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Ambient Nonmethane Hydrocarbon Levels Along Colorado's Northern Front Range: Acute and Chronic Health Risks

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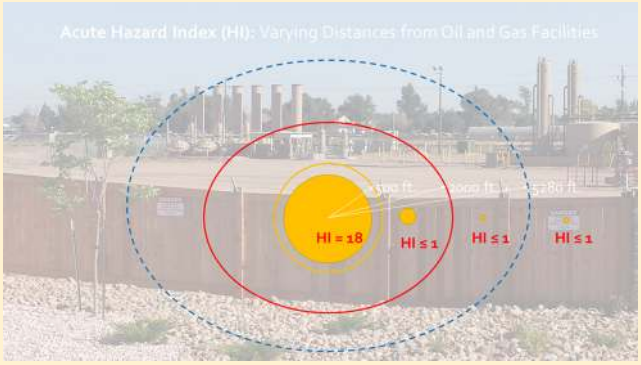
Supporting Information

ABSTRACT: Oil and gas (O&G) facilities emit air pollutants that are potentially a major health risk for nearby populations. We characterized prenatal through adult health risks for acute (1 h) and chronic (30 year) residential inhalation exposure scenarios to nonmethane hydrocarbons (NMHCs) for these populations. We used ambient air sample results to estimate and compare risks for four residential scenarios. We found that air pollutant concentrations increased with proximity to an O&G facility, as did health risks. Acute hazard indices for neurological (18), hematological (15), and developmental (15) health effects indicate that populations living within 152 m of an O&G facility could experience these health effects from inhalation exposures to benzene and alkanes. Lifetime excess cancer risks exceeded 1 in a million for all scenarios. The cancer risk estimate of 8.3 per 10 000 for populations living within 152 m of an O&G facility exceeded the United States Environmental Protection Agency's 1 in 10 000 upper threshold. These findings indicate that state and federal regulatory policies may not be protective of health for populations residing near O&G facilities. Health risk assessment results can be used for informing policies and studies aimed at reducing and understanding health effects associated with air pollutants emitted from O&G facilities.



INTRODUCTION

Horizontal drilling and high-volume hydraulic fracturing have resulted in a dramatic increase in the number of oil and gas (O&G) wells located on a single pad.[1,2] It is now common for O&G well sites to contain 20 to 40 wells, related infrastructure, and tank batteries to store and/or pipelines to transport petroleum products and exploration and production (E&P) waste.[3] Additional equipment and facilities, such as gathering lines, compressor stations, and E&P waste disposal sites may also be located in areas of intensive O&G development.[4]

In the Denver Julesberg Basin (DJB) on the Colorado Northern Front Range (CNFR), the O&G industry is rapidly expanding at the same time that housing construction is increasing to accommodate a rapidly growing population.[5] As a result, 19% of the population (~356 000 people) in the DJB live within 1600 m of an active O&G well site.[5] Between 2000 and 2012, the number of people living within 1600 m of an O&G well site grew almost 3 times faster than the population living further away.[5]

Colorado mandated regulatory exclusion zones around residential structures in which the drilling of O&G wells is discouraged are referred to as setback distances. Colorado setback distances were historically as short as 150 feet (46 m) and are currently at 500 feet (152 m).[6] Additionally, setback distances of 1000 feet (305 m) apply to high occupancy buildings serving 50 or more people (e.g., schools and hospitals) as well as operating child care centers for 5 or more children.[6] While the setback distances are intended to protect the general public's safety and welfare from environmental and nuisance impacts resulting from O&G develop-

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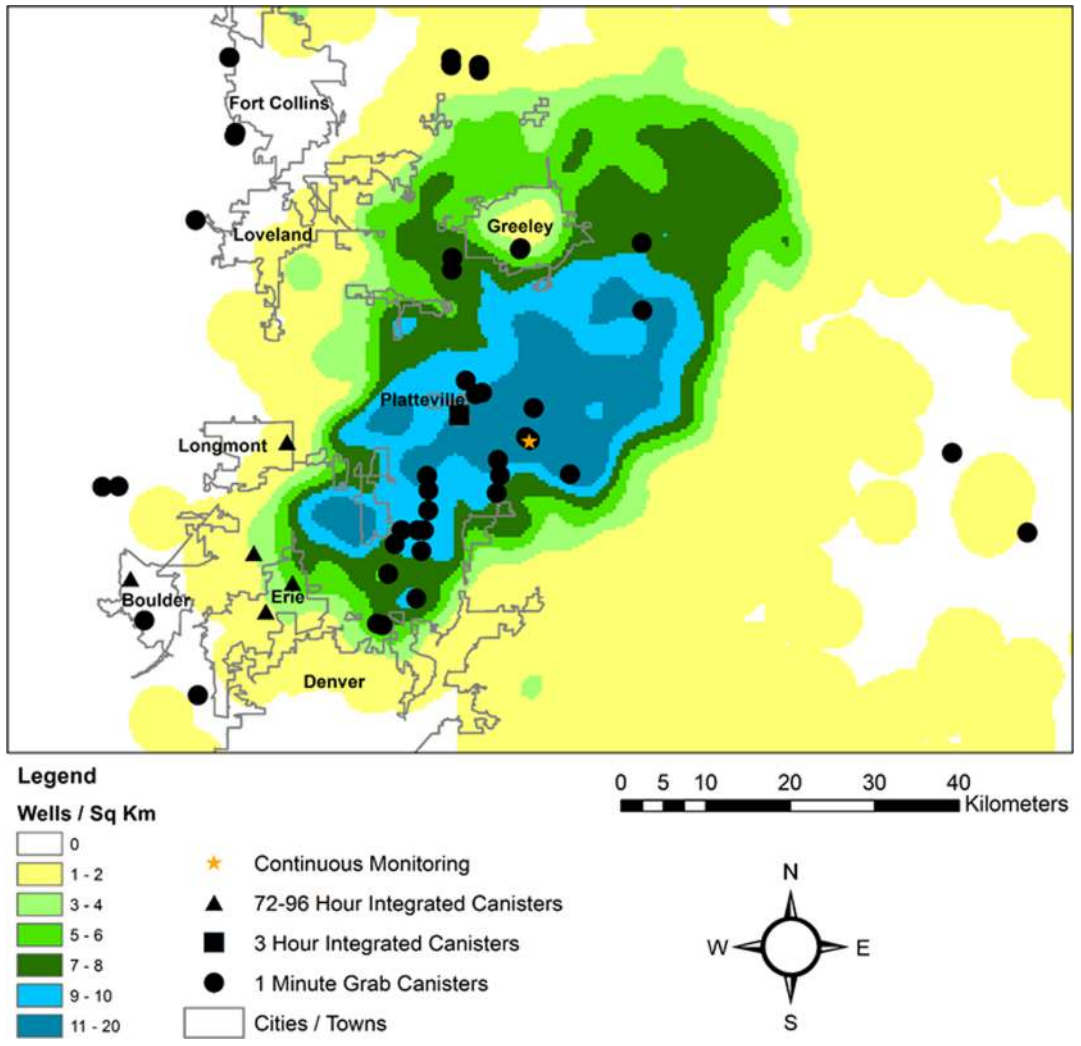

Figure 1. Colorado Northern Front Range: sample locations[37−39] and oil and gas well density.[36]

ment, they are not intended to address potential human health impacts associated with O&G development air emissions.[7]

Air pollution is one of the major potential health risks for populations living near O&G sites.[4,8] O&G sites directly emit nonmethane hydrocarbons (NMHCs) into the air,[9−11] and several studies have identified O&G facilities as major contributors to ambient NMHC levels along the CNFR.[12−17] Some of these NMHCs such as benzene, toluene, ethylbenzene, and xylenes (BTEX) are defined as hazardous air pollutants.[18] Because of higher atmospheric stability at night, nighttime emissions do not disperse as much as during the daytime, and average nighttime benzene levels are approximately twice daytime levels.[15]

Recent Colorado studies observed that infants with congenital heart defects and children diagnosed with leukemia are more likely to live in the densest areas of O&G wells.[19,20] Studies in Pennsylvania and Texas have observed associations between proximity to O&G wells and fetal death, low birthweight, preterm birth, asthma, fatigue, migraines, and chronic rhinosinusitis.[21−25]

The few previous human health risk assessments conducted in areas with O&G development have used results from ambient air samples to predict the risk for both noncancer and cancer health effects in the surrounding population.[8,26,27] Risks for noncancer health effects have been expressed as semi-quantitative hazard indices (HI), and cancer risks have expressed as risk in excess of the baseline lifetime cancer risk for Americans of 44 per 100 (lifetime excess cancer risk).[28] The previous assessments indicate the potential for short-term respiratory, neurological, hematological, and developmental effects and elevated estimated lifetime excess cancer risk for populations living within approximately 800 m of O&G well pads,[8] while the potential for chronic noncancer health effects and lifetime excess cancer risk are lower for populations living further from O&G sites.[8,26,29,30] One important shortcoming of previous risk assessments is that they did not consider short-term and repeated nighttime peak exposures. They did not explicitly address childhood exposures or incorporate findings from the most recent studies on health effects associated with ambient benzene exposure. Additionally, data sets supporting most of the previous risk assessments were not sufficient for assessment of short-term exposures to air pollution O&G facilities or the variance in health risks with differing setback distances from O&G facilities.

The goal of this analysis is to characterize prenatal through adult noncancer and cancer health risks from both short-term (acute) and long-term (chronic) residential exposures to NMHCs measured in CNFR O&G development areas and how health risks vary with proximity to O&G facilities.

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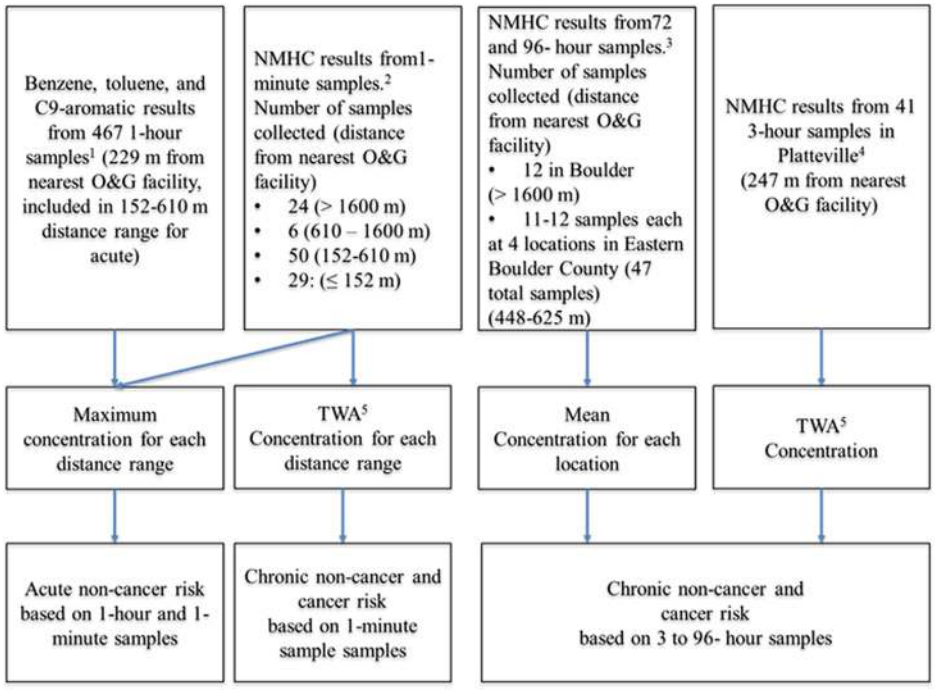

For each sample type this figure depicts the chemical measurement results used, number of samples collected, and the distance of the sampling location from the nearest oil and gas (O&G) facility single and multi- well sites, tank batteries, extraction and production waste disposal sites, gathering lines, and O&G processing facilities).
NMHC: non-methane hydrocarbon
[1] DISCOVER AQ Field Sampling Campaign: The nearest O&G facility is a multi-well pad. Sample collected every minute between July 17 and August 8, 2014 (n = 28,009 total measurements. Benzene, toluene, and C9 aromatic results determined by proton-transfer-reaction quadrupole mass spectrometry. The 1-hour results are the mean of 60 consecutive 1-s readings.[15]
[2] DISCOVER AQ Field Sampling Campaign: Samples collected between July 17 and August 13, 2014 primarily during daylight hours 6:00 and 21:00 hours (2 samples were collected in the 2:00 hour) at 3 to 14,870 meters from single and multi- well sites, tank batteries, extraction and production waste disposal sites, gathering lines, and O&G processing facilities. NMHC results determined by gas chromatography with flame ionization and quadrupole mass spectrometer detectors. 1-minute canister samples[15, 88]
[3] 2014 Boulder County Air Study: Samples were collected between May 23 and August 27, 2014: 12 sample at a single location in Boulder (> 1600 meters from an O&G facility) and 11-12 samples at each of four Erie locations (448 to 625 meters from multiple O&G well pad). NMHC results determined by gas chromatography with flame ionization and quadrupole mass spectrometer detectors. 72-96-hour integrated canister samples.[37]
[4] Colorado Department of Public Health and Environment (CDPHE) Platteville Air Monitoring Site: Nearest O&G facility is a multiple O&G well pad. Samples collected at a single location between 6:00 to 9:00 am (27 samples) and 1:00 to 4:00 pm (14 samples) from June 1 to August 31 2014. NMHC results determined by gas chromatography with flame ionization detector. 3-hour-integrated canister samples.[16, 38]
[5] Time Weighted Average: TWA mean = ((mean concentration x 12 hours x 2.34) + (mean concentration x 12 hours))/24 hour.

Figure 2. Samples collected along Colorado's Northern Front Range in summer 2014 used to develop exposure and risk estimates.

METHODS

We used California's Office of Environmental Health Hazard Assessment (OEHHA) Risk Assessment Guidelines to estimate acute and chronic noncancer hazards and cancer risks for exposures to NMHCs, including BTEX, in residential exposure scenarios.[31] California's OEHHA guidance addresses developmental outcomes not fully covered in standard United States Environmental Protection Agency's (USEPA) risk guidance.[32,33] Specifically, OEHHA guidance has incorporated recent research findings on the developmental toxicity of ambient level benzene into their toxicity factors as well as a lifespan beginning in the third trimester of pregnancy into their cancer risk assessment.[31,34,35]

Data Sources. We characterized risks for residential populations based on proximity to the nearest O&G facility, as recorded in the Colorado Oil and Gas Information System.[36] All samples included in this risk assessment were collected at plausible residential locations (i.e., at a distance greater that Colorado's historic 150 foot (46 m) setback distance from the nearest O&G facility) using NMHC measurement results from one of three CNFR studies conducted in the summer of 2014 (Figure 1, Figure 2, Supporting Information):

Study 1: 1-min canister samples (hereafter 1-min samples) and continuous air monitoring (1-s time resolution readings every minute: 60 consecutive minutes averaged to represent 1 h of exposure, hereafter 1-h samples) from the 2014 DISCOVER-AQ (Deriving Information on Surface conditions from Column and VERtically resolved observations relevant to Air Quality) field campaign.[37] The 1-min samples collected during the DISCOVER-AQ study targeted O&G, power generation, agricultural facilities, and high vehicle traffic areas. In situ methane, carbon dioxide, and carbon monoxide measurements were used to identify plume and background locations. In addition to residential plausibility-based setback distances, we

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Environ. Sci. Technol. 2018, 52, 4514−4525

reviewed Google Earth satellite images dated between June 2 and October 6, 2014 to determine if the sample location was appropriate for evaluating residential exposures. On the basis of these reviews, we excluded results from seven 1-min samples that had been collected at locations adjacent to large O&G processing plants or propane tank facilities because these locations were not plausible residential locations (Supporting Information Table S1). The 1-h samples were collected at a fixed site located in a rural area at 229 m from the nearest O&G facility.

Study 2: 72−96-h integrated canister samples (hereafter 72−96-h samples) collected for the 2014 Boulder County air quality monitoring study.[38] All sites were located in residential areas. The site in western Boulder was selected as a reference site (i.e., with minimal O&G development influence) and was located on the grounds of the Boulder County Public Health offices near a busy intersection. Results from this location are subjected to urban and traffic influences and thus provide a representative urban signature. Twelve summa canister samples were collected at the Boulder site. The sites in Eastern Boulder County, along the border between Boulder and Weld County, were selected to assess the geographical gradients of NMHCs resulting from dense O&G development. The Eastern Boulder County sites were public facilities (a school, park, church, and fire station) located in residential areas, and other obvious sources of NMHCs were avoided. A total of 47 summa canister samples were collected from 4 sites in Eastern Boulder County (11−12 samples at each site).

Study 3: 41 3-h integrated canister samples (hereafter 3-h samples) collected by the Colorado Department of Public Health and Environment (CDPHE) at a single site in a residential area of Platteville, CO located 247 m from the nearest O&G facility.[39]

Data Assessment. Field measurement results were grouped by exposure scenario and sample type, as indicated in Figure 2. Because the underlying measurements were not normally distributed, all data were log transformed prior to statistical analysis. We evaluated the remaining measurements from the 1-min samples as well as the 1-h, 3-h, and 72−96-h samples for outliers using Q-Q plots.[39] No results were removed based on the outlier analysis. For results below the limit of detection, we substituted the limit of detection for statistical evaluations and calculations of mean concentrations.[40] Supporting Information Tables S2−S4 contain summary statistics and limits of detection for NMHCs included in the risk assessment.

We used analysis of variance (ANOVA) to compare means of specific NMHC concentrations between the four scenarios described below. We evaluated differences between mean NMHC concentrations with post hoc Tukey's studentized range (HSD) tests. Results were considered statistically different at an α of 0.05. All statistical analyses were conducted using SAS software version 9.3 (Cary, NC).[40]

Exposure Assessment. Acute and chronic exposure estimates were developed for four scenarios based on Colorado regulatory setback distances between O&G wells and residential facilities of 152 m[6] and literature reference points of 1600 m:[5,41]

(1) No O&G facilities within 1600 m.
(2) Nearest O&G facility within 610−1600 m.
(3) Nearest O&G facility within 152 to 610 m.
(4) Nearest O&G facility within 152 m.

The nearest O&G facility from each sample location included well pads, tank batteries, E&P waste disposal sites, gathering lines, and processing facilities.

To estimate acute and chronic noncancer health hazards and cancer risks, we considered short and long-term exposures to NMHCs. For acute exposure, we used the maximum measured concentration of each NMHC from the 1-min samples to estimate the maximum 1-h ambient air concentration for all scenarios and compounds, except for benzene, toluene, and C9 aromatics in the 152−610 m scenario. For the 152−610 m acute scenario, we used maximum 1-h sample results for benzene, toluene, and C9 aromatics that were available only for this scenario. For chronic hazards and cancer risks, time-weighted average (TWA) mean (1-min and 3-h samples) over 24 h and mean (72−96-h samples) ambient NMHC concentrations were used to represent the average concentration and calculate a daily intake dose for each NMHC according to OEHHA Guidance (Supporting Information).[31] We calculated a TWA mean for the 1-min and 3-h samples because these samples were mostly collected in the daytime and do not represent nighttime concentrations. Continuous sampling results at the Platteville location indicate that the average mean benzene concentration from 19:00 in the evening to 7:00 the following morning is 2.34 times higher than between 7:00 and 19:00 h.[15] On the basis of these observations, eq 1 was used to calculate the TWA mean:

$$\text{TWA mean} = \frac{(\text{mean concentration} \times 12\ \text{h} \times 2.34) + (\text{mean concentration} \times 12\ \text{h})}{24\ \text{h}} \quad (1)$$

Toxicity Assessment and Risk Characterization. For noncarcinogens, we expressed inhalation toxicity health-based factors as a reference concentration (RfC) in units of $\mu g/m^3$ (Supporting Information Table S5). We used OEHHA chronic reference exposure levels (REL) to evaluate long-term exposures of 8 or more years (OEHHA 2015).[31] If an OEHHA chronic REL was not available, we used the USEPA's risk screening level (RSL) for ambient air.[42] The OEHHA chronic RELs and EPA chronic RSLs are applicable to 24-h per day exposures over 10 to ≥12% of a 70-year lifespan (i.e., 7 to 8 years of exposure).[31,34,42] We used OEHHA acute RELs to evaluate acute 1-h exposures.[31] If an acute OEHHA REL was not available, we used the ATSDR's acute MRLs.[43] If RELs, RSL, or MRL were not available, RfCs were obtained from (in order of preference) EPA's Integrated Risk Information System (IRIS) subchronic RfCs,[44] EPA's subchronic Provisional Peer-Reviewed Toxicity Values (PPRTV),[45] or Health Effects Assessment Summary Tables.[46] We used surrogate RfCs according to EPA guidance for C_5 to C_8 alkanes and C_9 aromatic hydrocarbons, which do not have a chemical-specific toxicity value.[45] We derived semiquantitative noncancer hazard quotients (HQs), defined as the ratio between the estimated exposure concentration and RfC.[31,32] We summed HQs for specific NMHCs to calculate the HI. We also separated the HQs specific to neurological, respiratory, hematological, and developmental effects and calculated a separate end point-specific HI for each of health effect. HQ's and HI's > 1 indicate that the estimated exposure exceeds the threshold exposure and the possibility of adverse health effects.[32] Because the HI is semiquantitative metric, it does not imply a multiplier. For example, an HI of 4 is not twice the risk of an HI of 2.

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Environ. Sci. Technol. 2018, 52, 4514−4525

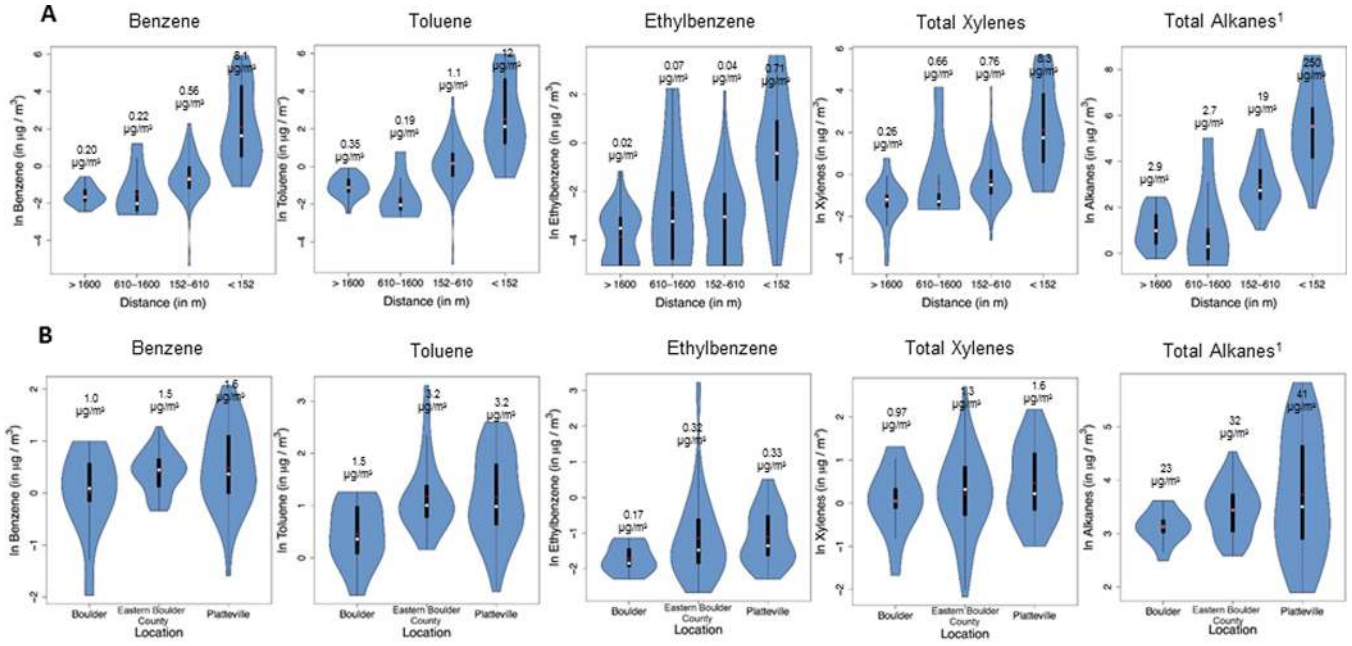

Figure 3. (A) Distributions and means of selected hydrocarbon concentrations from 1-min samples by distance from the nearest oil and gas facility. (B) Distributions and means of selected hydrocarbon concentrations from 3 to 96 h samples by distance from the nearest oil and gas facility.

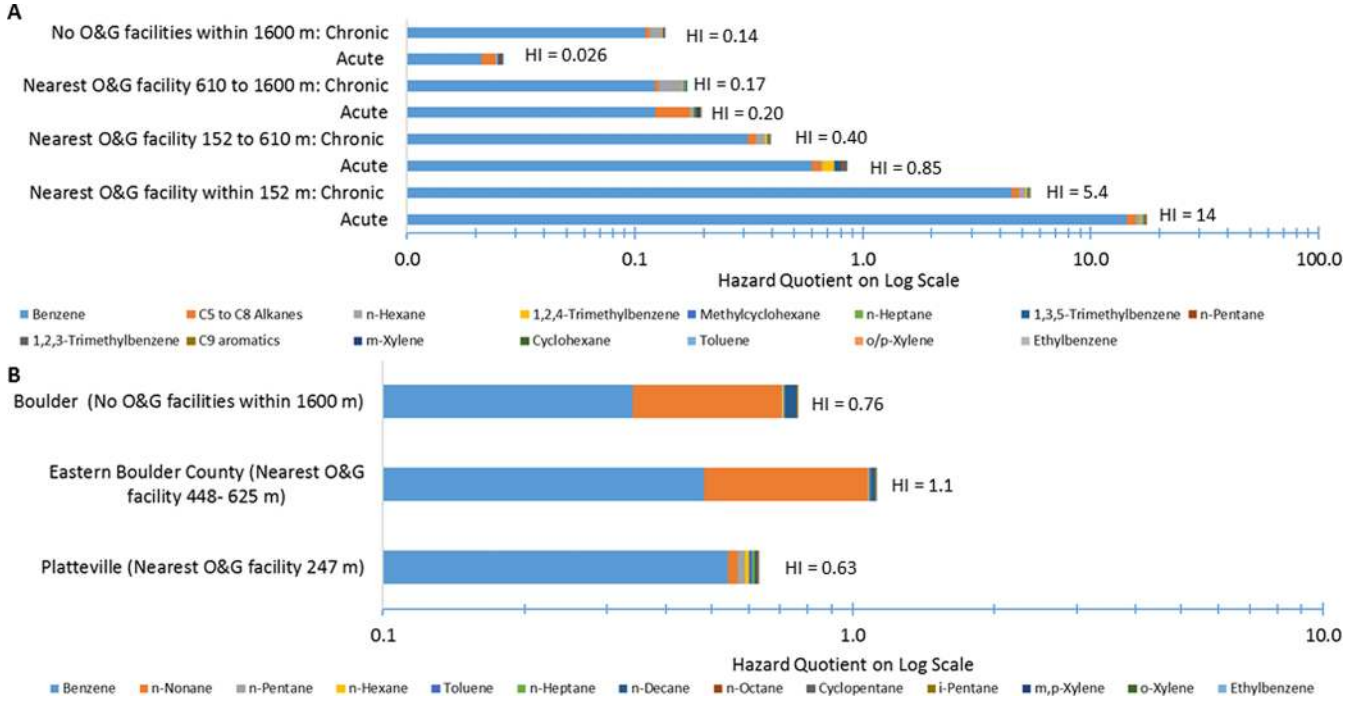

Figure 4. (A) Chronic and acute hazard quotients and hazard indices for residents living >1600, 610−1600, 152−610, and within 152 m from an oil and gas facility based on 1-min and 1-h sample results. (B) Chronic hazard quotients and hazard indices for residents living in Boulder, Eastern Boulder County, and Platteville based on 3-, 72-, and 96-h sample results.

For carcinogens, we expressed inhalation toxicity measurements as OEHHA inhalation cancer potency factors (CPFs) summarized in units of $(mg/kg\text{-}day)^{-1}$.[31] The lifetime excess cancer risk for each carcinogenic NMHC was derived per OEHHA guidance (Supporting Information).[31] We summed individual lifetime excess cancer risks for each NMHC to estimate cumulative lifetime excess risk. Risks are expressed as excess cancers over a lifetime per 1 million population based on exposure over 30 years, per OEHHA guidance,[34] which is consistent with the USEPA reasonable maximum exposure.[32]

To estimate the population cancer risk for residential scenarios of less than 1600 m, we adjusted the cumulative lifetime excess cancer risk by subtracting the risk for populations with no O&G facilities within 1600 m of their home from the risk for populations living in closer proximity to facilities. We derived 2014 population estimates by adjusting the DJB 2012 population estimates at specific distances from

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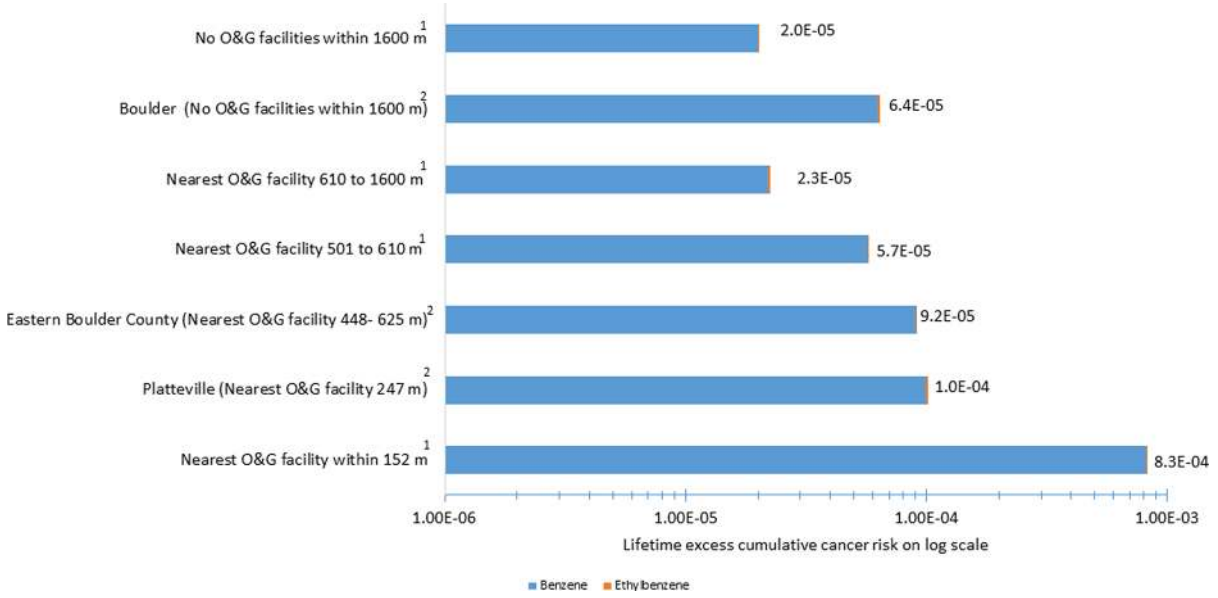

Figure 5. Lifetime excess cancer risks (30 year exposure duration) for residents >1600, 610−1600, 152−610, and within 152 m from an oil and gas facility based on 1-min sample results.

O&G wells for 2 years of population growth based on the average annual rate of growth between 2000 and 2012.[5] We then estimated the population risk for each scenario by multiplying the adjusted cumulative lifetime excess cancer risk by the estimated 2014 population estimate.[31]

RESULTS AND DISCUSSION

For the 1-min samples (Figure 3), mean ambient BTEX and total alkane concentrations increased as the distance of the sample collection from the nearest O&G facility decreased ($p < 0.001$). The mean ambient benzene, toluene, ethylbenzene, total xylene and total alkane concentrations from the 1-min samples collected within 152 m of the nearest O&G facility were 41, 34, 35, 32, and 86 times higher, respectively, than the mean from 1-min samples collected further than 1600 m from the nearest O&G facility ($p < 0.05$, Figure 3). Supporting Information Table S6 presents the ANOVA results comparing selected NMHC mean concentrations as a function of distance to O&G facility.

For the 3-, 72-, and 96-h samples (Figure 3b and Table S6b), the TWA mean concentration from the 3-h samples collected in Platteville (247 m from nearest O&G facility) was compared to the mean concentration from the 72- and 96-h samples collected in Boulder (>1600 m from nearest O&G facility) and Eastern Boulder County (448−625 m from nearest O&G facility). Mean ambient benzene, ethylbenzene, and total xylene concentrations did not vary significantly between locations, although the lowest mean concentrations occurred in samples collected in Boulder. Mean ambient toluene concentrations in Platteville and Eastern Boulder County were twice the mean concentration in Boulder ($p < 0.05$). Mean ambient total alkane concentrations in Platteville were 1.3 and 1.8 times greater than those in Eastern Boulder County and Boulder ($p < 0.05$) (Figure 3b).

Noncancer Hazards. Figure 4a presents acute and chronic noncancer HQ and HI estimates based on maximum 1-min and 1-h sample results, and TWA mean 1-min sample results, respectively (Supporting Information Tables S7). Acute and chronic HQs and HIs increased with decreasing distance to the nearest O&G facility. Acute HIs for nervous system (18), blood system (15), and developmental effects (15) were >1 for residents living within 152 m of an O&G facility, and benzene and alkanes contributed more than 80 and 13%, respectively, to these end point specific HIs. Acute respiratory HIs were <1 for all scenarios. Chronic HIs for blood system (4) and developmental effects (4) were >1 for residents living within 152 m of an O&G facility, and benzene contributed to 84% of the HI (Supporting Information Tables S7). Acute and chronic HIs for all effects were <1 at distances greater than 152 m from O&G facilities.

Figure 4 b presents chronic HQ and HI estimates based on TWA mean 3-h (Platteville) and mean 72−96 h (Boulder and Erie) sample results (Supporting Information Table S8). Total chronic HIs were highest in Eastern Boulder County, where the total HI was 1.1, followed by Boulder, and then Platteville. Nervous system, respiratory system, blood system, and developmental HIs were <1 for all locations.

The chronic HIs based on 72−96-h samples are 2−10 times greater than those reported for residential exposures to NMHC in O&G areas in previous risk assessments[8,26,27] primarily because the OEHHA chronic REL for benzene (3 $\mu g/m^3$) is 10 times less than the USEPA's chronic RfC (30 $\mu g/m^3$). The OEHHA chronic benzene REL[34] considers several studies published after USEPA's 2002 benzene assessment,[47] which found increased efficiency of benzene metabolism at low doses,[48−51] decreased peripheral blood cell counts at low doses (800−1860 $\mu g/m^3$) with no apparent threshold,[52−54] and large population variation in the response of metabolic enzymes involved in benzene activation and detoxification.[55]

Lifetime Excess Cancer Risk Estimates. Figure 5 presents lifetime excess cancer risks based on daily inhalation intake dose estimates calculated from 1-min, 3-h, and 72−96-h sample results (Supporting Information Tables S9 and S10). All cumulative lifetime excess cancer risks exceeded USEPA's de minimus benchmark of 1 in a million[58] with benzene representing more than 95% of the total risk estimate for all scenarios. The cumulative lifetime excess cancer risk increased with decreasing distance to the nearest O&G facility. For

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Environ. Sci. Technol. 2018, 52, 4514−4525

residents living within 152 m of an O&G facility, the risk exceeded the USEPA upper bound risk level of 1 in 10 000[56] with an overall risk of 8.3 per 10 000 (Supporting Information Table S9). The cumulative lifetime excess cancer risk was higher in Eastern Boulder County and Platteville than in Boulder and reached the USEPA's upper bound risk level of 1 in 10 000 in Platteville (nearest O&G facility 247 m) based on the 3-, 72-, and 96-h sample results (Supporting Information Table S10). For similar scenarios, the cumulative lifetime excess cancer risks based on mean 72−96-h sample results are greater than risks based on TWA mean 1-min and 3-h sample results.

These lifetime excess cancer risk estimates are 10−100 times greater than those reported in previous risk assessments in O&G development areas that used USEPA guidance.[8,26,27] This is partly because the OEHHA inhalation benzene CPF (0.1 $(mg/kg\text{-}day)^{-1}$ is 4 times higher than USEPA's benzene slope factor (0.027 $(mg/kg\text{-}day)^{-1}$.[31,44] The OEHHA approach addresses methodological shortcomings in the derivation of USEPA's current slope factor, which was calculated with a linear extrapolation model that assumes excess risk is proportional to the lifetime average exposure, is the same for all ages, and does not explicitly address the impact of episodic exposure peaks.[57] OEHHA's inhalation CPF was calculated using a weighted cumulative exposure/relative risk procedure that assumes with continuous exposure, age-specific cancer incidence continues to increase as a power function of the elapsed time since the initial exposure.[35] Additionally, OEHHA includes prenatal exposures in the calculation of lifetime excess cancer risk based on recent studies indicating increased susceptibility to benzene in early life.[35] Even using USEPA's current slope factor, which would reduce the lifetime excess cancer risk from benzene for residents living within 152 m of an O&G facility to 2.2 in 10 000, our results remain above USEPA's 1 in 10 000 upper bound for remedial action.

Overall Strengths and Limitations. We assessed acute and chronic health risks from air pollution associated with O&G operations using data collected in close proximity to O&G facilities and realistic residential scenarios tied to regulatory setback distances and literature reference points. This approach allowed us to incorporate proximity, spatial variability, and temporally relevant sampling durations into our exposure scenarios. The consistent application of exposure and toxicity parameters for all four scenarios allows for the comparison of hazards and risks between the scenarios. We found increasing (1) hematological and developmental HIs and (2) cumulative lifetime excess cancer risks with decreasing distance to the nearest O&G facility. These results are consistent with findings from observational epidemiological studies that indicate an increased likelihood of adverse birth outcomes and childhood acute lymphocytic leukemia with increasing proximity to O&G wells.[19−21,23,24] The weight of evidence increasingly suggests that plausible outcomes to explore in future epidemiological studies of exposure to O&G-related pollutants include: neural tube defects,[58] changes in blood cell and platelet counts and aberrant nucleic acid methylation patterns,[59−61] and increased levels of 8-hydroxydeoxygunaosine, a biomarker of short-term nucleic acid damage.[62−64]

However, the uncertainties in our risk assessment are substantial, and the results are best suited for scoping policy and future studies. Some of our assumptions are inherent in the risk assessment process (Table 1), while others are more specific to this study. Exposure to benzene had the largest contribution our predicted health risks. While there is extensive evidence that occupational benzene exposure is linked to leukemia, the evidence in nonoccupational populations is less robust. Nonetheless, the body of literature suggesting that exposures to ambient levels of benzene are associated with incidence of childhood leukemia is increasing. Additionally, recent studies that were included in the derivation of the RELs for toluene in this risk assessment suggest that low dose toluene exposure can alter fetal and adult testosterone levels.[65−67] Reductions in testosterone and mRNA 3B-hydroxysteroid dehydrogenase levels were observed in male fetal rats at low toluene exposures.[65] Using the lowest observed adverse effect level of 3400 $\mu g/m^3$ from that study results in chronic and acute toxicity values of approximately 300 and 30 000 times lower, respectively, than current toxicity values, resulting in a corresponding increase of acute and chronic toluene HQs > 1 for the <610 m exposure scenarios.

Table 1. Assumptions Adherent in Risk Assessment Process That Lead to Uncertainty

assumption	description
1	Maximum concentrations from 1-min samples to estimate acute exposure levels.
2	Chronic reference exposure levels and risk screening levels assume 24 h per day exposures, 365 and 350 days per year, respectively, for more than 7 years.
3	Multiple uncertainty factors applied in derivation of the reference concentrations.
4	The lifetime excess cancer risk assumed that residents spend 72−85% of their time at home over a 30 year period.
5	Reference concentrations that were mostly derived from occupational studies on adults or animal toxicity studies may not adequately represent the current understanding of developmental and reproductive effects.

Ideally, chronic HIs and cancer risk are estimated from a large number of air samples that represent 24-h exposure. In the summer of 2014, only the 72- to 96-h samples collected in Boulder and Eastern Boulder County captured full 24-h exposure periods. Because 24-h data was not available to estimate chronic HIs and cancer risks for populations living in close proximity to O&G facilities (i.e., 305 m),[5] we used 3-h and 1-min measurements as they were the best available to estimate 24-h exposures for this scenario. However, the 1-min and 3-h samples were collected mostly during the daytime and do not represent the contribution of what are likely higher nighttime ambient NMHC concentrations,[15] even after the TWA adjustment. This is likely the reason our chronic cumulative HIs and cancer risks based on mean 72−96-h sample results are greater than those based on TWA mean 1-min and 3-h sample results for similar scenarios. This also indicates that the HIs and cancer risks calculated from the 3-h and 1-min samples are likely not overestimated because they are an empirical estimate of local short-term concentrations of these compounds.

Our findings are based on ambient air samples collected in the summer of 2014 that may not capture temporal variations in NMHC concentrations associated with O&G activities. For example, NMHC concentrations likely differ by season and will vary in the future as O&G emission control technology evolves. Existing studies suggest that winter levels of these pollutants are higher because longer nights and cold daytime temperatures keep the atmospheric boundary layer lower than that in summer and thus increase NMHC concentrations near the surface.[12,68]

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Finally, exposure to other air pollutants, drinking water contaminants, and nonchemical stressors (e.g., noise) associated with upstream O&G operations could further contribute to the health risks estimated in this study. For example, alkanes emitted from O&G operations contribute to approximately 20% of summertime photochemical ozone production along the CNFR,[69] and each 10 ppb increase in ozone may result in an 2% increase in mortality.[70] Ozone levels in several CNFR cities exceed National Ambient Air Quality standards.[71]

To better understand health risks from air pollution originating from O&G operations, systematic ongoing sampling of NMHCs (especially BTEX), source tracers, and other air pollutants such as formaldehyde, acetaldehyde, and polycyclic aromatic hydrocarbons[72,73] associated with O&G activities is needed. Future research should focus on providing measured and modeled exposure estimates of key risk drivers (e.g., BTEX) for populations living near O&G operations.[74]

POLICY IMPLICATIONS

Our results indicate that State regulatory setback distances (the minimum distance an O&G wellhead may be located from a home) and reverse setback distances (the minimum distance a home may be located from an O&G wellhead) and related municipal codes may not protect nearby residents from health effects resulting from air pollutants emitted from these facilities. Setback distances between homes and other types of O&G facilities (e.g., tank batteries, waste disposal sites, gathering lines, compressor stations, etc.) have not been specified,[6] and very few municipal codes regulate the siting of homes near existing O&G well sites.[5,75,76] We found that Colorado populations within 152 m of an O&G facility are more likely to experience neurological, hematological, and developmental health effects from acute inhalation exposures to benzene and alkanes. We also estimated cumulative lifetime excess cancer risks for populations living within 610 m of an O&G facility exceed USEPA's upper threshold of 1 in 10 000.

Sources of air pollutants other than O&G facilities (e.g., non O&G related traffic) likely partially contributed to the health risks for all exposure scenarios. Nonetheless, our results indicate that air pollutants from O&G facilities increasingly contribute to the health risks as the distance from the nearest O&G facility decreases. For the more than 380 000 people along the CNFR estimated to be living within 1600 m of an O&G well in 2014, we estimate an additional 17 to 27 cases of cancer over a lifetime (70 years). We estimate that more than 50% of these additional cancers may occur in the population living within 152 m of an O&G facility (Supporting Information Table S11).

Our results could be useful in justifying and further scoping of Colorado regulations on air emissions from O&G facilities. In 2014, the Colorado Air Quality Control Commission fully adopted EPA's Standards of Performance for Crude Oil and Natural Gas Production, Transmission, and Distribution (NSPS OOOO) (40 C.F.R. Part 60, Subpart OOOO) into Colorado Regulation Number 6 and adopted complementary O&G emission control measures in Colorado Regulation Number 7.[77,78] EPA's NSPS OOOO stipulates that hydraulic fracturing and well completion operations begun on or after January 1, 2015 and storage tanks must use control measures to reduce VOC emissions.[77] In 2016, the Colorado Department of Public Health and Environment's Air Pollution Control Division implemented Regulation 7, which requires O&G operators to find and repair leaks and install devices to capture at least 95% of VOC emissions from new and existing wells, storage tanks, compressor stations, and glycol dehydrators.[78] Colorado's revised Regulations 6 and 7 aim to reduce ozone precursor and methane emissions from larger and newer O&G facilities and could eliminate 93 500 tons of VOCs per year.[78] Our results provide further justification for implementation of these regulations because such regulations could also reduce emissions of hazardous air pollutants such as benzene that drive our risk estimates.

However, our risk results include both older and smaller O&G facilities, and other studies indicate that older and smaller O&G facilities could emit significant levels of air pollutants that are important contributors to health risk. Because Colorado Regulations 6 and 7 are less stringent for older wells, controls on small emitters (<6 tons VOCs per year), and temporary frac tanks,[78] they may not be sufficiently protective for residents living near these facilities. The NSPS OOOO is applicable only to wells built or modified starting in 2015; the current United States administration is seeking delay of implementation, and the O&G industry is challenging the federal regulation in court.[77,79] A study in the Marcellus shale found that older well sites generally had much high production normalized methane emission rates than newer multiwell sites because of a range of issues, including a lack of maintenance.[80] Small emitters outside the nonattainment area for zone are required under Regulation 7 to conduct monthly audio, visual, and olfactory (AVO) inspections, and they are currently required to conduct only one inspection with an approved instrument monitoring method (e.g., an infrared [IR]camera capable of detecting hydrocarbon and VOC emissions) over the lifetime of the facility.[81] Additionally, the regulations exempt storage tanks from emission inspections and small emitters from emission's management plans.[81] A recent analysis conducted with an infrared camera in Boulder County, CO detected gas leaks at 65% of 145 inspected O&G sites, most of which were small emitters developed prior to 2011. Ninety-two percent of the detected gas leaks were at storage tanks, separators, or wellheads, and at least 31% involved pneumatic devices or equipment associated with them.[82] Several studies have implicated storage tanks, thief hatches, and pneumatic devices as major sources of VOC emissions from O&G facilities.[12,15,83−85] The Boulder County analysis found that only 2.5% of AVO inspections identified a gas leak, compared to 66% of inspections using an IR camera, indicating that in this program monthly AVO inspections are not effective in detecting VOC emissions from leaking equipment.[82] Intermittent and continuous bleed pneumatic devices may be a significant source of emissions even when operating properly.[86] Zero-bleed pneumatic devices could also significantly reduce emissions.[86] Ultimately, this means that the large number of old, low producing, and insufficiently inspected O&G operations could be a significant source of air pollutant emissions and related health risks.

While the magnitude of air pollutant emissions may vary by region, these results also have implications for policies in other O&G regions where homes are located near O&G facilities[75,76] and NMHCs have been measured. Studies in regions of dense O&G development in the Uintah basin, Marcellus Shale, Barnett Shale, and Eagle Ford Shale have documented elevated levels of NMHCs[11,27,87,88] as well as increased risks for several adverse health effects.[21−25] Risk assessments using air sampling results specific to these regions could be useful for informing

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policies aimed at reducing health risks associated with O&G facilities for nearby populations.

This study provides further evidence that populations living nearest to O&G facilities bear the greatest risk of acute and chronic health risk from exposures to NMHC air pollutants emitted from upstream O&G facilities. Therefore, this analysis supports and highlights the importance of policies aimed at reducing or eliminating air emissions from O&G equipment and facilities, particularly those near homes, and effective monitoring of emissions from these facilities.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.7b05983.

Details on sample collection and analysis, OEHHA Dose and Risk Equations for carcinogens, and tables including descriptive statistics and risk assessments (PDF)

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Notes

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■ REFERENCES

(1) Allshouse, W. B.; Adgate, J. L.; Blair, B. D.; McKenzie, L. M. Spatiotemporal Industrial Activity Model for Estimating the Intensity of Oil and Gas Operations in Colorado. *Environ. Sci. Technol.* **2017**, *51* (17), 10243−10250.

(2) Thout, K. On the Launch Pad: The Rise of Pad Drilling. *Drillinginfo* **2014**, 1.

(3) Manda, A. K.; Heath, J. L.; Klein, W. A.; Griffin, M. T.; Montz, B. E. Evolution of multi-well pad development and influence of well pads on environmental violations and wastewater volumes in the Marcellus shale (USA). *J. Environ. Manage.* **2014**, *142*, 36−45.

(4) Adgate, J. L.; Goldstein, B. D.; McKenzie, L. M. Potential Public Health Hazards, Exposures and Health Effects from Unconventional Natural Gas Development. *Environ. Sci. Technol.* **2014**, *48* (15), 8307−8320.

(5) McKenzie, L. M.; Allshouse, W. B.; Burke, T.; Blair, B. D.; Adgate, J. L. Population Size, Growth, and Environmental Justice Near Oil and Gas Wells in Colorado. *Environ. Sci. Technol.* **2016**, *50* (21), 11471−11480.

(6) Colorado Oil and Gas Conservation Commission. Rules and Regulations. Denver, CO, 2015; http://cogcc.state.co.us/reg.html#/rules.

(7) Colorado Oil and Gas Conservation Commission, Statement of Basis, Specific Statutory Authority, and Purpose, New Rules and Amendments to Current Rules of the Colorado Oil and Gas Conservation Commission, 2 CCR 404−1. In *2 CCR Commission*; COGCC: 2013; http://cogcc.state.co.us/reg.html#/rules.

(8) McKenzie, L. M.; Witter, R. Z.; Newman, L. S.; Adgate, J. L. Human Health Risk Assessment of Air Emissions from Development of Unconventional Natural Gas Resources. *Sci. Total Environ.* **2012**, *424*, 79−87.

(9) Collett, J. L.; Arsineh, H. *North Front Range Oil and Gas Air Pollutant Emission and Dispersion Study*; Colorado State University: Fort Collins, CO, 2016.

(10) Collett, J. L.; Pierce, J.; Arsineh, H.; Clements, A.; Shonkwiler, K.; Yong, Z.; Desyaterik, Y.; MacDonald, L.; Wells, B., Hilliard, N.; Tigges, M.; Bibeau, B.; Kirk, C. *Characterizing Emissions from Natural Gas Drilling and Well Completion Operations in Garfield County, CO*; Colorado State University: Fort Collins, CO, 2016.

(11) Helmig, D.; Thompson, C.; Evans, J.; Park, J.-H. Highly Elevated Atmospheric Levels of Volatile Organic Compounds in the Uintah Basin, Utah. *Environ. Sci. Technol.* **2014**, *48*, 4707−4715.

(12) Pétron, G.; Frost, G.; Miller, B. R.; Hirsch, A. I.; Montzka, S. A.; Karion, A.; Trainer, M.; Sweeney, C.; Andrews, A. E.; Miller, L.; Kofler, J.; Bar-Ilan, A.; Dlugokencky, E. J.; Patrick, L.; Moore, C. T.; Ryerson, T. B.; Siso, C.; Kolodzey, W.; Lang, P. M.; Conway, T.; Novelli, P.; Masarie, K.; Hall, B.; Guenther, D.; Kitzis, D.; Miller, J.; Welsh, D.; Wolfe, D.; Neff, W.; Tans, P. Hydrocarbon emissions characterization in the Colorado Front Range: A pilot study. *Journal of Geophysical Research: Atmospheres* **2012**, *117* (D4), D04304.

(13) Pétron, G.; Karion, A.; Sweeney, C.; Miller, B. R.; Montzka, S. A.; Frost, G. J.; Trainer, M.; Tans, P.; Andrews, A.; Kofler, J.; Helmig, D.; Guenther, D.; Dlugokencky, E.; Lang, P.; Newberger, T.; Wolter, S.; Hall, B.; Novelli, P.; Brewer, A.; Conley, S.; Hardesty, M.; Banta, R.; White, A.; Noone, D.; Wolfe, D.; Schnell, R. A new look at methane and nonmethane hydrocarbon emissions from oil and natural gas operations in the Colorado Denver-Julesburg Basin. *Journal of Geophysical Research: Atmospheres* **2014**, *119* (11), 6836.

(14) Gilman, J. B.; Lerner, B. M.; Kuster, W. C.; de Gouw, J. A. Source Signature of Volatile Organic Compounds from Oil and Natural Gas Operations in Northeastern Colorado. *Environ. Sci. Technol.* **2013**, *47* (3), 1297−1305.

(15) Halliday, H. S.; Thompson, A. M.; Wisthaler, A.; Blake, D.; Hornbrook, R. S.; Mikoviny, T.; Müller, M.; Eichler, P.; Apel, E. C.; Hills, A. J. Atmospheric benzene observations from oil and gas production in the Denver Julesburg basin in July and August 2014. *Journal of Geophysical Research: Atmospheres* **2016**, *121* (18), 11055−11074.

(16) Thompson, C. R.; Hueber, J.; Helmig, D. Influence of oil and gas emissions on ambient atmospheric non-methane hydrocarbons in residential areas of Northeastern Colorado. *Elem. Sci. Anth.* **2014**, *2* (1), 000035.

(17) Swarthout, R. F.; Russo, R. S.; Zhou, Y.; Hart, A. H.; Sive, B. C. Volatile organic compound distributions during the NACHTT campaign at the Boulder Atmospheric Observatory: Influence of urban and natural gas sources. *Journal of Geophysical Research: Atmospheres* **2013**, *118* (18), 10614−10637.

(18) United States Environmental Protection Agency. List of Hazardous Air Pollutants, Petition Process, Lesser Quantity

Designations, Source Category List. In *40 CFR 63 Federal Registar*; 2005; pp 75047−75059.
(19) McKenzie, L. M.; Allshouse, W. B.; Byers, T. E.; Bedrick, E. J.; Serdar, B.; Adgate, J. L. Childhood hematologic cancer and residential proximity to oil and gas development. *PLoS One* **2017**, *12* (2), e0170423.
(20) McKenzie, L. M.; Guo, R.; Witter, R. Z.; Savitz, D. A.; Newman, L. S.; Adgate, J. L. Birth outcomes and maternal residential proximity to natural gas development in rural Colorado. *Environ. Health Perspect* **2014**, *122*, 412−417.
(21) Whitworth, K. W.; Marshall, A. K.; Symanski, E. Maternal residential proximity to unconventional gas development and perinatal outcomes among a diverse urban population in Texas. *PLoS One* **2017**, *12* (7), e0180966.
(22) Rasmussen, S. G.; Ogburn, E. L.; McCormack, M.; Casey, J. A.; Bandeen-Roche, K.; Mercer, D. G.; Schwartz, B. S. ASsociation between unconventional natural gas development in the marcellus shale and asthma exacerbations. *JAMA Internal Medicine* **2016**, *176* (9), 1334−43.
(23) Stacy, S.; Brink, L.; Larkin, J.; Sadovsky, Y.; Goldstein, B.; Pitt, B.; Talbott, E. Perinatal Outcomes and Unconventional Natural Gas Operations in Southwest Pennsylvania. *PLoS One* **2015**, *10* (6), e0126425.
(24) Casey, J. A.; Savitz, D. A.; Rasmussen, S. G.; Ogburn, E. L.; Pollak, J.; Mercer, D. G.; Schwartz, B. S. Unconventional natural gas development and birth outcomes in Pennsylvania, USA. *Epidemiology (Cambridge, Mass.)* **2016**, *27* (2), 163.
(25) Tustin, A. W.; Hirsch, A. G.; Rasmussen, S. G.; Casey, J. A.; Bandeen-Roche, K.; Schwartz, B. S. Associations between Unconventional Natural Gas Development and Nasal and Sinus, Migraine Headache, and Fatigue Symptoms in Pennsylvania. *Environ. Health Perspect* **2017**, *125* (2), 189−197.
(26) Bunch, A. G.; Perry, C. S.; Abraham, L.; Wikoff, D. S.; Tachovsky, J. A.; Hixon, J. G.; Urban, J. D.; Harris, M. A.; Haws, L. C. Evaluation of impact of shale gas operations in the Barnett Shale region on volatile organic compounds in air and potential human health risks. *Sci. Total Environ.* **2014**, *468*, 832−842.
(27) Swarthout, R. F.; Russo, R. S.; Zhou, Y.; Miller, B. M.; Mitchell, B.; Horsman, E.; Lipsky, E.; McCabe, D. C.; Baum, E.; Sive, B. C. Impact of Marcellus Shale Natural Gas Development in Southwest Pennsylvania on Volatile Organic Compound Emissions and Regional Air Quality. *Environ. Sci. Technol.* **2015**, *49* (5), 3175−3184.
(28) Howlader, N.; Noone, A. M.; Krapcho, M.; Miller, D.; Bishop, K.; Kosary, C. L.; Yu, M.; Ruhl, J.; Tatalovich, Z.; Mariotto, A.; Lewis, D. R.; Chen, H. S.; Feuer, E. J.; KA, C. *SEER Cancer Statistics Review, 1975−2014*; National Cancer Institute: Bethesda, MD, 2017.
(29) Colorado Department of Public Health and Environment. *Garfield County Air Toxics Inhalation Screening Level Human Health Risk Assessment: Inhalation of Volatile Organic Compounds Measured in Rural, Urban, and Oil & Gas Areas in Air Monitoring Study (June 2005−May 2007)*; Disease Control and Environmental Epidemiology Division: Rifle, CO, 2007.
(30) Colorado Department of Public Health and Environment. *Air Emissions Case Study Related to Oil and Gas Development in Erie, Colorado*; Air Pollution Control Division: Rifle, CO, 2012.
(31) California Office of Health Hazard Assessement (OEHHA). Risk Assessment Guidelines. In *Air Toxics Hot Spots Program*; California Environmental Protection Agency: Sacramento, CA, 2015.
(32) U.S. Environmental Protection Agency. *Risk assessment guidance for superfund (Part A)*; Office of Emergency and Remedial Response, U.S. Environmental Protection Agency: Washington, DC, 1989; Vol. *1*.
(33) U.S. Environmental Protection Agency. *A Framework for Assessing Health Risks of Environmental Health Risks of Environmental Exposures to Children*; United States Environmental Protection Agency: Washington, DC, 2006.
(34) California Office of Health Hazard Assessement (OEHHA). *Technical Support Document for the Derivation of Noncancer Reference Exposure Levels Appendix D 2014 Update*; California Environmental Protection Agency: Oakland, CA, 2008.
(35) California Office of Health Hazard Assessement (OEHHA). *Technical Support Document for Cancer Potency Factors; Methodologies for Derivation, Listing of Available Values, and Adjustments to Allow for Early Life Stage Exposures*; California Environmental Protection Agency: Oakland, CA, 2009.
(36) Colorado Oil and Gas Information System on-line Database. Colorado Oil and Gas Conservation Commission, Colorado Department of Natural Resources. http://cogcc.state.co.us/data.html#/cogis (accessed March 12, 2018).
(37) National Aeronautics and Space Administration (NASA). Discover-AQ, Colorado 2014. http://www-air.larc.nasa.gov/missions/discover-aq/discover-aq.html (accessed April 2, 2016).
(38) Helmig, D.; Hannigan, M.; Milford, J.; Gordon, J. *Final Report-Boulder County Oil and Gas Development Air Quality Study*; University of Colorado: Denver, CO, 2015.
(39) Colorado Department of Public Health and Environment Air Quality Control Division Technical Services Program. http://apcd.state.co.us/about_us.aspx. (Accessed April 2, 2016).
(40) U.S. Environmental Protection Agency. *ProUCL Version 4.00.05 Technical Guide Statistical Software for Environmental Applications for Data Sets with and without Nondetect Observations*; Office of Research and Development: Washington, DC, 2010.
(41) Czolowski, E. D.; Santoro, R. L.; Srebotnjak, T.; Shonkoff, S. B. Toward Consistent Methodology to Quantify Populations in Proximity to Oil and Gas Development: A National Spatial Analysis and Review. *Environ. Health Perspect.* **2017**, *125* (8), 086004−1−11.
(42) United States Environmental Protection Agency. Risk-Based Screening Table, 2017. https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables-november-2017. (Accessed April 2, 2016).
(43) ATSDR Minimum Risk Levels. https://www.atsdr.cdc.gov/mrls/index.asp (accessed October 6, 2017).
(44) United States Environmental Protection Agency. Integrated Risk Information System. https://www.epa.gov/iris. (Accessed March 2, 2018).
(45) United States Environmental Protection Agency. *Provisional Peer Reviewed Toxicity Values for Complex Mixtures of Aliphatic and Aromatic Hydrocarbons*; United States Environmental Protection Agency: Cincinnati, OH, 2009.
(46) United States Environmental Protection Agency. *Health Effects Assessment Summary Tables*; United States Environmental Protection Agency: Washington, DC, 1997.
(47) United States Environmental Protection Agency. *Toxicological Review of Benzene (Noncancer Effects)*; United States Environmental Protection Agency: Washington, DC, 2002.
(48) Kim, S.; Vermeulen, R.; Waidyanatha, S.; Johnson, B. A.; Lan, Q.; Rothman, N.; Smith, M. T.; Zhang, L.; Li, G.; Shen, M.; Yin, S.; Rappaport, S. M. Using urinary biomarkers to elucidate dose-related patterns of human benzene metabolism. *Carcinogenesis* **2006**, *27* (4), 772−781.
(49) Kim, S.; Vermeulen, R.; Waidyanatha, S.; Johnson, B. A.; Lan, Q.; Smith, M. T.; Zhang, L.; Li, G.; Shen, M.; Yin, S.; Rothman, N.; Rappaport, S. M. Modeling Human Metabolism of Benzene Following Occupational and Environmental Exposures. *Cancer Epidemiol., Biomarkers Prev.* **2006**, *15* (11), 2246−2252.
(50) Rappaport, S. M.; Kim, S.; Lan, Q.; Li, G.; Vermeulen, R.; Waidyanatha, S.; Zhang, L.; Yin, S.; Smith, M. T.; Rothman, N. Human benzene metabolism following occupational and environmental exposures. *Chem.-Biol. Interact.* **2010**, *184* (1−2), 189−195.
(51) Rappaport, S. M.; Kim, S.; Lan, Q.; Vermeulen, R.; Waidyanatha, S.; Zhang, L.; Li, G.; Yin, S.; Hayes, R. B.; Rothman, N.; Smith, M. T. Evidence That Humans Metabolize Benzene via Two Pathways. *Environ. Health Perspect.* **2009**, *117* (6), 946−952.
(52) Lan, Q.; Zhang, L.; Li, G.; Vermeulen, R.; Weinberg, R. S.; Dosemeci, M.; Rappaport, S. M.; Shen, M.; Alter, B. P.; Wu, Y.; Kopp, W.; Waidyanatha, S.; Rabkin, C.; Guo, W.; Chanock, S.; Hayes, R. B.; Linet, M.; Kim, S.; Yin, S.; Rothman, N.; Smith, M. T. Hematotoxicity

DOI: 10.1021/acs.est.7b05983
Environ. Sci. Technol. 2018, 52, 4514−4525

in Workers Exposed to Low Levels of Benzene. *Science* **2004**, *306* (5702), 1774−1776.
(53) Qu, Q.; Shore, R.; Li, G.; Jin, X.; Chi Chen, L.; Cohen, B.; Melikian, A. A.; Eastmond, D.; Rappaport, S. M.; Yin, S.; Li, H.; Waidyanatha, S.; Li, Y.; Mu, R.; Zhang, X.; Li, K. Hematological changes among Chinese workers with a broad range of benzene exposures. *Am. J. Ind. Med.* **2002**, *42* (4), 275−285.
(54) Khuder, S. A. Assessment of Complete Blood Count Variations Among Workers Exposed to Low Levels of Benzene. *J. Occup. Environ. Med.* **2000**, *42* (2), 113.
(55) Chen, Y.; Li, G.; Yin, S.; Xu, J.; Ji, Z.; Xiu, X.; Liu, L.; Ma, D. Genetic polymorphisms involved in toxicant-metabolizing enzymes and the risk of chronic benzene poisoning in Chinese occupationally exposed populations. *Xenobiotica* **2007**, *37* (1), 103−112.
(56) United States Environmental Protection Agency. *Understanding Superfund Risk Assessment*, 9285.7-06FS; United States Environmental Protection Agency Office of Emergency and Remedial Response: Washington, DC, 1992.
(57) United States Environmental Protection Agency. *Carcinogenic Effects of Benzene: An Update*; United States Environmental Protection Agency: Washington, DC, 1998.
(58) Lupo, P.; Symanski, E.; Waller, D.; Chan, W.; Langlois, P.; Canfield, M.; Mitchell, L. Maternal Exposure to Ambient Levels of Benzene and Neural Tube Defects among Offspring, Texas 1999−2004. *Environ. Health Perspect.* **2010**, *119* (3), 397−402.
(59) D'Andrea, M. A.; Reddy, G. K. Adverse Health Effects of Benzene Exposure Among Children Following a Flaring Incident at the British Petroleum Refinery in Texas City. *Clin. Pediatr.* **2016**, *55* (3), 219−227.
(60) Bollati, V.; Baccarelli, A.; Hou, L.; Bonzini, M.; Fustinoni, S.; Cavallo, D.; Byun, H.-M.; Jiang, J.; Marinelli, B.; Pesatori, A. C.; Bertazzi, P. A.; Yang, A. S. Changes in DNA Methylation Patterns in Subjects Exposed to Low-Dose Benzene. *Cancer Res.* **2007**, *67* (3), 876−880.
(61) Smith, M. T. Advances in Understanding Benzene Health Effects and Susceptibility. *Annu. Rev. Public Health* **2010**, *31*, 133−148.
(62) Li, J.; Lu, S.; Liu, G.; Zhou, Y.; Lv, Y.; She, J.; Fan, R. Co-exposure to polycyclic aromatic hydrocarbons, benzene and toluene and their dose−effects on oxidative stress damage in kindergarten-aged children in Guangzhou, China. *Sci. Total Environ.* **2015**, *524*−*525*, 74−80.
(63) Franken, C.; Koppen, G.; Lambrechts, N.; Govarts, E.; Bruckers, L.; Den Hond, E.; Loots, I.; Nelen, V.; Sioen, I.; Nawrot, T. S.; Baeyens, W.; Van Larebeke, N.; Boonen, F.; Ooms, D.; Wevers, M.; Jacobs, G.; Covaci, A.; Schettgen, T.; Schoeters, G. Environmental exposure to human carcinogens in teenagers and the association with DNA damage. *Environ. Res.* **2017**, *152*, 165−174.
(64) Andreoli, R.; Manini, P.; Palma, G. D.; Alinovi, R.; Goldoni, M.; Niessen, W. M. A.; Mutti, A. Quantitative determination of urinary 8-oxo-7,8-dihydro-2′-deoxyguanosine, 8-oxo-7,8-dihydroguanine, 8-oxo-7,8-dihydroguanosine, and their non-oxidized forms: daily concentration profile in healthy volunteers. *Biomarkers* **2010**, *15* (3), 221−231.
(65) Tsukahara, S.; Nakajima, D.; Kuroda, Y.; Hojo, R.; Kageyama, S.; Fujimaki, H. Effects of maternal toluene exposure on testosterone levels in fetal rats. *Toxicol. Lett.* **2009**, *185* (2), 79−84.
(66) Kilcoyne, K. R.; Smith, L. B.; Atanassova, N.; Macpherson, S.; McKinnell, C.; van den Driesche, S.; Jobling, M. S.; Chambers, T. J. G.; De Gendt, K.; Verhoeven, G.; O'Hara, L.; Platts, S.; Renato de Franca, L.; Lara, N. L. M.; Anderson, R. A.; Sharpe, R. M. Fetal programming of adult Leydig cell function by androgenic effects on stem/progenitor cells. *Proc. Natl. Acad. Sci. U. S. A.* **2014**, *111* (18), E1924−E1932.
(67) Le Cornet, C.; Fervers, B.; Pukkala, E.; Tynes, T.; Feychting, M.; Hansen, J.; Togawa, K.; Nordby, K. C.; Oksbjerg Dalton, S.; Uuksulainen, S.; Wiebert, P.; Woldbaek, T.; Skakkebaek, N. E.; Olsson, A.; Schuz, J. Parental Occupational Exposure to Organic Solvents and Testicular Germ Cell Tumors in their Offspring: NORD-TEST Study. *Environ. Health Perspect.* **2017**, *125* (6), 067023.
(68) Seidel, D. J.; Zhang, Y.; Beljaars, A.; Golaz, J.-C.; Jacobson, A. R.; Medeiros, B. Climatology of the planetary boundary layer over the continental United States and Europe. *Journal of Geophysical Research: Atmospheres* **2012**, *117* (D17), D17106.
(69) Edwards, P.; McDuffie, E. E.; Gilman, J. B.; Lerner, B.; Dubé, W. P.; Trainer, M.; Wolfe, D. E.; deGouw, J.; Williams, E. J.; Tevlin, A. G. Influence of Oil and Gas Emissions on Summertime Ozone in the Colorado Northern Front Range. *Journal of Geophysical Research* **2016**, *121*, 8712−8729.
(70) Turner, M. C.; Jerrett, M.; Pope, C. A.; Krewski, D.; Gapstur, S. M.; Diver, W. R.; Beckerman, B. S.; Marshall, J. D.; Su, J.; Crouse, D. L.; Burnett, R. T. Long-Term Ozone Exposure and Mortality in a Large Prospective Study. *Am. J. Respir. Crit. Care Med.* **2016**, *193* (10), 1134−1142.
(71) Ramboll Environ, A. G. *Denver Metro/North Front Range 2017 8- hour Ozone State Implementation Plan: 2017 Attainment Demonstration Modeling Final Report*, 06-35902E1; Regional Air Quality Council: Denver, CO, 2017.
(72) Macey, G. P.; Breech, R.; Chernaik, M.; Cox, C.; Larson, D.; Thomas, D.; Carpenter, D. O. Air Concentrations of Volatile Compounds near Oil and Gas Production: A Community-based Exploartory Study. *Environmental Health* **2014**, *13*, 1 DOI: 10.2139/ssrn.2516589.
(73) Elliott, E. G.; Trinh, P.; Ma, X.; Leaderer, B. P.; Ward, M. H.; Deziel, N. C. Unconventional oil and gas development and risk of childhood leukemia: Assessing the evidence. *Sci. Total Environ.* **2017**, *576*, 138−147.
(74) Health Effects Institute. *Strategic Research Agenda on the Potential Impacts of 21st Century Oil and Natural Gas Development in the Appalachian Region and Beyond*; Boston, MA, 2015.
(75) Fry, M.; Brannstrom, C.; Sakinejad, M. Suburbanization and shale gas wells: Patterns, planning perspectives, and reverse setback policies. *Landscape and Urban Planning* **2017**, *168*, 9−21.
(76) Brasier, K.; Chandler, R.; Glenna, L.; Hesse, A.; Kelsey, T.; Monnat, S.; Perchinski, J.; Schaaft, K.; Suchyta, M. *The Marcellus Shale Impacts Study Wave 2: Chronicaling Social and Economic Change in Northern and Southwestern Pennsylvania*; The Center for Rural Pennsylvania, Pennsylvania General Assembly: Harrisburg, PA, 2017.
(77) U.S. Environmental Protection Agency, Oil and Natural Gas Sector. *New Source Performance Standards and National Emission Standards for Hazardous Air Pollutants*; United States Environmental Protection Agency: Washington, DC, 2012.
(78) Colorado Department of Public Health and Environment. *Revisions to Colorado Air Quality Control Commission's Regulation Numbers 3, 6, and 7 Fact Sheet*; Colorado Department of Public Health and Environment: Denver, CO, 2014.
(79) U.S. EPA Controlling Air Pollution for the Oil and Natural Gas Industry. https://www.epa.gov/controlling-air-pollution-oil-and-natural-gas-industry (accessed October 6, 2017).
(80) Omara, M.; Sullivan, M. R.; Li, X.; Subramanian, R.; Robinson, A. L.; Presto, A. A. Methane Emissions from Conventional and Unconventional Natural Gas Production Sites in the Marcellus Shale Basin. *Environ. Sci. Technol.* **2016**, *50* (4), 2099−2107.
(81) Colorado Air Quality Control Commission. *Regulation Number 7, Code of Colorado Regulations*; Colorado Secretary of State: 2014; Vol. 7.
(82) Armstrong, K. J. *Leak Inspection and Repair at Oil and Gas Well Sites Boulder County Voluntary Inspection Program Results 2014−2016*; Boulder County Public Health- Environmental Health Division: Boulder, CO, 2017.
(83) Allen, D. T.; Pacsi, A. P.; Sullivan, D. W.; Zavala-Araiza, D.; Harrison, M.; Keen, K.; Fraser, M. P.; Daniel Hill, A.; Sawyer, R. F.; Seinfeld, J. H. Methane Emissions from Process Equipment at Natural Gas Production Sites in the United States: Pneumatic Controllers. *Environ. Sci. Technol.* **2015**, *49* (1), 633−640.
(84) Eastern Research Group, City of Fort Worth. *Natural Gas Air Quality Study*; Forth Worth, TX, 2011.
(85) Harrison, R.; Retzer, K.; Kosnett, M. J.; al, e. Sudden Deaths Among Oil and Gas Extraction Workers Resulting from Oxygen

DOI: 10.1021/acs.est.7b05983
Environ. Sci. Technol. 2018, 52, 4514−4525

Deficiency and Inhalation of Hydrocarbon Gases and Vapors — United States, January 2010−March 2015. *MMWR Morb Mortal Wkly Rep* **2016**, *65*, 6−9.
(86) Saunier, S.; Darani, H.; Pederstad, A. *Zero emission controllers in the USA*, version 2.0; Carbon Limits AS: Oslo Norway, 2016.
(87) Zielinska, B.; Campbell, D.; Samburova, V. Impact of Emissions from Natural Gas Production Facilities on Ambient Air Quality in the Barnett Shale Area: a Pilot Study. *J. Air Waste Manage. Assoc.* **2014**, *64* (12), 1369−1383.
(88) Olaguer, E. P. The potential near-source ozone impacts of upstream oil and gas industry emissions. *J. Air Waste Manage. Assoc.* **2012**, *62* (8), 966−977.

DOI: 10.1021/acs.est.7b05983
Environ. Sci. Technol. 2018, 52, 4514−4525