



Unconventional natural gas development and pediatric asthma hospitalizations in Pennsylvania

Mary D. Willis^a, Todd A. Jusko^{b,c}, Jill S. Halterman^d, Elaine L. Hill^{a,b,*}

^a School of Biological and Population Health Sciences, College of Public Health and Human Sciences, Oregon State University, Corvallis, OR, USA

^b Department of Public Health Sciences, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

^c Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

^d Department of Pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

ARTICLE INFO

Keywords:

Pediatric asthma
Air pollution
Unconventional natural gas development
Environmental health
Industrial emissions

ABSTRACT

Background: Pediatric asthma is a common chronic condition that can be exacerbated by environmental exposures, and unconventional natural gas development (UNGD) has been associated with decreased community air quality. This study aims to quantify the association between UNGD and pediatric asthma hospitalizations.

Methods: We compare pediatric asthma hospitalizations among zip codes with and without exposure to UNGD between 2003 and 2014 using a difference-in-differences panel analysis. Our UNGD exposure metrics include cumulative and contemporaneous drilling as well as reported air emissions by site.

Results: We observed consistently elevated odds of hospitalizations in the top tertile of pediatric patients exposed to unconventional drilling compared with their unexposed peers. During the same quarter a well was drilled, we find a 25% increase (95% CI: 1.07, 1.47) in the odds of being hospitalized for asthma. Ever-establishment of an UNGD well within a zip code was associated with a 1.19 (95% CI: 1.04, 1.36) increased odds of a pediatric asthma hospitalization. Our results further demonstrate that increasing specific air emissions from UNGD sites are associated with increased risks of pediatric asthma hospitalizations (e.g. 2,2,4-trimethylpentane, formaldehyde, x-hexane). These results hold across multiple age groups and sensitivity analyses.

Conclusions: Community-level UNGD exposure metrics were associated with increased odds of pediatric asthma-related hospitalization among young children and adolescents. This study provides evidence that additional regulations may be necessary to protect children's respiratory health from UNGD activities.

1. Background

Unconventional natural gas development (UNGD) industry has exponentially grown throughout the United States (US) to accommodate growing domestic energy requirements, increasing from under 26,000 drilling sites in 2000 to over 300,000 drilling sites in 2015 (U.S. Energy Information Administration, 2017b). Recent estimates indicate that 17.6 million Americans now live within one mile of an active drilling site, which includes UNGD, thus there is a clear need to ascertain the children's health effects of living in a community with UNGD emissions (Czolowski et al., 2017).

Drilling for fossil fuel resources can be categorized in two ways: conventional (CONGD) and unconventional (UNGD) (U.S. Energy Information Administration, 2017a). CONGD involves drilling

vertically to pump natural gas out of a pocket found within geological formations. However, natural gas can sometimes be trapped within layers of shale, necessitating UNGD techniques such as hydraulic fracturing with high volumes of high pressure fluids and horizontal drilling parallel to the surface to extract natural gas. This new advance in UNGD technology has allowed communities with no previous drilling activity to be inundated by the industry. UNGD technology enabled increased shale gas production worldwide in countries such as the United States, Canada, China, Argentina, Algeria, and Mexico (U.S. Energy Information Administration (EIA), 2016). Within the United States, one of the most productive geological formations is the Marcellus Shale in rural Pennsylvania, yielding about 18% of total domestic natural gas production (U.S. Energy Information Administration, 2017a).

Throughout UNGD processes, numerous toxic air pollutants are

Abbreviations: UNGD, unconventional natural gas development; CONGD, conventional natural gas development; US, United States; PHC4, Pennsylvania Healthcare Cost Containment Council; NATA, National Air Toxics Assessment; RHI, respiratory hazard index

* Corresponding author at: Department of Public Health Sciences, University of Rochester School of Medicine and Dentistry, 265 Crittenden Blvd Box 420644, Rochester, NY 14642, USA.

E-mail address: elaine_hill@urmc.rochester.edu (E.L. Hill).

<https://doi.org/10.1016/j.envres.2018.06.022>

Received 5 April 2018; Received in revised form 21 May 2018; Accepted 11 June 2018

Available online 21 June 2018

0013-9351/ © 2018 Elsevier Inc. All rights reserved.

emitted that may cause adverse respiratory health outcomes. Existing environmental monitoring studies demonstrate air pollution above background levels in communities with UNGD sites for chemicals associated with UNGD processes, many of which are known respiratory irritants (McKenzie et al., 2012; Colborn et al., 2014; Macey et al., 2014; Swarthout et al., 2015; Webb et al., 2016). Specific toxicants that have been previously associated with air pollution from UNGD emissions include particulate matter (diesel PM, PM₁₀); volatile organic compounds (benzene, ethylbenzene, formaldehyde, n-hexane, toluene, and xylene); polycyclic aromatic hydrocarbons (naphthalene, chlorobenzene, phenol); and other pollutants (ethylene glycol, methanol) (Colborn et al., 2010, 2014; Adgate et al., 2014; Elliott et al., 2017; Paulik et al., 2016; Macey et al., 2014; McKenzie et al., 2012; Korfmacher et al., 2013). Children are especially sensitive to environmental toxicants and associated adverse health outcomes (Faustman et al., 1999).

Asthma is a common chronic illness that currently affects 8.4% of children and adolescents under eighteen in the US, or about six million children (CDC, 2017). This condition is characterized by recurrent episodes of cough and wheeze related to the narrowing of the airways and inflammation of the lungs (US Department of Health and Human Services National Institutes of Health National Heart, Lung, and Blood Institute, 2014). Pediatric asthma has a substantial impact on functional outcomes, as it is a key contributor to school absenteeism, lower quality of life, and limitation of physical activity (Stridsman et al., 2017). Patients under 18 years old with asthma cost 1.99 billion dollars per year in the United States, so this outcome represents a substantial burden to communities (CDC, 2005). Asthma prevalence varies by age group at 9.6% for children between 5 and 11, 10.3% for young teenagers between ages 12 and 14, and 9.8% for older teenagers between 15 and 17 (CDC, 2017). Asthma outcomes for children are typically considered within different age groups because the course of asthma can change over time, and a child's response to exposures and treatments may vary by age. The national guidelines for asthma management includes recommendations for control assessments and stepwise treatments based on child age category (NHLBI, 2007).

Although there are numerous triggers for asthma exacerbations, some types of outdoor environmental air pollution are known respiratory irritants (Adams et al., 2011; Pennsylvania Department of Health, 2016). Many chemicals that have been found at increased levels in areas located close to UNGD sites have also been implicated as environmental asthma triggers (Marrero et al., 2016; McKenzie et al., 2012; Pennsylvania Department of Health, 2016; Swarthout et al., 2015). It remains unclear what aspects of UNGD may be most associated with pediatric asthma such as the initial drilling of a new site or the ongoing activities as the site produces natural gas (Adgate et al., 2014; Czolowski et al., 2017).

Only one previous study exists on UNGD and respiratory health outcomes and it utilizes a Pennsylvania sample between ages 5 and 90 (Rasmussen et al., 2016). Their analyses find odds ratios ranging from 1.10 (95% CI: 0.92, 1.30) to 1.74 (95% CI: 1.45, 2.09) depending upon exposure metric. Additional community concern regarding the health effects of UNGD-related air pollution have also been raised, but no studies to date have examined specific components of UNGD air pollution and linked this information to population health effects (Macey et al., 2014; Maskrey et al., 2016; Paulik et al., 2016; Rabinowitz et al., 2015).

Our study demonstrates how age groups within the pediatric population may be at differing risks from exposure to UNGD-related air pollution and examining specific UNGD pollutants from reported site air emissions. We take into account potential co-exposures for our population such as pre-existing respiratory irritants and conventional oil and natural gas development (CONGD). Our results add to the body of literature on how UNGD is associated with asthma exacerbations among a vulnerable population of children.

2. Methods

2.1. Study population

We obtained data on individual inpatient hospitalization for the entire state of Pennsylvania (67 total counties) from the Pennsylvania Health Care Cost Containment Council (Pennsylvania Healthcare Cost Containment Council Inpatient Discharge Data). Each record contains the patient's residential zip code, which we used to assign exposure status. We included the zip codes in counties fully located on the Marcellus Shale, as zip codes not located on the Marcellus Shale have no potential for UNGD and may be inherently different than areas located on the Marcellus Shale. Furthermore, we excluded counties designated as urban by the Pennsylvania Department of Health's Asthma Prevalence report due to the large differences in urban versus rural air quality and other co-exposures (Pennsylvania Department of Health, 2016; Strosnider, 2017). By limiting our sample population to rural counties located on the Marcellus Shale, we are reducing the potential for residual confounding in our final risk estimates.

2.2. Study design

We use a difference-in-differences design to account for pre-existing time trends in pediatric asthma hospitalizations that may be present prior to the introduction of UNGD. This study design permits the comparison of trends in the outcome before and after the introduction of UNGD in a zip code, as well as contrast the trends to zip codes unexposed to UNGD over the entire study period.

2.3. Exposure metric

We obtained complete drilling wells dataset from the Pennsylvania Department of Environmental Protection (PADEP) and assigned wells' coordinates to specific zip codes and counties (PADEP, 2016b). Unlike residential-specific proximity exposure metrics, zip code and county exposures can consider how macroeconomic changes from UNGD may benefit the local area (e.g. decreased unemployment, increased private insurance), so these derived exposure metrics represent an effective community-level estimate of UNGD exposure. The database contains a field that indicates if a well site is permitted as unconventional as well as the exact date that drilling began, the combination of which we use to determine exposure status.

To assess exposure to UNGD within a zip code, we examined the number of wells drilled in the zip code in a specific quarter of a calendar year. We hypothesize that the immediate effect of a newly drilled well is more likely to affect local air quality and cause an asthma exacerbation than the long term cumulative effect of wells. However, the effect of an increasing amount of drilling activity in the zip code may create more air pollution for a longer period. Both exposure metrics have been used in previous epidemiologic work (Jemielita et al., 2015; Rasmussen et al., 2016; Tustin et al., 2016). Since there is little literature supporting either framework, we chose to create three metrics of UNGD exposure by zip code for each quarter and year observation: a binary contemporaneous variable for a newly spudded (initially drilled) well, a binary cumulative variable for ever-spudded wells, and tertiles of cumulative count of the wells ever drilled. We also incorporate similar exposure metrics for conventional oil and natural gas development (CONGD) to account for known co-occurrence of CONGD and UNGD.

We also leverage the Pennsylvania Unconventional Natural Gas Emission Inventory to assess the association between specific reported UNGD air pollutants and our pediatric asthma outcomes (PADEP, 2016a). This database contains annualized emissions data from all UNGD sites from 2011 through 2014 reported by companies for a number of pollutants: 2,2,4-trimethylpentane, benzene, carbon monoxide, carbon dioxide, ethylbenzene, formaldehyde, methane, nitrous

oxide, nitrogen oxides, PM_{2.5}, PM₁₀, toluene, volatile organic compounds, x-hexane, and xylenes. Although individual volatile organic compounds are in the emissions data, Pennsylvania regulates volatile organic compounds as a heterogeneous category and requires emissions to be reported as specific volatile organic compounds as well, thus we evaluate this category in both ways. All pollutants are reported in tons emitted per year. This database is one of the only ones that contains pollution by site from the UNGD process since UNGD sites are not subject to the national Toxic Release Inventory during our study period (US EPA, 2016). For all reporting UNGD sites, we linked our spud data from DrillingInfo to the emissions data by matching on company names, site names, and counties by year and determine how much pollution is being reported per zip code on an annual basis. This allows us to assess the annual sum of pollution in tons by chemical at the zip code level as an additional exposure metric in separate models. Our main models explore pollution in a log-sum framework to ascertain how different levels of emissions may affect our pediatric population.

2.4. Other respiratory hazards

We control for pre-existing respiratory hazards via the 2011 National Air Toxics Assessment (NATA) respiratory hazard index (RHI), a composite index of over 180 hazardous air pollutants from mobile and stationary sources (US Environmental Protection Agency, 2015). This data is available for the entire nation by census tract centroid, so we applied inverse distance interpolation to estimate NATA RHI for each zip code centroid in our analysis. To our knowledge, no other studies on respiratory health effects of UNGD have incorporated a composite metric for non-UNGD respiratory hazards.

2.5. Outcome metric

The Pennsylvania Healthcare Cost Containment Council (PHC4) hospitalization data include the diagnostic codes assigned to each patient upon discharge in Pennsylvania. Our analysis includes patients between the ages of 2 and 18 years with a 493.X ICD-9 code, which indicates acute asthma exacerbations. We excluded children under the age of 2 years from this analysis because an asthma hospitalization in this age group may be reflective of a viral illness, not a typical asthma case (Adams et al., 2011). Our outcome is a binary indicator of whether there is a pediatric asthma hospitalization in a specific zip code-quarter-year observation.

We stratified asthma-related hospitalizations into three age-specific categories (2–6, 7–12, and 13–18 years) to better examine the differences in asthma exacerbations throughout childhood and adolescence. These categorizations somewhat align with the age stratification scheme that the Center for Disease Control uses to report asthma incidence, but we categorize them into tertiles due to the exclusion of the children under 2 years (CDC, 2017). Hospitalizations were analyzed by year and quarter per zip code, thus considering spatiotemporal patterns. We also extracted patient sex, race, ethnicity, and insurance status for inclusion in our models.

2.6. Statistical analysis

The maximum number of observations in this analysis is fixed at the quantity of $(\text{Number of years of data}) * (\text{Number of quarters per year}) * (\text{Number of zip codes})$. To account for the hierarchical nature of the data, we fit mixed effects logistic regression models with a random intercept for zip code and fixed effects for year and quarter. While a similar study used fixed effects Poisson regression due to the count nature of hospitalizations, we hypothesize that a mixed effects logistic regression model is more appropriate due to our rare outcome and has been previously used to study associations between UNGD and asthma (Jemielita et al., 2015; Rasmussen et al., 2016). We assume that absence of an ICD-indicated asthma hospitalization within the zip code

during a specific quarterly timeframe indicates that a contemporaneous event did not occur.

For our analysis of reported emissions, we subset our hospitalizations to only 2011 through 2014, which aligns with the only available years of emissions data. We substitute our UNGD exposure metric for each annualized pollutant available in these four years of data but maintain the same models in all other regards, including the quarterly temporality to account for seasonal variation within a year.

Covariates in all of our asthma models include annual proportion of hospitalizations for sex, race, ethnicity, and insurance type by zip code derived from the individual-level PHC4 hospitalization data; zip code-level population density from the 2010 US Census and background respiratory hazard index from the 2011 National Air Toxics Assessment; and annual county-level unemployment, poverty for children under 18 years of age, and median household income from the US Census Small Area Income and Poverty Estimates (Surveillance, Epidemiology, and End Results Program, 2017; IPUMS NHGIS, 2016; US Environmental Protection Agency, 2015). Additional analyses stratify by pediatric age groups (2–6, 7–12, and 13–18 years) to examine potential heterogeneity across different stages of development. Our pollutant-specific models follow the same specifications.

In addition to assessing our results in calendar time, we also developed models to examine our results in terms of event time, which allows us to examine how the asthma hospitalization risk may change after the initial UNGD activity began. We collapse our data to the annual level and convert our data into years before and after UNGD started in each zip code. Our reference year is four quarters prior to the first UNGD site is spudded in the zip code. We limit this analysis to only eight years of before and after spudding since very few zip codes experience UNGD activity for greater than eight years of time in our study period.

2.7. Sensitivity analysis

First, we include a covariate for conventional oil and gas development (CONGD) to adjust for potential co-exposure effects. Second, we fit models using conditional likelihood logistic regression to confirm that the random intercept did not influence our effect estimates. Third, we examine cumulative count of UNGD wells within the zip code prior to hospitalization to estimate the effect of each additional well on asthma hospitalization. Fourth, we examine the relationship between the number of reporting UNGD sites regressed on the sum of emissions in each zip code by pollutant, which helps us ensure that these reported emissions are indicative of the number of sites in the zip code. Finally, we fit regressions for the quintile framework (lowest vs. highest quintiles) of specific pollutants to explore the association between our UNGD pollution and pediatric asthma hospitalizations for our most and least exposed communities.

3. Results

3.1. Descriptive statistics

Our inclusion criteria yield 29 counties containing 571 zip codes in Pennsylvania, which generates 27,296 observations by zip code, quarter, and year. In Pennsylvania between 2003 and 2014, new UNGD wells annually increases from 3 to 1372 with spuds drilled in 274 zip codes per year at its peak in 2011 (Fig. 1). In total, 5649 UNGD wells are drilled in our sample area between 2003 and 2014, with CONGD wells co-occurring within many zip codes across our study period (Fig. 2).

In total, 15,837 pediatric asthma-related hospitalizations are included. Our exposure distribution yields 1070 hospitalizations in 532 zip codes exposed to UNGD compared with 14,767 unexposed hospitalizations in 6794 zip codes, and most demographic information is similar among patients exposed and unexposed to UNGD activity

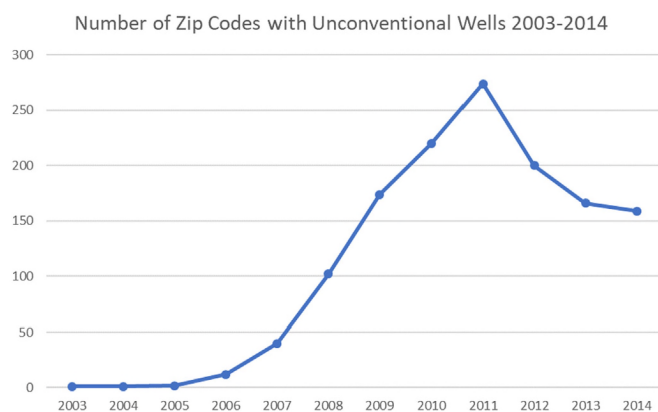


Fig. 1. Newly spudded UNGD sites by zip code 2003–2014.

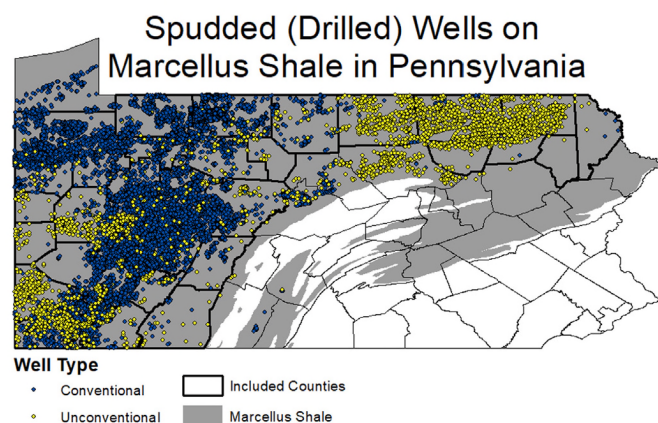


Fig. 2. Spatial distribution of UNGD and CONGD in Pennsylvania 2003–2014.

(Table 1). We note that patients exposed to UNGD tended to live in areas with slightly lower population densities.

3.2. Association of UNGD with pediatric asthma hospitalizations

We first determine that a logistic model is appropriate by graphing our hospitalizations counts means per quarter and zip code in a histogram (eFig. 1). After adjusting for secular time trends, children and adolescents exposed to newly spudded UNGD wells within their zip code have 1.25 (95% CI: 1.07, 1.47) times the odds of experiencing an asthma-related hospitalization compared with children who did not live in these communities (Table 2). When stratified by patient age, those between 2 and 6 years have the greatest odds of an asthma-related hospitalization (OR = 1.44; 95% CI: 1.18, 1.75) followed by ages 13–18 (OR = 1.34, 95% CI: 1.13, 1.60).

In the binary cumulative exposure framework, we observe similar results to the contemporaneous analysis (Table 2). Children and adolescents residing in a zip code with any current or previous drilling activity have 1.19 (95% CI: 1.04, 1.36) times the odds of experiencing an asthma-related hospitalization compared with children who do not live in these communities. Children between the ages of 2 and 6 have the most elevated odds ratio (OR = 1.35; 95% CI: 1.14, 1.60) followed by children ages 13–18 (OR = 1.29, 95% CI: 1.11, 1.49).

We conduct additional analyses using the number of UNGD sites ever drilled within a zip code to examine the effect of additional wells on pediatric asthma-related hospitalizations. The tertiles of exposure by number of wells ever drilled in the zip code is 1–2, 3–10, and > 11. The highest tertile of exposure is associated with increased odds of pediatric asthma hospitalizations for all age groups (OR = 1.39, 95% CI: 1.14, 1.71), while middle and lowest tertiles of exposure did not demonstrate clear dose-response (Table 2). Results for children between ages of 2

Table 1

Individual, zip code, and county demographic information for participants by exposure status.

| | Unexposed ^a | Exposed |
|---|------------------------|---------|
| Individual | | |
| Total Asthma Patients | 14,767 | 1070 |
| Age Group | | |
| 2–6 | 31% | 30% |
| 7–12 | 25% | 20% |
| 13–18 | 44% | 50% |
| Zip Code^b | | |
| Female (%) | 42% | 42% |
| Race/Ethnicity (%) | | |
| White | 88% | 90% |
| Black | 6% | 4% |
| Hispanic | 2% | 1% |
| Other | 4% | 5% |
| Insurance (%) | | |
| Medicaid | 51% | 52% |
| Private | 46% | 45% |
| Uninsured | 2% | 2% |
| Other or Missing | 1% | 1% |
| Hospitalization Quarter | | |
| 1 (Jan, Mar) | 25% | 23% |
| 2 (Apr, Jun) | 25% | 25% |
| 3 (Jul, Sep) | 25% | 27% |
| 4 (Oct, Dec) | 25% | 26% |
| Hospitalization Type (%) | | |
| Emergency | 50% | 44% |
| Urgent | 38% | 45% |
| Elective | 12% | 11% |
| Respiratory Hazard Index^b | | |
| | 1.1 | 1.2 |
| County | | |
| Median Income (\$) ^c | 41,059 | 43,596 |
| Population Density ^d | 48.0 | 34.5 |
| Poverty Under 18 (%) ^c | 20% | 21% |
| Unemployment Rate (%) ^e | 7% | 8% |

^a Exposure status determined by any UNGD well drilled in a zip code contemporaneously with the asthma hospitalization.

^b Zip code demographics determined using all pediatric hospitalizations in each zip code over the course of the study period.

^c Derived from annual U.S. Census Small Area Income & Poverty Estimates.

^d Derived from annual U.S. Intercensal County Population Data.

^e Derived from annual U.S. Bureau of Labor Statistics.

and 6 show the strongest evidence of dose-response, and in the highest tertile of exposure, UNGD is associated with a 1.73 higher odds (95% CI: 1.34, 2.23) of an asthma-related hospitalization compared with the no UNGD exposure group. Finally, we observe increases in the odds of an asthma-related hospitalization for years after the initial drilling begins (Fig. 3).

3.3. Association of UNGD site emissions with pediatric asthma hospitalizations

Our pollutant-specific emissions models demonstrate consistent increased risks of pediatric asthma hospitalizations across most of our models when we compare the lowest to highest quintiles of exposure (Table 3). Full descriptions of the pollutant distributions are available in our [Supplementary material data \(eTable 1\)](#). Briefly, we find odds ratios ranging from 1.08 (95% CI: 0.93, 1.26) for carbon dioxide to 1.42 (95% CI: 1.22, 1.66) for VOCs. Specific reported pollutants with associations across our all-ages models include 2,2,4-trimethylpentane, carbon dioxide, formaldehyde, nitrous oxide, VOCs, and x-hexane. Ages 2–6 hospitalizations are also associated with exposure to carbon monoxide, methane, nitrogen oxides, PM_{2.5}, PM₁₀, toluene, and xylenes while hospitalizations among children ages 7–12 and adolescents 13–18 are associated with no additional pollutants.

Table 2Associations between UNGD and pediatric asthma hospitalizations by exposure metric.^a

| Age group | Binary exposure metrics | | Tertile exposure metrics ^{de} | | | |
|-----------|------------------------------|-------------------------|--|-------------------|-------------------|-------------------|
| | Contemporaneous ^b | Cumulative ^c | No UNGD | Low | Medium | High |
| All | 1.25 (1.07, 1.47) | 1.19 (1.04, 1.36) | REF | 1.15 (0.97, 1.36) | 1.12 (0.94, 1.34) | 1.39 (1.14, 1.71) |
| 2–6 | 1.44 (1.18, 1.75) | 1.35 (1.14, 1.60) | REF | 1.24 (1.00, 1.54) | 1.27 (1.01, 1.59) | 1.73 (1.34, 2.23) |
| 7–12 | 1.03 (0.83, 1.29) | 1.05 (0.88, 1.25) | REF | 1.06 (0.84, 1.34) | 1.00 (0.79, 1.27) | 1.11 (0.84, 1.47) |
| 13–18 | 1.34 (1.13, 1.60) | 1.29 (1.11, 1.49) | REF | 1.28 (1.06, 1.55) | 1.25 (1.03, 1.53) | 1.35 (1.08, 1.70) |

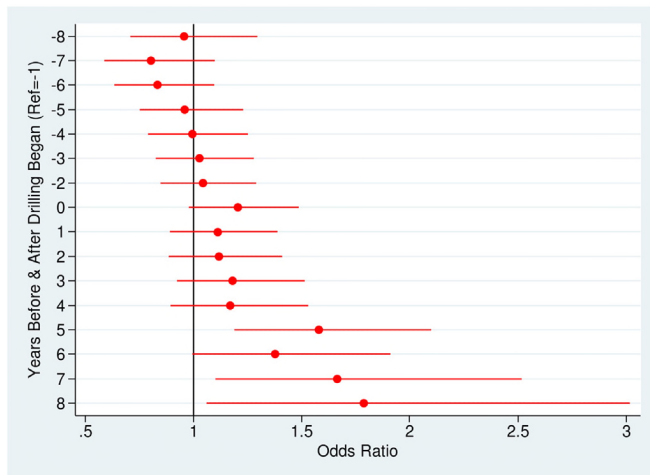
^a Multilevel logistic models with a random intercept for zip code adjusted for sex, race, year, quarter, insurance status, zip code respiratory hazard index, county median household income quartile, county unemployment, county poverty under 18 years old, and county log population density.

^b Exposure metric is whether any UNGD wells were drilled in the same zip code, quarter, and year as the hospitalization.

^c Exposure metric is whether any UNGD wells were ever drilled in the same zip code, quarter, and year as the hospitalization.

^d Reference group is zip codes with no UNGD activity in study period.

^e Exposure metric is tertile of UNGD site count in a zip code through the quarter that the hospitalization occurred.

**Fig. 3.** Odds ratios for pediatric asthma hospitalizations by years before and after first spudded UNGD site in zip code.

3.4. Sensitivity analyses

Given the high quantity of conventional drilling occurring within our study time frame across our study area (Fig. 2), we adjust for CONGD exposure within the zip code in an additional set of analyses. For the binary exposure analysis, results remain similar in both analyses

after adjusting for CONGD (Online Supplementary material eTable 2). For the tertile analysis, all results maintain similar, if slightly attenuated, risk estimates after controlling for CONGD. Our results likewise remain qualitatively similar when we use a fixed effects logistic regression instead of a mixed effects framework (Online Supplementary material eTable 3). We also find similar effect sizes for our cumulative UNGD metric for each additional well among the 2–6 age group but not others (Online Supplementary material eTable 4). In regressions of the sum of pollution on the number of reporting UNGD sites in a zip code, we find consistent positive associations, which demonstrates that the number of UNGD sites is sufficiently correlated with the self-reported emissions data (Online Supplementary material eTable 5). Our regression results for specific emissions in a quintile exposure framework also demonstrate similar, if higher, associations with wider confidence intervals between each pollutant and our pediatric asthma outcome (Online Supplementary material eTable 6).

4. Discussion

We conducted a difference-in-differences analysis of pediatric asthma-related hospitalizations in Pennsylvania using an administrative database from 2003 through 2014, which corresponds to the rapid development of the Marcellus Shale. This study examines the relationship between pediatric asthma hospitalizations and UNGD. In addition, this study shows how specific UNGD emissions may be linked to respiratory health outcomes. We are able to break down pediatric asthma hospitalizations by age group to examine the effects of UNGD

Table 3

Associations between log-sum UNGD emissions and pediatric asthma hospitalizations by pollutant.

| Pollutants ^a | All ages | 2–6 | 7–12 | 13–18 |
|------------------------------|-------------------|-------------------|--------------------|-------------------|
| 2,2,4-Trimethylpentane | 1.29 (1.01, 1.64) | 1.30 (1.07, 1.58) | 1.04 (0.83, 1.30) | 1.41 (1.12, 1.77) |
| Benzene | 1.12 (0.99, 1.27) | 1.09 (0.98, 1.21) | 1.08 (0.96, 1.23) | 1.04 (0.92, 1.17) |
| Carbon Monoxide | 1.08 (0.93, 1.26) | 1.20 (1.05, 1.37) | 1.07 (0.93, 1.25) | 1.03 (0.90, 1.19) |
| Carbon Dioxide | 1.16 (1.02, 1.33) | 1.20 (1.05, 1.36) | 1.17 (1.01, 1.37) | 1.11 (0.97, 1.28) |
| Ethylbenzene | 1.11 (0.95, 1.30) | 0.94 (0.82, 1.08) | 1.01 (0.87, 1.17) | 1.07 (0.93, 1.23) |
| Formaldehyde | 1.20 (1.06, 1.36) | 1.18 (1.06, 1.31) | 1.06 (0.94, 1.20) | 1.12 (1.00, 1.25) |
| Methane | 1.10 (0.96, 1.26) | 1.17 (1.04, 1.31) | 1.05 (0.92, 1.19) | 1.04 (0.92, 1.18) |
| Nitrous Oxide | 1.17 (1.02, 1.33) | 1.19 (1.06, 1.34) | 1.16 (1.00, 1.34) | 1.07 (0.94, 1.22) |
| NO _x | 1.21 (0.98, 1.48) | 1.23 (1.05, 1.45) | 1.088 (0.90, 1.32) | 1.20 (0.99, 1.45) |
| PM _{2.5} | 1.06 (0.92, 1.22) | 1.18 (1.04, 1.34) | 1.04 (0.90, 1.20) | 1.02 (0.89, 1.16) |
| PM ₁₀ | 1.08 (0.94, 1.24) | 1.23 (1.09, 1.40) | 1.03 (0.90, 1.19) | 1.04 (0.91, 1.18) |
| Toluene | 1.09 (0.97, 1.24) | 1.14 (1.03, 1.26) | 0.99 (0.88, 1.12) | 1.05 (0.94, 1.18) |
| SO _x | 1.09 (0.96, 1.24) | 1.08 (0.98, 1.21) | 1.05 (0.93, 1.19) | 1.11 (0.99, 1.25) |
| Volatile Organic Compounds | 1.42 (1.22, 1.66) | 1.34 (1.17, 1.54) | 1.12 (0.97, 1.29) | 1.32 (1.15, 1.52) |
| x-Hexane | 1.23 (1.05, 1.43) | 1.13 (0.99, 1.30) | 1.129 (0.97, 1.32) | 1.25 (1.08, 1.44) |
| Xylenes (Isomers & Mixtures) | 1.16 (0.98, 1.36) | 1.18 (1.03, 1.35) | 1.09 (0.94, 1.27) | 1.13 (0.98, 1.31) |

^a Models only include data 2011 through 2014. Multilevel logistic regression models with a random intercept for zip code adjusted for sex, race, year, quarter, insurance status, zip code respiratory hazard index, county median household income quartile, county unemployment, county poverty under 18 years old, and county log population density.

across the child developmental stages and demonstrate that specific pediatric age groups respond differently to UNGD in their community. Pediatric asthma hospitalization rates may be changing in our study period for reasons unrelated to UNGD, thus our analysis ensures that these secular trends are not influencing the results. Furthermore, we restrict our analysis to a relatively homogenous rural population in counties that are located on the Marcellus Shale, so our analysis reduces external confounding factors. We control for pre-existing respiratory health risks, which we adjust for via the National Air Toxics Assessment (NATA) respiratory hazard index (RHI). This method is more effective than controlling for individual ambient pollutants since the NATA RHI considers over 180 hazardous air pollutants from stationary and mobile sources at the local level. Our results appear to be driven by the highest exposure tertile, which insinuates that the intensity of pollution from UNGD is more important than the initial introduction of UNGD into a community.

Our results remain consistent with the existing literature on UNGD and respiratory health, though we observed attenuated estimates across all age groups and exposure levels (Rasmussen et al., 2016; Rabinowitz et al., 2015). The results presented in this study build upon the associations found in Rasmussen et al., 2016 by using the population of inpatient pediatric asthma hospitalizations between 2003 and 2014. We also show that the risk of a pediatric asthma hospitalization remains increased for years after the introduction of UNGD. Our findings further demonstrate that children between 2 and 6 years old are more susceptible to experiencing an asthma-related hospitalization in a UNGD zip code. After controlling for co-occurrence of CONGD, we continue to find an elevated risk of asthma-related hospitalizations with exposure to UNGD, which has not been previously shown. These results provide support that increased drilling activity may be associated with an increased risk of pediatric asthma hospitalizations.

In our analysis of individual pollutants from the emissions reports, we find evidence of specific pollutants from UNGD processes that may be driving increases in pediatric asthma hospitalization, including several known respiratory irritants such as volatile organic compounds and formaldehyde (Gordian et al., 2010; Kampa and Castanas, 2008; Webb et al., 2016). These results imply that the pollution from the UNGD sites themselves, as opposed to only UNGD-related traffic, may be contributing to pediatric asthma hospitalizations. Although this data is self-reported by the UNGD companies themselves, this data likely represents an underreporting of true UNGD site emissions, thus our results may be underreporting the risk of pediatric asthma from specific UNGD pollutants. We interpret these results with caution due to the self-reported nature of the emissions data; however, these results provide preliminary insights into the effects of specific UNGD pollutants on pediatric asthma hospitalizations.

Shale gas development has previously been implicated in decreased air quality, but these assessments have focused on UNGD and did not assess the CONGD co-exposure (Czolowski et al., 2017; Marrero et al., 2016; McKenzie et al., 2012; Swarthout et al., 2015; Walters et al., 2015). Any reductions in air quality are likely to be adversely experienced by the most vulnerable asthmatic patients in the local population, whom we captured in our study via their hospitalization records. Pediatric patients experiencing breathing difficulties are usually taken to the hospital, even in rural settings. The administrative nature of our data allows us to capture exacerbations among young patients, who are hard to access otherwise. Importantly, these episodes represent not only a significant event for the patient and his or her family, but also are associated with missed days of school and work, and substantial healthcare cost.

The present study has some limitations. Exposure and outcome were examined at the zip code level, which contributes to potential exposure misclassification. Our tertiles of drilling exposure by zip code attempt to examine the dose response relationship, but this imprecise exposure metric is not ideal for individual exposures since we cannot assess exactly where the patients reside in relation to the UNGD sites. However,

our results indicate that community-level UNGD is associated with decreased respiratory health, which can be more easily translated into local policy decisions. Our results are further bolstered by our use of the UNGD emissions data in addition to accounting for background respiratory hazards, where we demonstrate that specific pollutants are more likely to be associated with pediatric asthma hospitalizations. Additionally, the reliance on hospitalization data did not permit the investigation of how patients with less severe asthma may be affected, which previous literature has shown to be susceptible to UNGD-related air pollution (Rasmussen et al., 2016).

Our analysis focuses on asthma-related hospitalizations among children and adolescents while adequately controlling for pre-existing outcome trends that occurred prior to the introduction of UNGD. We also leverage a unique database of UNGD pollution to examine specific chemicals with respect to respiratory health outcomes, which has not been done in the UNGD and human health literature to date. Difference-in-differences designs can take these time trends into account, so future analyses of other outcomes should incorporate pre-existing outcome trends into their models to minimize spatiotemporal confounding. We supplement our results with models that demonstrate specific UNGD pollutants that may be creating the higher risks of pediatric asthma hospitalizations associated with community UNGD exposures. We also assess CONGD co-exposures with respect to a health outcome. Our populations of patients were relatively homogenous in terms of socio-demographic factors, and all had to be at risk for UNGD, which should reduce potential unmeasured confounding. Furthermore, our outcome data come from a standardized source and we focus on the children most vulnerable to air pollution increases. Finally, the zip code nature of our exposure allows for a community-level assessment of UNGD and demonstrate that community-level exposures to UNGD are associated with increased risk of pediatric asthma hospitalizations, which may better measure the amount of drilling exposure for policy implications.

5. Conclusions

Previous studies observe associations between UNGD and poorer local air quality. This study examines the associations between community-level UNGD activity and pediatric asthma while considering pre-existing time trends, co-occurrence of CONGD, and UNGD site-specific emissions reports. Additional work is needed to understand how UNGD air pollution may affect respiratory health, which could include detailed exposure assessments for UNGD and CONGD sites.

Acknowledgements

Ms. Willis and Dr. Hill had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. This study was funded by NIH grant DP5OD021338 (Dr Hill). The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. We thank Richard DiSalvo and Alina Denham (University of Rochester) for database construction aid and valuable comments on the article; Perry Hystad, Ph.D. (Oregon State University) for additional comments on the article. We would like to thank PHC4 for their support in gaining access to the hospitalization data. All except Dr. Hystad received compensation for their contributions.

Funding

Research reported in this publication was supported by the Office of the Director of the National Institutes of Health under award number DP5OD021338. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Data provider disclaimer

The Pennsylvania Health Care Cost Containment Council (PHC4) is an independent state agency responsible for addressing the problem of escalating health costs, ensuring the quality of health care, and increasing access to health care for all citizens regardless of ability to pay. PHC4 has provided data to this entity to further PHC4's mission of educating the public and containing health care costs in Pennsylvania. PHC4, its agents, and staff, have made no representation, guarantee, or warranty, express or implied, that the data, – financial, patient, payor, and physician specific information, – provided to this entity, are error-free, or that the use of the data will avoid differences of opinion or interpretation. This analysis was not prepared by PHC4. This analysis was done by Dr. Hill and her collaborators. PHC4, its agents and staff, bear no responsibility or liability for the results of the analysis, which are solely the opinion of this entity.

Human subjects protection

This research was approved by University of Rochester Research Subjects Review Board (RSRB).

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.envres.2018.06.022>.

References

- Adams, J., Sutter, M., Alberman, T., 2011. The patient with asthma in the emergency department. *Clin. Rev. Allerg. Immunol.* 43, 14–29.
- Adgate, J.L., Goldstein, B.D., McKenzie, L.M., 2014. Potential public health hazards, exposures and health effects from unconventional natural gas development. *Environ. Sci. Technol.* 48, 8307–8320. <http://dx.doi.org/10.1021/es404621d>.
- CDC, 2005. Preventing Chronic Disease. Centers for Disease Control and Prevention. Available: https://www.cdc.gov/pcd/issues/2005/jan/04_0053.htm (Accessed 5 May 2018).
- CDC, 2017. Most Recent Asthma Data.
- Colborn, T., Kwiatkowski, C.F., Schultz, K., Bachran, M., 2010. Natural gas operations from a public health perspective. *Hum. Ecol. Risk Assess. Int. J.* 17, 1040–1056.
- Colborn, T., Schultz, K., Herrick, L., Kwiatkowski, C., 2014. An exploratory study of air quality near natural gas operations. *Hum. Ecol. Risk Assess. Int. J.* 20, 86–105. <http://dx.doi.org/10.1080/10807039.2012.749447>.
- 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.
- Elliott, E.G., Trinh, P., Ma, X., Leaderer, B.P., Ward, M.H., Deziel, N.C., 2017. Unconventional oil and gas development and risk of childhood leukemia: assessing the evidence. *Sci. Total Environ.* 576, 138–147. <http://dx.doi.org/10.1016/j.scitotenv.2016.10.072>.
- Faustman, E., Silbernagel, S., Fenske, R., Burbacher, T., Ponce, R., 1999. Mechanisms underlying children's susceptibility to environmental toxicants. *Environ. Health Perspect.* 108, 13–21.
- Gordian, M.E., Stewart, A.W., Morris, S.S., 2010. Evaporative gasoline emissions and asthma symptoms. *Int. J. Environ. Res. Public Health* 7, 3051–3062. <http://dx.doi.org/10.3390/ijerph7083051>.
- IPUMS NHGIS, 2016. National Historical Geographic Information System. Available: <https://www.nhgis.org/> (Accessed 12 January 2018).
- Jemielita, T., Gerton, G.L., Neidell, M., Chillrud, S., Yan, B., Stute, M., et al., 2015. Unconventional gas and oil drilling is associated with increased hospital utilization rates. *PLoS ONE* 10, e0131093. <http://dx.doi.org/10.1371/journal.pone.0131093>.
- Kampa, M., Castanas, E., 2008. Human health effects of air pollution. *Environ. Pollut.* 151, 362–367. <http://dx.doi.org/10.1016/j.envpol.2007.06.012>.
- Korfmaier, K.S., Jones, W.A., Malone, S.L., Vinci, L.F., 2013. Public health and high volume hydraulic fracturing. *New Solut. J. Environ. Occup. Health Policy* NS 23, 13–31. <http://dx.doi.org/10.2190/NS.23.1.c>.
- Macey, G.P., Breech, R., Chernaik, M., Cox, C., Larson, D., Thomas, D., et al., 2014. Air concentrations of volatile compounds near oil and gas production: a community-based exploratory study. *Environ. Health* 13, 82. <http://dx.doi.org/10.1186/1476-069X-13-82>.
- Marrero, J.E., Townsend-Small, A., Lyon, D.R., Tsai, T., Meinardi, S., Blake, D.R., 2016. Estimating emissions of toxic hydrocarbons from natural gas production sites in the Barnett shale region of Northern Texas. *Environ. Sci. Technol.* 50, 10756–10764. <http://dx.doi.org/10.1021/acs.est.6b02827>.
- Maskrey, J.R., Insley, A.L., Hynds, E.S., Panko, J.M., 2016. Air monitoring of volatile organic compounds at relevant receptors during hydraulic fracturing operations in Washington County, Pennsylvania. *Environ. Monit. Assess.* 188, 1–12. <http://dx.doi.org/10.1007/s10661-016-5410-4>.
- McKenzie, L.M., Witter, R.Z., Newman, L.S., Adgate, J.L., 2012. Human health risk assessment of air emissions from development of unconventional natural gas resources. *Sci. Total Environ.* 424, 79–87. <http://dx.doi.org/10.1016/j.scitotenv.2012.02.018>.
- NHLBI, 2007. Guidelines for the Diagnosis and Management of Asthma (EPR-3). National Heart, Lung, and Blood Institute. Available: <https://www.nhlbi.nih.gov/health-topics/guidelines-for-diagnosis-management-of-asthma> (Accessed 14 May 2018).
- PADEP, 2016a. Instructions for Completing Air Quality Emission Inventory Forms.
- PADEP, 2016b. Oil and Gas Reports.
- Paulik, L.B., Donald, C.E., Smith, B.W., Tidwell, L.G., Hobbie, K.A., Kincl, L., et al., 2016. Emissions of polycyclic aromatic hydrocarbons from natural gas extraction into air. *Environ. Sci. Technol.* 50, 7921–7929. <http://dx.doi.org/10.1021/acs.est.6b02762>.
- Pennsylvania Department of Health, 2016. 2015 Pennsylvania Asthma Prevalence Report. Pennsylvania Healthcare Cost Containment Council Inpatient Discharge Data.
- Rabinowitz, P.M., Slizovskiy, I.B., Lamers, V., Trufan, S.J., Holford, T.R., Dziura, J.D., 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, 21–26. <http://dx.doi.org/10.1289/ehp.1307732>.
- Rasmussen, S., Ogburn, E., McCormack, M., Casey, J., Bandeen-Roche, K., Mercer, et al., 2016. Association between unconventional natural gas development in the Marcellus Shale and asthma exacerbations. *JAMA Intern. Med.* 176, 1334–1343. <http://dx.doi.org/10.1001/jamainternmed.2016.2436>.
- Stridsman, C., Dahlberg, E., Zandrén, K., Hedman, L., 2017. Asthma in Adolescence Affects Daily Life and School Attendance –Two Cross-sectional Population-based Studies 10 Years Apart.
- Strosnider, H., 2017. Rural and urban differences in air quality, 2008–2012, and community drinking water quality, 2010–2015 — United States. *MMWR Surveill. Summ.* 66. <http://dx.doi.org/10.15585/mmwr.mm6613a1>.
- Surveillance, Epidemiology, and End Results Program, 2017. National Cancer Institute. Available: <https://seer.cancer.gov/> (Accessed 12 January 2018).
- Swarthout, R.F., Russo, R.S., Zhou, Y., Miller, B.M., Mitchell, B., Horsman, E., et al., 2015. Impact of marcellus shale natural gas development in Southwest Pennsylvania on volatile organic compound emissions and regional air quality. *Environ. Sci. Technol.* 49, 3175–3184. <http://dx.doi.org/10.1021/es504315f>.
- Tustin, A.W., Hirsch, A.G., Rasmussen, S.G., Casey, J.A., Bandeen-Roche, K., Schwartz, B.S., 2016. Associations between unconventional natural gas development and nasal and sinus, migraine headache, and fatigue symptoms in Pennsylvania. *Environ. Health Perspect.* <http://dx.doi.org/10.1289/EHP281>.
- U.S. Energy Information Administration (EIA), 2016. Shale Gas Production Drives World Natural Gas Production Growth. Available: <https://www.eia.gov/todayinenergy/detail.php?id=27512> (Accessed 10 January 2018).
- U.S. Energy Information Administration, 2017a. Natural Gas Explained: Where Our Natural Gas Comes From.
- U.S. Energy Information Administration, 2017b. U.S. Energy Information Administration Annual Energy Outlook 2017.
- US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute, 2014. What Is Asthma?.
- US Environmental Protection Agency, 2015. National Air Toxics Assessment. US EPA. Available: <https://www.epa.gov/national-air-toxics-assessment> (Accessed 12 January 2018).
- US EPA, 2016. Addition of Natural Gas Processing Facilities to the Toxics Release Inventory Proposed Rule. US EPA. Available: <https://www.epa.gov/toxics-release-inventory-tri-program/addition-natural-gas-processing-facilities-toxics-release> (Accessed 7 May 2018).
- Walters, K., Jacobson, J., Kroening, Z., Pierce, C., 2015. PM2.5 airborne particulates near frac sand operations. *J. Environ. Health* 78, 8–12.
- Webb, E., Hays, J., Dyrszka, L., Rodriguez, B., Cox, C., Huffling, K., et al., 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.* <http://dx.doi.org/10.1515/reveh-2014-0070>.