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Residential Proximity to Unconventional Oil and Gas Development and Birth Defects in Ohio

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Abstract

Background: Chemicals used or emitted by unconventional oil and gas development (UOGD) include reproductive/developmental toxicants. Associations between UOGD and certain birth defects were reported in a few studies, with none conducted in Ohio, which experienced a thirty-fold increase in natural gas production between 2010 and 2020.

Methods: We conducted a registry-based cohort study of 965,236 live births in Ohio from 2010–2017. Birth defects were identified in 4,653 individuals using state birth records and a state surveillance system. We assigned UOGD exposure based on maternal residential proximity at birth to active UOG wells and a metric specific to the drinking-water exposure pathway that identified UOG wells hydrologically connected to a residence ("upgradient UOG wells"). We estimated odds ratios (ORs) and 95% confidence intervals (CIs) for all structural birth defects combined and specific birth defect types using binary exposure metrics (presence/absence of any UOG

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Declaration of interests

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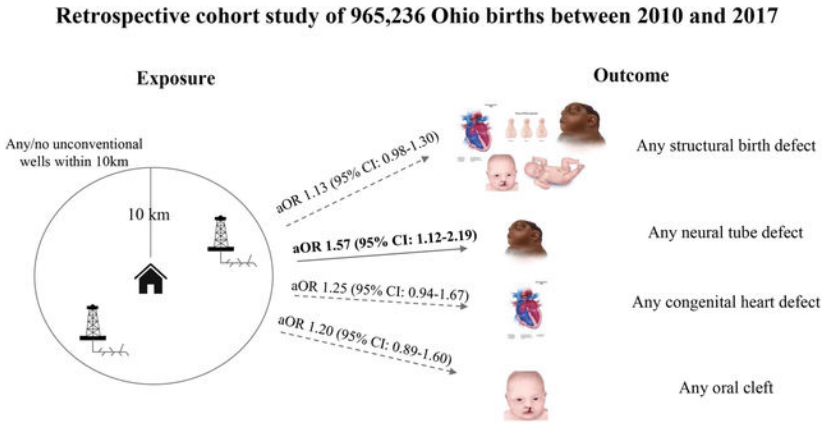
well and presence/absence of an upgradient UOG well within 10 km), adjusting for confounders. Additionally, we conducted analyses stratified by urbanicity, infant sex, and social vulnerability.

Results: The odds of any structural defect were 1.13 times higher in children born to mothers living within 10 km of UOGD than those born to unexposed mothers (95%CI: 0.98–1.30). Odds were elevated for neural tube defects (OR: 1.57, 95%CI: 1.12–2.19), limb reduction defects (OR: 1.99, 95%CI: 1.18–3.35), and spina bifida (OR 1.93; 95%CI 1.25–2.98). Hypospadias (males only) was inversely related to UOGD exposure (OR: 0.62, 95%CI: 0.43–0.91). Odds of any structural defect were greater in magnitude but less precise in analyses using the hydrological-specific metric (OR: 1.30; 95%CI: 0.85–1.90), in areas with high social vulnerability (OR: 1.27, 95%CI: 0.99–1.60), and among female offspring (OR: 1.28, 95%CI: 1.06–1.53).

Conclusions: Our results suggest a positive association between UOGD and certain birth defects, and findings for neural tube defects corroborate results from prior studies.

Graphical Abstract



Keywords

oil and gas; birth defects; fracking; congenital malformations; congenital anomalies; epidemiology; Ohio; hydraulic fracturing

1. Introduction

Unconventional oil and gas development (UOGD) refers to the extraction of oil and gas from previously inaccessible reservoirs through the use of directional drilling and high-volume hydraulic fracturing.[1, 2] High-volume hydraulic fracturing uses the injection of large quantities of fluids to liberate oil and natural gas from low permeability rock, such as shale.[1, 2] Widespread application of these techniques transformed the United States (U.S.) from a net importer to net exporter of natural gas.[3–5] The state of Ohio, which is situated above the Marcellus and Utica Shales and ranks seventh in the nation with regard to natural gas production, experienced a thirty-fold increase in the volume of natural gas produced between 2010 and 2020.[6, 7]

In addition to the U.S. “shale boom,” widespread exploration and/or development of UOG reserves is occurring in numerous countries and on every continent except Antarctica.[8–15]

Proponents of UOGD support natural gas as a “transition fuel” that will enable a shift from coal to renewable energy, create jobs, and decrease reliance on foreign countries for energy needs.[5, 16–18] Others contend that economic benefits have been overstated[19,20, 21] investments in new natural gas infrastructure will prolong the production of greenhouse gas emitting fossil fuel resources[22, 23] and that energy independence would be more safely and reliably achieved through more expeditious adoption of renewable energy sources.[24–26] Finally, there is growing evidence of the negative health implications associated with living in proximity to UOGD, particularly with regard to children’s health, including birth defects.[5, 27–30]

Annually, an estimated 5 million babies are born with a birth defect worldwide.[31] Birth defects, also known as congenital anomalies, are defined as a change to an organ or body part that can negatively impact a baby’s survival, health status, and/or ability to thrive developmentally.[32] Approximately 3% of infants in the U.S. are born with a defect, and birth defects are the leading cause of infant mortality in the U.S.[32] Globally, birth defects result in an estimated 400,000 deaths in children under five years.[31] Children born with a defect may experience a lifelong disability and have specialized healthcare and social needs.[31, 33, 34] The etiology of birth defects is multifactorial and as many as 60% of birth defects have an unknown cause.[35–38] Established risk factors include genetics, maternal age, alcohol use, and medication use; however, certain involuntary and modifiable environmental exposures are also potential risk factors (e.g., radiation, air pollution, chemical toxicants), likely in combination with genetic determinants of vulnerability, but evidence remains limited.[34, 39–41]

UOGD can release air pollutants, water contaminants, and other stressors that could result in an increased risk of adverse birth outcomes for those living in proximity to these sites.[29] Hydraulic fracturing fluids and UOGD wastewater contain numerous known and suspected reproductive and developmental toxicants including metals (e.g., arsenic, cadmium, lead and mercury), polycyclic aromatic hydrocarbons, and volatile organic compounds (e.g. benzene and toluene).[36, 42–45] Although management of these wastewaters is intended to reduce human exposure, surface spills, leaks, or containment failure could lead to migration of chemicals into groundwater or surface water.[46–48] Increased vehicle emissions and diesel equipment emissions near well sites may also expose pregnant women to environmental teratogens such as fine particulate matter, nitrous oxides, and other airborne pollutants.[49–53] UOGD can also lead to increased noise exposure, particularly at night,[54] which can activate the sympathetic nervous system and potentially contribute to sleep disturbance, cardiovascular disease, and adverse birth outcomes, although evidence for birth defects specifically is limited.[55, 56] UOGD has also been associated with increased psychosocial stress in proximal communities,[49, 57, 58] another potential risk factor for birth defects.[59–63] Hypothesized mechanistic pathways connecting UOGD hazards with birth defects include oxidative stress,[36, 64, 65] fetal hypoxia,[66] insulin resistance,[60] inflammation,[67] and endocrine disruption.[68]

To our knowledge, eight studies have evaluated associations between UOGD exposure and risk of structural birth defects. All studies reported evidence of a relationship, although the direction and statistical significance of associations vary by birth defect and study (Table

1).[69–75] Studies have been conducted in Colorado, Texas, Pennsylvania, Oklahoma, and Alberta, Canada. The most common associations reported were with congenital heart and neural tube defects. These studies primarily applied aggregate UOG proximity metrics, while McKenzie et al. 2019 applied an intensity-adjusted inverse distance-weighted metric that reflected additional detail about air pollution-emitting activities at the UOG well site.[74] A study conducted in Texas by Willis et al. 2023 used a variety of metrics specific to the volume of oil, gas, and waste water produced within 5 km of maternal address.[19] To help clarify the relationship between UOGD exposure and risk of a range of structural birth defects in a less studied region, we conducted a registry- and population-based study in the state of Ohio and applied a new UOGD metric specific to the drinking water exposure pathway. The study protocol was approved by the Institutional Review Board of Yale University (HIC #2000021809) and by the Ohio Department of Health.

2. Methods

2.1 Study Population

The source study population included all live singleton births in Ohio from 2010–2017, obtained from birth records from the Ohio Department of Health (n=1,029,682) (Figure 1). We geocoded the maternal addresses at birth using SAS 9.4 PROC GEOCODE. Addresses unable to be geocoded to street level were excluded (n=60,070; 5.8%). In addition, records were excluded if they were missing infant sex (n=11; 0.0011%), had unknown or implausible values for term birth weight (<500 g or >5500 g) or gestational age (<18 weeks or >47 weeks) (n=4329; 0.42%), or had geocoded birth addresses outside of Ohio (n=35; 0.0025%). Application of exclusion criteria yielded a final cohort of 965,236 births.

2.2 Outcome Assessment

Birth defects can be categorized into “structural birth defects” which primarily affect the structure of body parts, and “functional birth defects,”[31, 76] which primarily affect the development and function of whole-body systems. In this study, we focus on structural birth defects because they are more likely to be accurately identified and diagnosed at birth, while functional abnormalities require a longer follow up and more sensitive outcome assessment methods to ascertain.[77]

Information on structural birth defect outcomes was obtained from two sources: (i) “congenital anomalies” identified on the Ohio Department of Public Health birth records (obtained for 2010–2017), and (ii) the Ohio Connections for Children with Special Needs (OCCSN) birth defects surveillance system (available at time of data acquisition for 2012–2017). The birth records were available for all live births and for more years than the surveillance data and therefore the state birth records were used in the primary analyses. However, because these are typically based on a visual examination, defects not overtly manifested at birth may be missed.[78] The OCCSN is a passive surveillance system in which all hospitals, physicians, and freestanding birthing centers in Ohio are required to report cases of children from birth to 5 years of age with specific birth defects via file upload to a secure website.[35] The OCCSN data was available for fewer years than the state birth records, but provided the data for more specific birth defect subtypes.

The birth record data included diagnoses for nine types of structural birth defects: anencephaly, meningomyocele/spina bifida, cyanotic congenital heart disease, gastroschisis, omphalocele, diaphragmatic hernia, limb reduction defects, cleft lip with or without cleft palate, and cleft palate alone. The surveillance data included another ten diagnoses, seven of which fall within the category of "cyanotic congenital heart disease"—common truncus, transposition of the great arteries, tetralogy of Fallot, pulmonary valve atresia, tricuspid valve atresia and stenosis, hypoplastic left heart syndrome, and total anomalous pulmonary venous connection—as well as aortic valve stenosis and coarctation of the aorta, which are only cyanotic if critical, and encephalocele. Individuals with multiple diagnoses were selected as cases for each diagnosis present and considered a single case for the aggregate "any structural birth defect" outcome.

2.3 Exposure Assessment

We retrieved oil and gas well location and production datasets from the Ohio Department of Natural Resources Division of Oil and Gas Resources Risk Based Data Management System to identify all active wells, defined as having been drilled or producing as confirmed by having a reported spud date or production report.[79, 80] The data were cleaned and quality checked to address missing data, remove duplicates, and harmonize variables that changed over time. For example, for wells reporting gas, oil, or brine production from Marcellus and Utica formations but a missing spud date, we assigned a spud date equal to the first day of the earliest producing production reporting period minus 251 days (the median number of days between the spud date and the first reported production period). Wells with a missing spud date and no production reporting periods were considered inactive and excluded. The final Ohio UOGD well dataset included 2,290 ever active Marcellus and Utica coalbed methane, gas, and oil wells, with spud dates between January 21, 2008, and December 31, 2017.

We applied three UOG proximity-based metrics used in prior studies: (i) a binary metric for presence or absence of any active UOG wells within the buffer distance, (ii) an inverse-distance-square-weighted (ID^2W) metric capturing the density of active UOG wells within the buffer, which was categorized into tertiles, and (iii) a hydrological metric that is specific to the drinking water exposure pathway (ID_{ups}). Due to the low prevalence in UOGD exposure, we were unable to apply our exposure metrics with more than three categories or use them continuously. The ID^2W metric uses the following formula:

$$ID^2W \text{ well count} = \sum_{i=1}^{n} \frac{1}{d_i^2} \quad [1]$$

where d is the distance between the ith UOG well and a residence, and n the number of active UOG wells. This metric accounts for all UOG wells within a buffer zone while weighting closer wells more heavily than distant wells. Variations of the inverse-distance-weighted metric have been used in several previous health studies (Table 1).[29]

The details and programming code for the ID_{ups} metric was previously presented; this metric considers only the closest active UOG well that could be hydrologically connected to a

residence.[81–83] This exposure metric assumes that UOG wells that are located upgradient of a residence contribute more to exposure than downgradient wells.

The ID_{ups} metric is expressed as

$$ID_{ups} = \frac{1}{u} \quad [2]$$

where u is the distance to the nearest topographically upgradient UOG well, as determined by the D-infinity algorithm in TauDEM.[84] ID_{ups} was found to be a highly informative predictor in physics-informed models of groundwater vulnerability in regions of hill-and-valley topography where groundwater tends to flow in the downhill direction, parallel to the local topographic gradient. The ID_{ups} metric was applied in one previous exposure study and one previous epidemiologic analysis of children's health.[85, 86] In using the ID_{ups} metric, we implicitly assume that consumption or contact with groundwater from domestic wells is an important exposure source.[83] In Ohio, more than 40% of the population is served by groundwater[87], and approximately 15–20% of residences utilize a domestic well as a source of drinking water;[88, 89] this percentage is likely higher in the rural northeast of the state, where UOGD is most prevalent.

Buffer distances of 2, 5, and 10 km were used based on plausible dispersion of air and water pollutants and to facilitate comparisons to prior literature. With respect to exposure timing, we examined two etiologically important exposure windows for our UOGD exposure metrics: (i) the year prior to birth, called the "primary window," and (ii) the first trimester only, as this is a particularly vulnerable time in fetal development with regard to teratogen exposure.[90] The time window corresponding to the first trimester was calculated using the date of birth and the obstetric estimate of gestation.

2.4 Covariates

A list of candidate individual and community-level factors was compiled *a priori* based on the published literature including known or suspected risk factors for birth defects and covariates used in prior studies of UOGD and birth defects. These included the following individual-level demographic, socioeconomic, health, and lifestyle factors obtained from state birth records: infant sex, birth year, season of birth, maternal age, maternal race, maternal ethnicity, maternal educational attainment, maternal marital status, maternal smoking status during pregnancy, maternal alcohol use during pregnancy, parity (nulliparious, one or more previous live births), primary payer for delivery (Medicaid, private insurance), use of federal Women Infants and Children (WIC) program, pre-pregnancy body mass index (BMI), whether a mother received prenatal care, and maternal hypertension or diabetes.

We also obtained community-level variables such as urbanicity/rurality as captured by the 2010 Rural Urban Commuting Area (RUCA) codes which classify U.S. census tracts into 10 categories based on population density, urbanization, and daily commuting[91] and the 2014 Social Vulnerability Index (SVI) developed by the U.S. Center for Disease Control (CDC), which combines 15 U.S. Census variables into a percentile ranking capturing the

likelihood of experiencing disproportionate harm from environmental disasters with a higher percentile indicating greater vulnerability.[92] The SVI has been associated with preterm birth and other health outcomes.[93–95] We used agricultural data from the Cropland Data Layer of the USDA CropScape tool (USDA 2009–2016) to classify individuals with a maternal geocoded residence with any/none cropland within 500 m as a proxy for the potential for pesticide exposures.[96, 97] In addition, each birth was linked to the mean average daily fine particulate matter ($PM_{2.5}$) concentration in their census tract during the first trimester of pregnancy, a previously identified sensitive time window, using data from the U.S. Environmental Protection Agency[98–100] Both $PM_{2.5}$ and SVI were modeled as tertiles. We considered including SVI as a time-varying factor, but none of the tracts changed tertiles across 2010, 2014, and 2018.

2.5 Statistical Analysis

We used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for all structural birth defects combined, categories of birth defects (e.g., neural tube defects), and individual birth defects (e.g., anencephaly). Our primary analyses used defects identified from the state birth records for the years 2010–2017. The exposure metric used in our main model was presence or absence of a UOG well within 10 km, informed by the overall low exposure prevalence and rarity of birth defects. Our main model included the following potential confounding factors as covariates, selected based on the published literature, evidence of associations with the exposure or outcome, sufficient variability in the distribution of subjects across categories, and to avoid overadjustment and unnecessary adjustment:[101] year of birth, parity, maternal race, maternal smoking, use of WIC, SVI, and ambient $PM_{2.5}$ concentrations. A directed acyclic graph (Supplemental Figure 1) illustrates how we have conceptualized the relationship between covariates included in the models. The main model was run separately for each birth outcome data source (state birth records and surveillance system) and for several variations on the exposure metrics (different time windows, buffer sizes, tertiles of inverse-distance weighted well count, water-pathway specific metric). Models for hypospadias were restricted to males only.

In addition, we conducted several sensitivity analyses to test the robustness of our main findings to inclusion of other covariates, as some of the relationships depicted in our directed acyclic graph could be debated. Additional analyses included (a) main model + additional sociodemographic (infant sex, maternal ethnicity, maternal marital status), (b) main model + lifestyle factors (maternal alcohol consumption during pregnancy), (c) main model + maternal health (hypertension, diabetes, previous risk pregnancy), (d) main model + socioeconomic factors (maternal education, use of WIC), and (e) main model + other environmental factors (season of birth percent cropland). In stratified analyses, we ran our main model separately for urban (RUCA codes 1–7) and rural census tracts (RUCA codes 8–10), male and female infants, and three SVI categories (<33rd percentile, 33–66th percentile, and >66th percentile). In addition, we considered whether ambient $PM_{2.5}$ concentrations could be on the causal pathway between UOGD and birth defects, although we assumed these data would reflect general, regional air pollution and would not be sensitive enough to detect intermittent emissions from oil and gas well pads. However, we reran our models

with and without $PM_{2.5}$. All statistical analyses were conducted within the R Statistical Environment (http://www.R-project.org/).

3. Results

There were 4,112 individuals in our 2010–2017 cohort with at least one structural defect recorded in state birth records and 2,321 identified from surveillance data (2012–2017). Population characteristics for the full population and those identified as having birth defects from either state birth records or the surveillance system are presented in Table 2. The most prevalent birth defect categories based on state birth records were hypospadias (n=943), followed by congenital heart defects (n=904), and oral clefts (n=874). These categories were also the most prevalent based on the surveillance data (Table 3). Between 2010 and 2017, there were 41,152 births to mothers who resided within 10 km of an UOGD well during pregnancy (4.3% of the total cohort) (Table 4).

In our main model using outcome data from state birth records only (2010–2017), we observed an elevated odds ratio for any structural defect among those living within 10 km of a UOGD well (OR 1.13; 95% CI 0.98–1.30) (Table 3). UOGD exposure based on the binary metric was positively associated with several categories of birth defects, including neural tube defects (OR 1.57; 95% CI 1.12–2.19), spina bifida (OR 1.93; 95% CI 1.25–2.98), and limb reduction defects (OR 1.99; 95% CI 1.18–3.35) (Table 3). In contrast, an inverse association was observed for hypospadias (OR 0.62; 95% CI 0.43–0.91).

Table 4 presents the magnitude of observed ORs for all structural defects combined for variations in the exposure assessment including buffer size (5 km versus 10 km), exposure time window (year prior to birth versus first trimester only), and exposure metric (binary, inverse distance squared weighted, and ID_{ups}) (Table 4). Restricting the buffer distance to 5 km and limiting the exposure window to the first trimester each yielded ORs of larger magnitudes and wider confidence intervals. The ORs across tertiles of the inverse-distance-squared-weighted metric were similar to those observed with the binary metric. The largest magnitude OR was observed for ID_{ups}, the water-pathway specific metric (OR: 1.30, 95% CI: 0.85–1.97).

In stratified analyses, the OR for structural defects in relation to UOGD exposure were higher among individuals living in Census tracts with greatest neighborhood social vulnerability (OR: 1.26, 95% CI: 0.99–1.60), compared to the OR for the lowest tertile of neighborhood social vulnerability (OR: 1.06, 95% CI: 0.79–1.43) (Figure 1). Sex stratified analyses yielded stronger associations between UOGD exposure and structural birth defects among female offspring (OR: 1.33, 95% CI: 1.08–1.65), but not males (OR: 1.01, 95% CI: 0.84–1.21) (Figure 1). ORs did not differ by rural/urban designation (Figure 1). Results from sensitivity analyses in which additional covariates were added to the main model were consistent with the findings from the main model (Table 5). Excluding ambient $PM_{2.5}$ concentrations had negligible impact on the results (Supplemental Table 2).

4. Discussion

In our study of birth defects in Ohio, we observed elevated ORs of several types of structural birth defects in relation to residential proximity to UOGD, with positive associations observed for neural tube defects and the specific anomalies of spina bifida and limb reduction defects. Hypospadias was inversely associated with potential UOGD exposure. These results add to the current limited body of evidence with analyses from a different state and application of a new water-specific exposure metric.

The positive associations observed in our analysis are generally consistent with the eight existing studies of UOGD and birth defects, with some variations in findings (Table 1). Of the four other studies that assessed neural tube defects, two also observed a positive association with UOGD exposure in the principal metric.[19, 73, 75] We found elevated but not statistically significant ORs for congenital heart defects, consistent with findings from four of the five prior studies examining this endpoint.[73–75] Our study reports results for limb reduction defects, which was positively associated with UOGD exposure, and for hypospadias, which was inversely associated with the exposure. The unexpected inverse association with hypospadias could be due to chance, or could be indicative of the possibility that endocrine disruptors can produce effect estimates in different directions.[102–104] For example, hypospadias is linked to exposure to hormone disruptors,[102, 105] and both androgenic and anti-androgenic chemicals have been detected in hydraulic fracturing fluid and wastewater.[68, 106–108] Another reason for the inverse relationship could be there are other dominant sources of endocrine disruptors that we did not assess that may have confounded for this endpoint. Of the eight birth defect studies previously mentioned, none reported results for hypospadias specifically. One reported marginally elevated odds of being born with a genitourinary defect in association with maternal residential proximity to oil and gas.[19]

Ours is one of the few health studies on oil and gas conducted in Ohio, and the only study regarding unconventional oil and gas and birth defects in this state. It is valuable to conduct similar studies in different states, where regulations, geology, demographics, and covariates may vary, to facilitate cross-cohort comparisons, triangulate evidence, and enhance generalizability of findings.[109] For example, Ohio has among the shortest allowable setback distances (the allowable distance between a directionally drilled well and a sensitive receptor such as a residence, drinking water well), ranging from 50 to 200 feet depending on the circumstance.[110, 111] State-specific studies can hold more weight for policy makers seeking to update state policies.

The low exposure prevalence in conjunction with the rarity of birth defects prevented more refined exposures assessments and posed challenges in terms of statistical power, common issues in research of rare outcomes.[78] Our study included 4,653 cases, which is comparable to 2014 and 2019 studies done in Colorado but substantially fewer than a 2020 study conducted in the larger and more populous state of Texas, which included over 50,000 cases.[73–75] We grouped specific diagnoses with potentially different etiologies into broader categories to increase sample size, which may have biased results towards the null. Similarly, the ID_{ups} metric, which offers more detail and specificity for the drinking water

pathway, was only able to be evaluated in a binary fashion and in relation to “any birth defects”, our most aggregate outcome. A study with a larger population size could increase statistical power and enable more refined exposure assessments. We focused on UOGD, which is deep, water-intensive, has had documented well integrity issues, and has been linked to numerous increased health risks in children.[1, 28, 29, 112] However, Ohio also has conventional oil and gas development, which emits several similar pollutants[113] and future work could expand this analysis to include both conventional and unconventional oil and gas wells.

Although outcome misclassification is possible with administrative birth defects datasets, we used two data sources and observed similar results, lending confidence to the findings. Ohio follows a passive rather than active surveillance system, which means the overall number of birth defects are likely underreported.[78, 114] Studies in states with active surveillance systems or in which researchers themselves abstract hospital records would be expected to yield more complete case ascertainment; the 2020 study done by Tang et al. in Texas is an example of this.[75, 78, 114] On the other hand, the passive surveillance offers an advantage in terms of providing a lower likelihood of false positives.

Other possible limitations include the use of maternal address at birth to estimate prenatal residential exposure does not account for residential mobility during pregnancy; however, this has been shown to have minimal impact on exposure misclassification.[115–117] Finally, live birth bias could be an issue and may underestimate the effect if UOG exposure increases the risk for fetal or neonatal death, especially among those with or susceptible to birth defects.[118, 119]

5. Conclusions

In this Ohio study, we observed associations between residential proximity to UOGD and neural tube defects, corroborating prior findings. We presented new findings of relationships with the specific anomalies of limb reduction and spina bifida and presented results using a newly developed metric specific to the drinking water exposure pathway. These results, in conjunction with the broader literature, underscore the need to consider impacts to children’s health specifically when developing or improving public health protections around UOGD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights:

- Higher odds of neural tube defects in infants born near oil and gas development
- Higher odds of limb reduction defects in infants born near oil and gas development
- Higher odds of spina bifida in infants born near oil and gas development
- Lower odds of hypospadias in infants born near oil and gas development
- Greater risk in areas with high neighborhood social vulnerability

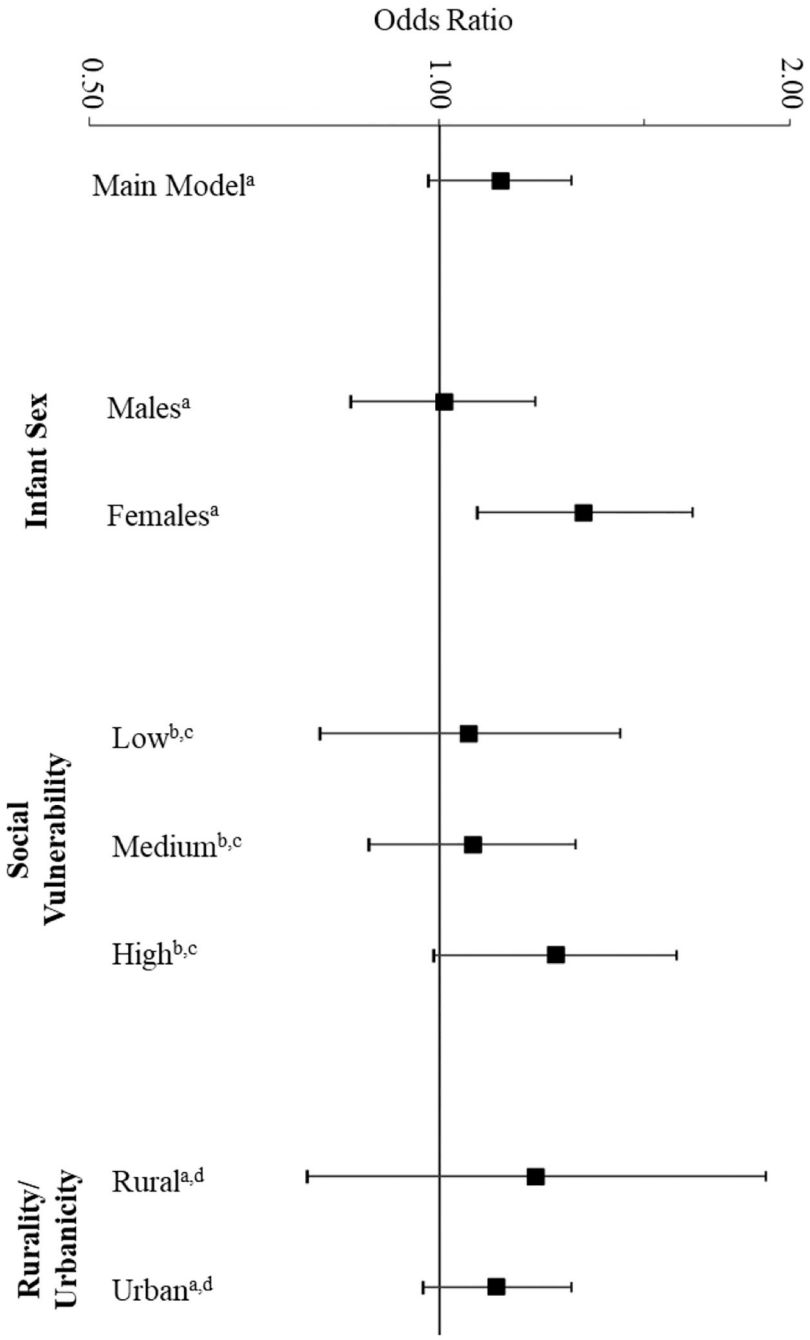

Figure 1.

Stratified analyses of odds of any structural defect in relation to presence of unconventional oil and gas well within 10 km of maternal residence at birth (2010–2017).

[a]Odds Ratios and confidence intervals are for logistic regression including the following covariates: year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentration.

[b]Neighborhoods with "low," "moderate," and "high" social vulnerability are defined as those census tracts which had a Social Vulnerability Index in the bottom 33%, the middle 33%,

or the top 33% compared to other census tracts across the state, as ranked in the Center for Disease Control 2014 Social Vulnerability Index dataset

[c]Odds Ratios and confidence intervals are for logistic regression including the following covariates: year of birth, parity, maternal race, maternal smoking, use of WIC, and ambient $PM_{2.5}$ concentration.

[d]Rural" and "urban" are defined in accordance with 2010 Rural-Urban Commuting Area (RUCA) codes from the United States Department of Agriculture. Individuals living in a census tract with a RUCA code of 1–7 are considered "urban"; individuals living in a census tract with a RUCA code of 8–10 are considered "rural."

Table 1.

Characteristics and results of studies of exposure to UOGD and birth defects.

Lead author (year)	State/ region	Study design	Exposure metric	Study population	Covariates	Findings
McKenzie (2014)	Colorado	Retrospective cohort	IDW well count (10 mi buffer)	124,842 births between 1996 and 2009	Maternal age, ethnicity, tobacco use, alcohol use, parity at time of pregnancy, education, elevation of residence, and infant sex	**CHDs ↑ (aOR: 1.3, 95% CI: 1.2–1.5)** **NTDs ↑ (aOR: 2.0, 95% CI: 1.0–3.9)** Oral clefts ↘ (aOR: 0.82, 95% CI: 0.55–1.2)
Ma (2016)	Pennsylvania	Semiecological	Presence of 1+ well in zip code	1,401,813 births between 2003 and 2012	Maternal age, maternal highest education level, self-designated race, maternal pre-pregnancy BMI, primary payer for delivery, mother receiving WIC assistance, maternal pre and during pregnancy diabetes status, maternal hypertension, maternal smoking, and maternal infection during pregnancy reported in birth registry	Zip codes with UOGD: **Any birth defects ↑ (OR: 1.22, 95% CI: 1.13–1.32)** **Structural birth defects ↑ (OR: 1.21, 95% CI: 1.111.32)** **Functional or developmental birth defects: ↗ (OR:1.23, 95% CI: 1.06–1.43)** Increase in UOG well density per square kilometer: Any birth defects prevalence ↘ (OR: 0.93, 95% CI: 0.851.01) Structural birth defects prevalence ↘ (OR: 0.95, 95% CI: 0.86–1.04) Functional or developmental birth defects prevalence ↘ (OR: 0.90, 95% CI: 0.76–1.07)
Hill (2018)	Pennsylvania	Difference-indifference	Nearest UOG well Buffers (2km, 2.5km, 3km, 3.5km, 4km, 4.5km, 5km), Well density at 2.5 km	1,098,884 births between 2003 and 2010	Race, education, age, marital status, WIC status, insurance type, previous risky pregnancy, whether the mother smoked during her pregnancy, month of birth, year of birth, month/year interaction, and gender of the child	Any congenital anomaly ↔
Janitz (2019)	Oklahoma	Retrospective cohort	IDW well count (2, 5 and 10 mi buffers)	476,000 births between 1997 and 2009	Birth year, infant sex, race/ethnicity, gestational age, birth weight, urban/ rural status of census block, maternal age, marital status, prenatal care, parity, maternal tobacco use during pregnancy, maternal education	At the 2-mile buffer: NTD ↗ (PPR: 1.20, 95% CI: 0.82–1.75) Oral clefts ↔ (PPR: 1.03, 95% CI: 0.82–1.29) CCHD ↘ (PPR: 0.91, 95% CI: 0.75–1.11) Exposure to any natural gas activity compared to none, at the 2-mile buffer: Mix of insignificant positive and negative associations for a variety of specific congenital malformations (common truncus, etc.) ↔
McKenzie (2019)	Colorado	Nested case-control	Intensity adjusted inverse distance weighted well count (10 mi buffer) during second month of pregnancy	469 cases, 2860 controls born between 2005 and 2011	IDW count of other oil and gas facilities, IA-IDW count of non oil and gas air pollution sources, maternal age, socioeconomic status index, parity, infant sex	Overall: **Any CHD ↑ (OR: 1.7, 95% CI: 1.1–2.6)**; Insignificant positive association with various specific heart defects Rural: **Any CHD ↑ (OR: 2.47, 95% CI: 1.3–4.4); Conotruncal defects ↑ (OR: 4.07, 95% CI: 1.4–12)**; Insignificant positive associations with various specific heart defects ↗ Urban:- Any CHD ↘ (OR: 0.95, 95% CI: 0.47, 1.9); Insignificant positive and negative associations with various specific heart defects
Tang (2020)	Texas	Case-control	Well count (1, 3, and 7.5 km buffers)	52,955 cases and 642,399 controls	- Maternal Characteristics: smoking status, plurality of birth, maternal age, race/ethnicity, and education status	Within 1 km of maternal address: **Anencephaly ↑ (aOR: 2.44, 95% CI: 1.55–3.86)** **Spina bifida ↑ (aOR: 2.09, 95% CI: 1.47–2.99)**

Lead author (year)	State/ region	Study design	Exposure metric	Study population	Covariates	Findings
				between 1999 and 2011	- Neighborhood Characteristics: median household income at maternal address block group, urbanicity in 2010, and average daily vehicle miles traveled for all trucks by county	**Gastrochisis (older mothers) ↑ (aOR: 3.19, 95% CI: 1.77–5.73)** **Atrial septal defect (1.66, 95% CI: 1.54–1.79)** **Aortic valve stenosis ↑ (aOR: 1.90, 95% CI: 1.33–2.71)** **Hypoplastic left heart syndrome ↑ (aOR: 2.00, 95% CI: 1.39–2.86)** **Pulmonary valve atresia/stenosis ↑ (aOR: 1.36, 95% CI: 1.10–1.66)** Orofacial clefts: no effect
Cairncross (2022)	Alberta, Canada	Retrospective cohort	Presence of 1+ wells within 10 km	34,873 births between 2013 and 2018	Parental age at delivery, multiple births (ie, twins, triplets), infant sex, obstetric comorbidities, and area-level socioeconomic status (Pampalon Index)	Major congenital anomalies (aRR: 1.31; 95% CI, 1.01–1.69)
Willis (2023)	Texas	Retrospective cohort	Tertiles of inverse distance-squared weighting within 5 km for drilling site count, gas production, oil production, and produced water	2,234,138 births between 1999 and 2009	-Individual Characteristics infant sex, gestational age, birth weight, maternal age, maternal race and ethnicity, maternal education, maternal smoking, maternal alcohol usage, prenatal care, distance to nearest highways, birth year, county -Neighborhood Characteristics: unemployment, % White population, median household income	Temporal comparison, inverse distance-squared well count within 5km: **All defects ↑ (aOR: 1.25, CI: 1.21–1.30)** **> 1 site ↑ (aOR: 1.19, CI: 1.10–1.33)** **Cardiac and circulatory ↑ (aOR: 1.20, CI: 1.13–1.28)** Central nervous system ↔ (aOR: 1.00, CI: 0.82–1.21) **Eye and ear ↑ (aOR: 1.53, CI: 1.10–2.12)** Gastrointestinal ↗ (aOR: 1.10, CI: 0.97–1.24) **Genitourinary ↑ (aOR: 1.12, CI: 1.03–1.21)** Musculoskeletal ↗ (aOR: 1.11, CI: 0.96–1.29) Oral clefts ↔ (aOR: 1.02, CI: 0.85–1.22) Respiratory ↔ (aOR: 0.96, CI: 0.69–1.35) **Chromosomal ↑ (aOR: 1.32, CI: 1.10–1.59)**
Current study	Ohio	Retrospective	Presence of 1+ wells within 10 km, presence of upgradient UOG well within 10 km, IDW well count	965,236 births between 2010 and 2017	Year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentration	Any UOG wells within 10km: Any structural defect ↗ (aOR: 1.11, 95% CI: 0.99–1.25) Any CHD ↗ (aOR: 1.16, 95% CI: 0.94–1.44) **Any NTD ↑ (aOR: 1.45, 95% CI: 1.07–1.97)** Oral clefts ↗ (aOR: 1.18, 95% CI: 0.99–1.81) **Limb reduction ↑ (aOR: 2.13, 95% CI: 1.30–3.49)** **Hypospadias ↓ (aOR: 0.65, 95% CI: 0.45–0.93)**

IDW—inverse distance-weighted; OR—odds ratio; CI—confidence interval; UOG—unconventional oil and gas; CHD—congenital heart defect; NTD—neural tube defect; aOR—adjusted odds ratio; aRR—absolute risk reduction; CCHD—critical congenital heart defects; PPR—prevalence proportion ratios ↑ = significant increase; ↓ = significant decrease; ↗ = non-significant increase; ↘ = non-significant decrease; ↔ = non-significant direction not reported or zero effect

Table 2.

Population characteristics by outcome data source.

Maternal or infant characteristics	Full cohort (N = 965,236)	Individuals with structural birth defects identified on birth record (N = 3,976)	Individuals with structural birth defects identified in surveillance database (N = 2,246)
	N (%)	N (%)	N (%)
Birth year			
2010	115011 (11.9)	374 (9.1)	0 (0)
2011	114324 (11.8)	354 (8.6)	0 (0)
2012	122019 (12.6)	441 (10.7)	327 (14.1)
2013	122683 (12.7)	515 (12.5)	417 (18)
2014	123395 (12.8)	555 (13.5)	383 (16.5)
2015	123759 (12.8)	591 (14.4)	438 (18.9)
2016	122395 (12.7)	656 (16)	419 (18.1)
2017	121651 (12.6)	626 (15.2)	337 (14.5)
Parity			
0	372287 (38.6)	1693 (41.2)	917 (39.5)
1+	586729 (60.8)	2404 (58.5)	1396 (60.1)
Unknown	6221 (0.6)	15 (0.4)	8 (0.3)
Maternal race			
Black	168437 (17.5)	710 (17.3)	322 (13.9)
White	735025 (76.1)	3173 (77.2)	1862 (80.2)
Other	31352 (3.2)	112 (2.7)	60 (2.6)
Unknown	30423 (3.2)	117 (2.8)	77 (3.3)
Maternal smoking			
Yes	151065 (15.7)	757 (18.4)	385 (16.6)
No	810522 (84)	3335 (81.1)	1921 (82.8)
Unknown	3650 (0.4)	20 (0.5)	15 (0.6)
Use of WIC			
Yes	371497 (38.5)	1672 (40.7)	919 (39.6)
No	586685 (60.8)	2400 (58.4)	1381 (59.5)
Unknown	7055 (0.7)	40 (1)	21 (0.9)
Social vulnerability index			

Maternal or infant characteristics	Full cohort (N = 965,236)	Individuals with structural birth defects identified on birth record (N = 3,976)	Individuals with structural birth defects identified in surveillance database (N = 2,246)
	N (%)	N (%)	N (%)
Least vulnerable (Tertile 1)	314335 (32.6)	1194 (29)	728 (31.4)
Moderately vulnerable (Tertile 2)	318778 (33)	1442 (35.1)	803 (34.6)
Most vulnerable (Tertile 3)	332124 (34.4)	1476 (35.9)	790 (34)
Ambient PM2.5 Concentrations During First Trimester			
Low (Tertile 1)	319730 (33.1)	1575 (38.3)	942 (40.6)
Medium (Tertile 2)	322256 (33.4)	1264 (30.7)	760 (32.7)
High (Tertile 3)	323251 (33.5)	1273 (31)	619 (26.7)

Table 3.

Odds ratios (ORs) and 95% confidence intervals (CIs) of structural birth defects for infants exposed to unconventional oil and gas development as defined as having an active UOGD well within 10 km of the maternal residence at birthcompared to unexposed for outcomes based on birth records alone and birth records or surveillance data.

Birth defect type	Defect recorded in certificate data-2010–2017 cohort (n = 965,236)			Defect recorded in either certificate or surveillance data 2012–2017 cohort (n = 735,901)		
	Exposed Cases/ All Cases	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	Exposed Cases/ All Cases	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
Any structural birth defect	216/4112	1.25 (1.09–1.43)	1.13 (0.98–1.3)	287/4824	1.1 (0.98–1.24)	1.06 (0.94–1.2)
Neural tube defect						
Any	38/545	1.68 (1.21–2.34)	1.57 (1.12–2.19)	45/584	1.45 (1.07–1.97)	1.42 (1.05–1.93)
Anencephaly	16/294	1.29 (0.78–2.14)	1.28 (0.77–2.13)	17/238	1.34 (0.82–2.19)	1.41 (0.86–2.32)
Spina bifida	23/256	2.22 (1.44–3.4)	1.93 (1.25–2.98)	25/313	1.51 (1.00–2.27)	1.4 (0.93–2.12)
Congenital heart defect						
Any	50/904	1.32 (0.99–1.75)	1.25 (0.94–1.67)	52/984	0.97 (0.73–1.28)	0.96 (0.73–1.27)
Cyanotic congenital heart disease	50/904	1.32 (0.99–1.75)	1.25 (0.94–1.67)	74/1281	1.07 (0.84–1.35)	1.09 (0.86–1.38)
Coarctation of aorta	N/A	*	*	21/311	1.26 (0.81–1.96)	1.21 (0.77–1.89)
Tetralogy of Fallot	N/A	*	*	14/232	1.12 (0.65–1.92)	1.17 (0.68–2.03)
Oral clefts						
Any	49/874	1.33 (1–1.78)	1.2 (0.89–1.6)	79/1240	1.18 (0.94–1.49)	1.08 (0.86–1.36)
Cleft lip	33/576	1.36 (0.96–1.94)	1.24 (0.87–1.77)	46/643	1.34 (0.99–1.81)	1.23 (0.91–1.67)
Cleft palate	16/298	1.27 (0.77–2.11)	1.12 (0.67–1.85)	34/624	1 (0.71–1.42)	0.91 (0.64–1.29)
Other						
Gastroschisis	21/408	1.22 (0.79–1.89)	1.03 (0.66–1.61)	20/331	1.12 (0.71–1.76)	0.99 (0.63–1.57)
Diaphragmatic hernia	11/197	1.33 (0.72–2.44)	1.24 (0.67–2.29)	11/187	1.09 (0.59–2)	1.13 (0.61–2.08)
Limb reduction defects	16/174	2.27 (1.36–3.8)	1.99 (1.18–3.35)	17/155	2.14 (1.30–3.55)	2.02 (1.21–3.37)
Hypospadias	28/943	0.69 (0.47–1)	0.62 (0.43–0.91)	30/879	0.61 (0.43–0.88)	0.62 (0.43–0.89)

[a]Adjusted odds ratios included the following covariates: year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentrations.

““N/A”” identifies those birth defects for which there was no available record in a given data source. Cells are occupied with a ““*”” when they correspond to models for which there were insufficient exposed cases to calculate a meaningful odds ratio (< 10 cases).

Table 4.

Sensitivity analyses of odds of any structural defect in relation to unconventional oil and gas development (2010–2017) using different exposure metrics.

Model description	Buffer size	Exposure time window	Type of exposure metric	N exposed (cases/total)	OR[a] (95% CI)
Main model	10 km	Year prior to birth	Presence of UOG well	216/41152	1.13 (0.98–1.30)
Smaller buffer size	5 km	Year prior to birth	Presence of UOG well	63/11959	1.12 (0.87–1.44)
Narrow time window	10 km	First trimester	Presence of UOG well within buffer	193/35467	1.14 (0.99–1.32)
Inverse distance squared (ref: $ID^2W=0$)	10 km	Year prior to birth	Inverse distance-squared-weighted: Tertile 1	66/13717	1.07 (0.83–1.36)
Inverse distance squared (ref: $ID^2W=0$)	10 km	Year prior to birth	Inverse distance-squared-weighted: Tertile 2	75/13717	1.18 (0.94–1.48)
Inverse distance squared (ref: $ID^2W=0$)	10 km	Year prior to birth	Inverse distance-squared-weighted: Tertile 3	75/13718	1.14 (0.90–1.43)
Water-specific metric (ID_{ups})	10 km	Year prior to birth	Presence of upgradient UOG well	22/3564	1.30 (0.85–1.97)

[a]Odds ratios (ORs) adjusted for the following covariates: year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentrations.

Table 5.

Sensitivity analyses of odds of any structural defect in relation to presence of unconventional oil and gas well within 10 km of maternal residence at birth (2010–2017).

Model	Variables	OR (95% CI)*
Main Model	year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentration	1.13 (0.98–1.30)
Model A (Main model + additional sociodemographic factors)	year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, ambient $PM_{2.5}$ concentration, infant sex, maternal ethnicity, maternal marital status	1.13 (0.98–1.29)
Model B (Main model + lifestyle factors)	year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentration, maternal alcohol consumption	1.11 (0.97–1.28)
Model C (Main model + maternal health factors)	year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentration, hypertension, diabetes, previous risky pregnancy	1.14 (0.99–1.30)
Model D (Main model + socioeconomic factors)	year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentration, maternal education, primary payer for delivery	1.12 (0.97–1.29)
Model E (Main model + environmental factors)	year of birth, parity, maternal race, maternal smoking, use of WIC, social vulnerability index, and ambient $PM_{2.5}$ concentration, season of birth, percent cropland	1.12 (0.98–1.29)