HEI energy

A Health Effects Institute Affiliate

RESEARCH BRIEF 1

FALL 2021

Potential Human Health Effects Associated with Unconventional Oil and Gas Development: A Categorical Update to the Literature, 2019–2021

This Research Brief is part of a series of periodic updates on the literature about potential human exposures and health effects associated with unconventional oil and natural gas development (UOGD) in the United States

HEI Energy
Health Effects Institute Energy
75 Federal St., Suite 1400
Boston, MA 02110, USA
+1-617-488-2300
www.HEIenergy.org

Trusted Science, Clean Environment, Better Health

Potential Human Health Effects Associated with Unconventional Oil and Gas Development: An Update to the Literature, 2019–2021

Health Effects Institute Energy

Boston, MA

TRUSTED SCIENCE, CLEAN ENVIRONMENT, BETTER HEALTH

Publishing history: This document was posted at *www.heienergy.org* in January 2022.

Citation for document:

Rosofsky AR, Adelsheim LA. 2022. Potential Human Health Effects Associated with Unconventional Oil and Gas Development: An Update to the Literature, 2019–2021. Research Brief 1. Boston, MA: Health Effects Institute Energy.

CONTENTS

About HEI Energy

The Health Effects Institute (HEI) Energy is a national research program formed to identify and conduct high-priority research on potential population exposures and health effects from development of oil and natural gas from shale and other unconventional resources across the United States. HEI Energy supports community exposure research in multiple regions. To enable exposure research planning, HEI Energy conducts periodic reviews of the relevant scientific literature. Once initial research is completed, HEI Energy will assess the results to identify additional exposure research priorities and, where feasible and appropriate, health research needs for funding in subsequent years.

The scientific review and research provided by HEI Energy will contribute high-quality and credible science that supports decisions about how best to protect public health. To achieve this goal, HEI Energy has put into place a governance structure that mirrors the one successfully employed for nearly forty years by its parent organization, the Health Effects Institute, with several critical features:

- HEI Energy receives joint funding from the U.S. Environmental Protection Agency under a contract that funds HEI Energy exclusively and from the oil and natural gas industry;
- HEI Energy's independent Board of Directors consists of leaders in science and policy who are committed to fostering the public–private partnership that is central to the organization;
- HEI Energy's research program is governed independently by individuals having no direct ties to, or interests in, sponsor organizations;
- HEI Energy's Research Committee consists of members who are internationally recognized experts in one or more subject areas relevant to the Committee's work, have demonstrated their ability to conduct and review scientific research impartially, and have been vetted to avoid conflicts of interest;
- All research undergoes rigorous peer review by HEI Energy's Review Committee;
- HEI Energy staff and committees engage in open and extensive stakeholder engagement before, during,and after research, and communicate all results in the context of other relevant research;
- HEI Energy makes publicly available all literature reviews and original research that it funds and provides summaries written for a general audience; and
- Without advocating policy positions, HEI Energy provides impartial science, targeted to make better-informed decisions.

HEI Energy is a separately funded affiliate of the Health Effects Institute (*www.healtheffects.org*).

AUTHORS

Anna Rosofsky, *Staff Scientist, HEI Energy*

Lee Ann Adelsheim, *Research Assistant, HEI Energy*

ACKNOWLEDGMENTS

HEI ENERGY AND HEI PROJECT STAFF

Kristin Eckles, *Senior Editorial Manager, HEI*

Daniel S. Greenbaum, *President, HEI*

Robert M. O'Keefe, *President, HEI Energy*

Allison P. Patton, *Staff Scientist, HEI* and *Quality Assurance Manager, HEI Energy*

Annemoon van Erp, *Deputy Director of Science, HEI*

Donna J. Vorhees, *Vice President and CEO, HEI Energy*

PURPOSE OF THIS RESEARCH BRIEF

In 2019, the HEI Energy Research Committee (the Committee) conducted a systematic review of the analytical epidemiology literature about unconventional oil and gas development (UOGD)[1] in the United States (HEI Energy Research Committee 2019). Additional studies have been published since the completion of that review.

The purpose of this document is to provide a summary of the newly published studies — providing information on study methods and the exposures, health outcomes, and regions that have been studied. In addition, we briefly compare methods used in these studies and in the studies that were included in the Committee's systematic review (HEI Energy Research Committee 2019). This document is not a systematic review of the literature; instead, it provides a general update on the UOGD analytical epidemiology literature.

UOGD HEALTH LITERATURE

The expansion of UOGD in the United States has given rise to questions about associated exposures and their possible effects on human health. In response, a body of scientific literature has emerged that has helped to answer some of these questions.

Overview of the Literature

The UOGD health literature published to date includes original research and reviews about the toxicity of chemicals associated with UOGD (e.g., Balise et al. 2019; Hansen et al. 2019; Kassotis et al. 2016, 2018; Sapouckey et al. 2018), assessments of human health risk associated with chemicals in air and water that may have originated from UOGD operations (e.g., McKenzie et al. 2012; Rish and Pfau 2018), and descriptive and analytical epidemiology studies of populations living in proximity to UOGD.

In the analytical epidemiology literature, investigators have assessed exposure to UOGD using a variety of exposure surrogates, such as distance-based metrics, and examined associations with a range of health outcomes, including perinatal, respiratory, cardiovascular, physiological and mental health symptoms, as well as cancer. Systematic reviews of the analytical epidemiology literature have reported insufficient or limited evidence for causal associations between UOGD and the assessed health outcomes (Bamber et al. 2019; HEI Energy Research Committee 2019). Qualitative reviews of both analytical and descriptive epidemiology studies have come to mixed conclusions about the strength of evidence for causal associations among a variety of health outcomes (Deziel et al. 2020; Ferrar et al. 2019; Gorski and Schwartz 2019; Johnston et al. 2019; Krupnick and Echarte 2017; Wollin et al. 2020). Though several investigators have described the evidence for adverse birth outcomes as "modest" (Bamber et al. 2019), "strong preliminary" (Gorski and Schwartz 2019), and "growing" (Deziel et al. 2020), there is much to be learned.

The 2019 Systematic Review of Analytical Epidemiology Literature

The review of the epidemiology literature (HEI Energy Research Committee 2019) took the form of a systematic review, designed to yield a transparent, reproducible, and critical assessment of the literature. The review addressed the question: Are there adverse human health effects associated with environmental exposures originating directly from UOGD?

[1] UOGD refers to the development and production of oil and natural gas as practiced starting around the beginning of the 21st century through multistage hydraulic fracturing in horizontal wells.

Peer-reviewed and gray literature published electronically or in print were identified using three electronic databases: PubMed, Web of Science, and Embase. Application of the literature search phrase returned 3,929 studies published between January 1, 2000 and December 31, 2018. To ensure completeness of the search, the Committee additionally examined reference lists of relevant reviews, reviewed commentaries, and consulted with knowledgeable experts to identify both peer-reviewed and gray literature publications that may not have appeared in the electronic literature searches. Twenty-five studies met the Committee's selection criteria: (1) analytical epidemiology studies; (2) peer-reviewed or gray literature in final and complete form; (3) assessed relationships between exposures originating from UOGD operations in North America and human health outcomes.

Literature Summarized in this Research Brief

This Research Brief summarizes the methods and main results of the analytical epidemiology literature related to UOGD that has been published since the Committee's 2019 systematic review (HEI Energy Research Committee 2019). Future Research Briefs will summarize other types of literature (e.g., human health risk assessments) that assesses UOGD's potential effects on health.

ANALYTICAL EPIDEMIOLOGY LITERATURE PUBLISHED SINCE THE 2019 SYSTEMATIC REVIEW

Approach to Identifying and Extracting Data from the Literature

We used the same approach employed in the Committee's 2019 systematic review (HEI Energy Research Committee 2019) to identify analytic epidemiology studies published between December 31, 2018 (the cutoff date for the 2019 review) and February 1, 2021. Twelve studies emerged from this search, and the following data were extracted from each study:

- Study design
- Study population
- Outcome assessment
- Exposure assessment
- Control of confounding
- Analytic methods
- Reported findings

General Description of the Literature

In total, 37 analytic epidemiology studies have been published that assess relationships between surrogates of UOGD exposure and various health outcomes (Table 1 and Figure 1). Of these studies, 12 were published since the Committee's 2019 review.

Six of the more recent studies assessed perinatal outcomes, one assessed respiratory-related hospitalizations (e.g., asthma exacerbation), one assessed cardiovascular disease, three assessed symptoms, and one assessed all hospitalizations. Two studies used an ecologic study design, three used a cross-sectional design, three used a case–control design, and four used a retrospective cohort design. As with the studies reviewed by the Committee in 2019, none used a prospective cohort design.

The new studies have covered the same states, and in some cases the same study populations (e.g., Casey et al. 2019; McAlexander et al. 2020; McKenzie et al. 2019a) as the studies in the original systematic review (Figure 1). In total, the greatest number of studies took place in Pennsylvania (Figure 1). One study (Caron-Beaudoin et al. 2020) took place in Canada.

Table 1. Health Outcomes by Exposure Surrogate Assessed in the Studies

Health Outcome (as defined by studies)	Exposure Surrogate											
	Earthquake[1]	Time Period[2]	Pre- or Post- Spud Date[3]	Distance from Wells[4]	Well Count or Density[5]	Intensity[6]	Time and Distance from Wells[7]	IDW[8]	IDW by Activity Level[9]	Spatio-temporal Activity Model[10]	Estimated Concen-trations[11]	Flaring[12]
PERINATAL												
Birth Weight (birth weight; term birth weight; low birth weight; term low birth weight; small for gestational age)					Apergis et al. 2019*		Currie et al. 2017; Hill 2018	Caron-Beaudoin et al. 2020*; Currie et al. 2017; Cushing et al. 2020*; Hill 2018; McKenzie et al. 2014; Stacy et al. 2015; Whitworth et al. 2017	Casey et al. 2016; Casey et al. 2019*			Cushing et al. 2020*
Gestational Age (preterm birth; gestational age)							Hill 2018	Caron-Beaudoin et al. 2020*; Cushing et al. 2020*; McKenzie et al. 2014; Stacy et al. 2015; Whitworth et al. 2017	Casey et al. 2016; Whitworth et al. 2018; Casey et al. 2019*			Cushing et al. 2020*
Apgar Score (5-minute APGAR Score <7)							Hill 2018		Casey et al. 2016			
Infant Health Index					Apergis et al. 2019*		Currie et al. 2017; Hill 2018					
Birth Defects (CHDs, NTDs, and oral clefts; structural and developmental anomalies; any birth defect)			Ma et al. 2016	Janitz et al. 2018	Ma et al. 2016; Tang et al. 2020*		Hill 2018	McKenzie et al. 2014; Janitz et al. 2018		McKenzie et al. 2019a*		

Table 1. Health Outcomes by Exposure Surrogate Assessed in the Studies

Health Outcome (as defined by studies)	Exposure Surrogate											
	Earthquake[1]	Time Period[2]	Pre- or Post- Spud Date[3]	Distance from Wells[4]	Well Count or Density[5]	Intensity[6]	Time and Distance from Wells[7]	IDW[8]	IDW by Activity Level[9]	Spatio-temporal Activity Model[10]	Estimated Concen-trations[11]	Flaring[12]
High-Risk Pregnancy (clinical indication on electronic medical record)									Casey et al. 2016			
Mortality (fetal death, early infant mortality)		Busby & Mangano 2017			Busby & Mangano 2017			Whitworth et al. 2017				
CANCER												
All Cancer			Fryzek et al. 2013									
Lymph (leukemia; non-Hodgkin lymphoma; acute lymphoblastic leukemia)		Finkel et al. 2016;	Fryzek et al. 2013					McKenzie et al. 2017				
CNS		Mokry 2010	Fryzek et al. 2013									
Thyroid		Finkel et al. 2016										
Urinary Bladder		Finkel et al. 2016										
Breast		Mokry 2010										
RESPIRATORY												
Asthma (oral corticosteroid order; asthma emergency department; inpatient asthma hospitalization)			Peng et al. 2018; Willis et al. 2018		Willis et al. 2018; Willis et al. 2020*	Peng et al. 2018; Willis et al. 2018; Willis et al. 2020*			Rasmussen et al. 2016			Willis et al. 2020*
Pneumonia			Peng et al. 2018			Peng et al. 2018						
URI			Peng et al. 2018			Peng et al. 2018						

Table 1. Health Outcomes by Exposure Surrogate Assessed in the Studies

Health Outcome (as defined by studies)	Exposure Surrogate											
	Earthquake[1]	Time Period[2]	Pre- or Post- Spud Date[3]	Distance from Wells[4]	Well Count or Density[5]	Intensity[6]	Time and Distance from Wells[7]	IDW[8]	IDW by Activity Level[9]	Spatio-temporal Activity Model[10]	Estimated Concen-trations[11]	Flaring[12]
COPD			Peng et al. 2018			Peng et al. 2018						
CARDIOVASCULAR												
Biomarkers of Effect (augmentation index; systolic blood pressure; diastolic blood pressure; IL1β, IL-6, IL-8, tumor necrosis factor-α)										McKenzie et al. 2019b		
Heart Failure Hospitalization										McAlexander et al. 2020*		
Acute Myocardial Infarction			Peng et al. 2018									
SYMPTOMS												
Physiologic Symptoms (Dermal, respiratory, neurological, GI, cardiac; other [stress and fatigue]; CRS, migraines, fatigue)				Elliott et al. 2018; Rabinowitz et al. 2015	Brown et al. 2019*; Blinn et al. 2020*			Elliott et al. 2018; Rabinowitz et al. 2015; Blinn et al. 2020*	Elliott et al. 2018; Tustin et al. 2017		Brown et al. 2019*; Blinn et al. 2020*	
Mental Health Symptoms (life satisfaction; bad mental health days; Google search for "anxiety"; depression symptoms and disordered sleep; self-rated health)	Casey et al. 2018a				Maguire & Winters 2017; Mayer et al. 2020*				Casey et al. 2018b			

Table 1. Health Outcomes by Exposure Surrogate Assessed in the Studies

Health Outcome (as defined by studies)	Exposure Surrogate											
	Earthquake[1]	Time Period[2]	Pre- or Post- Spud Date[3]	Distance from Wells[4]	Well Count or Density[5]	Intensity[6]	Time and Distance from Wells[7]	IDW[8]	IDW by Activity Level[9]	Spatio-temporal Activity Model[10]	Estimated Concen-trations[11]	Flaring[12]
OTHER												
Multiple Hospitalization Diagnoses					Denham et al. 2019*; Jemielita et al. 2015;							

[1] Earthquakes: Number of USGS-recorded earthquakes ≥4 in magnitude.
[2] Time period: Exposure defined as a specified date range or whether outcome occurred before or after the spud date.
[3] Pre- or post-spud date: Outcome rate before or after earliest spud date in geographic unit.
[4] Distance from wells: Distance between a household and nearest well or number of wells within a specified radius.
[5] Well count or density: Total number of UOGD sources within geographic area (e.g., ZIP code, county, radius around home).
[6] Intensity: Natural gas output or annual tons of emissions from UOGD sites.
[7] Indicator of time and distance: Product of two binary variables indicating (1) if spud date of nearest well occurred before or after birth and (2a) if distance of active well from residence is within specified radius or (2b) the density of wells within specified radius.
[8] IDW: Inverse of distance between a household and each well within a specified radius, summed across all wells within that radius.
[9] IDW by activity: Inverse of distance between a household and each well, summed across all wells within a specified radius around the residence and categorized by separate UOGD phases (e.g., drilling, production).
[10] Spatio-temporal activity model: A score incorporating well-specific information on location, number of wells, activity phase, use of green completion, production volume, number of tanks on well pad, and intensity.
[11] Sum of ambient concentrations of $PM_{2.5}$, carbon monoxide, nitrous oxides, volatile organic compounds, and formaldehyde predicted from a box air pollution dispersion model with emissions factors from multiple UOGD sources and wind speed as inputs.
[12] Flaring: Number of nightly flares within 5 km of residence and the total flared area (m^2) from all flares within 5km of maternal residence (Cushing et al. 2020); The monthly flaring volume by zip code (Willis et al. 2020)

*Studies published between January 1, 2019 and February 28, 2021.

Abbreviations: CHDs: congenital heart defects; CNS: central nervous system; COPD: chronic obstructive pulmonary disease; CRS: chronic rhinosinusitis; GI: gastrointestinal; IL: interleukin; NTDs: neural tube defects; URI: upper respiratory infection.

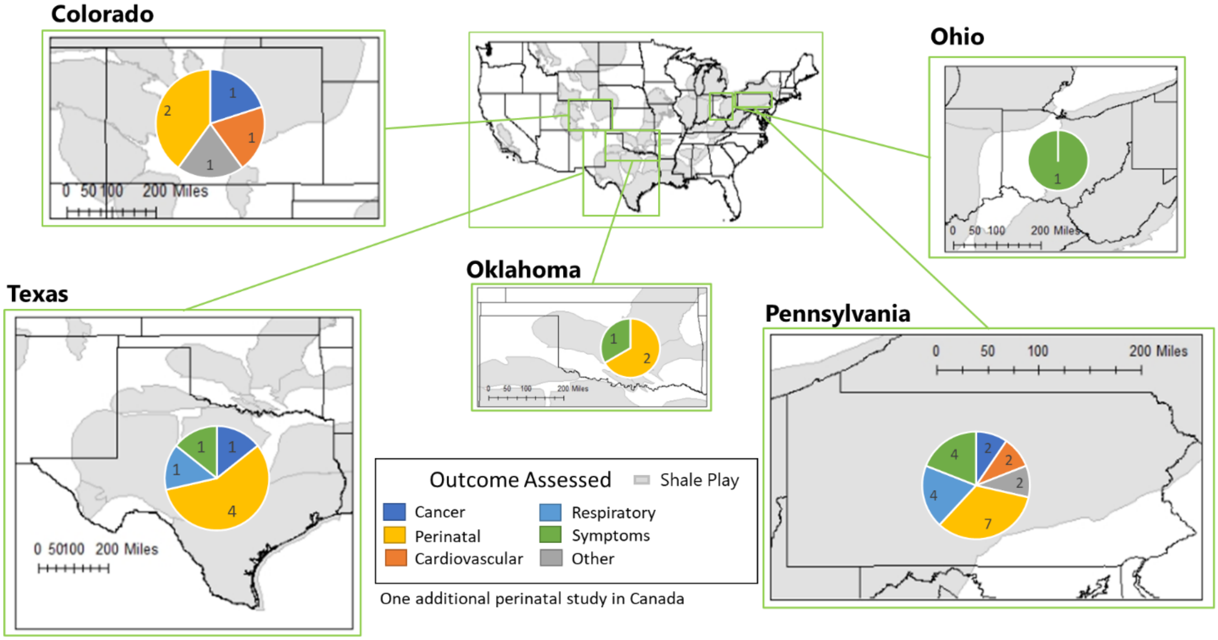

Figure 1. Studies included in and published since HEI Energy Research Committee (2019) shown by location and assessed health outcome.

Locations of new studies published since HEI Energy Research Committee (2019):
Canada: Caron-Beaudoin et al. (2020); Colorado: McKenzie et al. (2019), Mayer et al. (2020); Oklahoma: Apergis et al. (2019); Pennsylvania: Brown et al. (2019), Casey et al. (2019), Denham et al. (2019), Blinn et al. (2020), McAlexander et al. (2020); Texas: Cushing et al. (2020), Tang et al. (2020), Willis et al. (2020).

Note: Within the pie charts, each color represents a different health outcome category and each number represents the number of studies assessing each outcome.

Summary of Literature by Assessed Health Outcomes

This section describes the 12 more recent studies, categorized by the type of health outcomes assessed in each one. The phrase "earlier studies" refers to those that the Committee reviewed in its 2019 systematic review.

Perinatal Outcomes

Most of the recent studies focused on a variety of perinatal outcomes, including two on birth defects (McKenzie et al. 2019a; Tang et al. 2020), and four on other birth outcomes (Apergis et al. 2019; Caron-Beaudoin et al. 2020; Casey et al. 2019; Cushing et al. 2020) such as preterm birth (PTB), birthweight, gestational age, small for gestational age (SGA), and composite health indices. All studies applied exposure surrogates used in the earlier literature, including phase-specific inverse distance weighting (IDW), well density, distance to wells, and a spatio-temporal activity model (defined in Table 1). Two of the seven studies controlled for potential non-UOGD sources of exposure (McKenzie et al. 2019a; Tang et al. 2020).

Birth defects. McKenzie et al. (2019a) is a case–control study focused on congenital heart defects (CHDs) for all births in Colorado from 2005 to 2011. In this study, the investigators built on their original study, which examined associations between the IDW exposure surrogate (defined in Table 1) and birth defects (McKenzie et al. 2014), by using a more detailed exposure assessment (Allshouse et al. 2017) and control for confounding (with non-UOGD air pollution sources included as model covariates), and conducting detailed residential history in the same study population. They reported stronger positive associations between UOGD and congenital heart defects than those reported in their earlier work (McKenzie et al. 2014). It is unclear whether results differ as a function of the methods used to assess exposure, control for confounding, or other factors.

Tang et al. (2020), a case–control study, examined associations between well density within three different distances (1 km, 3 km, and 7.5 km radii) from the maternal residence and 16 birth defects for births between 1999 and 2011. They divided the exposure surrogate at each radius into tertiles. The investigators described their exposure proxy as a surrogate of UOGD-related chemical exposure through air and water pathways. They included socioeconomic covariates in their models, as well as rural or urban status and average daily vehicle miles traveled by county — two variables that had not been considered in the earlier literature. In addition, the investigators assessed effect modification by race/ethnicity and socioeconomic status. The investigators reported inconsistent results across well density tertiles within 1, 3, and 7.5 km radii around homes. Tests of trend were significant for five of the birth defects assessed. They also reported increased odds of neural tube defects and congenital heart defects in the third tertile across all radii in the Hispanic population, but not in the non-Hispanic population.

<u>Other Birth Outcomes</u>. Four studies assessed a range of birth outcomes related to birth weight and gestational age (Apergis et al. 2019; Caron-Beaudoin et al. 2020; Casey et al. 2019; Cushing et al. 2020). Apergis et al. (2019), a retrospective cohort study, included all births in Oklahoma between 1996 and 2017 and examined the relationship between birth weight, low birth weight, and a composite health index and well density within specified radii (1 km, 1–5 km, 5–10 km, and 10–20 km) around the maternal residence ZIP code. They stratified their results by conventional and unconventional wells and by year of birth (1996–2005 and 2006–2017). They controlled for covariates related to the mother's age, race, educational attainment, and child parity. They reported significant ($p<0.05$) positive associations between well density within 0-1 and 1-5-km radii around the maternal residence and probability of low birth weight and decreased health index value for births between 2006 and 2017.

Caron-Beaudoin et al. (2020), a retrospective cohort study, examined associations between the IDW exposure surrogate within a 2.5, 5, and 10 km radii around the maternal residence and head circumference, birthweight, SGA, and PTB for births at one hospital in northeastern British Columbia between 2006 and 2016. Their models included maternal age, parity, smoking status, infant sex, and year of birth. The investigators reported inconsistent results across quartiles and radii. Tests for trend were not significant for any models.

Casey et al. (2019), a retrospective cohort study, focused on maternal anxiety and depression as potential mediators in the relationship between birth outcomes (preterm birth and term birth weight) and UOGD exposure. This is the first UOGD analytic epidemiology study to examine the role of mediation. The team utilized Geisinger health system data in Pennsylvania for births between 2009–2013 and extracted information on mental health diagnosis and antidepressant medication orders during pregnancy. They also stratified results by medical assistance (a surrogate for socioeconomic status). They used a phase-specific IDW to assess exposure (described in Table 1). The investigators reported increased risk of PTB in the fourth compared with the first exposure quartile and reported relationships consistent with the null between antenatal anxiety or depression and adverse birth outcomes and no mediation effect.

Cushing et al. (2020), a retrospective cohort study, assessed the relationship between UOGD flaring and PTB, SGA, birthweight, and gestational age for births in the Texas Eagle Ford Shale play counties from 2012 to 2015. Along with Willis et al. 2020 (discussed below under respiratory outcomes), Cushing et al. (2020) were the first to explore the associations between UOGD-related flaring and health. They identified flares using satellite observations and defined three exposure surrogates: (1) number of nightly flares during pregnancy for each participant within 5 km of their residence, (2) total flared area during pregnancy, and (3) IDW of each nightly flare observation. Their models included numerous covariates: maternal age, race/ethnicity, U.S. or foreign born, educational attainment, pre-pregnancy body mass index, smoking status, insurance type, parity, high-risk pregnancy status, infant sex, adequacy of prenatal care, number of wells, and the year and season of birth. Of the 23,487 births included in the study, 92% were not exposed to flaring within a 5 km radius of the residence. As with Tang et al. (2020), they examined effect modification by Hispanic and non-Hispanic populations. They reported that prenatal exposure to flaring was associated with an increased odds of PTB and shorter gestational age for the "high flaring" groups (i.e., highest quartile). Results were consistent with the null for SGA and birthweight among both groups.

Cancer Outcomes

Studies quantifying associations UOGD exposure and cancer outcomes have not been published since HEI Energy Research Committee (2019).

Respiratory Outcomes

Willis et al. (2020), an ecologic study, focused on pediatric asthma hospitalizations occurring between 2000 and 2010 at the ZIP code level in Texas, and included only ZIP codes with geographic overlap with shales or basins. The investigators created three exposure surrogates at the ZIP code level: (1) well density, (2) flaring volume as reported by operators, which the investigators identify as being inaccurately reported, and (3) production volume. They ran separate analyses for conventional and unconventional wells and stratified models by race, ethnicity, household income, urbanicity, and age. Models included the following covariates: population density, age, percent non-White, percent Hispanic, National Air Toxic Assessment respiratory hazard index from 2005, and other county-level socioeconomic covariates. They also ran models that included year, quarter, and county-level fixed effects to allow for assessment of associations within counties over time. In their full models that include these variables, investigators reported significant increased odds of at least one pediatric asthma hospitalization within each tertile of the well density and production volume exposure surrogates and in the first tertile of flaring volume, as well as a significant inverse association in the third tertile of flaring volume. They reported similar results across age, racial, and income groups for the three exposure surrogates, and stronger results for flaring volume in urban as compared to rural ZIP codes. The investigators did not estimate exposure at a temporal resolution that would allow for assessment of acute outcomes.

Cardiovascular Outcomes

McAlexander et al. (2020), a case–control study, examined associations between phase-specific IDW and heart failure cases, extracted from Pennsylvania Geisinger healthcare system data from 2008 to 2015. They described their exposure surrogate as encompassing air pollution and non–air pollution exposures. They considered a detailed set of individual-level and community-level covariates, including age, smoking status, information about smoking status, medication use, body mass index, duration of care, comorbidities, socioeconomic status, residential greenness, and roadway proximity. In their full model, the research team reported increased odds of heart failure in the second, third, and fourth quartiles compared to the referent (first quartile) for the pad preparation phase, increased odds in the third and fourth quartiles for the stimulation phase, and increased odds in the fourth quartile as compared with the referent in the production phase. They reported null associations during the drilling phase.

Symptoms

Three studies focused on self-reported health symptoms. Mayer et al. (2020), a cross-sectional study, examined odds of lower self-rated health (answering the question on a Likert scale "How satisfied are you with your health”) between three Colorado towns, each town representing varying UOGD activity levels. They controlled for respondent race, age, income, employment and education status, trust in state-level regulatory agencies, and UOGD-related stress derived from the question: “As a result of oil and gas development, in my community, I experience more daily stress.” They reported that the communities with high and medium levels of UOGD activity had lower self-rated health compared with the community with no UOGD activity.

Two studies (Blinn et al. 2020; Brown et al. 2019), both cross-sectional, examined associations between UOGD and a broad range of symptoms in a group of adults and children who participated in the study because they had concerns about UOGD exposure. The participants reported health concerns to the Southwest Pennsylvania Environmental Health Project. The investigators included the following covariates in their models: age, sex, smoking status (Brown et al. 2019 only), and water source. To assess exposure, both studies used simple air pollution modeling methods to predict concentrations of five compounds (nitrogen oxides, carbon monoxide, volatile organic compounds, and particulate matter ≤ 2.5 µm in aerodynamic diameter). In addition, they assessed exposure using several other surrogates: Brown et al. (2019) quantified number of UOGD sources in each prevailing wind direction of the residence (in other words, the number of UOGD sources to the north, south, east and west of each residence); Blinn et al. (2020) applied the IDW exposure surrogate and quantified well density within a 5 km radius of the residence. Brown et al. (2019) reported significant, decreased odds of all respiratory symptoms with an increased number of UOGD sources to the north of the residence and significant, increased odds with an increased number of UOGD sources to the west. Results were consistent with the null for the air pollution model–based exposure surrogate. Blinn et al. (2020) reported mixed results depending on the assessed symptom and exposure surrogate.

Hospitalizations — All Diagnostic Codes

Denham et al. (2019), an ecologic and exploratory study, examined associations between county-level well count and density and non-targeted hospitalization diagnoses in Pennsylvania. This study built on the work of Jemielita et al. (2015) by extending the number of counties included and years assessed (2003–2014). They included county and year fixed effects in their models but did not control for other covariates. For both well count and density exposure surrogates, they reported positive associations for 2 of the 17 health outcome categories (genitourinary disease and diseases of the skin) and results consistent with the null for the other 15 health outcome categories.

Summary and Next Steps

This review summarizes a growing body of literature about the potential health effects of UOGD. Many of the studies expand on earlier research by controlling for additional potential confounders, performing effect modification assessments and mediation analyses, and using exposure metrics designed to minimize measurement error. However, the studies have many of the limitations identified in the Committee’s original report, notably limited-to-no control of potential confounding in some studies, including non-UOGD environmental sources and inconsistent results across studies. Also, some differences in study design and methods hinder the ability to perform inter-study comparison.

HEI’s Energy Research Committee will continue to track this literature and other health and exposure literature related to UOGD. The Committee will use published criteria (e.g., Bhide and Acharya 2015; Khan et al. 2003; Munn et al. 2018) to assess whether additional systematic review of the literature is merited.

ACKNOWLEDGMENTS AND FUNDING

Although this document was produced with partial funding by the United States Environmental Protection Agency under Contract No. 68HERC19D0010 to the Health Effects Institute–Energy, it has not been subject to the Agency's review and therefore does not necessarily reflect the views of the Agency, and no official endorsement by the Agency should be inferred. Oil and natural gas companies also provided funding to produce this document; however, it has not been subject to their review and therefore does not necessarily reflect the views of any of the oil and natural gas companies, and no endorsement by them should be inferred.

REFERENCES

Allshouse WB, Adgate JL, Blair BD, McKenzie LM. 2017. Spatiotemporal industrial activity model for estimating the intensity of oil and gas operations in Colorado. Env Sci Technol 51:10243–10250; doi:10.1021/acs.est.7b02084.

Apergis N, Hayat T, Saeed T. 2019. Fracking and infant mortality: Fresh evidence from Oklahoma. Environ Sci Pollut Res; doi:10.1007/s11356-019-06478-z.

Balise VD, Cornelius-Green JN, Kassotis CD, Rector RS, Thyfault JP, Nagel SC. 2019. Preconceptional, gestational, and lactational exposure to an unconventional oil and gas chemical mixture alters energy expenditure in adult female mice. Front Endocrinol 10; doi:10.3389/fendo.2019.00323.

Bamber AM, Hasanali SH, Nair AS, Watkins SM, Vigil DI, Van Dyke M, et al. 2019. A systematic review of the epidemiologic literature assessing health outcomes in populations living near oil and natural gas operations: study quality and future recommendations. Int J Environ Res Public Health 16:2123; doi:10.3390/ijerph16122123.

Bhide A, Acharya G. 2015. When is it appropriate to conduct a(nother) systematic review? Acta Obstet Gynecol Scand 94:1151–1152; doi:10.1111/aogs.12782.

Blinn HN, Utz RM, Greiner LH, Brown DR. 2020. Exposure assessment of adults living near unconventional oil and natural gas development and reported health symptoms in southwest Pennsylvania. USA. PLOS ONE 15:e0237325; doi:10.1371/journal.pone.0237325.

Brown DR, Greiner LH, Weinberger BI, Walleigh L, Glaser D. 2019. Assessing exposure to unconventional natural gas development: using an air pollution dispersal screening model to predict new-onset respiratory symptoms. J Environ Sci Health Part A 1–7; doi:10.1080/10934529.2019.1657763.

Busby C, Mangano J. 2017. There's a world going on underground—infant mortality and fracking in Pennsylvania. Journal of Environmental Protection 381–393; doi:10.4236/jep.2017.84028.

Caron-Beaudoin É, Whitworth KW, Bosson-Rieutort D, Wendling G, Liu S, Verner M-A. 2020. Density and proximity to hydraulic fracturing wells and birth outcomes in Northeastern British Columbia, Canada. J Expo Sci Environ Epidemiol; doi:10.1038/s41370-020-0245-z.

Casey JA, Goin DE, Rudolph KE, Schwartz BS, Mercer D, Elser H, et al. 2019. Unconventional natural gas development and adverse birth outcomes in Pennsylvania: The potential mediating role of antenatal anxiety and depression. Environ Res 177:108598; doi:10.1016/j.envres.2019.108598.

Casey JA, Goldman-Mellor S, Catalano R. 2018a. Association between Oklahoma earthquakes and anxiety-related Google search episodes. Environmental Epidemiology 2:e016; doi:10.1097/ee9.0000000000000016.

Casey JA, Savitz DA, Rasmussen SG, Ogburn EL, Pollak J, Mercer DG, et al. 2016. Unconventional natural gas development and birth outcomes in Pennsylvania, USA. Epidemiology 27:163–172; doi:10.1097/EDE.0000000000000387.

Currie J, Greenstone M, Meckel K. 2017. Hydraulic fracturing and infant health: New evidence from Pennsylvania. Science Advances 3; doi:10.1126/sciadv.1603021.

Cushing LJ, Vavra-Musser K, Chau K, Franklin M, Johnston JE. 2020. Flaring from unconventional oil and gas development and birth outcomes in the Eagle Ford Shale in south Texas. Environ Health Perspect 128:077003; doi:10.1289/EHP6394.

Denham A, Willis M, Zavez A, Hill E. 2019. Unconventional natural gas development and hospitalizations: evidence from Pennsylvania, United States, 2003–2014. Public Health 168:17–25; doi:10.1016/j.puhe.2018.11.020.

Deziel NC, Brokovich E, Grotto I, Clark CJ, Barnett-Itzhaki Z, Broday D, et al. 2020. Unconventional oil and gas development and health outcomes: A scoping review of the epidemiological research. Environ Res 182:109124; doi:10.1016/j.envres.2020.109124.

Elliott EG, Ma X, Leaderer BP, McKay LA, Pedersen CJ, Wang C, et al. 2018. A community-based evaluation of proximity to unconventional oil and gas wells, drinking water contaminants, and health symptoms in Ohio. Environ Res; doi:10.1016/j.envres.2018.08.022.

Ferrar K, Jackson E, Malone S. 2019. Categorical review of health reports on unconventional oil and gas development: Impacts in Pennsylvania. Available: https://www.fractracker.org/2019/05/health-economic-impacts-of-fracking-in-pa/ [accessed 8 September 2021].

Finkel ML. 2016. Shale gas development and cancer incidence in southwest Pennsylvania. Public health 141:198–206; doi:10.1016/j.puhe.2016.09.008.

Fryzek J, Pastula S, Jiang X, Garabrant DH. 2013. Childhood cancer incidence in Pennsylvania counties in relation to living in counties with hydraulic fracturing sites. J Occup Environ Med 55:796–801; doi:10.1097/JOM.0b013e318289ee02.

Gorski I, Schwartz BS. 2019. Environmental health concerns from unconventional natural gas development. In: Oxford Research Encyclopedia of Global Public Health. NewYork:Oxford University Press.

Hansen BH, Sørensen L, Størseth TR, Nepstad R, Altin D, Krause D, et al. 2019. Embryonic exposure to produced water can cause cardiac toxicity and deformations in Atlantic cod (Gadus morhua) and haddock (Melanogrammus aeglefinus) larvae. Mar Environ Res 148:81–86; doi:10.1016/j.marenvres.2019.05.009.

HEI Energy Research Committee. 2019. Potential human health effects associated with unconventional oil and gas development: A systematic review of the epidemiology literature.

Hill EL. 2018. Shale gas development and infant health: Evidence from Pennsylvania. Journal of Health Economics 61:134–150; doi:https://doi.org/10.1016/j.jhealeco.2018.07.004.

Janitz AE, Dao HD, Campbell JE, Stoner JA, Peck JD. 2018. The association between natural gas well activity and specific congenital anomalies in Oklahoma, 1997-2009. Environ Int; doi:10.1016/j.envint.2018.12.011.

Jemielita T, Gerton GL, Neidell M, Chillrud S, Yan B, Stute M, et al. 2015. Unconventional gas and oil drilling is associated with increased hospital utilization rates. PloS One 10:e0131093; doi:10.1371/journal.pone.0131093.

Johnston JE, Lim E, Roh H. 2019. Impact of upstream oil extraction and environmental public health: A review of the evidence. Sci Total Environ 657:187–199; doi:https://doi.org/10.1016/j.scitotenv.2018.11.483.

Kassotis CD, Iwanowicz LR, Akob DM, Cozzarelli IM, Mumford AC, Orem WH, et al. 2016. Endocrine disrupting activities of surface water associated with a West Virginia oil and gas industry wastewater disposal site. Sci Total Env 557–558:901–910; doi:10.1016/j.scitotenv.2016.03.113.

Kassotis CD, Nagel SC, Stapleton HM. 2018. Unconventional oil and gas chemicals and wastewater-impacted water samples promote adipogenesis via PPARγ-dependent and independent mechanisms in 3T3-L1 cells. Sci Total Environ; doi:10.1016/j.scitotenv.2018.05.030.

Khan KS, Kunz R, Kleijnen J, Antes G. 2003. Five steps to conducting a systematic review. J R Soc Med 96: 118–121.

Krupnick AJ, Echarte I. 2017. Health impacts of unconventional oil and gas development. https://media.rff.org/archive/files/document/file/RFF-Rpt-ShaleReviews_Health_0.pdf [accessed October 1, 2021]

Ma ZQ, Sneeringer KC, Liu L, Kuller LH. 2016. Time Series Evaluation of Birth Defects in Areas with and without Unconventional Natural Gas Development. J Epidemiol Public Health Rev 1; doi:10.16966/2471-8211.107.

Maguire K, Winters JV. 2017. Energy Boom and Gloom? Local Effects of Oil and Natural Gas Drilling on Subjective Well-Being. Growth Change 48:590–610; doi:10.1111/grow.12204.

Mayer A, Malin S, McKenzie L, Peel J, Adgate J. 2020. Understanding self-rated health and unconventional oil and gas development in three Colorado communities. Soc Nat Resour; doi:10.1080/08941920.2020.1734702.

McAlexander TP, Bandeen-Roche K, Buckley JP, Pollak J, Michos ED, McEvoy JW, et al. 2020. Unconventional natural gas development and hospitalization for heart failure in Pennsylvania. J Am Coll Cardiol 76:2862–2874; doi:10.1016/j.jacc.2020.10.023.

McKenzie LM, Allshouse WB, Byers TE, Bedrick EJ, Serdar B, Adgate JL. 2017. Childhood hematologic cancer and residential proximity to oil and gas development. PloS one 12:e0170423; doi:10.1371/journal.pone.0170423.

McKenzie LM, Allshouse W, Daniels S. 2019a. Congenital heart defects and intensity of oil and gas well site activities in early pregnancy. Environ Int 104949; doi:10.1016/j.envint.2019.104949.

McKenzie LM, Crooks J, Peel JL, Blair B, Brindley S, Allshouse W, et al. 2019b. Relationships between indicators of cardiovascular disease and intensity of oil and natural gas activity in Northeastern Colorado. Environ Res 170:56–64; doi:10.1016/j.envres.2018.12.004.

McKenzie LM, Guo R, Witter RZ, Savitz DA, Newman LS, Adgate JL. 2014. Birth outcomes and maternal residential proximity to natural gas development in rural Colorado. Env Health Perspect 122:412–417; doi:10.1289/ehp.1306722.

McKenzie LM, Witter RZ, Newman LS, Adgate JL. 2012. Human health risk assessment of air emissions from development of unconventional natural gas resources. Sci Total Environ 424:79–87; doi:10.1016/j.scitotenv.2012.02.018.

Mokry BJ. 2010. Summary of Investigation into the Occurrence of Cancer: Zip Codes 75022 and 75028, Flower Mound Denton County, Texas 1998–2007, 2007–2009.

Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. 2018. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 18:143; doi:10.1186/s12874-018-0611-x.

Peng L, Meyerhoefer C, Chou SY. 2018. The health implications of unconventional natural gas development in Pennsylvania. Health economics; doi:10.1002/hec.3649.

Rabinowitz PM, Slizovskiy IB, Lamers V, Trufan SJ, Holford TR, Dziura JD, et al. 2015. Proximity to natural gas wells and reported health status: results of a household survey in Washington County, Pennsylvania. Environmental health perspectives 123:21–26; doi:10.1289/ehp.1307732.

Rasmussen SG, Ogburn EL, McCormack M, Casey JA, Bandeen-Roch K, Mercer DG, et al. 2016. Association between unconventional natural gas development in the marcellus shale and asthma exacerbations. JAMA Intern Med 176:1334–1343; doi:10.1001/jamainternmed.2016.2436.

Rish WR, Pfau EJ. 2018. Bounding analysis of drinking water health risks from a spill of hydraulic fracturing flowback water. Risk Anal 38:724–754.; doi:10.1111/risa.12884.

Sapouckey SA, Kassotis CD, Nagel SC, Vandenberg LN. 2018. Prenatal exposure to unconventional oil and gas operation chemical mixtures altered mammary gland development in adult female mice. Endocrinology 159:1277–1289; doi:10.1210/en.2017-00866.

Stacy SL, Brink LL, Larkin JC, Sadovsky Y, Goldstein BD, Pitt BR, et al. 2015. Perinatal Outcomes and Unconventional Natural Gas Operations in Southwest Pennsylvania. PloS one 10:e0126425; doi:10.1371/journal.pone.0126425.

Tang IW, Langlois PH, Vieira VM. 2020. Birth defects and unconventional natural gas developments in Texas, 1999–2011. Environ Res 110511; doi:10.1016/j.envres.2020.110511.

Tustin A, Hirsch A, Rasmussen S, Casey J, Bandeen-Roche K, Schwartz B. 2017. Associations between Unconventional Natural Gas Development and Nasal and Sinus, Migraine Headache, and Fatigue Symptoms in Pennsylvania. Environmental health perspectives 125:189–197; doi:http://dx.doi.org/10.1289/EHP281.

Whitworth KW, Marshall AK, Symanski E. 2018. Drilling and Production Activity Related to Unconventional Gas Development and Severity of Preterm Birth. Environmental health perspectives 126; doi:10.1289/EHP2622.

Whitworth KW, Marshall AK, Symanski E. 2017. Maternal residential proximity to unconventional gas development and perinatal outcomes among a diverse urban population in Texas. PloS one 12:e0180966; doi:10.1371/journal.pone.0180966.

Willis M, Hystad P, Denham A, Hill E. 2020. Natural gas development, flaring practices and paediatric asthma hospitalizations in Texas. Int J Epidemiol 49(6):1883–1896. doi: 10.1093/ije/dyaa115.

Willis MD, Jusko TA, Halterman JS, Hill EL. 2018. Unconventional natural gas development and pediatric asthma hospitalizations in Pennsylvania. Environ Res 166:402–408; doi:https://doi.org/10.1016/j.envres.2018.06.022.

Wollin K-M, Damm G, Foth H, Freyberger A, Gebel T, Mangerich A, et al. 2020. Critical evaluation of human health risks due to hydraulic fracturing in natural gas and petroleum production. Arch Toxicol; doi:10.1007/s00204-020-02758-7.

HEI Energy Board, Research Committee, and Staff