



To: Earthworks

Re: Summarization of health research related to unconventional oil and gas operations, with an emphasis on Colorado

Date: October 3, 2019

The Endocrine Disruption Exchange (TEDX) is a US 501(c)3 non-profit organization dedicated to disseminating scientific evidence on the health and environmental effects of exposure to chemicals that interfere with hormone (endocrine) action, otherwise known as endocrine disrupting chemicals (EDCs). A major concern with endocrine disruptors is that they are associated with adverse health effects at very low concentrations, particularly when exposure occurs prenatally or in early childhood.

In 2005, TEDX became aware of the large number of chemicals used during unconventional oil and gas operations (UOG; which includes drilling, hydraulic fracturing, and associated activities). In 2011, we published the first peer-reviewed study identifying such chemicals as a public health threat. We also made this research publicly available through an online database, in order to inform stakeholders, including the public, advocacy groups, and government agencies.

UOG utilizes horizontal drilling to penetrate tight geological formations (e.g. shale), and it uses hydraulic fracturing (fracking) to create openings in the rock that release the target hydrocarbons to the surface. Fracking requires millions of gallons of water and chemicals, and thousands of pounds of proppants per well. In addition, UOG releases tons of polluting chemicals into the air and produces millions of gallons of sometimes toxic wastewater over the lifetime of a well.

As UOG unlocks vast shale resources in the US, it is contributing to the industrialization of rural areas as well as encroaching on urban centers. Large populations are now exposed to harmful chemicals where they live, work, and play. The frequent proximity of oil and gas facilities, such as refineries, near minority or low-income residences is an environmental justice issue. Research also suggests that UOG wells are disproportionately located in disadvantaged communities. Further, certain subpopulations are more susceptible to the health harms of UOG, including children, the elderly, and those with compromised immune function.

Before epidemiological research studies were conducted on the health effects of exposure to UOG, TEDX identified 353 chemicals used during UOG and searched the literature for known health effects of those chemicals. We found the following:

- Nearly 75% could have skin/eye/sensory organ, respiratory, and gastrointestinal effects
- Approximately 40–50% could affect the brain/nervous system, immune and cardiovascular systems, and the kidneys
- Over 30% could affect the endocrine system
- 25% could cause cancer and mutations¹

More recently, the US Environmental Protection Agency (EPA) compiled a list of over 1000 chemicals used in fracking². Elliott et al. analyzed these chemicals and found 49 were known, probable, or possible human carcinogens³. A previous Elliott et al. study identified 95 fracking chemicals potentially associated with adverse reproductive and developmental effects⁴. In addition to chemicals introduced during the processes of drilling and fracking, UOG contributes to air and water pollution by releasing chemicals into the environment from ‘native’ underground sources. Now that nearly a decade has passed since TEDX’s first published study, over 200 original research papers have been published on the health effects of UOG. Much of that research has been conducted in Colorado, a state hit particularly hard by the recent boom in UOG.

Adverse Health Effects of UOG

Research on fracking and health is growing rapidly, as evidenced by TEDX’s FrackHealth Database, an online resource providing information on the peer reviewed studies of fracking and various health endpoints⁵. Figure 1 displays the number of studies published each year, including human, animal, and in vitro research, health impact assessments, and reviews. As of August 2019, 200 studies are included in this database.

¹ Colborn T, Kwiatkowski C, Schultz K, Bachran M. 2011. Natural gas operations from a public health perspective. *Hum Ecol Risk Assess* 17(5):1039-1056, doi: 10.1080/10807039.2011.605662.

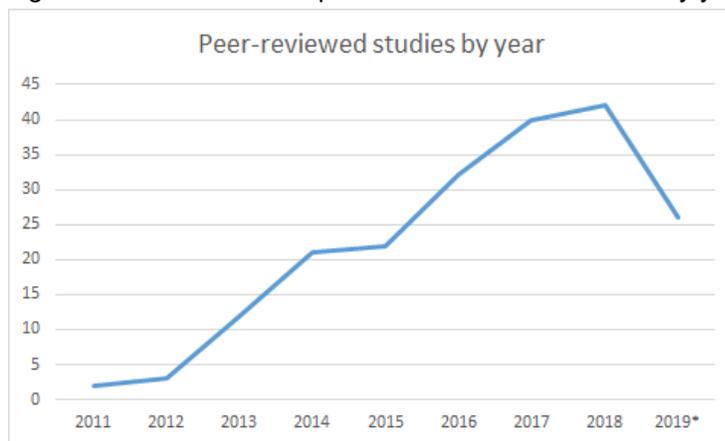
² US Environmental Protection Agency. 2016. Hydraulic Fracturing for Oil and Gas: Impacts from the Hydraulic Fracturing Water Cycle on Drinking Water Resources in the United States. Report #EPA-600-R-16-236Fb. Available at www.epa.gov/hfstudy.

³ Elliott EG, Trinh P, Ma X, Leaderer BP, Ward MH, Deziel NC. 2017. Unconventional oil and gas development and risk of childhood leukemia: Assessing the evidence. *Sci Total Environ* 576:138-147, doi: 10.1016/j.scitotenv.2016.10.072.

⁴ Elliott EG, Ettinger AS, Leaderer BP, Bracken MB, Deziel NC. 2017. A systematic evaluation of chemicals in hydraulic-fracturing fluids and wastewater for reproductive and developmental toxicity. *J Expos Sci Environ Epidemiol* 27(1):90-99, doi: 10.1038/jes.2015.81.

⁵ The Endocrine Disruption Exchange. FrackHealth Database. Available at: <https://endocrinedisruption.org/audio-and-video/fracking-related-health-research-database/search-the-database>.

Figure 1. Number of UOG peer-reviewed health studies by year of publication



*Includes studies through August, 2019

Colorado research

Public health scientists from the University of Colorado School of Public Health have published numerous studies on possible health effects of living in close proximity to UOG. Two studies published in 2019 consider the relationship between oil and gas operations and cardiovascular function. The first study published by McKenzie et al. looked at intensity of oil and gas activity near homes and cardiovascular disease in adults⁶. An association was found between increased activity and several indicators of cardiovascular health (augmentation index, blood pressure, inflammatory markers).

In the second study, McKenzie et al. used an intensity adjusted proximity model to estimate maternal exposure from three months preconception through the second gestational month. This nested case-control study used data from 3324 infants born in 34 Colorado counties with active oil and gas operations. Results indicated higher congenital heart defects (pulmonary artery and valve, aortic artery and valve, conotruncal, tricuspid valve) in babies born near oil and gas activity, especially in rural areas⁷. This research built on a previous, 2014 study using a retrospective cohort of 125K birth records in 57 rural Colorado counties, which showed a linear relationship between well density/proximity and the likelihood of a baby having a congenital heart defect, as well as an association with neural tube defects⁸.

In 2018, McKenzie et al. conducted a risk assessment demonstrating that both air pollutants and acute and chronic health risks, such as neurological and development effects and cancer,

⁶ McKenzie LM, Crooks J, Peel JL, Blair BD, Brindley S, Allshouse WB, Malin S, Adgate JL. 2019(a). 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.

⁷ McKenzie LM, Allshouse W, Daniels S. 2019(b). 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.

⁸ 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. *Environ Health Perspect*: 122(4):412-417, doi: 10.1289/ehp.1306722.

increased with increasing proximity to UOG⁹. Earlier work from this team concluded that residents living less than a half mile from wells were at greater risk of experiencing health effects than those living further away¹⁰. In a case-control study of childhood risk, McKenzie et al. concluded that children with acute lymphocytic leukemia were more likely to live near oil and gas wells¹¹.

Another Colorado risk assessment by Witter et al. in 2013 identified cancer, birth defects, and exacerbation of chronic diseases like asthma, COPD and cardiac disease as possible long term health effects of UOG. They also identified more immediate, probable health effects from air emissions, including headaches and other neurological symptoms, and airway and mucous membrane irritation¹². These immediate effects were supported by symptoms of residents living within a half mile of well development, as reported in the Colorado Oil and Gas Conservation Commission inspection/incident database.

Evidence from other states

Evidence from other states support the findings in Colorado. In addition, many studies assessed different endpoints, such as hospitalizations, respiratory effects, and acute symptoms.

Birth outcomes

In addition to the two studies from Colorado reporting increased birth defects in UOG exposed offspring, eight studies from other states identified significant associations including altered birth

⁹ McKenzie LM, Blair BD, Hughes J, Allshouse WB, Blake N, Helmig D, Milmoie P, Halliday H, Blake DR, Adgate JL. 2018. Ambient non-methane hydrocarbon levels along Colorado's northern Front Range: Acute and chronic health risks. *Environ Sci Technol* 52(8):4514-4525, doi: 10.1021/acs.est.7b05983.

¹⁰ 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.

¹¹ 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(2):e0170423, doi: 10.1371/journal.pone.0170423.

¹² Witter RZ, McKenzie L, Stinson KE, Scott K, Newman LS, Adgate J. 2013. The use of health impact assessment for a community undergoing natural gas development. *Am J Public Health* 103(6):1002-1010, doi: 10.2105/AJPH.2012.301017.

weight^{13,14,15}, small for gestational age^{16,17}, infant mortality^{18,19}, preterm birth^{20,21,22,23}, and birth defects²⁴. An additional study found no associations²⁵. Some of these outcomes, such as preterm birth and small for gestational age, have been associated with learning disabilities, lower IQ, and behavioral problems in children as they mature. These retrospective studies only report the conditions apparent at birth. The longitudinal research required to follow a child's development is rare, as it is costly and time consuming to conduct.

Hospitalizations

There are five studies suggesting an association between increased hospitalization rates and living near fracking operations. Respiratory complaints (asthma, pneumonia, general complaint) were the most common cause for hospitalization^{26,27,28}. Additional research reported positive associations between well density and genitourinary hospitalizations^{29,30}, as well as inpatient prevalence rates for cardiovascular, neurological, and dermatological conditions, and oncology visits³¹.

¹³ Stacy SL, Brink LL, Larkin JC, Sadovsky Y, Goldstein BD, Pitt BR, Talbott EO. 2015. Perinatal outcomes and unconventional natural gas operations in southwest Pennsylvania. PLoS ONE 10(6):e0126425, doi: 10.1371/journal.pone.0126425.

¹⁴ Currie J, Greenstone M, Meckel K. 2017. Hydraulic fracturing and infant health: New evidence from Pennsylvania. Sci Adv 3(12), doi: 10.1126/sciadv.1603021.

¹⁵ Hill EL. 2018. Shale gas development and infant health: Evidence from Pennsylvania. J Health Econ 61:134-150, doi: 10.1016/j.jhealeco.2018.07.004.

¹⁶ Stacy et al. 2015

¹⁷ Hill 2018

¹⁸ Busby C, Mangano JJ. 2017. There's a world going on underground —infant mortality and fracking in Pennsylvania. J Environ Prot 8(4):381-393, doi: 10.4236/jep.2017.84028.

¹⁹ 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(7):e0180966, doi: 10.1371/journal.pone.0180966.

²⁰ Casey JA, Savitz DA, Rasmussen SG, Ogburn EL, Pollak J, Mercer DG, Schwartz BS. 2015. Unconventional natural gas development and birth outcomes in Pennsylvania, USA. Epidemiology 27(2):163-172, doi: 10.1097/ede.0000000000000387.

²¹ Whitworth et al. 2017

²² Hill 2018

²³ Whitworth K, Marshall A, Symanski E. 2018. Drilling and production activity related to unconventional gas development and severity of preterm birth. Environ Health Perspect 126(3):037006, doi: 10.1289/EHP2622.

²⁴ Janitz AE, Dao HD, Campbell JE, Stoner JA, Peck JD. 2019. The association between natural gas well activity and specific congenital anomalies in Oklahoma, 1997–2009. Environ Inter 122:381-388, doi: 10.1016/j.envint.2018.12.011.

²⁵ Ma Z, Sneeringer K, Liu L, Kuller L. 2016. Time series evaluation of birth defects in areas with and without unconventional natural gas development. J Public Health Epidemiol 1(2): doi: 10.16966/2471-8211.107.

²⁶ Peng L, Meyerhoefer C, Chou SY. 2018. The health implications of unconventional natural gas development in Pennsylvania. Health Econ doi: 10.1002/hec.3649.

²⁷ Rasmussen SG, Ogburn EL, McCormack M, Casey JA, Bandeen-Roche K, Mercer DG, Schwartz BS. 2016. Association between unconventional natural gas development in the Marcellus Shale and asthma exacerbations. JAMA Intern Med 176(9):1334-1343, doi: 10.1001/jamainternmed.2016.2436.

²⁸ 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: 10.1016/j.envres.2018.06.022.

²⁹ 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.

³⁰ Jemielita T, Gerton GL, Neidell M, Chillrud S, Yan B, Stute M, Howarth M, Saberi P, Fausti N, Penning TM, et al. 2015. Unconventional gas and oil drilling is associated with increased hospital utilization rates. PloS One 10(7):e0131093, doi: 10.1371/journal.pone.0131093.

³¹ Jemielita et al. 2015

Respiratory system

Impacted respiratory function can occur immediately with acute exposure to UOG activity. Residents exposed to high levels of UOG activity, as determined by well data, had increased odds of asthma exacerbations³². A related study by Koehler et al. looked at additional activity metrics (compressor stations, impoundments, flaring events) and confirmed an association with asthma exacerbations³³. Respiratory symptoms reported by residents living near UOG include coughing, wheezing, shortness of breath, and increased prevalence of asthma^{34,35,36,37}.

Other health effects

Studies of self-reported conditions in residents living in close proximity to UOG include a variety of other symptoms as well. Examples include neurological symptoms (headaches, dizziness, and seizures), dermatological conditions (rashes, burning or itchy skin, and dermatitis), cardiovascular effects (irregular heartbeat, high blood pressure, and heart palpitations), and other symptoms (nosebleeds, nausea, eye irritation, muscle aches, and fatigue)^{38,39,40,41,42,43,44,45}.

Laboratory research

Laboratory research is a critical component of the total body of evidence available to answer the question of whether UOG affects human health. It is used precisely because it helps scientists predict human outcomes in the natural environment and can lend support to findings from

³² Rasmussen et al. 2016

³³ Koehler K, Ellis JH, Casey J, Manthos D, Bandeen-Roche K, Platt R, Schwartz B. 2018. Exposure assessment using secondary data sources in unconventional natural gas development and health studies. *Environ Sci Technol* 52(10):6061-6069, doi: 10.1021/acs.est.8b00507.

³⁴ Elliott EG, Ma X, Leaderer BP, McKay LA, Pedersen CJ, Wang C, Gerber CJ, Wright TJ, Sumner AJ, Brennan M, 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* 167:550-557, doi: 10.1016/j.envres.2018.08.022.

³⁵ Weinberger B, Greiner LH, Walleigh L, Brown D. 2017. Health symptoms in residents living near shale gas activity: A retrospective record review from the Environmental Health Project. *Prev Med Rep* 8:112-115, doi: 10.1016/j.pmedr.2017.09.002.

³⁶ Rabinowitz PM, Slizovskiy IB, Lamers V, Trufan SJ, Holford TR, Dziura JD, Peduzzi PN, Kane MJ, Reif JS, Weiss TR, et al. 2015. Proximity to natural gas wells and reported health status: Results of a household survey in Washington County, Pennsylvania. *Environ Health Perspect* 123(1):21-26, doi: 10.1289/ehp.1307732.

³⁷ Shamasunder B, Collier-Oxandale A, Blickley J, Sadd J, Chan M, Navarro S, Hannigan M, Wong N. 2018. Community-based health and exposure study around urban oil developments in South Los Angeles. *Int J Environ Res Public Health* 15(1):138, doi: 10.3390/ijerph15010138.

³⁸ Ferrar KJ, Kriesky J, Christen CL, Marshall LP, Malone SL, Sharma RK, Michanowicz DR, Goldstein BD. 2013. Assessment and longitudinal analysis of health impacts and stressors perceived to result from unconventional shale gas development in the Marcellus Shale region. *Int J Occup Env Health* 19(2):104-112, doi: 10.1179/2049396713Y.0000000024.

³⁹ Tustin AW, Hirsch A, Rasmussen S, Casey J, Bandeen-Roche K, Schwartz B. 2016. Associations between unconventional natural gas development and nasal and sinus, migraine headache, and fatigue symptoms in Pennsylvania. *Environ Health Perspect* 125:189-197, doi: 10.1289/EHP281.

⁴⁰ Saberi P, Propert K, Powers M, Emmett E, Green-McKenzie J. 2014. Field survey of health perception and complaints of Pennsylvania residents in the Marcellus Shale region. *Int J Environ Res Public Health* 11(6):6517-6527, doi: 10.3390/ijerph110606517.

⁴¹ Steinzor N, Subra W, Sumi L. 2013. Investigating links between shale gas development and health impacts through a community survey project in Pennsylvania. *New Solut* 23(1):55-83, doi: 10.2190/NS.23.1.e.

⁴² Elliott et al. 2018

⁴³ Rabinowitz et al. 2015

⁴⁴ Jemielita et al. 2015

⁴⁵ Weinberger et al. 2017

epidemiological studies. In particular, it can address the limitations of such research with regard to exposure timing (e.g. during prenatal development), dose, and control of covariates.

In laboratory experiments using rodent models, exposure to UOG chemicals resulted in numerous adverse impacts. Specifically, male rodents exposed prenatally to a mixture of chemicals used during hydraulic fracturing were shown to have increased testosterone, decreased sperm counts, and heavier testes and thymus⁴⁶. Effects in female rodents included hormone suppression, changes in uterine, ovary, heart, and body weights, and disrupted ovarian folliculogenesis⁴⁷. Additionally, recent research found altered mammary gland development⁴⁸, impaired immune system development and function⁴⁹, and altered adult energy expenditure^{50,51} in prenatally exposed female mice.

Other species provide supporting evidence as well. Zebrafish embryos exposed to flowback/produced water had increased embryo deformations and mortality, reduced metabolic rates, and altered cardio-respiratory gene expression^{52,53}, and juveniles exposed embryonically had decreased metabolic rates and fitness⁵⁴. Exposure in juvenile rainbow trout showed adverse impacts to multiple pathways, including biotransformation and oxidative stress pathways, and potential endocrine disruptive effects⁵⁵. Finally, exposure of *Daphnia* to

⁴⁶ Kassotis CD, Klemp KC, Vu DC, Lin C-H, Meng C-X, Besch-Williford CL, Pinatti L, Zoeller RT, Drobnis EZ, Balise VD, et al. 2015. Endocrine-disrupting activity of hydraulic fracturing chemicals and adverse health outcomes after prenatal exposure in male mice. *Endocrinology* 156(12):4458-4473, doi:10.1210/en.2015-1375.

⁴⁷ Kassotis CD, Bromfield JJ, Klemp KC, Meng CX, Wolfe A, Zoeller RT, Balise VD, Isiguzo CJ, Tillitt DE, Nagel SC. 2016. Adverse reproductive and developmental health outcomes following prenatal exposure to a hydraulic fracturing chemical mixture in female C57Bl/6 mice. *Endocrinology* 157(9):3469-3481, doi: 10.1210/en.2016-1242.

⁴⁸ 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(3):1277-1289, doi: 10.1210/en.2017-00866.

⁴⁹ Boulé LA, Chapman TJ, Hillman SE, Kassotis CD, O'Dell C, Robert J, Georas SN, Nagel SC, Lawrence BP. 2018. Developmental exposure to a mixture of 23 chemicals associated with unconventional oil and gas operations alters the immune system of mice. *Toxicol Sci* 163(2):639-654, doi: 10.1093/toxsci/kfy066.

⁵⁰ Balise VD, Cornelius-Green JN, Parmenter B, Baxter S, Kassotis CD, Rector RS, Thyfault JP, Paterlini S, Palanza P, Ruiz D, et al. 2019. Developmental exposure to a mixture of unconventional oil and gas chemicals increased risk-taking behavior, activity and energy expenditure in aged female mice after a metabolic challenge. *Front Endocrinol* 10(460), doi: 10.3389/fendo.2019.00460.

⁵¹ 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(323), doi: 10.3389/fendo.2019.00323.

⁵² He Y, Flynn SL, Folkerts EJ, Zhang Y, Ruan D, Alessi DS, Martin JW, Goss GG. 2017. Chemical and toxicological characterizations of hydraulic fracturing flowback and produced water. *Water Res* 114:78-87, doi: 10.1016/j.watres.2017.02.027.

⁵³ Folkerts EJ, Blewett TA, He Y, Goss GG. 2017. Cardio-respirometry disruption in zebrafish (*Danio rerio*) embryos exposed to hydraulic fracturing flowback and produced water. *Environ Pollut* 231:1477-1487, doi: 10.1016/j.envpol.2017.09.011.

⁵⁴ Folkerts EJ, Blewett TA, He Y, Goss GG. 2017. Alterations to Juvenile Zebrafish (*Danio rerio*) Swim Performance after Acute Embryonic Exposure to Sub-lethal exposures of hydraulic fracturing flowback and produced water. *Aquat Toxicol* 193:50-59, doi: 10.1016/j.aquatox.2017.10.003.

⁵⁵ He Y, Folkerts EJ, Zhang Y, Martin JW, Alessi DS, Goss GG. 2017. Effects on biotransformation, oxidative stress, and endocrine disruption in rainbow trout (*Oncorhynchus mykiss*) exposed to hydraulic fracturing flowback and produced water. *Environ Sci Technol* 51(2):940-947, doi: 10.1021/acs.est.6b04695.

flowback/produced water resulted in decreased reproduction and altered gene expression⁵⁶ and physical immobility⁵⁷.

Research using *in vitro* assays also supports the laboratory and epidemiological findings. For example, studies of chemicals detected in water collected near UOG operations, such as spill sites and surface water near wastewater injection sites, were shown to have hormone activity in estrogen, androgen, progesterone, glucocorticoid, and thyroid hormone receptor assays^{58,59}. Altered hormone activity was also found in extracted groundwater samples near UOG sites in Wyoming⁶⁰. One study of wastewater samples demonstrated dose-dependent toxicity in human and rat cells, altered gene expression, and impaired cell behavior, with some effects at very low concentrations⁶¹. A study using Marcellus Shale flowback water induced malignant cell transformation *in vitro*⁶². Most recently, fracking chemicals, wastewater, and surface water collected near UOG activity spurred fat cell development and proliferation in mouse cells⁶³.

Notably, many of the effects described above were found in developing organisms (i.e. via prenatal exposure), are related to the endocrine system, and occurred at low exposure concentrations. This highlights the importance of assessing impacts on the endocrine system with regard to UOG exposure. Such effects can have widespread and long lasting implications for overall health.

Indirect health impacts

In addition to the effects from chemical exposure, there are also non-chemical stressors, including noise pollution, traffic, and other community impacts, that could be affecting health on their own or in combination with chemical exposure. Also, risks from fires or explosions on well pads pose a safety issue that is not well studied^{64,65}.

⁵⁶ Blewett TA, Delompre PL, He Y, Folkerts EJ, Flynn SL, Alessi DS, Goss GG. 2017. The sub-lethal and reproductive effects of acute and chronic exposure to flowback and produced water from hydraulic fracturing on the water flea *Daphnia magna*. *Environ Sci Technol* 51(5):3032-3039, doi: 10.1021/acs.est.6b05179.

⁵⁷ Blewett TA, Delompre PL, Glover CN, Goss GG. 2018. Physical immobility as a sensitive indicator of hydraulic fracturing fluid toxicity towards *Daphnia magna*. *Sci Total Environ* 635:639-643, doi: 10.1016/j.scitotenv.2018.04.165.

⁵⁸ Kassotis CD, Tillitt DE, Davis JW, Hormann AM, Nagel SC. 2014. Estrogen and androgen receptor activities of hydraulic fracturing chemicals and surface and ground water in a drilling-dense region. *Endocrinology* 155(3):897-907, doi: 10.1210/en.2013-1697.

⁵⁹ Kassotis CD, Iwanowicz LR, Akob DM, Cozzarelli IM, Mumford AC, Orem WH, Nagel SC. 2016. Endocrine disrupting activities of surface water associated with a West Virginia oil and gas industry wastewater disposal site. *Sci Total Environ* 557-558:901-910, doi: <http://dx.doi.org/10.1016/j.scitotenv.2016.03.113>.

⁶⁰ Kassotis CD, Vu DC, Vo PH, Lin C-H, Cornelius-Green JN, Patton S, Nagel SC. 2018. Endocrine-disrupting activities and organic contaminants associated with oil and gas operations in Wyoming groundwater. *Arch Environ Contam Toxicol* doi: 10.1007/s00244-018-0521-2.

⁶¹ Crosby LM, Tatu CA, Varonka M, Charles KM, Orem WH. 2018. Toxicological and chemical studies of wastewater from hydraulic fracture and conventional shale gas wells. *Environ Toxicol Chem* doi: 10.1002/etc.4146.

⁶² Yao Y, Chen T, Shen SS, Niu Y, DesMarais TL, Linn R, Saunders E, Fan Z, Liou P, Kluz T, et al. 2015. Malignant human cell transformation of Marcellus Shale gas drilling flow back water. *Toxicol Appl Pharmacol* 288(1):121-130, doi: 10.1016/j.taap.2015.07.011.

⁶³ Kassotis CD, Nagel SC, Stapleton HM. 2018. Unconventional oil and gas chemicals and wastewater-impacted water samples promote adipogenesis via PPAR γ -dependent and independent mechanisms in 3T3-L1 cells. *Sci Total Environ* doi: 10.1016/j.scitotenv.2018.05.030.

⁶⁴ Blair BD, McKenzie LM, Allshouse WB, Adgate JL. 2017. Is reporting "significant damage" transparent? Assessing fire and explosion risk at oil and gas operations in the United States. *Energy Res Soc Sci* 29:36-43, doi: 10.1016/j.erss.2017.04.014.

⁶⁵ Haley M, McCawley M, Epstein AC, Arrington B, Bjerke EF. 2016. Adequacy of current state setbacks for directional high-volume hydraulic fracturing in the Marcellus, Barnett, and Niobrara Shale plays. *Environ Health Perspect* 124(9):1323-1333, doi: 10.1289/ehp.1510547.

Noise

There is a growing body of evidence that UOG activities produce noise at high enough levels that it may be harmful to health. Researchers documented noise levels at a residential UOG site in the Denver-Julesburg Basin where noise mitigation measures were in place. They found both daytime and nighttime levels exceeding 50 dBA, a threshold above which adverse health effects may be seen⁶⁶. Additionally, noise levels were measured during different phases of development (drilling, fracking, flowback, production) and exceedances were found during all four phases⁶⁷. Environmental noise exposure has been associated with annoyance, sleep disturbance, and cardiovascular disease⁶⁸.

Traffic

Increased volume of traffic at oil and gas locations is a big concern for nearby communities. The risk of injury rises with increased trucking activity. One Colorado study recorded nine heavy truck trips per hour, 24 hours a day, in a residential area during the fracking phase alone⁶⁹. Data shows that Colorado counties with increased oil and gas operations have more trucking accidents per capita than those with less activity, with higher populations and well density impacting injury numbers⁷⁰. Associated air and noise pollution from diesel trucks affects individuals living near well pads as well as those living along access roads.

Socio-environmental stress

Many social stressors are brought on by the underlying uncertainty surrounding oil and gas development, especially in areas with no previously existing extraction activities. Concern over quality of life, health effects, environmental contamination, and property values begin when drilling is proposed, and conflicting information around these impacts can lead to stress and community tension^{71,72}. Residents in Battlement Mesa Colorado reported increased anxiety and depression as well as negative community impacts (increased crime and sexually transmitted disease) during a previous natural gas boom⁷³.

⁶⁶ Blair BD, Brindley S, Dinkeloo E, McKenzie LM, Adgate JL. 2018. Residential noise from nearby oil and gas well construction and drilling. *J Expo Sci Environ Epidemiol* 28(6):538-547, doi: 10.1038/s41370-018-0039-8.

⁶⁷ Allshouse WB, McKenzie LM, Barton K, Brindley S, Adgate JL. 2019. Community noise and air pollution exposure during the development of a multi-well oil and gas pad. *Environ Sci Technol* 53(12):7126-7135, doi: 10.1021/acs.est.9b00052.

⁶⁸ Hays J, McCawley M, Shonkoff SBC. 2017. Public health implications of environmental noise associated with unconventional oil and gas development. *Sci Total Environ* 580:448-156, doi: 10.1016/j.scitotenv.2016.11.118.

⁶⁹ Allshouse et al. 2019

⁷⁰ Blair BD, Hughes J, Allshouse WB, McKenzie LM, Adgate JL. 2018. Truck and multivehicle truck accidents with injuries near Colorado oil and gas operations. *Int J Environ Res Public Health* 15(9):1861, doi: 10.3390/ijerph15091861.

⁷¹ Malin SA, Mayer A, Crooks JL, McKenzie L, Peel JL, Adgate JL. 2019. Putting on partisan glasses: Political identity, quality of life, and oil and gas production in Colorado. *Energy Policy* 129:738-748, doi: 10.1016/j.enpol.2019.01.049.

⁷² Hirsch JK, Bryant Smalley K, Selby-Nelson EM, Hamel-Lambert JM, Rosmann MR, Barnes TA, Abrahamson D, Meit SS, GreyWolf I, Beckmann S, et al. 2017. Psychosocial impact of fracking: a review of the literature on the mental health consequences of hydraulic fracturing. *Int J Ment Health Ad* 16(1):1-15, doi: 10.1007/s11469-017-9792-5.

⁷³ Witter RW, McKenzie L, Towle M, Stinson K, Scott K, Newman L, Adgate J. 2010. Health impact assessment for Battlement Mesa, Garfield County Colorado. Colorado School of Public Health. Available at <http://www.garfield-county.com/public-health/documents/1%20%20%20Complete%20HIA%20without%20Appendix%20D.pdf>

Environmental Pollution

The population exposed to environmental pollution associated with UOG is not limited to the frontline communities living near UOG sites. Air and water pollution can occur throughout the UOG extraction and supply chain, with local, regional, and even global impacts.

Air pollution

Numerous studies attest to the fact that UOG creates air pollution. A recent study identified 61 Hazardous Air Pollutants (HAPs) associated with upstream oil and gas operations (drilling, fracking, production)⁷⁴. Fifteen were measured in Colorado. The US EPA defines HAPs as chemicals known or suspected to cause cancer or other serious health effects. In addition to HAPs, many endocrine disrupting chemicals have been detected near upstream operations. A TEDX review of 48 peer-reviewed studies reported over 200 chemicals in the air⁷⁵. Thirty-four of these chemicals are EDCs, shown to impact hormone function or hormone mediated outcomes. Benzene, ethylbenzene, toluene and xylenes (BTEX) were among the top 10 most frequently found chemicals. They are HAPs, with well known respiratory, cardiovascular, neurological and carcinogenic, and endocrine disrupting effects. Ten of the studies in our review sampled the air in Colorado, with eight being in the Denver-Julesburg Basin (detecting approximately 76 chemicals).

Atmospheric research conducted on the Front Range provides some of the most compelling evidence for UOG related air pollution^{76,77,78,79}. For example, multiple studies from National Oceanic and Atmospheric Administration researchers, collecting top-down emission concentrations, found high levels of non-methane volatile organic compounds and traced it to UOG extraction. Air pollution from UOG development in rural locations in Colorado has also been studied, identifying dozens of toxic chemicals^{80,81}.

⁷⁴ Garcia-Gonzales DA, Shonkoff SBC, Hays J, Jerrett M. 2019. Hazardous air pollutants associated with upstream oil and natural gas development: A critical synthesis of current peer-reviewed literature. *Annu Rev Public Health* 40(1):283-304, doi: 10.1146/annurev-publhealth-040218-043715.

⁷⁵ Bolden AL, Schultz K, Pelch KE, Kwiatkowski CF. 2018. Exploring the endocrine activity of air pollutants associated with unconventional oil and gas extraction. *Environ Health* 17(1):26, doi: 10.1186/s12940-018-0368-z.

⁷⁶ Gilman JB, Lerner BM, Kuster WC, de Gouw JA. 2013. Source signature of volatile organic compounds from oil and natural gas operations in Northeastern Colorado. *Environ Sci Technol* 47(3):1297-1305, doi: 10.1021/es304119a.

⁷⁷ Pétron G, Frost G, Miller BR, Hirsch AI, Montzka SA, Karion A, Trainer M, Sweeney C, Andrews AE, Miller L, et al. 2012. Hydrocarbon emissions characterization in the Colorado Front Range: A pilot study. *J Geophys Res Atmos* 117:D04304, doi: 10.1029/2011JD016360.

⁷⁸ Pétron G, Karion A, Sweeney C, Miller BR, Montzka SA, Frost GJ, Trainer M, Tans P, Andrews A, Kofler J, et al. 2014. A new look at methane and nonmethane hydrocarbon emissions from oil and natural gas operations in the Colorado Denver-Julesburg Basin. *J Geophys Res Atmos* 119(11):6836-6852, doi: 10.1002/2013JD021272.

⁷⁹ Swarthout RF, Russo RS, Zhou Y, Hart AH, Sive BC. 2013. Volatile organic compound distributions during the NACHTT campaign at the Boulder Atmospheric Observatory: Influence of urban and natural gas sources. *J Geophys Res Atmos* 118(18):10,614-610,637, doi: 10.1002/jgrd.50722.

⁸⁰ Colborn T, Schultz K, Herrick L, Kwiatkowski C. 2014. An exploratory study of air quality near natural gas operations. *Hum Ecol Risk Assess* 20(1):86-10, doi: 10.1080/10807039.2012.749447.

⁸¹ McKenzie et al. 2012

Ozone

Many air pollutants associated with UOG are ozone precursors, volatile organic compounds (VOCs) that mix with nitrogen oxides (NO_x) in sunlight to form ozone. UOG emits both VOCs and NO_x. Once emitted, these compounds can travel downwind, contributing to ozone formation in cities near shale plays. In Colorado, this has led to both urban and rural areas being out of compliance with current US standards^{82,83,84}. A report by the Clean Air Task Force quantified the health impacts from ozone produced by the US oil and gas sector. They attributed over 25,000 summertime asthma attacks in Colorado children per year to oil and gas related ozone pollution with predicted cases exceeding 32,000 per year in 2025⁸⁵. Similarly, 2025 models estimate 70 premature deaths per year in Colorado based on oil and gas ozone and PM_{2.5} emissions⁸⁶.

Even relatively low levels of ozone can cause health effects in humans. In the short term, ozone can cause coughing, difficulty breathing, and sore throat. It can also make the lungs more susceptible to infection and can continue to damage the lungs even when the symptoms have disappeared. In the long term, ozone can inflame and damage the airways, aggravating lung diseases including asthma, emphysema, and chronic bronchitis⁸⁷. Children are particularly vulnerable because their lungs are still developing until about age 18, and they don't process chemicals as efficiently as adults because their immune and metabolic systems are not fully developed. As their lungs grow in the presence of ozone, children may suffer from decreased lung function and immune response making them more susceptible to lung infections⁸⁸. Women exposed to higher ozone during pregnancy have been shown to deliver preterm, low birth weight babies with decreased lung function⁸⁹.

⁸² Evans JM, Helmig D. 2016. Investigation of the influence of transport from oil and natural gas regions on elevated ozone levels in the Northern Colorado Front Range. *J Air Waste Manage* 67(2):196-211, doi: 10.1080/10962247.2016.1226989.

⁸³ McDuffie EE, Edwards PM, Gilman JB, Lerner BM, Dubé WP, Trainer M, Wolfe DE, Angevine WM, deGouw J, Williams EJ, et al. 2016. Influence of oil and gas emissions on summertime ozone in the Colorado Northern Front Range. *J Geophys Res- Atmos* 121(14):8712-8729, doi: 10.1002/2016JD025265.

⁸⁴ Musselman RC, Korfmacher JL. 2014. Ozone in remote areas of the Southern Rocky Mountains. *Atmos Environ* 82(0):383-390, doi: 10.1016/j.atmosenv.2013.10.051.

⁸⁵ Clean Air Task Force. 2016. Gasping for Breath: An analysis of the health effects from ozone pollution from the oil and gas industry. Available at http://catf.us/resources/publications/files/Gasping_for_Breath.pdf

⁸⁶ Fann N, Baker KR, Chan EAW, Eyth A, Macpherson A, Miller E, Snyder J. 2018. Assessing human health PM_{2.5} and ozone impacts from U.S. oil and natural gas sector emissions in 2025. *Environ Sci Technol* 52(15):8095-8103, doi: 10.1021/acs.est.8b02050.

⁸⁷ Epstein AC. 2017. The Human Health Implications of Oil and Natural Gas Development. In: *Environmental Issues Concerning Hydraulic Fracturing*, Volume 1, p. 113-145; doi: 10.1016/bs.apmp.2017.08.002.

⁸⁸ Webb E; Hays J; Dyrszka L; Rodriguez B; Cox C; Huffling K; Bushkin-Bedient S. 2016. Potential hazards of air pollutant emissions from unconventional oil and natural gas operations on the respiratory health of children and infants. *Rev Environ Health* 31(2):225-243, doi: 10.1515/reveh-2014-0070.

⁸⁹ American Lung Association. 2017. State of the Air. Available at <http://www.lung.org/assets/documents/healthy-air/state-of-the-air/sota-2018-full.pdf>

Water pollution

UOG operations can contaminate ground and surface water through multiple pathways such as faulty well casings, spills, and leaks^{90,91}. Spills and leaks of fracking chemicals and produced water occur on pads, and also during transport of fluids to and from the well site and during disposal. Spill data from over 30,000 wells across four states reported hydrocarbon spills at 2-16% of wells each year, most within the first few years when production volumes are highest. Colorado alone accounted for 476 spills, many from wells reporting more than one spill⁹².

Wastewater

It is estimated that over 900 billion gallons of wastewater are generated each year from oil and gas production in the US⁹³. This includes the initial flowback of the fracking fluid as well as the produced water that surfaces for the life of the well. Current management and disposal practices include deep well injection, storage in impoundments, recycling for reuse in UOG, and treatment in industrial or municipal facilities⁹⁴. There is limited reuse of wastewater outside of oil and gas production (beneficial reuse), but interest is mounting in Colorado. Wastewater has been used in some states for crop irrigation, livestock watering, and road spreading for dust suppression or deicing^{95,96}.

TEDX participated in a review of 101 studies identifying over 1000 chemicals in UOG wastewater (flowback and/or produced water) from onshore oil and gas production⁹⁷. Twenty-one studies reported wastewater constituents in Colorado including carcinogens and EDCs^{98,99,100}. The majority of the identified chemicals have no toxicological hazard data, so risk estimates may be based on only a few well-studied chemicals. For example, naturally occurring radioactive materials (NORM) are a known component in wastewater, including the carcinogen

⁹⁰ Gorski I, Schwartz BS. 2019. Environmental Health Concerns From Unconventional Natural Gas Development. Oxford University Press, doi: 10.1093/acrefore/9780190632366.013.44.

⁹¹ Vengosh A, Jackson RB, Warner N, Darrah TH, Kondash A. 2014. A critical review of the risks to water resources from unconventional shale gas development and hydraulic fracturing in the United States. *Environ Sci Technol* 48(15):8334-8348, doi: 10.1021/es405118y.

⁹² Patterson LA, Konschnik KE, Wiseman H, Fargione J, Maloney KO, Kiesecker J, Nicot J-P, Baruch-Mordo S, Entekin S, Trainor A, et al. 2017. Unconventional oil and gas spills: Risks, mitigation priorities, and state reporting requirements. *Environ Sci Technol* 51(5):2563-2573, doi: 10.1021/acs.est.6b05749.

⁹³ Danforth C, Chiu WA, Rusyn I, Schultz K, Bolden A, Kwiatkowski C, Craft E. (in press). An integrative method for identification and prioritization of constituents of concern in produced water from onshore oil and gas extraction. *Environ Int*.

⁹⁴ Sun Y, Wang D, Tsang DCW, Wang L, Ok YS, Feng Y. 2019. A critical review of risks, characteristics, and treatment strategies for potentially toxic elements in wastewater from shale gas extraction. *Environ Int* 125:452-469, doi: 10.1016/j.envint.2019.02.019.

⁹⁵ Hill LAL, Czolowski ED, DiGiulio D, Shonkoff SBC. 2019. Temporal and spatial trends of conventional and unconventional oil and gas waste management in Pennsylvania, 1991–2017. *Sci Total Environ* 674:623-636, doi: 10.1016/j.scitotenv.2019.03.475.

⁹⁶ Tasker TL, Burgos WD, Piotrowski P, Castillo-Meza L, Blewett TA, Ganow KB, Stallworth A, Delompré PLM, Goss GG, Fowler LB, et al. 2018. Environmental and human health impacts of spreading oil and gas wastewater on roads. *Environ Sci Technol* 52(12):7081-7091, doi: 10.1021/acs.est.8b00716.

⁹⁷ Danforth et al. in press

⁹⁸ Rosenblum JS, Thurman EM, Ferrer I, Aiken GR, Linden KG. 2017. Organic chemical characterization and mass balance of a hydraulically fractured well: From fracturing fluid to produced water over 405 days. *Environ Sci Technol* 51(23):14006-14015, doi: 10.1021/acs.est.7b03362.

⁹⁹ Thurman EM, Ferrer I, Rosenblum J, Linden K, Ryan JN. 2017. Identification of polypropylene glycols and polyethylene glycol carboxylates in flowback and produced water from hydraulic fracturing. *J Hazard Mater* 323:11-17, doi: 10.1016/j.jhazmat.2016.02.041.

¹⁰⁰ Kassotis et al. 2014

radium. Long-term exposure to radium, as well as exposure to other chemicals of concern in UOG wastewater including benzene, polycyclic aromatic hydrocarbons, and heavy metals, can increase excess lifetime cancer risk¹⁰¹. Based on this limited knowledge, caution should be used in exploring options to re-use UOG wastewater, particularly in light of the many more millions of people who will then be at risk.

CDPHE Review of the Evidence

The evidence presented thus far is overwhelmingly in support of numerous health hazards and risks from UOG. In fact, a recent review found only two studies since 2000 failed to find significant health effects associated with UOG¹⁰². However, in 2019 the Colorado Department of Public Health and Environment (CDPHE) published a review of the epidemiological evidence and claimed there was only “limited evidence” of harmful health effects¹⁰³. Unfortunately, their conclusions were compromised by severe flaws in their application of systematic review methods.

As recognized by the CDPHE authors, systematic reviews are the gold standard for answering research questions in clinical medicine and have recently been adapted by the US National Toxicology Program and others^{104,105} to accommodate features unique to environmental health. However, the authors chose not to follow the adapted frameworks in at least two critical steps.

One, despite the fact that adapted frameworks specifically state that observational studies in environmental health should begin with a moderate certainty rating when assessing evidence of an effect¹⁰⁶, CDPHE chose to use a baseline rating of low certainty. Had studies been accurately characterized as moderate quality at the start, it is highly likely the authors’ overall conclusions would have been very different. Two, they used a study quality scoring system that is invalid according to the National Toxicology Program. Scoring systems are not advised because they are affected by the number of questions used, which is arbitrary, and by the assumption that all questions are weighted equally. Most frustrating is that the authors were aware of this, as written in their limitations section, yet failed to apply readily available valid methods.

Further, if CDPHE had followed approved systematic review methods, they would have published their protocol online *a priori*, providing an opportunity for systematic review experts to

¹⁰¹ Elliott et al. 2017

¹⁰² Wright R, Muma RD. 2018. High-volume hydraulic fracturing and human health outcomes: A scoping review. *J Occup Environ Med* 60(5):424-429, doi: 10.1097/jom.0000000000001278.

¹⁰³ Bamber AM, Hasanali SH, Nair AS, Watkins SM, Vigil DI, Van Dyke M, McMullin TS, Richardson K. 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(12):2123, doi: 10.3390/ijerph16122123.

¹⁰⁴ Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. 2014. Systematic review and evidence integration for literature-based environmental health science assessments. *Environ Health Perspect* 122(7):711–718, doi: 10.1289/ehp.1307972.

¹⁰⁵ Woodruff TJ, Sutton P. 2014. The navigation guide systematic review methodology: A rigorous and transparent method for translating environmental health science into better health outcomes. *Environ Health Perspect* 122(10):1007–1014, doi: 10.1289/ehp.1307175.

¹⁰⁶ Woodruff and Sutton 2014

improve their methodological approach. TEDX has participated in worldwide collaborations to develop systematic review methods and has published several peer-reviewed systematic and scoping reviews. We would have welcomed the opportunity to comment. In addition to providing the above input, we would have urged CDPHE to include the growing body of animal and mechanistic studies in the review, which is a key feature of systematic reviews in environmental health.

Colorado has been a frontrunner in producing the strongest science available on the impacts of UOG on health and the environment. It is very concerning that the Colorado health department's scientifically compromised review of the evidence could have damaging repercussions on the ability of the state to protect its citizens from the harmful effects of UOG.

In sum

The current body of scientific evidence indicates that people are at risk for health effects from UOG. It is likely that risk is underestimated, given that these studies do not account for all possible chemical interactions, vulnerabilities of sensitive populations (e.g. infants), or outcomes that may arise long after initial exposures. Amplifying this risk is the fact that in many areas, UOG is now being conducted in close proximity to large populations, bringing it closer to more people in their homes, schools, hospitals, and businesses. A recent study demonstrated that in the US alone, 17.6 million people live within 1,600 m (~1 mi) of at least one active oil and/or gas well¹⁰⁷, including at least 6% of the Colorado population¹⁰⁸. Efforts to find uses for UOG wastewater, such as dust suppression or deicing of roads, similarly threatens to expose a greater number of people to the hazards of UOG.

Further, the scale of UOG operations is growing, posing threats to even more people. As the industry has evolved, the number of wells per unit area has increased, with up to 50 horizontal wellbores that can now extend two miles in any direction. These large capacity well pads require more chemicals, water, sand, and truck trips, and produce more waste. Compared to conventional wells, this can be as much as 50 times more water and associated fracking chemicals - up to 20 million gallons per well. Thousands of tons of sand must be mined and transported to the pad, and millions of gallons of hazardous wastewater must be transported off the pad, stored, and disposed. Industrial activity on the well pad now lasts for months or years, leading to increased air pollution from diesel and truck engines. Larger scale operations mean higher risk of spills, water contamination, air pollution, truck hazards, etc.

Due to these concerns, states and localities across the country are asking what is a safe distance for UOG in relation to human activity. The answer is ultimately a question of how much risk one is willing to accept. As of yet, there is no scientific basis for a gradient of safe distances. Significant health effects have been demonstrated at distances up to 3,280

¹⁰⁷ Czolowski E, Santoro R, Srebotnjak T, Shonkoff S. 2017. Toward consistent methodology to quantify populations in proximity to oil and gas development: a national spatial analysis and review. *Environ Health Perspect* 125(8):086004, doi: 10.1289/EHP1535.

¹⁰⁸ McKenzie et al. 2019(b)

feet^{109,110,111,112,113,114}. In a review published in 2016, Haley et al. concluded that even the most protective setbacks, up to 1500 feet among the three states evaluated (PA, TX and CO), are not sufficient¹¹⁵. Unfortunately, it could be decades before we have conclusive evidence of how close is too close. Meanwhile, the health and well-being of entire communities continues to be threatened. In the interest of the people of the state of Colorado, and as a model for the nation, we urge you to make the most health protective decisions possible.

¹⁰⁹ McKenzie LM et al. 2012

¹¹⁰ Whitworth KW et al. 2017

¹¹¹ McKenzie LM et al. 2018

¹¹² Currie J et al. 2017

¹¹³ Weinberger B et al. 2017

¹¹⁴ Rabinowitz PM et al. 2015

¹¹⁵ Haley et al. 2016