Original Research

Unconventional natural gas development and hospitalizations: evidence from Pennsylvania, United States, 2003–2014

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ARTICLE INFO

ABSTRACT

Objectives: To examine relationships between short-term and long-term exposures to unconventional natural gas development, commonly known as fracking, and county hospitalization rates for a variety of broad disease categories.

Study design: This is an ecological study based on county-level data for Pennsylvania, United States, 2003–2014.

Methods: We estimated multivariate regressions with county and year fixed effects, using two 12-year panels: all 67 Pennsylvania counties and 54 counties that are not large metropolitan.

Results: After correcting for multiple comparisons, we found a positive association of cumulative well density (per km^2) with genitourinary hospitalization rates. When large metropolitan counties were excluded, this relationship persisted, and positive associations of skin-related hospitalization rates with cumulative well count and well density were observed. The association with genitourinary hospitalization rates is driven by females in 20–64 years group, particularly for kidney infections, calculus of ureter, and urinary tract infection. Contemporaneous wells drilled were not significantly associated with hospitalizations after adjustment for multiple comparisons.

Conclusions: Our study shows that long-term exposure to unconventional gas development may have an impact on prevalence of hospitalizations for certain diseases in the affected populations and identifies areas of future research on unconventional gas development and health.

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Introduction

Rapid growth in unconventional natural gas development (UNGD) over the last two decades has raised serious concerns about its impact on population health. Although the economic boom that generally accompanies UNGD may have positive effects on the local communities, pollutants and stressors associated with drilling may affect public health in predictable as well as unpredictable ways. While community members and politicians voice extensive concern over the impact of UNGD on health[1–3] and the importance of research in this area has been emphasized in public health literature,[4–8] few epidemiological studies have quantified its impact on a range of health outcomes to date.

UNGD is a process to extract natural gas from shale, a compressed fine-grained sedimentary rock, which recently became possible because of hydraulic fracturing technology, commonly known as fracking. In this process, a well is drilled vertically for approximately 6 km, after which drilling proceeds horizontally. Hydraulic fracturing involves pumping a large volume of water and chemicals under high pressure into the drilling pipe to create fractures in the rock so that natural gas can be released and captured from the shale formation. The UNGD boom has been most pronounced in the United States—particularly in Pennsylvania, Texas, Colorado, West Virginia, and Louisiana—and in Canada. Europe is still amidst a debate, with some countries allowing exploratory or small-scale UNGD and some banning the practice over concerns about increased seismic activity, water and air contamination, and associated health risks.

The UNGD process uses a number of toxic chemicals that are released into the atmosphere and can enter water supply. There is widespread consensus that these chemicals contribute to water contamination[9–11] and air pollution.[12–14] Air and water pollutants from UNGD have been linked to potential harmful effects on health, including but not limited to birth outcomes and reproductive, respiratory, skin, neurological, digestive, and cardiovascular health.[3,15,16]

Recent academic studies on UNGD and health confirm some of these projections and public concerns. Multiple studies show that community members report symptoms associated with UNGD.[3,17–19] Studies have also found that UNGD is associated with higher odds of asthma exacerbations,[20,21] increased prevalence of childhood hematologic cancer,[22] and higher rates of hospitalizations for pneumonia among the elderly.[23] A number of studies have found an impact of UNGD exposure on birth outcomes, including low birth weight,[24–27] small for gestational age,[24,25,27] premature birth,[24,25,27–29] and certain birth defects.[30]

Whereas most research so far has focused on the effects of UNGD on specific health outcomes that reflect most plausible biological mechanisms, we analyzed how UNGD may impact hospitalizations for broad disease groups and thus identify avenues for future research. Given that UNGD can financially benefit local communities but is also linked to air, water, noise, and light pollution, the impact of UNGD on health may come from a mixture of these exposures in ways that may not be readily thought of a priori and thus have not yet been explored. One small-scale study has examined hospitalizations for broad diagnosis groups thus far and found positive associations between UNGD and hospitalizations for cardiovascular and neurological conditions.[31] This study examined hospitalizations in three Pennsylvania counties, two of which are exposed, in 2007–2011. Our research improves on this study in important ways. By including all Pennsylvania counties, we examined the potential impact of UNGD across the whole state. We also extended the studied exposure period, including both the pre-boom period (2003–2006) and the period following the peak of annual drilled well count (2012–2014), allowing us to capture potential effects of approximately 3600 additional wells drilled in these 3 years and examine long-term effects of UNGD exposure. This may be particularly important given that hospitalizations generally reflect serious underlying health conditions that cannot be addressed in an outpatient setting or at home. Our study offers substantial methodological improvements as well.

Methods

Data and measures

Unconventional gas well data were obtained from the Carnegie Museum of Natural History's Pennsylvania Unconventional Gas Wells Geodatabase.[32] We included unconventional gas wells drilled into the Marcellus Shale with the start drilling date between January 1, 2003 and December 31, 2014. We aggregated well-level data to county-year level and used three annual county-specific exposure measures: contemporaneous wells (i.e. unconventional gas wells drilled in a year), cumulative well count (i.e. the total number of unconventional gas wells drilled up to the end of that year), and cumulative well density (i.e. cumulative well count divided by the county land area in square kilometers). The contemporaneous measure represents short-term and the cumulative measures long-term exposure to UNGD. Because the drilling phase is the most polluting and disruptive to the local communities, we are interested in drilled wells and do not differentiate between producing and non-producing wells or between active wells and wells that are inactive, plugged, or abandoned.

For our outcome variables, we abstracted inpatient discharge records from 2003 through 2014 from Pennsylvania Health Care Cost Containment Council (PHC4) data. Variables used included patient's county of residence, year of discharge, and primary diagnosis based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Observations were included if the principal diagnosis fell under any of the 16 major categories, determined by the ICD-9-CM groupings. We also calculated a total hospitalizations count, encompassing all hospitalizations in the 16 groups. Our outcome variables are annual county-level total and category-specific hospitalization rates per 10,000 residents that we calculated using population estimates from the Surveillance, Epidemiology, and End Results (SEER) program. We aggregated hospitalizations at the county level, which aligns with previous research in Pennsylvania.[23] However, the aforementioned small-scale study of UNGD and hospitalizations[31] used

hospitalization rates at the zip code level, which requires the assumption that zip code population did not change during the study period. If zip code population sizes did in fact change, our estimates would be biased. In our analyses of county-level demographics over the same study period, we observed demographic changes across Pennsylvania in response to unconventional well drilling. This suggests that zip code populations must have changed in this period as well. To avoid introducing bias into our estimates, we chose county-level aggregation.

We adjusted for annual county characteristics in terms of demographics, economy, and healthcare resources. Demographics data, encompassing distributions by age, sex, and race/ethnicity, were obtained from the SEER program. Poverty estimates and median income data came from small area income and poverty estimates (SAIPE) and unemployment rates were obtained from the Bureau of Labor Statistics. County-level hospital counts were abstracted from the Area Health Resource File. We adjusted for uninsured rate using a proxy variable, obtained by dividing the number of uninsured hospitalizations in a county year by the total annual county population. Under the assumption that the uninsured group has a stable hospitalization rate over the years, this proxy variable captures temporal trends in the county-level rate of the uninsured. These adjustments allow for county-level demographic-, economic-, and healthcare system–related changes that may affect hospitalization rates independently of exposure to UNGD.

Statistical analysis

We estimated a series of fixed-effects multivariate linear regressions. In the main analysis, we considered a 12-year panel of 67 Pennsylvania counties (N = 804). We included county and year fixed effects to control for time-invariant county characteristics and secular trends in hospital admissions and adjusted for time-varying county characteristics described above. In a subsequent analysis, we removed the effect of pollution in large urban areas by excluding large metropolitan counties, defined by the 2013 National Center for Health Statistics urban-rural classification. This analysis used a 12-year panel of 54 Pennsylvania counties (N = 648). Conducting analyses for three different exposure variables on the samples of 804 and 648 county years, we obtained six subsets of results for our 17 outcomes. Because chance findings are possible when multiple hypotheses are tested simultaneously, we adjusted for multiple comparisons in each subset of analyses. We used the Benjamini and Hochberg correction method, which relies on controlling the false discovery rate.[33] We set the false discovery rate to 0.10; in other words, we are willing to accept up to 10% of the significant results as erroneously significant. We used R software to obtain Benjamini and Hochberg adjusted P-values.[34]

For outcomes that were significantly associated with UNGD, we performed further analyses to explore potential effects of UNGD on health in more detail. First, we estimated the relationships by sex and age group: children, non-elderly adults, and the elderly. Then, for demographic groups in which statistically significant relationships persisted, we analyzed disease subcategories and specific diseases. We only examined further subcategories and specific diseases, if the subcategory findings at the higher level of grouping matched our main findings, in terms of statistical significance in models by exposure metric and panel of counties.

Results

Descriptive statistics

Table 1 shows 2003–2014 changes in summary statistics of our variables. Increases in all three UNGD measures over the study period are dramatic. We demonstrate the rapid and extensive growth of UNGD in Fig. A (see online supplementary material). The spatial distribution of unconventional gas wells drilled between 2003 and 2014 across Pennsylvania counties is shown in Fig. B (see online supplementary material).

There were significant changes in hospitalization rates for the broad disease categories and overall between 2003 and 2014 (Table 1). Fig. B (see online supplementary material) illustrates the across-county variation in total hospitalization rate changes across Pennsylvania. Although the state overall experienced a decrease in the total hospitalization rate as shown in Table 1, seven counties experienced increases in total hospitalization rate of 1.5 or more standard deviations from the state mean. Changes in state-level mean population characteristics from 2003 to 2014 are shown in Table 1.

UNGD and hospitalizations

For our main analyses, we first report statistically significant findings at 5% level before the adjustment for multiple comparisons. Then, we report the findings that remain statistically significant at 5% level after the adjustment.

Tables 2 and 3 present fixed-effects regression estimates. In the panel of all Pennsylvania counties, we found a positive association between cumulative well count and hospitalizations for genitourinary diseases (Table 2). On average, one additional cumulative well in a county is associated with an increase of 0.008 hospitalizations for genitourinary diseases per 10,000 residents (P = .007, 95% confidence interval [CI] 0.002–0.01). Compared with the baseline average rate of 67.8 in 2003, this point estimate indicates that the addition of 100 cumulative wells is associated with a 1.2% relative increase in the genitourinary hospitalization rate. We found no evidence of association between county-level cumulative well count and hospitalizations for the rest of the broad disease categories or overall hospitalizations in the panel of all Pennsylvania counties.

When modeling exposure as cumulative well density, we found negative associations with hospitalizations for infectious diseases and musculoskeletal diseases and a positive association with genitourinary hospitalizations (Table 2). An increase of one well per square kilometer is associated with 27.7 fewer infectious disease hospitalizations per 10,000 residents (P = .03; 95% CI −52.0 to −3.5; relative decrease 89.4%) and with 13.7 fewer musculoskeletal disease hospitalizations (P = .04; 95% CI −27.1 to −0.4; relative decrease 16.7%). As for genitourinary diseases, an increase of one well per square kilometer is associated with 20.0 more hospitalizations per

Table 1 – Summary statistics of UNGD exposure measures, county hospitalization rates, and county characteristics in Pennsylvania, 2003 and 2014.

Variable	2003		2014	
	Mean	SD	Mean	SD
UNGD exposure measure				
Contemporaneous spudded wells	0.015**	0.12	17.8**	48.2
Cumulative well count	0.015***	0.12	124.6***	295.5
Cumulative well density (per sq.km.)	7×10^{-6}***	6×10^{-5}	0.057***	0.129
County hospitalizations rates, per 10,000				
Total hospitalizations	1204.6**	216.0	1086.8**	192.9
Infectious diseases	31.0 ***	8.3	69.3***	18.3
Neoplasms	64.6***	12.8	45.6***	10.6
Endocrine, nutritional and metabolic diseases, and immunity disorders	51.9***	14.3	39.7***	10.1
Diseases of the blood and blood-forming organs	11.0***	4.0	13.7***	4.9
Mental disorders	87.3*	31.8	100.0*	29.3
Diseases of the nervous system and sense organs	19.6***	6.5	26.5***	6.8
Diseases of the circulatory system	276.5***	60.6	195.2***	37.7
Diseases of the respiratory system	135.4***	35.8	108.5***	27.7
Diseases of the digestive system	125.2***	25.6	111.9***	19.9
Diseases of the genitourinary system	67.8***	14.9	56.1***	15.7
Complications of pregnancy and childbirth	111.0***	18.0	99.2***	18.0
Diseases of the skin and subcutaneous tissues	21.5*	6.4	23.9*	7.4
Diseases of the musculoskeletal system and connective tissue	81.9**	13.7	89.9**	18.4
Congenital anomalies	4.2*	1.4	3.6*	1.3
Conditions originating in the perinatal period	3.6	1.7	3.7	2.3
Injury and poisoning	112.1***	20.3	100.0***	19.1
County demographic characteristics				
% White	94.7	7.2	92.7	8.1
% Black	4.1	6.3	5.4	6.8
% Hispanic	2.3**	2.7	4.1**	4.4
% Female	50.7	1.6	50.0	2.5
% 0–19 y	25.8***	1.6	22.9***	2.5
% 20–39 y	24.5	2.8	23.6	3.2
% 40–64 y	33.6***	1.8	35.0***	2.1
% 65+ y	16.1***	2.2	18.4***	2.4
County economic characteristics				
% In poverty	10.4***	2.5	13.6***	3.3
% Unemployed	6.1	1.4	6.1	1.0
Median income ($2010)	46,462	9372	46,139	8656
Healthcare system characteristics				
Total number of hospitals	3.7	5.7	3.5	4.9
Uninsured proxy (number of uninsured hospitalizations/10,000 population)	22.2	9.3	20.4	7.5

UNGD = unconventional natural gas development. SD = standard deviation.

The well data are from the Carnegie Museum of Natural History, 2003–2014. Hospitalization rates calculated by dividing the number of hospitalizations in a county year by the estimate of the population count in the county year. We obtained hospitalization data from Pennsylvania Health Care Cost Containment Council (PHC4) and population count estimates from the Surveillance, Epidemiology, and End Results (SEER) Program.

***Changes from 2003 to 2014 statistically different (t-test) at <0.001 level, ** at <0.01 level, * at <0.05 level.

10,000 residents (*P* = .001; 95% CI 8.2–31.8; relative increase 29.5%). When contemporaneous wells were considered as the exposure variable, we found a negative relationship with hospitalizations for musculoskeletal diseases; an additional well in a year is associated with a decrease of 0.025 hospitalizations per 10,000 residents (*P* = .01; 95% CI −0.05 to −0.005) (Table 2), translating into a 0.03% relative decrease.

When large metropolitan counties were excluded, the positive relationships between cumulative measures of UNGD and genitourinary hospitalizations persisted (Table 3). In addition, both cumulative UNGD measures are positively associated with hospitalizations for diseases of the skin: on average, an additional cumulative well is associated with an increase of 0.004 hospitalizations per 10,000 residents

(*P* < .001; 95% CI 0.002–0.007), and each additional well per square kilometer is associated with an increase of 12.2 hospitalizations per 10,000 residents (*P* = .002; 95% CI 4.5–20.0) (Table 3), translating into 0.02% and 59.5% relative increases, respectively, relative to the baseline 2003 rate of 20.5 in this panel. There is no evidence of association between contemporaneous wells and any outcome variables in the panel of 54 counties (Table 3).

After correction for multiple comparisons, four associations remained statistically significant: the positive associations between genitourinary hospitalizations and cumulative well density, in both panels (corrected *P* = .02 for both estimates) and the positive associations between skin-related hospitalizations and both cumulative UNGD

Table 2 – Associations of unconventional natural gas development measures and hospitalization rates, per 10,000, Pennsylvania, all counties, 2003–2014.

Outcomes	Well count, coefficient (P-value) [95% CI]	Well density, coefficient (P-value) [95% CI]	Contemporaneous wells, coefficient (P-value) [95% CI]
Overall hospitalizations	0.05 (0.32) [−0.05 to 0.16]	64.3 (0.60) [−178.9 to 307.4]	0.002 (0.99) [−0.28 to 0.28]
Infectious diseases	−0.01 (0.07) [−0.02 to 0.001]	−27.7* (0.03) [−52.0 to −3.5]	−0.037 (0.07) [−0.08 to 0.003]
Neoplasms	0.00002 (0.99) [−0.004 to 0.004]	1.1 (0.81) [−7.9 to 10.1]	0.002 (0.79) [−0.02 to 0.02]
Endocrine, nutritional and metabolic diseases, and immunity disorders	0.008 (0.09) [−0.001 to 0.02]	13.3 (0.26) [−10.00 to 36.6]	0.006 (0.59) [−0.02 to 0.03]
Diseases of the blood and blood-forming organs	−0.001 (0.17) [−0.003 to 0.001]	−2.75 (0.14) [−6.4 to 0.9]	−0.003 (0.32) [−0.01 to 0.003]
Mental disorders	0.0003 (0.95) [−0.009 to 0.01]	7.8 (0.62) [−23.3 to 38.8]	0.015 (0.46) [−0.03 to 0.05]
Diseases of the nervous system and sense organs	0.006 (0.07) [−0.0004 to 0.01]	10.3 (0.18) [−4.7 to 25.4]	0.007 (0.42) [−0.01 to 0.03]
Diseases of the circulatory system	0.023 (0.19) [−0.011 to 0.06]	26.6 (0.51) [−54.4 to 107.7]	0.024 (0.59) [−0.06 to 0.11]
Diseases of the respiratory system	0.006 (0.54) [−0.014 to 0.03]	8.6 (0.73) [−41.4 to 58.6]	0.001 (0.98) [−0.06 to 0.06]
Diseases of the digestive system	0.006 (0.34) [−0.006 to 0.02]	4.8 (0.74) [−23.3 to 32.9]	−0.001 (0.97) [−0.04 to 0.04]
Diseases of the genitourinary system	0.008** (0.007) [0.002 to 0.01]	20.00** (0.001) [8.2 to 31.8]	0.011 (0.36) [−0.01 to 0.03]
Complications of pregnancy, childbirth, and the puerperium	0.001 (0.63) [−0.003 to 0.005]	−0.4 (0.94) [−10.7 to 10.0]	−0.009 (0.14) [−0.02 to 0.003]
Diseases of the skin and subcutaneous tissues	0.003 (0.06) [−0.0001 to 0.006]	7.9 (0.10) [−1.4 to 17.3]	0.003 (0.60) [−0.007 to 0.01]
Diseases of the musculoskeletal system and connective tissue	−0.005 (0.11) [−0.011 to 0.001]	−13.7* (0.04) [−27.1 to −0.4]	−0.025* (0.01) [−0.05 to −0.005]
Congenital anomalies	0.0002 (0.53) [−0.0004 to 0.001]	0.5 (0.55) [−1.2 to 2.2]	0.001 (0.37) [−0.001 to 0.004]
Conditions originating in the perinatal period	0.0006 (0.39) [−0.001 to 0.002]	0.6 (0.74) [−2.7 to 3.8]	−0.0002 (0.92) [−0.004 to 0.003]
Injury and poisoning	0.008 (0.21) [−0.005 to 0.02]	7.4 (0.62) [−22.4 to 37.2]	0.008 (0.66) [−0.03 to 0.05]
N	804	804	804

We calculated hospitalization rates by dividing the number of hospitalizations in a county year by the estimate of the population count in the county year. We obtained hospitalization data from Pennsylvania Health Care Cost Containment Council (PHC4) and population count estimates from the Surveillance, Epidemiology, and End Results (SEER) Program. The well data are from Carnegie Museum of Natural History.
P values from 2-tailed tests are reported in parentheses, 95% confidence intervals (CIs) are reported in square brackets.
*** Statistically significant at <0.001 level, ** at <0.01 level, * at <0.05 level.

measures in the panel of 54 counties (corrected P = .009 and P = .02, respectively).

In further analyses, we found that the associations between cumulative UNGD measures and genitourinary hospitalizations in the general population are driven by hospitalizations among non-elderly adult (20–64 years old) females. The magnitudes of the associations in this demographic group are 2–3 times higher than the estimates in the general population. The associations between cumulative UNGD measures and skin-related hospitalizations in the general population in the panel excluding large metropolitan counties are driven by hospitalizations among non-elderly adult males. Estimates across all models by sex and age group are shown in Table A (see online supplementary material).

In further exploration of what specific diseases account for these findings, we found statistically significant positive associations between cumulative UNGD and the following specific diseases within the genitourinary category among non-elderly adult females: kidney infections (ICD-9-CM 590), calculus of ureter (ICD-9-CM 592.1), and urinary tract infection (ICD-9-CM 599.0), across both measures and both panels (Table 4). As for specific diseases driving skin-related hospitalizations among non-elderly males, we found statistically significant associations between cumulative density and cellulitis and abscess of four body parts, but the findings were mixed, likely because of the relative rarity of these conditions (results not shown but available upon request).

Sensitivity analyses

We performed several sensitivity analyses. First, we accounted for potential UNGD effects from neighboring counties by including an additional covariate that measures UNGD exposure in adjacent Pennsylvania counties. The negative association between cumulative well density and musculoskeletal hospitalizations and the positive association between cumulative well count and skin-related hospitalization rate in the reduced panel remained statistically significant before correction for multiple comparisons (P = .03 and P = .05, respectively) but lost statistical significance after the correction. The estimates of the other associations reported in the main analyses were no longer precise.

In addition to UNGD, other industrial activity in Pennsylvania, such as coal mining and electricity production, may confound our findings. In the second sensitivity analysis, we adjusted our models by coal production measures (facility, surface, and underground) in each county year. Our main estimates for genitourinary and skin-related hospitalizations are robust to this model specification. Additionally, estimates for skin-related hospitalizations in the all-county panel gain precision after the adjustment for county coal production: 0.003 (P = .008) for cumulative count and 8.9 (P = .02) for cumulative density. In the third sensitivity analysis, we adjusted for the total number of power plants in each county year. Our

Table 3 − Associations of unconventional natural gas development measures and hospitalization rates, per 10,000, Pennsylvania, excluding large metropolitan counties, 2003−2014.

Outcomes	Well count, coefficient (P-value) [95% CI]	Well density, coefficient (P-value) [95% CI]	Contemporaneous wells, coefficient (P-value) [95% CI]
Overall hospitalizations	0.08 (0.19) [−0.04 to 0.20]	125.5 (0.44) [−195.2 to 446.3]	0.05 (0.76) [−0.3 to 0.4]
Infectious diseases	−0.01 (0.13) [−0.02 to 0.003]	−29.0 (0.05) [−58.4 to 0.4]	−0.04 (0.12) [−0.09 to 0.01]
Neoplasms	−0.00003 (0.99) [−0.005 to 0.005]	1.6 (0.77) [−9.4 to 12.7]	0.003 (0.76) [−0.02 to 0.02]
Endocrine, nutritional and metabolic diseases, and immunity disorders	0.009 (0.11) [−0.002 to 0.02]	14.9 (0.33) [−15.3 to 45.2]	0.003 (0.77) [−0.02 to 0.03]
Diseases of the blood and blood-forming organs	−0.0005 (0.48) [−0.002 to 0.001]	−1.2 (0.51) [−5.0 to 2.5]	−0.001 (0.63) [−0.007 to 0.004]
Mental disorders	0.003 (0.59) [−0.008 to 0.01]	15.7 (0.40) [−21.3 to 52.8]	0.02 (0.20) [−0.01 to 0.06]
Diseases of the nervous system and sense organs	0.006 (0.12) [−0.002 to 0.01]	10.5 (0.31) [−9.8 to 30.7]	0.007 (0.55) [−0.02 to 0.03]
Diseases of the circulatory system	0.03 (0.11) [−0.007 to 0.07]	41.7 (0.43) [−63.2 to 146.6]	0.03 (0.51) [−0.07 to 0.13]
Diseases of the respiratory system	0.01 (0.33) [−0.011 to 0.03]	20.1 (0.51) [−40.6 to 80.9]	0.009 (0.80) [−0.06 to 0.08]
Diseases of the digestive system	0.009 (0.20) [−0.005 to 0.02]	11.5 (0.53) [−25.2 to 48.2]	0.006 (0.80) [−0.04 to 0.05]
Diseases of the genitourinary system	0.008* (0.02) [0.002 to 0.02]	23.1** (0.002) [8.7 to 37.5]	0.01 (0.36) [−0.01 to 0.04]
Complications of pregnancy, childbirth, and the puerperium	0.002 (0.39) [−0.003 to 0.007]	1.3 (0.84) [−11.1 to 13.6]	−0.006 (0.31) [−0.02 to 0.005]
Diseases of the skin and subcutaneous tissues	0.004*** (<0.001) [0.002 to 0.007]	12.2** (0.002) [4.5 to 20.0]	0.005 (0.32) [−0.005 to 0.02]
Diseases of the musculoskeletal system and connective tissue	−0.003 (0.44) [−0.009 to 0.004]	−6.9 (0.41) [−23.3 to 9.6]	−0.02 (0.07) [−0.04 to 0.002]
Congenital anomalies	0.0001 (0.79) [−0.0006 to 0.0008]	0.29 (0.78) [−1.8 to 2.4]	0.001 (0.43) [−0.002 to 0.004]
Conditions originating in the perinatal period	0.0005 (0.51) [−0.001 to 0.002]	0.07 (0.97) [−4.1 to 4.3]	−0.0003 (0.87) [−0.004 to 0.004]
Injury and poisoning	0.009 (0.22) [−0.006 to 0.02]	9.6 (0.63) [−30.6 to 49.8]	0.01 (0.61) [−0.03 to 0.06]
N	648	648	648

We calculated hospitalization rates by dividing the number of hospitalizations in a county year by the estimate of the population count in the county year. We obtained hospitalization data from Pennsylvania Health Care Cost Containment Council (PHC4) and population count estimates from the Surveillance, Epidemiology, and End Results (SEER) Program. The well data are from Carnegie Museum of Natural History.
P values from 2-tailed tests are reported in parentheses, 95% confidence intervals (CIs) are reported in square brackets.
*** Statistically significant at <0.001 level, ** at <0.01 level, * at <0.05 level.

Table 4 − Associations between cumulative UNGD measures and hospitalization rates for specific diseases within genitourinary disease category, non-elderly adult females, Pennsylvania, 2003−2014.

Outcomes	All counties (N = 804)		Excluding large metropolitan counties (N = 648)	
	Well count coefficient (P-value) [95% CI]	Well density coefficient (P-value) [95% CI]	Well count coefficient (P-value) [95% CI]	Well density coefficient (P-value) [95% CI]
Genitourinary, females (20-64y)				
Kidney infections	0.002* (0.027) [0.0003−0.004]	6.19* (0.04) [0.40−12.0]	0.003* (0.010) [0.0007−0.005]	8.44** (0.009) [2.20−14.68]
Calculus of ureter	0.003** (0.003) [0.001−0.005]	7.91** (0.004) [2.63−13.20]	0.003** (0.009) [0.0009−0.006]	8.21* (0.013) [1.82−14.61]
Urinary tract infection	0.003** (0.004) [0.001−0.005]	7.16** (0.003) [2.52−11.80]	0.004** (0.003) [0.001−0.006]	9.70** (0.001) [4.22−15.19]

We calculated hospitalization rates by dividing the number of hospitalizations in a county year by the estimate of the population count in the demographic group (females, 20−64 years old) in the county year. We obtained hospitalization data from Pennsylvania Health Care Cost Containment Council (PHC4) and population count estimates from the Surveillance, Epidemiology, and End Results (SEER) Program. The well data are from Carnegie Museum of Natural History.
P values from 2-tailed tests are reported in parentheses, 95% confidence intervals (CIs) are reported in square brackets.
*** Statistically significant at <0.001 level, ** at <0.01 level, * at <0.05 level.

reported estimates for genitourinary and skin-related hospitalizations remain essentially the same.

Discussion

In the main analysis of this study, we identified two broad categories of disease that may be affected by long-term exposure to UNGD: genitourinary diseases and diseases of the skin and subcutaneous tissue. Disease subgroupings as well as examples of specific diseases within these categories are given in Appendix B of the online supplementary material. We found that annual county-level genitourinary hospitalization rates are strongly and positively associated with cumulative well density in the two panels and that skin-related hospitalizations are strongly and positively associated with both cumulative UNGD measures in the panel excluding large metropolitan counties. The

associations between UNGD and genitourinary diseases and diseases of the skin are consistent with raised concerns over the potential effects of the chemicals found near UNGD sites in Pennsylvania on health.[3] Skin-related symptoms were also reported in a Pennsylvania-based household survey.[18] A 2018 report on community complaints to the Pennsylvania Department of Health showed that 39.7% of all formal health complaints about unconventional oil and gas production in the period from 2011 to February 2018 included dermatological symptoms and 10.0% included urogenital symptoms.[35]

The estimated associations of hospitalizations with cumulative well count and density are generally consistent with each other, indicating that both the total number of wells in the county, regardless of its size, and total well density have a similar effect on the considered outcomes. Since we found statistically significant associations with cumulative well measures but did not find evidence of associations with contemporaneously spudded wells, our results suggest that exposure to UNGD may have long-term effects, especially when considering hospitalizations, which imply serious acute illnesses or exacerbations of chronic diseases. It is possible that the risk of developing certain diseases accumulates with repeated exposure to drilling. This supposition is in agreement with previous literature that suggests a persistent effect of UNGD on health after the initial drilling and fracking phase.[18,19,24,25,27] If data on outpatient utilization of health services were available, investigations into whether contemporaneous drilling is related to minor health conditions and complaints would be possible. Another explanation may be that, although the well drilling phase generates more pollutants than other UNGD phases and is the most disruptive for the community, later stages of UNGD can be harmful for population health as well. Existing studies in Pennsylvania show that UNGD sites can remain in production for decades after the initial drilling, which could present an ongoing public health hazard for the affected communities.[18]

Whereas we did not find evidence of the association between UNGD and hospitalizations for other broad disease categories after correction for multiple testing, the null findings do not preclude effects of UNGD on hospitalizations for specific diseases within these categories. Previous research found significant associations of UNGD exposure with asthma hospitalizations[20,21] and pneumonia hospitalizations among the elderly;[23] however, the corresponding outcome in our study includes hospitalizations for all respiratory diseases at a higher level of aggregation, and our estimation model could not identify these relationships.

In further analyses, we found that the positive relationships between cumulative UNGD measures and genitourinary hospitalization rates are driven by hospitalizations among females in the 20–64 years age group and, in particular, by their hospitalizations for kidney infections, calculus of ureter, and urinary tract infection. To our knowledge, this is first evidence of a potential effect of long-term exposure to UNGD on genitourinary health of non-elderly adult women. However, we are only able to indicate strength of the associations, and a definite causal link should not be inferred. Further research into the causal mechanisms is needed to enhance

our understanding of how UNGD might be affecting genitourinary health. One mechanism by which UNGD may compromise genitourinary health, leading to hospital admissions, could be consumption of and contact with water contaminated with UNGD-related chemicals. It has been shown that UNGD drilling in proximity to community water systems increases shale-related contaminants in public drinking water in Pennsylvania.[10] Another mechanism could potentially be an increase in risk behaviors in areas with UNGD. A recent study showed that Pennsylvania counties with UNGD activities had higher rates of certain sexually transmitted infections and higher prostitution-related arrests.[36] It is plausible that behaviors related to these outcomes are linked to declines in genitourinary health among non-elderly adult women observed in our study. The mechanism may be composed of the complex mixture of pollutants from UNGD activity, increased risky behaviors in areas with UNGD, and economic changes that UNGD brings. Future research should untangle how UNGD affects health and address why these effects on genitourinary health may exist.

As for skin health, the positive relationships between cumulative UNGD measures and skin-related hospitalization rates in counties other than large metropolitan are driven by hospitalizations among males in the 20–64 years age group; however, investigation into which specific diseases may account for these relationships yielded mixed findings, likely because of the relative rarity of these diseases. More research into potential effects of long-term UNGD exposure on skin health is warranted.

Hospitalizations, in contrast with outpatient physician visits, reflect acute illness or serious exacerbations of chronic disease and are a reason for public health concern. An effect of UNGD on hospitalization rates suggests that there are likely effects on outpatient utilization, underlying more minor symptoms and conditions. Public health and healthcare professionals should be aware of the potential effects of UNGD exposure on genitourinary health among non-elderly adult women and should encourage those who live in close proximity to unconventional well drilling and have genitourinary symptoms to seek appropriate and timely health care, hopefully thus preventing serious disease and the need for hospitalizations. Future research can inform specific public health interventions.

We acknowledge limitations of our study. First, we are limited by the information included in the hospital discharge data. Because these data do not include patients' street address, we are unable to utilize more precise exposure measures based on distance between place of residence and wells, and we therefore utilize an ecological study design. One considerable drawback of an ecological study is that residents living near the centroid of the area are not differentiated from individuals residing near area borders, with the latter group potentially experiencing the exposure of the adjacent areas. To account for these potential spillover effects, we conducted a sensitivity analysis including measures of exposure in adjacent counties. Although our estimates were no longer precise, the direction of estimates remained the same and our conclusions do not change. Additionally, ecological study design does not allow for causal inference. Second, we were unable to appropriately

adjust for annual county-level uninsured rates because of data unavailability. Healthcare utilization depends to a large extent on whether individuals have health insurance. If our proxy measure does not appropriately capture temporal and geographic variation in the uninsured rate, our estimates may be biased.

In the absence of a large and conclusive body of evidence on the impact of UNGD on public health, several European countries, including France, Germany, Bulgaria, Ireland, and Scotland, and three states in the United States — Vermont, New York, and Maryland — as well as select counties have taken a precautionary approach and prohibited hydraulic fracturing. Our investigation into associations between UNGD exposure measures and annual county-level hospitalization rates in Pennsylvania shows that UNGD may cause or exacerbate genitourinary diseases and diseases of the skin, leading to hospital admissions. More specifically, genitourinary health of non-elderly adult women seems to be particularly affected. Our findings suggest that public health and healthcare professionals should be aware of these potential effects and advise the exposed patients to seek care early. If our findings are confirmed in future research as causal, improved regulations to protect affected communities may also be needed.

Author statements

Acknowledgements

Ethical approval

This study has been approved by University of Rochester Institutional Review Board.

Funding support

Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Appendix A and B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2018.11.020.