons or could be spurious. The trend test assessed the linear relationship of the exposure tertiles, and some trend tests were statistically significant even when odds ratios (or term birthweights) were close to the reference level. It may also be the case that, although we used as our comparison those residing greater than 10 miles from UNGD activity, there is no such thing as a truly non-exposed group given the large density of wells, and the relatively few births in the unexposed group. It may also be true that air pollution is acting as a confounder here, where the unexposed controls who were slightly more likely to reside in Allegheny County, were not impacted by fracking, but have higher levels of PM2.5. Future models should include PM2.5 measurements with UNGD activity.

In contrast to Casey et al.[6] which included births from 2009 to 2013, we examined 11 years of birth data and corresponding UNGD activity data during a period of high activity in Southwestern PA (2010-2020). We anticipate that technological changes may have occurred over that time that may modify the associations with UNGD in more recent years.

Our results provide important new information about the associations between UNGD activity and birth outcomes, but also provide direction for future analyses. The findings related to oil and gas infrastructure need to be examined in more detail, particularly the types and amounts of waste accepted by such facilities. Moreover, additional work is needed to ascertain why the production phase seems to pose the most risk for reduced term birthweight, and to a lesser extent, SGA. The similar associations related to the production phase among term birthweight and SGA, both outcomes related to in utero growth, lend support to the consistency of those findings. Of the previous studies which examined both SGA and term birthweight, Stacy[5] and Tran[27] also identified associations with UNGD activity and both outcomes. Hill[26] found an association with SGA but not term birthweight; Willis[18] found an association with term birthweight but not SGA, and Casey[6] and Whitworth[10] did not find associations with either outcome.

While we focused here on term birthweight and preterm birth 22-36 weeks, those infants born preterm with low birthweight or preterm prior to 31 weeks may be especially vulnerable and those associations should be examined. Finally, the exposures associated with UNGD are complex and multi-faceted. As recently advocated by Deziel et al.[19], future work should include multiple exposures and identify ways in which exposure pathways can be delineated.

Appendix

Table 1. Peer-Reviewed Literature on Birth Outcomes and Associations with UNGD

Year	First Author	Journal	Geographic Area	Population	Distance (miles/km)	Metric (e.g., IDW, CWD)	Data Source (e.g., DEP, self-report,)	Findings
2014	McKenzie	Environmental Health Perspectives	CO – restricted to rural areas and towns with pops < 50,000 in 57 counties	Singleton live births from 1996 through 2009, excluding non-white births due to low %	10 mi radius of maternal residence	IDW natural gas well counts (tertiles; referent group = 0 wells w/i 10 mi)	Colorado Oil and Gas Information System (COGIS)	Association between density and proximity of natural gas wells within a 10-mile radius of maternal residence and prevalence of CHDs
2015	Casey	Epidemiology	PA	Singleton births delivered at Geisinger, 2006-2013 (but then excluded births < 2009)	N/A – used all wells in the state	ID^2W, incorporating four phases of well development (quartiles)	PA DEP, PA DCNR, SkyTruth	Association between UNGD activity and preterm birth that increased across quartiles, 4^{th} q OR=1.4
2015	Stacy	PLoS ONE	PA -- Butler, Washington, and Westmoreland counties	Singleton births in the study counties from 2007-2010	10 mi radius of maternal residence and within the study counties	IDW well count (quartiles); Used active unconventional gas drilling wells from 2007-2010	PA DEP	Lower birth weight (21 g) and higher incidence of SGA (4.8% vs 6.5%) comparing most to least exposed
2016	Ma	Journal of Epidemiology and Public Health Reviews	PA	Singleton live births from 2003-2012	N/A – zip-code level	Well density = total number of unconventional wells	PA DEP	UNGD was not associated with birth defects prevalence rate

						per sq km for each zip-code		trend and level changes
2017	Currie	Science Advances	PA	Singleton births in the state from 2004-2013; Subset of births to mothers residing w/I 15 km of a well site	0-1 km, 1-2 km, 2-3 km, …, 10-15 km (with 0-1, 1-2, 2-3 km distance bands being defined as "near"; 3-15 km as "far")	Binary variable indicating if there is at least one well within the specified radius of the mother's residence; Used all oil and gas wells marked as unconventional and not currently plugged at time of study (i.e., active)	PA DEP Internal Operator Well Inventory	Greater incidence of low birthweight and lower birthweight within 1 km and 3km; little evidence for health effects at distances beyond 3 km
2017	Whitworth	PLoS ONE	TX – 24-county Barnett Shale area	Singleton births and fetal deaths from 11/30/2010-11/29/2012	0.5, 2, and 10 mi radius of maternal residence	ID^2W well count (tertiles; referent group = women with at least 1 well > 10 km but < 20 km of residence)	DrillingInfo	Increased adjusted odds of preterm birth in highest tertiles of the ½-, 2-, and 10-mile metrics. Little indication of association with SGA or term birthweight.
2017	Busby	Journal of Environmental Protection	PA	Live births and infant deaths (0-28 days, 0-1 year), 2003-2010	N/A -- county level	Comparison of time period before (2003-2006) and after fracking expansion (2007-2010); violations per birth; water wells per birth	PA DEP (fracking wells, violations), PA DCNR (drilled water wells)	Fracking associated with early infant mortality
2018	Hill	Journal of Health Economics	PA	Births from 2003-2010	2.5 km of maternal residence (also tested radii of 2, 3, 3.5, 4, 4.5, 5 km)	Binary variable indicating presence of any gas wells w/i specified radius;	PA DEP (also including permit data)	Associated with reduced average birth weight among infants born to mothers

						CWD of gas wells w/i specified radius		living within a 2.5 km
2018	Whitworth	Environmental Health Perspectives	TX – 24-county Barnett Shale area	Singleton births from 11/30/2010-11/29/2012	0.5 mi of maternal residence	ID^{2}W count of wells in the drilling phase (tertiles; referent group = 0 wells w/i 0.5 mi); ID2W sum of cumulative daily gas production volume (MCF) among wells in the production phase (tertiles; referent group = 0 wells w/i 0.5 mi)	DrillingInfo	Evidence of differences in phase- and trimester-specific associations of UNGD and preterm birth and indication of particular risk associated with extremely preterm birth
2019	Apergis	Environmental Science and Pollution Research	OK	Births from 2006-2017	0-1, 1-5, 5-10, and 10-20 km of maternal residence	CWD (number of wells within buffer)	Oklahoma Corporation Commission Oil and Gas Division	Unidirectional causal relationship between fracking and infant's health
2019	Casey	Environmental Research	PA	Singleton births delivered at Geisinger to women w/ and w/o depression or anxiety, 2009-2013	N/A – used all wells in the state	ID^{2}W, incorporating four phases of well development (quartiles)	PA DEP, PA DCNR, SkyTruth	Increased antenatal anxiety or depression in mothers in highest quartile of UNGD activity
2019	Janitz	Environment International	OK	Singleton births from 1997-2009	2 mi of maternal residence (also tested radii of 5 and 10 mi)	ID^{2}W well count (tertiles); IDW well count (tertiles)	Oklahoma Corporation Commission	Increased prevalence of neural tube defects among children with

								natural gas activity compared to no wells)
2019	McKenzie	Environment International	CO -- restricted to 34 counties with 20 or more active wells (areas with intense oil and gas activity)	All non-chromosomal congenital heart defect (CHD) cases and randomly selected singleton live birth controls, 2005-2011	10 mi radius of maternal residence	IDW well count; intensity adjusted IDW well count (IA-IDW) incorporating relative intensity of air pollution sources not associated with oil and gas activities	Colorado Oil and Gas Information System; EPA TRI; US Geological Survey (mines), Colorado Department of Public Health	CHDs more likely in medium and high intensity exposure groups
2020	Cushing	Environmental Health Perspectives	TX -- rural areas of the 27 counties comprising the Eagle Ford Shale	Singleton births from 2012-2015	5 km of maternal residence	CWD (number of wells within 5 km of maternal residence categorized as none, low, med, high); Number of individual nightly flaring events (median split); Total flared area (median split); ID2W sum of flares (median split)	DrillingInfo; VIIRS	Exposure to a high number of nightly flare events was associated with 50% higher odds of preterm birth and shorter gestation compared with no exposure. Women exposed to a high number of wells vs. no wells within 5km had a higher odds of preterm birth shorter gestation and lower average birthweight

2020	Gonzalez	Environmental Epidemiology	CA – 8 counties comprising San Joaquin valley region	Singleton births from 1998 to 2011 delivered at nonmilitary hospitals in the study region	10 km radius of maternal residence	ID^2W well count (tertiles)	California Geologic Energy Management Division (CalGEM; formerly DOGGR), Enverus (private data aggregation service)	Increased ORs for preterm birth with high exposure to wells in the first and second trimesters for births delivered at ≤31 weeks, confined to births to Hispanic and non-Hispanic Black women and to women with ≤12 years of educational attainment
2020	Tran	Environmental Health Perspectives	CA -- Sacramento Valley, San Joaquin Valley, South Central Coast, and South Coast air basins (where well densities were highest)	Singleton births from 2006-2015 to mothers living w/i 10 km of a well	1 km of maternal residence	Total oil and gas production volume among active wells (categorized as none, moderate, high); CWD for inactive wells (categorized as none, low, mod, high)	CA Division of Oil, Gas, and Geothermal Resources	Associations found with low birthweight, SGA, and decreased term birthweight in rural areas
2021	Willis	Environmental Health Perspectives	TX	Singleton births from 1996-2009 to mothers living w/i 10 km of a well	Exposed w/i 3 km; Unexposed 3-10km	Binary exposure to well within buffer on day of birth	TX Dept of Vital Stats; Enverus Drilling Info	Small reduction in term birthweight; no association with SGA

IDW: Inverse distance weighting

CWD: Cumulative well density

Table 2. Zip codes excluded from the City of Pittsburgh

Zip code	All or part City of Pittsburgh
15106	Part City
15120	Part City
15201	All City
15203	All City
15204	Part City
15205	Part City
15206	All City
15207	All City
15208	All City
15210	Part City
15211	All City
15212	Part City
15213	All City
15214	Part City
15215	Part City
15216	Part City
15217	All City
15218	Part City
15219	All City
15220	Part City
15221	Part City
15222	All City
15224	All City
15226	Part City
15227	Part City
15230	All City
15232	All City
15233	All City
15234	Part City
15235	Part City
15240	Part City
15260	All City
15282	All City

Table 3. Body Mass Index (BMI) calculation and cutoff values

For births to mothers aged 20 years or younger, we used the following criteria based on the CDC's recommended youth BMI-for-age cutoffs:
• **Underweight:** <5th percentile
• **Normal:** 5th to <85th percentile
• **Overweight:** 85th to <95th percentile
• **Obese:** ≥ 95th percentile
• Unknown: missing height and/or weight
For births to mothers aged 21 years or older, or for births for which maternal age was missing, we used the following criteria based on the CDC's recommended cutoffs for adults:
• **Underweight:** BMI <18.5
• **Normal:** BMI ∈ [18.5, 25)
• **Overweight:** BMI ∈ [25, 30)
• **Obese:** BMI ≥ 30
• Unknown: missing height and/or weight

Table 4. Calculation of Community Socioeconomic Deprivation Index

An index of socioeconomic deprivation incorporating six indicators from the 2015-2019 American Community Survey 5-year estimates from the US Census:
• Percent less than high school education
• Percent in poverty
• Percent not in the labor force
• Percent on public assistance
• Percent does not own a vehicle
• Percent civilian unemployment
The six indicators were standardized for direction, natural log-transformed, if necessary, z-scored using the standard deviations for Pennsylvania, and summed to create the final, unitless index for each county, township, or census tract. The total number of communities was divided into quartiles of socioeconomic deprivation index. Higher values of the index reflect greater community socioeconomic deprivation.

Table 5. Additional environmental exposure data sources considered for inclusion

Category	Description	Time period	Data source
Other oil and gas-related activity	Impoundment ponds	2005-2017	SkyTruth
	Oil and gas waste facilities	2000-2020	Pennsylvania Department of Environmental Protection (PA DEP)
	Underground injection disposal wells	2000-2021	United States Environmental Protection Agency (US EPA)
	Compressor stations	2000-2019	PA DEP
	Gas well and compressor station air emissions	2012-2019	PA DEP

	Hydraulic fracturing chemical disclosure registry	2008-2021	FracFocus
	Conventional wells	1985-2020	PA DEP
Other industries	Toxic Release Inventory (TRI) sites	1990-2019	US EPA
	Superfund/National Priorities List (NPL) sites	1985-2021	US EPA
Air quality	National Air Toxics Assessment (NATA)	1996, 1999, 2002, 2005, 2011, 2014	US EPA
	Ambient monitoring air pollution data	2000-2021	US EPA, PA DEP
	Satellite imagery-based air pollution data	2000-2018	Dalhousie University
Water quality	National Pollutant Discharge Elimination System (NPDES) and Water Quality Management (WQM) permitted wastewater facilities	1985-2021	PA DEP
	Electronic Discharge Monitoring Report (eDMR)	2007-2020	PA DEP
	Safe Drinking Water Act standards	2020	PA DEP
	Clean Water Act standards	2021	US EPA
	Safe Drinking Water Information System (SDWIS)	1985-2021	US EPA
	Water Quality Portal (WQP)	1985-2020	US EPA & United States Geological Survey (USGS)
	Assessment and Total Maximum Daily Load Tracking and Implementation System (ATTAINS)	2002-2015	US EPA

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