



Changes in emergency department visits for respiratory and cardiovascular disease after closure of a coking operation near Pittsburgh, PA

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ABSTRACT:

Introduction: In Allegheny County (AC), PA, US, closure of a large coke plant in January 2016 presented an opportunity to investigate the contribution of air pollutants to health outcomes in a nearby community.

Materials and methods: The Allegheny County Health Department, (ACHD), Division of Air Quality, had begun monitoring pollutants near the plant since June 2011. The rates of hospitalizations and ED visits for cardiovascular and respiratory disease were compared in the exposed community and two control areas: exposed control, with another coking operation; and unexposed control.

Results: Of the study and two control areas, particulate matter concentrations decreased the most in the study area, from 10.9 $\mu\text{g}/\text{m}^3$ to 9.7 $\mu\text{g}/\text{m}^3$. Benzene decreased substantially in that area, from 0.27 ppm to 0.10 ppm. ED visits for cardiovascular, respiratory, and asthma were significantly higher in the exposed group in 2015 compared to 2016. There were no temporal differences in either control groups. There was a 26.5% decrease in cardiovascular ED visits, a 37.9% decrease in respiratory ED visits, and a 3-5 fold decrease in ED visits due to asthma. These decreases were not seen in exposed and unexposed control areas. A case-crossover analysis confirmed that daily ED visits were significantly associated with daily particulate matter levels, controlling for temperature.

Conclusion: With the closure of a large coke plant facility, we found that a modest decrease in particulate matter and a notable decrease in benzene concentration were associated with a significant decrease in emergency room visits not previously documented in other studies.

Introduction

In the fall of 1948, seventeen people died, and hundreds fell ill due to air pollution in Donora, a small town in Western Pennsylvania. This led to the first public health investigation of air. The National Public Health Service investigated this incident, which began with a temperature inver-

sion that started on a Wednesday and persisted for five days. Because air pollution was not yet systematically measured, neither the concentration nor the constituents of the pollution during the incident were known. Interestingly, a retrospective look at death records in the community revealed that during previous temperature inver-

sions, which traps pollution, mortality rates had also increased, or even doubled [1].

Since the passing of the Clean Air Act by the United States Environmental Protection Agency (USEPA) in 1970, six criteria air pollutants are now measured and regulated [2]. Nationally, there has been a commensurate reduction in pollution levels. However, even with decreasing pollution levels, acute and chronic health effects of air pollutants (particularly PM₁₀ and PM_{2.5}) have been demonstrated at the national [3, 4] and local level [5-9].

In 2004, the American Heart Association issued a statement concluding that exposure to particulate matter contributes to cardiovascular morbidity and mortality [3]. Since then, much has been discovered regarding the mechanism of action of particulate matter on cardiovascular health. When fine particles, including metals and organic compounds, are breathed in, the body's response includes pulmonary and systemic oxidative stress and inflammation, as evidenced by elevated biomarkers, vasoconstriction and resultant hypertension. Exposure also coincides with coagulation and thrombotic events, long-term increased risk of atherosclerosis, and plaque. It is also associated with imbalance in the autonomic nervous system, and with arrhythmias. Daily increases of 10 µg/m³ are generally associated with a 1% increase in cardiovascular death [10].

Beyond the observations of health effects of air pollution noted during extreme circumstances like Donora, a variety of natural experiments have illustrated the impact of decreased particulate air pollution on health outcomes. One of the earliest studies in which pollution levels were quantified was done by many researchers, who studied health effects of air quality improvements during worker strikes at a steel mill in Utah in the 1980's [11, 12]. In the study period between April 1985

and February 1988, 24-h PM₁₀ levels were more than 150 µg/m³. While the mill was open and PM₁₀ levels were at their highest, there was twice the pollution and a 3-fold increase in children's hospitalizations for respiratory issues, compared to when the mill was closed. Additional studies have reached similar conclusions. For example, short-term changes in air pollution and health effects have been noted when alternative transportation strategies were employed during Olympic events [14, 15]. While these studies examine the before and after impact of pollution, they represent quasi experimental conditions that may have coincided with other population changes. Unfortunately, experimental designs to measure the impact of pollutants is difficult and largely unethical. Rather additional studies of natural scenarios may help shed additional light on the health outcomes of changes in air quality.

Here in Allegheny County (AC), PA, the closure of a large coke plant: Shenango, Inc., located in the Neville Island area of AC, which was the source of distinctive and substantial air pollutants presented a unique opportunity to investigate the contribution of air pollutants to health outcomes in a nearby community. Shenango, Inc. located on Neville Island in the Ohio River approximately 8 miles outside of Pittsburgh, PA, was a significant source of air pollution in Allegheny County. According to the Allegheny County 2014 Emissions Inventory, compared to other point sources, Shenango ranked 4th in volatile organic compound (VOC) emissions, 5th in sulfur dioxide (SO₂) emissions, 8th in PM_{2.5} emissions, 5th in NO_x emissions, and 1st in methane emissions. Additionally, it was one of the two coke plants in the county, which are the only contributors of coke oven emissions. Shenango, Inc. completed its last coke push in the first week of January 2016.

The purpose of this study was to examine hos-

pital and emergency department visits for cardiovascular and respiratory outcomes before and after Shenango closure compared to Allegheny County control communities with similar and varying fine particulate matter levels.

Materials and methods

The study period, including evaluation of both air pollution levels and health effects, was limited to calendar years 2015 and 2016, as the plant shut down during the first week of January 2016. This allowed both air and health comparisons to be made easily, without adjustment for seasonality.

Air Monitoring

The Allegheny County Health Department, (ACHD), Division of Air Quality, began monitoring volatile organic pollutants (VOCs) near the plant in February of 2015 using radiello® tubes. These tubes were changed every two weeks. VOCs monitored include those known to be associated with coke oven gas emissions, including benzene, toluene, ethylbenzene, m,p-xylene, o-xylene, and n-hexane. Monitors were placed where prevailing winds would dictate pollution would be distributed. Eight monitors were placed. See Fig. 1.

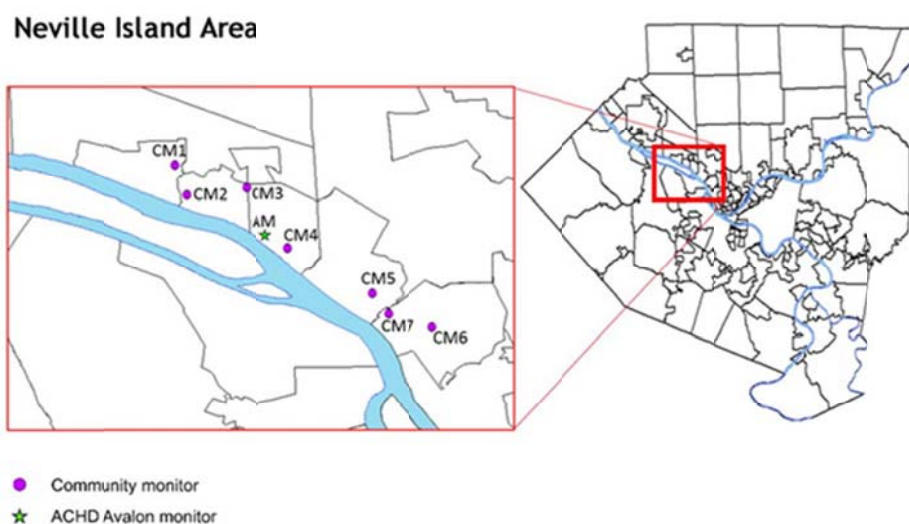


Fig. 1. Map of temporary community monitors and permanent regulatory monitor in study area

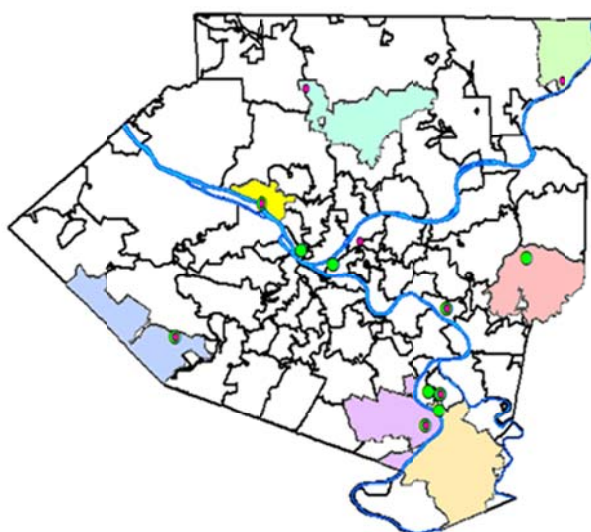


Fig. 2. EPA monitoring sites in Allegheny County with study area zip codes highlighted

There has been an EPA PM_{2.5} Beta-Attenuation Monitor (BAM) monitor located strategically in Avalon (as noted in Fig. 1 with a star) to capture hourly emissions from the industrial sites on Neville Island since June 8, 2011. It is collocated with a sulfur dioxide monitor that has been monitoring Neville Island emissions since January 1, 2006. The ACHD monitoring network is found in Fig. 2. Other monitors used in this study include another BAM monitor at Liberty Borough, directly across from the currently operating coking operation, which collects hourly particulate concentrations, and the Partisol monitor in Harrison Township that collects PM_{2.5} data every three days. These samples were taken using US Environmental Protection Agency (EPA) sampling guidelines set forth under the Clean Air Act. The daily mean PM_{2.5} concentrations were used in our analysis. The meteorological data, including daily mean temperature and humidity, were derived from the US National Climatic Data Center database for the monitoring site located at the Pittsburgh International Airport, Allegheny County.

Population

The population exposed to Shenango, Inc, resides in zip code 15202. Two control communities were chosen using the following criteria – presence of

a PM_{2.5} monitor and similar sociodemographics, with respect to poverty and minority status. See Table 1.

The following zip codes were assessed as unexposed: unexposed Control -- 15014 (Brackenridge), 15065 (Harrison, Natrona Heights), 15084 (Tarentum). This area was chosen as it also has a PM_{2.5} monitor with a similar 2015 concentration and among areas with a PM_{2.5} monitor, it is most similar demographically to the Shenango area. A second control population was selected – Exposed Control, 15025 (Clairton) 15037 (Liberty). This population is in proximity to another coking operation still running in Allegheny County.

Clinical outcomes

Two large electronic databases that include hospitalizations as well as Emergency Department (ED) visits for this population, were used to capture health care utilization data. Hospitalization data were obtained from the Pennsylvania Health Care Cost Containment Council (PHC4). Both respiratory and cardiovascular health outcomes were included in this study. Inpatient hospital visits for cardiovascular visits included ICD-10 codes I00-I99.9, Circulatory System Disease. Hospitalizations for respiratory disease were defined as J00-99.9, and those for asthma were J45.0-45.9.

Table 1. Sociodemographic characteristics of study populations

Zip Code	Population	Poverty	% nonwhite	PM _{2.5} (2015)	PM _{2.5} (2016)	% PM change (15-16)
Exposed 15202	19,536	9.6%	11.2%	10.9	9.7	-12%
Unexposed control	24,645	13.1	6.5%	9.8	9.5	-3%
15014	3,184	7.6%	7.6%	-----		
15065	11,588	11.7%	4.2%	9.8	9.5	-3%
15084	10,130	9.4%	5.8%	-----		
Exposed Control	26,818	12.4%	13.5%			
15025	16,426	7.7%	21.2%	10.4	9.3	-12%
15037	11,041	7.4%	3.3%	12.9	12.8	-1%

ED visits were downloaded from the EpiCenter data portal. EpiCenter uses ED registration data and aggregates into syndromes. EpiCenter receives data from all EDs in Pennsylvania, and were queried by patient residence. Syndromes for respiratory syndrome, asthma syndrome and traumatic injury ED visits were aggregated by zip code and day to create a database. Cardiovascular syndrome was defined by taking all the long descriptions of cardiovascular-related codes from ICD-9/10 and putting them into EpiInfo (version 7.2.0.1) to create a word cloud of the top 50 responses. Common words like “the” or “and” were not included. The codes were downloaded from the Centers for Medicare & Medicaid Services (CMS) website and filtered in Excel for codes 390-459 or I00-I78. Traumatic injury visits were used as a control health outcome in some analyses. Neither hospitalizations nor ED visits contained identifiable information and could therefore not be deduplicated, accounting for visits, rather than individuals.

Case-crossover analysis

A case-crossover analysis was conducted, controlling for temperature. This analysis was conducted only in the exposed and exposed control areas, as these two have particulate matter monitors that operate daily. These analyses were conducted using the case-crossover analysis tool (C-CAT) developed by Apex Epidemiology Research in collaboration with the New York State Department of Health for use with SAS [16]. It provides an easy-to-use interface to SAS code that implements time stratified case-crossover analysis to estimate the association between acute health effects and transient changes in environmental exposures. Because each subject serves as his/her own control, the case-crossover approach controls for the effects

of stable subject-specific covariates such as gender and race. If the case and control periods in each risk set are relatively close in time, this method also controls for potential time-varying confounders such as seasonal effects or personal habits by design [17].

In this study, the case period referred to the day when respiratory ED visits occurred. Controls were defined as all days within a 28-day interval with the same day-of-the-week as the case period. Therefore, a match setting consisted of 1 case period and 3 control periods. The referent day could be on the same day of the week 3 consecutive weeks before and none after; 2 weeks before and 1 week after; or 1 week before and 2 after; or 3 weeks after, all occurring within the 28 days. C-CAT performed conditional logistic regression to calculate the risk of $PM_{2.5}$. Temperature on the day of the event was evaluated as a covariate in each conditional logistic regression as we explored the relationship between air pollution and asthma ED visits in our study populations.

Because of the potentially lagged effect of air pollution on respiratory ED visits [9], lagged-day exposures up to 3 days and a 4-day average (day 0 to day 3) were used in the analyses. The 3-day averages were calculated as the mean of air pollution levels on the lag 0, 1, 2, and 3 days before the event (or the control day), which allowed us to evaluate the potential cumulative effect of 3 days of air pollution exposure on asthma ED visits. The variables of air pollution concentration for the lag 0, 1, 2, and 3 days and the 3-day average were fitted into separate models and the independent health effects of air pollution on asthma ED visits were estimated for these exposure periods. Results are presented as odds ratios and associated 95% confidence intervals for every $\mu\text{g}/\text{m}^3$ increase in concentration of $PM_{2.5}$.

Results and discussion

Air pollution levels

Radiello® monitors (Exposed only)

There was a significant decrease in maximum benzene (from 1.52 to 0.81 ppbv) after plant closure. Maximum toluene concentrations increased from 0.8 to 1.24 ppbv (NS), while other measured volatile organic compounds (VOCs) – ethylbenzene, ethylbenzene, m,p-xylene, o-xylene, naphthalene, styrene, and n-hexane – had no appreciable change. See Table 2.

Network monitors (Exposed, Unexposed Control, and Exposed Control)

Of the study and two control areas, particulate matter concentrations decreased the most in the study area, from 10.9 $\mu\text{g}/\text{m}^3$ to 9.7 $\mu\text{g}/\text{m}^3$. Ben-

zene decreased substantially in that area as well, from 0.27 ppm to 0.10 ppm. In the exposed control area in which a coking facility continued to operate through the study period, both particulate matter and benzene concentrations remained constant. Interestingly, hydrogen sulfide decreased more in the exposed control area than in the study area (89% and 23% respectively). See Table 3.

Clinical outcomes

Hospitalizations

There were 17 asthma hospitalizations in 2015 and 16 in 2016 in the study area. Because of small numbers, rates were not calculated. Table 4 indicates that there were no significant changes in hospitalization rates for cardiovascular disease in the exposed or in either control population between 2015 and 2016.

Table 2. Results of radiello sampling for VOCs, before and after plant closure

Compounds tested	Inhalation reference concentration (RfC, converted to ppb)	Maximum concentrations found (ppbv)	
		Plant open	Plant closed
Benzene	9.39	1.52	0.81
Toluene	1326.8	0.8	1.24
Ethylbenzene	230.3	0.13	0.15
M,p-xylenes	23	0.38	0.49
o-xylene	23	0.13	0.16
Naphthalene	0.57	ND	ND
Styrene	234.8	ND	ND
n-hexane	198.6	1.14	1.07

ND=Not detected

Ppbv=parts per billion volume

Table 3. Network monitor annual averages through study period for areas of interest

Zip Code	PM _{2.5} (2015)	PM _{2.5} (2016)	% PM change (15-16)	H ₂ S (1-hr max -- 2015)	H ₂ S (1-hr max -- 2016)	%H ₂ S change (15-16)	Benzene (2015)	Benzene (2016)	% Benzene change (15-16)
15202	10.9	9.7	-12%	0.016	0.013	23%	0.27	0.10	-270%
15037	12.9	12.8	-1%	0.140	0.074	89%	1.59	1.52	-5%
15065	9.8	9.5	-3%	NA	NA	NA	NA	NA	NA

NA=data Not Available/no monitor

ED visits

ED visits for respiratory and cardiovascular disease were measured for the exposed, exposed control, and unexposed control areas for 2015 and 2016. ED visits for these outcomes were significantly higher in the exposed group in 2015 compared to 2016. There were no temporal differences in either control group. In order to validate these findings, a control outcome, injuries, was assessed temporally to determine if there was a change in healthcare access that influenced ED visits. Injury visits increased during this time frame in the exposed and unexposed control areas, and remained unchanged in the exposed control area. See Table 5 for rates per 10,000. Inter-

estingly, CVD ED visits were 2.5 times higher in the Exposed Study area when compared to the Exposed Control in 2015. The Exposed geographic area consistently had the highest rate of ED visits for all outcomes. Unexposed control and Exposed control were second and third, respectively.

Next, asthma ED visits were evaluated for change after plant closure. Again, changes were noted in only the Exposed area, with an over 5-fold reduction in pediatric asthma after plant closure and a 3.3-fold reduction in all asthma. Asthma ED visits did not change between 2015 and 2016 in Control areas. See Table 6.

Table 4. Age adjusted circulatory system disease hospitalization rates in study areas

Exposure	Age-Adjusted rate per 10,000 2015 (95% CI)	Age-Adjusted rate per 10,000 2016 (95% CI)
Exposed	171.3 (154.9, 187.8)	167.6 (151.2, 183.8)
Unexposed control	176.8 (162.93, 190.579)	169.3 (155.70, 182.95)
Exposed control	150.3 (138.3, 162.4)	156.5 (144.1, 168.9)

Table 5. ED visit rates (per 10,000) by study area and year

Area	CVD 2015 (95%CI)	CVD 2016	Respiratory 2015	Respiratory 2016	Injury 2015	Injury 2016
Exposed	938.8 (898.6-980.2)	689.9 (655.1-725.9)	1,021.6 (979.8-1,065.0)	634.4 (601.1-669.2)	717.3 (681.9-753.9)	1,029.7 (987.8-1,073.0)
Exposed Control	376.0 (353.7-399.2)	403.2 (380.1-427.2)	482.5 (458.8-510.4)	484.0 (458.8-510.4)	746.7 (715.7-778.6)	763.1 (731.8-795.3)
Unexposed Control	577.5 (549.0-607.0)	593.1 (564.3-622.9)	748.5 (716.3-781.7)	767.4 (734.9-801.0)	790.3 (757.3-824.3)	861.3 (827.0-896.7)

Table 6. ED visits for asthma per 10,000

Area	Pediatric Asthma 2015 (95%CI)	Pediatric Asthma 2016 (95%CI)	Total Asthma 2015	Total Asthma 2016
Exposed	200.0 (158.4-249.0)	37.8 (21.5-61.9)	149.4 (133.1-167.1)	45.7 (37.0-55.9)
Exposed control	64.8 (45.6-88.6)	49.9 (33.5-71.3)	41.0 (33.8-49.1)	35.0 (28.5-42.7)
Unexposed control	37.6 (23.3-57.5)	29.7 (17.2-47.8)	34.9 (28.1-42.9)	46.6 (38.7-55.7)

Although there was no change in hospitalizations for environmentally sensitive conditions in the study area, there was a 26.5% decrease in cardiovascular ED visits, a 37.9% decrease in respiratory ED visits, and a 3-5 fold decrease in ED visits due to asthma. This decrease was not seen in areas of the county without environmental changes (exposed and unexposed controls).

The case-crossover analysis indicated that daily ED visits were significantly associated with daily particulate matter levels, after controlling for temperature. Daily exacerbations of cardiovascular disease were associated with daily particulate matter concentrations in the exposed control and combined areas, but not the exposed area alone. Daily exacerbations of respiratory disease were noted to be significantly associated with daily particulate concentrations in the exposed and combined areas, but not in the exposed control area alone. See Table 7.

In this study, we found that ED visits for cardiovascular and respiratory conditions significantly decreased after the closure of a local coke plant compared to control communities. This adds to the literature on natural experiments of changes in industrial air pollution and their impact on health.

Our results are somewhat in contrast with those from a study by other researchers [12], who found that hospitalizations for respiratory events were

significantly higher while the mill was in operation. During this period (1985-1988), PM₁₀ was the contaminant of concern, and comparison levels were <150 ug/m³ and ≥150 μg/m³. The 2015 Allegheny County PM₁₀ annual averages are much lower; the PM₁₀ concentration was 22.0 μg/m³ at the exposed control monitor and 18.1 at the exposed study monitor 2016 Allegheny County PM₁₀ annual average concentration is 20.1 μg/m³ at the exposed control monitor and 14.7 at the exposed study monitor. No changes in hospitalizations were noted during the study period.

Hospitalizations are less frequent and typically represent more severe outcomes, and an older population than ED visits [18]. A 73% agreement between CVD ED and hospitalization rate but only a 15% agreement for respiratory disease was noted previously. A stronger effect between air pollution and ED visits has been noted before, but in this case both outcomes were significant [19].

In two study, it were found significant decreases in asthma acute care visits post-Olympic intervention in their respective cities. It was noted in one of the mentioned studies, a 16.1% decrease in daily acute-care asthma visits among Medicaid-enrolled children associated with changes in PM₁₀. Adults in Beijing were found to have a 2% decrease in asthma outpatient visits during curtailment of polluting activities [14, 15]. In our

Table 7. Significant effects of daily particulate concentrations in exposed communities

	2015	2015-16 combined
Exposed Control CVD	3-day lag: 1.023 (1.005-1.041)	1-day lag: 1.015 (1.002-1.028) 3-day lag: 1.011 (1.001-1.021)
Combined Exposed CVD	3-day lag: 1.016 (1.002-1.029)	3-day lag: 1.011 (1.001-1.021)
Exposed Respiratory	3-day lag: 1.024 (1.002-1.047)	
Combined Exposed Respiratory	3-day lag: 1.015 (1.001-1.029)	3-day lag: 1.011 (1.001-1.021)

study area, a 5-fold decrease in children's asthma ED visits (200.0/10000 in 2015 to 37.8/10000 in 2016) was noted. A 3-fold decrease in adult asthma ED visits was noted for the population in the study area (149.4/10000 in 2015 and 45.7/10000 in 2016). Significant decreases were not noted in the control communities.

Our study not only compared the study area with two environmentally unchanged control areas; it also assessed an outcome that was not environmentally sensitive (injury) to determine if the change in number of exacerbations was likely associated with the plant closure, or to changing access to healthcare. In addition, a case-crossover analysis was conducted, which showed that daily ED visits were significantly associated with daily particulate matter levels, after controlling for temperature. Daily exacerbations of cardiovascular disease were associated with daily particulate matter concentrations in the exposed control and combined areas, but not the exposed area alone. Daily exacerbations of respiratory disease were noted to be significantly associated with daily particulate concentrations in the exposed and combined areas, but not in the exposed control area alone.

While other studies have noted changes in asthma ED visits following daily fluctuations in PM_{2.5}, this is the first study to demonstrate such a large change- a 2.4% change in respiratory ED visits per 1 µg/m³ change in daily particulate matter concentration (3-day lag). Prior studies have demonstrated far more modest changes. For example, a 10 µg/m³ increment in PM_{2.5} 1 day prior to the ED visit (1-day lag) was associated with a 3.6% increased risk of ED visits (OR = 1.036; 95% CI, 1.001–1.073) in a case-crossover analysis conducted in the same area a decade prior (9). In a recent meta-analysis, for each 10 µg/m³ increase in PM_{2.5}, the risk of asthma ED visits increased

by 1.5% (Fan, 2017). Previously observed city-to-city heterogeneity in PM–health associations (20, 21) may be driven by differences in population or exposure characteristics, such as susceptibility or air conditioning use, respectively, or by differences between cities in the chemical composition of source-specific PM_{2.5}. The differences noted could be related to the change of the chemical composition of the PM_{2.5} since the closure of the coke plant.

To further assess why the magnitude of change in ED visits was so great, we conducted an additional sensitivity analysis to examine trends over time. The results of this assessment demonstrated that several years pre-plant closure, (2013 and 2014 respectively), pediatric asthma visit rates within the study area were 59.5 (38.2-88.4) and 62.1 (40.4-91.7) per 10,000. For an unknown reason, they then peaked in 2015 at 200.0 (158.4-249.0), then dropped to 37.8 (21.5-61.9) and 32.4 (17.6-55.1) in 2016 and 2017. The years before plant closure were characterized by pediatric asthma rates that were higher than years after; there was a 64% decrease between 2014 and 2016 within the study area that was not statistically significant. In the control areas – when comparing 2014 and 2016 – there were also small decreases in pediatric ED visits (22% in exposed control and 15% in unexposed control) that were not statistically significant. In the study areas, we did not see major changes in insurance during the years in question (expansion of Medicaid occurred in 2014) nor was the flu season particularly aggressive in the years in question.

One explanation may be the heightened awareness of risk and the concomitant experience of stress. The community most affected by the emissions of the coking facility was actively advocating for cleaner air during the study period. They held many meetings and asked for placement of

special monitors in their community. They frequently contacted the health department with complaints of bad smells. In a study, it was determined that in Sweden, respondents not only were more annoyed by industrial odors before the shutdown of an industry, they also perceived a higher risk of environmental hazards [22]. In the other study, it was noted that the effect of NO₂ on asthma was modified by social stressors, including crowded conditions and poor access to resources [23]. Asthma is well known to be impacted by a variety of stressors [24, 25].

Some limitations to the data should be noted. First, in Pennsylvania, hospital admissions are not available by date, but quarter of year, restricting analysis to yearly rates. Second, we were unable to deduplicate or quantify ED visits by individual; there could have been a subset of the affected population that frequently sought acute care for cardiovascular or respiratory issues, possibly exacerbated by the stress of living near industry. Third, and unknown variable such as changes in specific managed care plans, or availability of physicians could have also contributed to changes in utilization patterns. We as yet, do not understand the trends in asthma ED utilization that occurred before (2013-2014) the study time-frame. More work is required to better understand these shifts.

With regard to air quality, although there was only a small decrease in the overall concentration of particulate matter after plant closure, there may have been changes in the constituent makeup of the particulate matter or in other pollutants and allergens that was not assessed in this study may have affected the health effects [26].

Conclusion

With the closure of a large coke plant facility, we found that a modest decrease in particulate matter

and a notable decrease in benzene concentration were associated with a significant decrease in emergency room visits not previously documented in other studies. This is suggestive that the impact of industry on health outcomes is critical. While we cannot establish causation, we did not identify similar changes in control communities. To validate these results, further work is needed.

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Competing interests

None of the authors have competing interests to disclose.

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Ethical considerations

Ethical considerations (including plagiarism, informed consent, misconduct, data fabrication or falsification, double publication and submission) have been completely observed by the authors.

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