Associations between Source-Specific Particulate Matter and Respiratory Infections in New York State Adults

Daniel P. Croft,∗† Wangjian Zhang,‡ Shao Lin,‡ Sally W. Thurston,‡ Philip K. Hopke,‡§# Edwin van Wijngaarden,§∥ Stefania Squizzato,§ Mauro Masiol,§ Mark J. Utell,∥§‡ and David Q. Rich‡§∥

†Department of Medicine, ‡Department of Biostatistics and Computational Biology, §Department of Public Health Sciences, and ∥Department of Environmental Medicine, University of Rochester Medical Center, Rochester, New York 14642, United States
‡Department of Environmental Health Sciences, University at Albany, The State University of New York, Rensselaer, New York 12203, United States
§Center for Air Resources Engineering and Science, Clarkson University, Potsdam, New York 13699, United States

ABSTRACT: The response of respiratory infections to source-specific particulate matter (PM) is an area of active research. Using source-specific PM2.5 concentrations at six urban sites in New York State, a case-crossover design, and conditional logistic regression, we examined the association between source-specific PM and the rate of hospitalizations and emergency department (ED) visits for influenza or culture-negative pneumonia from 2005 to 2016. There were at most N = 14 764 influenza hospitalizations, N = 57 522 culture-negative pneumonia hospitalizations, and N = 274 226 culture-negative pneumonia ED visits included in our analyses. We separately estimated the rate of respiratory infection associated with increased concentrations of source-specific PM2.5, including secondary sulfate (SS), secondary nitrate (SN), biomass burning (BB), pyrolyzed organic carbon (OP), road dust (RD), residual oil (RO), diesel (DIE), and spark ignition vehicle emissions (GAS). Increased rates of ED visits for influenza were associated with interquartile range increases in concentrations of GAS (excess rate [ER] = 9.2%; 95% CI: 4.3%, 14.3%) and DIE (ER = 3.9%; 95% CI: 1.1%, 6.8%) for lag days 0–3. There were similar associations between BB, SS, OP, and RO, and ED visits or hospitalizations for influenza, but not culture-negative pneumonia hospitalizations or ED visits. Short-term increases in PM2.5 from traffic and other combustion sources appear to be a potential risk factor for increased rates of influenza hospitalizations and ED visits.

INTRODUCTION

Previous studies have linked increased concentrations of ambient fine particles (PM2.5; particulate diameter <2.5 μm) with respiratory infection in adults.1−3 Recently, we observed an increased rate of hospitalization for culture-negative pneumonia and emergency department (ED) visits for culture-negative pneumonia and influenza, associated with increased PM2.5 concentrations in the previous 1, 4, and 7 days among adult residents of six New York State urban regions.4 An important next step to better understand the health effects of exposure to PM and guide policies is to identify PM components and sources with the highest toxicity.

PM2.5 is composed of numerous components that arise from different manmade sources (e.g., diesel, industry, spark ignition [gasoline] vehicles) and natural sources (e.g., sea salt). Source apportionment is an established method of identifying components of PM air pollution using spatial and temporal patterns,5 with apportioned PM source contributions used to examine acute morbidity and mortality events associated with individual PM sources.6 Previously, using positive matrix factorization (PMF) to estimate the mass concentration of particles corresponding to specific pollution sources at six urban centers in NY State,7 we identified major PM sources present at all six sites, including secondary nitrate [SN], secondary sulfate [SS], diesel [DIE], spark ignition vehicle emissions [GAS], pyrolyzed organic-rich emissions [OP], biomass burning [BB], and road dust [RD]. Three sources were identified only at New York City sites (fresh sea salt [FSS], aged sea salt [AGS], and residual oil [RO]). Further descriptions of these PM sources are provided by Squizzato et al.8

As described previously,10 there were significant reductions in air pollutant concentrations in New York State (NYS) from 2005 to 2016. These reductions were driven by economic changes due to the 2008 recession, changes in the relative prices of natural gas and coal for electricity production, and a number of policy initiatives to improve air quality in NYS, the United States, and Canada. In addition to reduced concentrations of gaseous pollutants and bulk PM2.5, there were also changes in particle composition.11 Generally, decreasing concentrations...
were observed across the state for SS and SN, while GAS was the only source with increasing concentrations over this period.\textsuperscript{11} Secondary organic carbon (SOC), estimated by the elemental carbon trace method, also increased from 2005 to 2016.\textsuperscript{9} Matching a statewide dataset of respiratory infectious disease hospitalizations and emergency department visits in NYS to estimates of source-specific PM, we estimated the rate of influenza and culture-negative pneumonia associated with increased PM source contributions in the previous 1, 4, and 7 days (driven by findings from our previous study).\textsuperscript{6} In our prior study, we observed increased respiratory infection hospitalizations and ED visits associated with increased PM 2.5 concentrations in the previous 7 days and increased SOC concentrations over the same time period.\textsuperscript{6} Based on our findings, we hypothesized that increased contributions of diesel (DIE), spark ignition vehicle emissions (GAS), secondary nitrate (SN), and secondary sulfate (SS) would be associated with increased rates of hospitalizations and ED visits for culture-negative pneumonia and influenza.

**Table 1. Characteristics of Hospitalizations and ED Visits of Patients by Type of Respiratory Infection**

|                      | Influenza                  |          | Emergency Department Visits \(N = 57,522\) |          |
|----------------------|----------------------------|----------|-----------------------------------------------|----------|
|                      | Hospitalizations \(N = 14,764\) |          | Hospitalizations \(N = 274,226\) |          |
| Gender               | n  | %  | n  | %  | n  | %  | n  | %  |
| male                 | 6335 | 43 | 22,828 | 40 | 128,888 | 47 | 54,471 | 48 |
| female               | 8429 | 57 | 34,692 | 60 | 145,337 | 53 | 59,520 | 52 |
| Age                  |     |     |     |     |     |     |     |     |
| years: mean (st. deviation) |     |     |     |     |     |     |     |
| 18–39                | 1880 | 13 | 34,606 | 60 | 20,266 | 7 | 38,213 | 34 |
| 40–49                | 1370 | 9  | 9,969  | 17 | 22,078 | 8 | 21,596 | 19 |
| 50–59                | 2044 | 14 | 7,106  | 12 | 35,343 | 13 | 21,243 | 19 |
| 60–69                | 2292 | 16 | 3,265  | 6  | 43,166 | 16 | 14,283 | 13 |
| 70–79                | 2695 | 18 | 1,509  | 3  | 55,847 | 20 | 9,486  | 8  |
| ≥80                  | 4483 | 30 | 1,067  | 2  | 97,526 | 36 | 9,176  | 8  |
| Race                 |     |     |     |     |     |     |     |     |
| white                | 7304 | 49 | 18,772 | 33 | 146,914 | 54 | 49,596 | 44 |
| black                | 3202 | 22 | 20,199 | 35 | 62,154 | 23 | 34,214 | 30 |
| native American/Alaskan | 56   | 0  | 261    | 0  | 1384   | 1  | 531    | 0  |
| Asian                | 259  | 2  | 1315   | 2  | 8904   | 3  | 2666   | 2  |
| native Hawaiian      | 1    | 0  | 20     | 0  | 122    | 0  | 50     | 0  |
| Ethnicity            |     |     |     |     |     |     |     |     |
| hispanic             | 1456 | 10 | 9497   | 17 | 32,375 | 12 | 14,348 | 13 |
| Year                 |     |     |     |     |     |     |     |     |
| 2005                 | 585  | 4  | 1998   | 3  | 31,211 | 11 | 7,620  | 7  |
| 2006                 | 306  | 2  | 1459   | 3  | 29,202 | 11 | 7,884  | 7  |
| 2007                 | 175  | 1  | 1,354  | 3  | 27,504 | 10 | 8,029  | 7  |
| 2008                 | 528  | 4  | 3,363  | 6  | 25,359 | 9  | 8,410  | 7  |
| 2009                 | 1594 | 11 | 12,116 | 21 | 24,373 | 9  | 9,911  | 9  |
| 2010                 | 561  | 4  | 2,552  | 4  | 22,378 | 8  | 8,290  | 7  |
| 2011                 | 871  | 6  | 3,317  | 6  | 22,792 | 8  | 9,970  | 9  |
| 2012                 | 855  | 6  | 3,250  | 6  | 21,419 | 8  | 10,845 | 10 |
| 2013                 | 1901 | 13 | 7,837  | 14 | 19,682 | 7  | 10,284 | 9  |
| 2014                 | 2489 | 17 | 7,490  | 13 | 17,464 | 6  | 10,014 | 9  |
| 2015                 | 2179 | 15 | 4,639  | 8  | 16,771 | 6  | 11,115 | 10 |
| 2016                 | 2720 | 18 | 7,967  | 14 | 16,071 | 6  | 11,625 | 10 |
| Season               |     |     |     |     |     |     |     |     |
| fall                 | 989  | 7  | 7,930  | 14 | 61,704 | 23 | 27,948 | 25 |
| spring               | 4379 | 30 | 15,913 | 28 | 72,750 | 27 | 28,665 | 25 |
| summer               | 647  | 4  | 3,953  | 7  | 59,291 | 22 | 22,845 | 20 |
| winter               | 8749 | 59 | 29,726 | 52 | 80,481 | 29 | 34,539 | 30 |

**METHODS**

**Study Population and Hospital Admission Data.** We used the same hospitalization and ED visit data as our previous study.\textsuperscript{6} Briefly, we included adult (age > 18 years old) patients from the NYS Department of Health Statewide Planning and Research Cooperative System (SPARCS), which includes hospitalizations from nearly 95% of hospitals in NYS, who lived within 15 miles of a central monitoring site in Buffalo, Rochester, Albany, Bronx, Manhattan, or Queens from Jan 1, 2005 to Dec 31, 2016. We included patients with a primary diagnosis (at the time of hospitalization or ED visit) of influenza (ICD9 = 487.0, 487.8, 488.0, 488.01, 488.02, 488.1, 488.11, 488.12, 488.8, 488.81, 488.82; ICD10 = J09, J09.X1, J09.X2, J10.0, J10.00, J10.01, J10.08, J10.1, J11.0, J11.00, J11.08, J11.1) or culture-negative pneumonia (ICD9 = 485, 486; ICD10 = J18). This study was approved by the Institutional Review Board at the State University of New York at Albany.

**PM\textsubscript{2.5} Sources and Weather Data.** We retrieved PM\textsubscript{2.5} concentration for these six sites (Albany, Buffalo, Rochester,
Patients hospitalized with influenza and culture-negative pneumonia were older (mean ± standard deviation) age of 65 ± 20 and 69 ± 18 years, respectively) than patients being treated in the ED (38 ± 16 and 49 ± 19 years old, respectively) (Table 1). Patients with influenza were predominantly female (57–60%). Compared to hospitalized influenza patients, influenza patients only treated in the ED were more racially diverse (33% white and 35% black). Similarly, hospitalized culture-negative pneumonia patients were more often white (54%) than culture-negative pneumonia patients treated in the ED (44% white) (Table 1). Influenza hospitalizations and ED visits were more often from latter years of the study period (hospitalized patients after 2012: 63%; ED visits after 2012: 59%) and predominantly from the winter and spring (hospitalized patients: 89%; ED visits: 80%). Culture-negative pneumonia hospitalizations and ED visits were less often from the latter years (hospitalized patients after 2012: 25%; ED visits after 2012: 38%), and more evenly distributed across seasons (Table 1). Distributions of the source-specific PM$_{2.5}$ mass contributions are shown in Table 2, with more detailed source descriptions provided by Squizzato et al. (2018).9 Minimum values for the source-specific mass concentrations often have small negative values as a result of the uncertainties in the PMF analysis.15 However, we did not left-censor the values to avoid the potential bias that such truncation would induce.17

For influenza, increased hospitalization rates were significantly associated with interquartile range (IQR) increases in the total PM$_{2.5}$ concentrations on the lag day 0 and lag days 0–3 (excess rate [ER] = 12.2%; 95% CI: 0.7%, 25.0%) (Table 3 and Figure 1). Similarly, increases in SN concentrations on lag day 0 were associated with an increase in the rate of influenza hospitalizations (ER = 5.0%; 95% CI: 0.1%, 10.1%). Although not statistically significant, similarly sized increased rates of influenza hospitalization were associated with IQR increases in concentrations of SS (ER = 3.0%; 95% CI: −0.7%, 6.8), GAS (ER = 6.0%; 95% CI: −0.1%, 12.5%), RO (ER = 2.7%; 95% CI: −3.0%, 8.6%), and BB (ER = 6.3%; 95% CI: −0.5%, 13.5%) on lag day 0. The magnitude of the increased rates of influenza hospitalizations associated with increases in DIE (ER = 1.1%; 95% CI: −0.8%, 3.1%) was smaller than observed for other pollutants on lag day 0. No consistent associations were observed between influenza hospitalizations and the OP, RD, FSS, or AGS concentrations.

### Table 2. Distribution of Daily PM$_{2.5}$ Source Concentrations ($\mu g/m^3$) for Control Periods (lag day 0)

| PM$_{2.5}$ Source | Mean | Standard Deviation | Minimum | 5th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 95th Percentile | Maximum |
|------------------|------|--------------------|---------|---------------|---------------|---------------|---------------|---------------|---------|
| Total PM$_{2.5}$| 10.98| 6.87               | 1.00    | 3.60          | 6.10          | 9.10          | 13.90         | 25.50         | 47.00   |
| Road dust (RD)  | 0.45 | 0.52               | −0.20   | 0.00          | 0.14          | 0.30          | 0.58          | 1.39          | 6.39    |
| Secondary sulfate (SS) | 3.12 | 3.93               | −0.94   | −0.38         | 0.76          | 2.04          | 4.09          | 10.50         | 42.47   |
| Secondary nitrate (SN) | 1.81 | 2.80               | −0.78   | −0.16         | 0.13          | 0.75          | 2.37          | 7.65          | 24.12   |
| Diesel (DIE)     | 1.09 | 0.89               | −0.38   | −0.09         | 0.53          | 0.92          | 1.44          | 2.67          | 10.26   |
| Spark ignition emissions (GAS) | 1.60 | 1.67               | −0.44   | −0.17         | 0.41          | 1.13          | 2.32          | 4.92          | 14.60   |
| Biomass burning (BB) | 0.37 | 0.53               | −0.22   | −0.05         | 0.04          | 0.18          | 0.53          | 1.38          | 9.92    |
| Pyrolyzed organic rich (OP) | 1.31 | 1.81               | −0.34   | −0.18         | 0.11          | 0.83          | 1.83          | 4.35          | 20.24   |

New York City Sites Only

| Source          | Mean | Standard Deviation | Minimum | 5th Percentile | 25th Percentile | 50th Percentile | 75th Percentile | 95th Percentile | Maximum |
|-----------------|------|--------------------|---------|---------------|---------------|---------------|---------------|---------------|---------|
| Fresh sea salt (FSS) | 0.20 | 0.66               | −0.08   | −0.01         | 0.00          | 0.02          | 0.10          | 0.98          | 10.64   |
| Aged sea salt (AGS) | 0.60 | 0.74               | −0.15   | −0.03         | 0.10          | 0.37          | 0.80          | 2.08          | 7.93    |
| Residual oil (RO) | 0.63 | 0.80               | −0.20   | −0.07         | 0.11          | 0.38          | 0.85          | 2.20          | 7.17    |
Table 3. Excess Rate of Acute Hospitalizations for Respiratory Infections Associated with Each Interquartile Range Increase in Total PM$_{2.5}$ or PM$_{2.5}$ Source Concentration$^a$

| Outcome                        | Lag  | $N$ cases | IQR ($\mu g/m^3$) | Excess Rate % (95% CI) | $p$-value | Outcome                        | Lag  | $N$ cases | IQR ($\mu g/m^3$) | Excess Rate % (95% CI) | $p$-value |
|--------------------------------|------|-----------|-------------------|------------------------|-----------|--------------------------------|------|-----------|-------------------|------------------------|-----------|
| Culture-Negative Pneumonia     | 0    | 56 181    | 5.8               | 0.8 (−0.2, 1.8)        | 0.130     |                                |      |           |                   |                        |           |
|                                | −3   | 40 554    | 5.05              | 0.4 (−1.0, 1.9)        | 0.580     |                                |      |           |                   |                        |           |
|                                | −6   | 42 332    | 4.2               | 0.1 (−1.4, 1.6)        | 0.942     |                                |      |           |                   |                        |           |
| Influenza                      | 0    | 32 463    | 5.2               | 0.6 (−1.8, 10.8)       | 0.005     |                                |      |           |                   |                        |           |
|                                | −3   | 19 232    | 7.1               | 12.2 (0.7, 25.0)       | 0.038     |                                |      |           |                   |                        |           |
|                                | −6   | 20 437    | 6.78              | 6.7 (−5.1, 20.0)       | 0.279     |                                |      |           |                   |                        |           |
| Spark Ignition Emissions (GAS) | 0    | 55 000    | 2.51              | 0.2 (−1.8, 2.2)        | 0.831     |                                |      |           |                   |                        |           |
|                                | −3   | 39 000    | 1.9               | 0.2 (−2.3, 2.8)        | 0.867     |                                |      |           |                   |                        |           |
|                                | −6   | 40 384    | 1.42              | 1.0 (−1.3, 3.4)        | 0.391     |                                |      |           |                   |                        |           |
| Influenza                      | 0    | 31 942    | 2.15              | 6.0 (−0.1, 12.5)       | 0.052     |                                |      |           |                   |                        |           |
|                                | −3   | 18 542    | 0.95              | −0.1 (−4.5, 4.6)       | 0.974     |                                |      |           |                   |                        |           |
|                                | −6   | 19 782    | 0.9               | 2.2 (−2.4, 7.0)        | 0.353     |                                |      |           |                   |                        |           |
| Road Dust (RD)                 | 0    | 55 000    | 0.3               | 0.8 (−0.0, 1.6)        | 0.053     |                                |      |           |                   |                        |           |
|                                | −3   | 39 000    | 0.24              | 1.1 (0.0, 2.2)         | 0.046     |                                |      |           |                   |                        |           |
|                                | −6   | 40 384    | 0.27              | 1.1 (−0.3, 2.6)        | 0.136     |                                |      |           |                   |                        |           |
| Influenza                      | 0    | 31 942    | 0.28              | −0.7 (−5.3, 4.0)       | 0.760     |                                |      |           |                   |                        |           |
|                                | −3   | 18 542    | 0.21              | −4.1 (−10.1, 2.3)      | 0.207     |                                |      |           |                   |                        |           |
|                                | −6   | 19 782    | 0.16              | 0.8 (−4.5, 6.4)        | 0.773     |                                |      |           |                   |                        |           |
| Pyrolyzed Organic Rich (OP)    | 0    | 33 581    | 1.43              | −0.5 (−1.8, 0.8)       | 0.447     |                                |      |           |                   |                        |           |
|                                | −3   | 23 498    | 0.96              | 0.8 (−0.6, 2.3)        | 0.261     |                                |      |           |                   |                        |           |
|                                | −6   | 24 517    | 0.9               | 0.4 (−1.4, 2.2)        | 0.650     |                                |      |           |                   |                        |           |
| Influenza                      | 0    | 28 682    | 0.89              | −0.0 (−3.8, 3.9)       | 0.993     |                                |      |           |                   |                        |           |
|                                | −3   | 16 932    | 0.94              | 2.5 (−4.8, 10.4)       | 0.506     |                                |      |           |                   |                        |           |
|                                | −6   | 18 332    | 0.86              | −2.5 (−9.5, 5.0)       | 0.499     |                                |      |           |                   |                        |           |
| Aged Sea Salt (AGS)            | 0    | 47 231    | 0.7               | 0.2 (−1.0, 1.4)        | 0.783     |                                |      |           |                   |                        |           |
|                                | −3   | 35 658    | 0.64              | −0.3 (−2.1, 1.4)       | 0.697     |                                |      |           |                   |                        |           |
|                                | −6   | 35 168    | 0.63              | −0.6 (−2.8, 1.7)       | 0.600     |                                |      |           |                   |                        |           |
| Influenza                      | 0    | 25 600    | 0.61              | −3.4 (−7.7, 1.1)       | 0.133     |                                |      |           |                   |                        |           |
|                                | −3   | 16 166    | 0.61              | 0.6 (−6.9, 8.6)        | 0.888     |                                |      |           |                   |                        |           |
|                                | −6   | 16 082    | 0.49              | −3.9 (−10.7, 3.4)      | 0.290     |                                |      |           |                   |                        |           |
| Residual Oil (RO)              | 0    | 47 231    | 0.7               | 0.2 (−1.0, 1.4)        | 0.783     |                                |      |           |                   |                        |           |
|                                | −3   | 35 658    | 0.64              | −0.3 (−2.1, 1.4)       | 0.697     |                                |      |           |                   |                        |           |
|                                | −6   | 35 168    | 0.63              | −0.6 (−2.8, 1.7)       | 0.600     |                                |      |           |                   |                        |           |
| Biomass Burning (BB)           | 0    | 31 942    | 0.63              | 6.3 (0.5, 13.5)        | 0.070     |                                |      |           |                   |                        |           |
| Culture-Negative Pneumonia     | 0    | 18 542    | 0.43              | −2.0 (−11.3, 8.2)      | 0.688     |                                |      |           |                   |                        |           |
|                                | −6   | 19 782    | 0.5               | 10.1 (−1.9, 23.4)      | 0.102     |                                |      |           |                   |                        |           |

$^a$PM$_{2.5}$ filters/measurements, on which PMF sources were identified, were only available in Buffalo every 6 days.
The pattern of influenza ED visit rate ratios was generally similar to the rate ratios for hospitalizations (Table 4 and Figure 2). Interquartile range (IQR) increases in total PM$_{2.5}$ concentration on lag day(s) 0, 0−3, and 0−6 were significantly associated with increased rates of ED visits (e.g., lag days 0−3: ER = 7.7%; 95% CI: 3.7%, 11.8%). Increased rates of influenza ED visits were also significantly associated with IQR increases in GAS concentration over lag days 0−3 (ER = 9.2%; 95% CI: 4.3%, 14.3%) and DIE concentration for lag days 0−3 (ER = 3.9%; 95% CI: 1.1%, 6.8%), as well as other lag times. Although not statistically significant and less precise, similarly sized increased rates of influenza ED visits were also associated with IQR increases in concentrations of SS (ER = 3.5%; 95% CI: 0.5%, 6.6%), OP (ER = 4.9%; 95% CI: 2.2%, 7.7%), RO (ER = 6.1%; 95% CI: 1.0%, 11.5%), and BB (ER = 4.9%; 95% CI: −0.5%, 10.5%) over the lag days 0−3. Increased concentrations of RD, RSS, and AGS were not associated with increased rates of influenza ED visits.

No consistent patterns of effect were observed for increases in PM$_{2.5}$ source contributions and the rates of culture-negative pneumonia hospitalizations or ED visits. The exception was a protective patterns for fresh sea salt PM$_{2.5}$ and culture-negative pneumonia ED visits (Table 4).

**DISCUSSION**

Previously, in a study of adult residents of six urban centers in NY State from 2005 to 2016, we observed an increased rate of ED visits for influenza (1−4%) and culture-negative pneumonia (1−2%) associated with IQR increases in PM$_{2.5}$ concentration in the previous 1−7 days. Using the same health data, we examined whether increases in the ambient concentration of specific sources of PM$_{2.5}$ were associated with increased rates of influenza and culture-negative pneumonia hospitalizations and ED visits for the lag day(s) 0, 0−3, 0−6. Consistent with our hypothesis, increased concentrations of GAS and DIE (traffic sources) were associated with increased rates of influenza ED visits at multiple lag times. While positive associations between increased concentrations of OP, RO, BB, and SS and influenza ED visits were also observed, these estimates were less precise, not statistically significant, and smaller in magnitude. Similarly, associations between increased concentrations of GAS, DIE, SS, BB, and SN in the 0, 0−3, and 0−6 day lags and influenza hospitalizations were also positive, but not statistically significant. Associations were independent of ambient temperature and relative humidity since they were included in our statistical models and independent of any nontime varying patient characteristics (e.g., age, gender, socioeconomic status) via the case-crossover study design (case and control periods within the same month of the same patient). Finally, there were no consistent associations between any PM$_{2.5}$ source and culture-negative pneumonia hospitalizations or ED visits.

There have been a relatively limited number of prior epidemiological studies using source-specific PM obtained from the application of receptor models. Most of these...
| Outcome                        | Lag | N cases | IQR (μg/m³) | Excess Rate % (95% CI) | p-value | N cases | IQR (μg/m³) | Excess Rate % (95% CI) | p-value |
|-------------------------------|-----|---------|-------------|------------------------|---------|---------|-------------|------------------------|---------|
| **Total PM₂.₅ (in the PMF File)** |     |         |             |                        |         |         |             |                        |         |
| Culture-Negative Pneumonia   | 0   | 22 024  | 6           | 0.4 (−1.4, 2.3)        | 0.67    | 21 540  | 2.1         | 0.7 (−0.6, 2.0)        | 0.30    |
|                              | 0−3 | 15 403  | 4.8        | 0.3 (−2.2, 2.8)        | 0.83    | 14 826  | 1.75        | 3.0 (1.1, 5.0)         | 0.002   |
|                              | 0−6 | 16 750  | 4.05       | −1.3 (−3.7, 1.2)       | 0.30    | 16 040  | 1.41        | 1.4 (−0.5, 3.3)        | 0.14    |
| Influenza                     | 0   | 11 490  | 5.7         | 2.3 (−0.2, 4.9)        | 0.07    | 11 293  | 1.74        | 3.3 (1.4, 5.4)         | <0.001  |
|                              | 0−3 | 7741    | 4.93        | 7.7 (3.7, 11.8)        | <0.001  | 7530    | 1.47        | 3.5 (0.5, 6.6)         | 0.02    |
|                              | 0−6 | 8509    | 6.03       | 6.0 (0.5, 11.8)        | 0.03    | 8190    | 1.18        | −2.9 (−5.7, −0.1)      | 0.04    |
| **Pyrolized Organic Rich (OP)** |     |         |             |                        |         |         |             |                        |         |
| Culture-Negative Pneumonia   | 0   | 21 540  | 2.68       | 1.5 (−1.6, 4.7)        | 0.36    | 21 540  | 0.49        | −0.8 (−2.0, 0.4)       | 0.20    |
|                              | 0−3 | 14 826  | 1.73       | 0.5 (−2.9, 4.0)        | 0.77    | 14 826  | 0.71        | −1.9 (−4.9, 1.2)       | 0.23    |
|                              | 0−6 | 16 040  | 1.44       | 1.3 (−2.0, 4.7)        | 0.44    | 16 040  | 0.76        | −3.7 (−7.4, 0.2)       | 0.06    |
| Influenza                     | 0   | 11 293  | 2.26       | 5.3 (1.7, 9.1)         | 0.004   | 11 293  | 0.43        | −0.2 (−1.9, 1.4)       | 0.77    |
|                              | 0−3 | 7530    | 1.77       | 9.2 (4.3, 14.3)        | <0.001  | 7530    | 0.38        | 3.9 (1.1, 6.8)         | 0.01    |
|                              | 0−6 | 8190    | 1.09       | 6.5 (3.1, 10.0)        | <0.001  | 8190    | 0.33        | 5.2 (2.6, 7.9)         | <0.001  |
| **Aged Sea Salt (AGS)**       |     |         |             |                        |         |         |             |                        |         |
| Culture-Negative Pneumonia   | 0   | 16 099  | 1.39       | −0.9 (−2.2, 0.5)       | 0.22    | 16 099  | 0.29        | 1.0 (−1.0, 0.0)        | 0.97    |
|                              | 0−3 | 11 033  | 0.91       | 0.6 (−1.5, 2.8)        | 0.57    | 12 922  | 0.14        | −0.9 (−1.6, −0.2)      | 0.02    |
|                              | 0−6 | 12 005  | 0.73       | −0.1 (−2.3, 2.1)       | 0.90    | 12 718  | 0.17        | −1.9 (−3.0, −0.8)      | <0.001  |
| Influenza                     | 0   | 9828    | 1.12       | 0.2 (−2.2, 2.4)        | 0.57    | 8890    | 0.14        | −0.8 (−1.6, −0.1)      | 0.03    |
|                              | 0−3 | 6560    | 0.77       | 4.9 (2.2, 7.7)         | <0.001  | 6582    | 0.2         | −2.2 (−3.8, −0.5)      | 0.01    |
|                              | 0−6 | 7106    | 0.82       | 6.8 (3.5, 10.2)        | <0.001  | 6522    | 0.25        | −2.1 (−4.5, 0.5)       | 0.11    |
| **Residual Oil (RO)**         |     |         |             |                        |         |         |             |                        |         |
| Culture-Negative Pneumonia   | 0   | 16 698  | 0.68       | 1.8 (−3.7, 0.2)        | 0.08    | 16 698  | 0.08        | −0.3 (−0.6, −0.0)      | 0.04    |
|                              | 0−3 | 12 922  | 0.6        | −1.9 (−4.5, 0.8)       | 0.17    | 12 922  | 0.68        | −1.4 (−5.0, 2.4)       | 0.46    |
|                              | 0−6 | 12 718  | 0.57       | −2.5 (−5.7, 0.8)       | 0.14    | 12 718  | 0.63        | −5.0 (−8.9, −0.9)      | 0.02    |
| Influenza                     | 0   | 8990    | 0.67       | −3.5 (−6.3, −0.7)      | 0.02    | 8990    | 0.88        | −0.1 (−3.5, 3.5)       | 0.96    |
|                              | 0−3 | 6582    | 0.6        | −1.5 (−5.3, 2.7)       | 0.48    | 6582    | 0.71        | 6.1 (1.0, 11.5)        | 0.02    |
|                              | 0−6 | 6522    | 0.51       | −8.0 (−12.0, −3.8)     | <0.001  | 6522    | 0.71        | 7.6 (1.5, 14.2)        | 0.01    |
| **Biomass Burning (BB)**      |     |         |             |                        |         |         |             |                        |         |
| Culture-Negative Pneumonia   | 0   | 55 000  | 0.58       | 0.4 (−0.7, 1.7)        | 0.462   | 55 000  | 1.02        | 1.4 (0.2, 2.2)         | 0.462   |
|                              | 0−3 | 39 000  | 0.48       | −0.8 (−2.5, 1.1)       | 0.41    | 39 000  | 1.46        | 1.4 (0.2, 2.7)         | 0.41    |
|                              | 0−6 | 40 384  | 0.4        | 1.3 (−0.6, 3.1)        | 0.175   | 40 384  | 3.39        | 6.0 (1.8, 11.3)        | 0.01    |
| Influenza                     | 0   | 3194    | 0.63       | 6.0 (2.8, 9.3)         | <0.001  | 3194    | 0.63        | 6.0 (2.8, 9.3)         | <0.001  |
|                              | 0−3 | 1854    | 0.43       | 4.9 (−0.5, 10.5)       | 0.076   | 1854    | 0.43        | 2.9 (−0.4, 6.2)        | 0.042   |
|                              | 0−6 | 1978    | 0.5        | 6.0 (0.2, 12.0)        | 0.042   | 1978    | 0.5         | 6.0 (0.2, 12.0)        | 0.042   |

*PM₂.₅ filters/measurements, on which PMF sources were identified, were only available in Buffalo every 6 days.*
studies examine relatively short time intervals (5 years) and did not focus on respiratory infections. Our source-specific analysis represents the largest population of patients with respiratory infection analyzed over the longest time period in which substantive changes in air pollution sources including gasoline formulation and energy generation occurred.

Multiple prior studies have examined the association between air pollution and respiratory infection.\textsuperscript{1,4,5,27} Locally, Lall et al.\textsuperscript{4} reported increased respiratory and specifically pneumonia hospitalizations among adult New York City residents associated with increased concentrations of PM$_{2.5}$ from steel (World Trade Center cleanup) at the 3 day lag time. Increased cardiovascular hospitalizations were also associated with increased traffic PM in the previous day.\textsuperscript{4} A source apportionment study of four U.S. cities (including PMF analyses) observed an increased excess risk (1–2%) of pneumonia ED visits associated with each IQR increases in PM$_{2.5}$ in Birmingham, AL.\textsuperscript{27} Similarly, our study observed increased relative rates of ED visits for influenza associated with IQR increases in PM$_{2.5}$ (2–8%), spark ignition vehicle emissions (5–9%), and diesel emissions (0–5%). Though we also observed positive associations between ED visits for influenza and BB, these were imprecise.

Short-term increases in concentrations of PM$_{2.5}$ from traffic-related sources (i.e., diesel and spark ignition vehicle emissions) may be responsible for our prior finding of an association between ED visits for influenza and increased concentrations of overall PM$_{2.5}$.\textsuperscript{6} Despite decreases in overall PM$_{2.5}$ over the course of our prior study, the toxicity of remaining PM$_{2.5}$ may have increased per unit mass. As described by Zhang et al.,\textsuperscript{14} GAS contributions increased, while DIE contributions remained constant across the NY State over the study period. During this same study period, the contributions of other PM sources decreased (and their PM$_{2.5}$ mass fractions).\textsuperscript{9} Thus, given our current finding of an association between GAS/influenza, the increasing GAS contribution may be one explanation for the increased toxicity of the PM$_{2.5}$ in our prior study. In our current study, the lack of associations between air pollution and culture-negative pneumonia may be related to an increased variability from a decreased sample size due to measurements being made every 3rd or 6th day. The lack of these associations may also be from outcome misclassification given the heterogeneous nature of culture-negative pneumonia, which is a common diagnosis used by physicians for infections that are not clearly determined to be from bacterial or viral sources.\textsuperscript{28}

Within our own broader New York State Accountability study, we observed similar findings between acute cardiovascular hospitalizations, PM$_{2.5}$ mass, and individual PM$_{2.5}$ sources. Using the same health and source apportioned PM$_{2.5}$ data, we reported increased rates of hospitalizations for cardiac arrhythmia, ischemic stroke, congestive heart failure, and ischemic heart disease associated with increased PM$_{2.5}$ concentrations in the previous few days.\textsuperscript{14} Similar to the
influenza findings reported in this study, increased rates of specific cardiovascular hospitalizations were associated with increased spark ignition vehicle emissions (GAS), diesel (DIE), road dust (RD), residual oil (RO), and secondary nitrate (SN) PM concentrations in the previous 1−7 days. These cardiovascular findings and our respiratory infectious disease findings suggest a role of traffic-related sources of PM$_{2.5}$ in NYS in the triggering of these events.

Our study focused on air pollution as one possible contributor to the risk of respiratory infection, recognizing that underlying immunity, smoking, vaccination status, comorbid cardiopulmonary diseases, and other environmental factors may have a greater effect on risk. These traffic-related PM sources may be associated with increased rates of health-care encounters for influenza via their impact on pulmonary inflammation and oxidative stress. The observation of both respiratory infection and cardiovascular outcomes being associated with acute increases in PM$_{2.5}$ in several prior studies suggests that inflammation and oxidative stress may serve as a common mechanism for both pulmonary and cardiovascular health effects. Traffic PM sources may be contributing to an increase in secondary organic carbon (SOC) concentrations (associated with increased oxidative stress) observed in our prior studies. While the vehicle-related PM (spark ignition vehicle and diesel emissions) appears to have the strongest association with increased SOC concentrations in prior studies, the metal content of residual oil may also lead to oxidative stress similar to SOC. Exposure to diesel emissions in human epithelial cell models and in vivo mouse models resulted in disruptive inflammation that may be linked to an increased susceptibility to viral infections.

We did not observe an association between road dust and respiratory infection. This null finding may, in part, be due to the large size of this particle and its deposition in the upper airway rather than the lower airway deposition of traffic emissions. Further, the road dust is heterogeneous, including tailpipe and nontailpipe emissions from traffic mixed with deposited soil and road surface material. It can contain redox-active transition metals (i.e., Fe, Ni, Cu, Zn) from tire and brake wear, muffler ablation, and combusted lubricating oil that can induce the formation of endogenous oxidants. Between deposition rates and reactivity, studying the association between road dust and respiratory infections may vary from location to location.

The increasing concentrations of GAS and increased SOC formation over the study periods are likely related to increased numbers of spark ignition vehicles in NYS (by registration data), alterations to gasoline formulations from 2010 to 2014 that reduced benzene content, and the use of gasoline direct injection technology. The sources specific to energy production (particularly secondary sulfate and a portion of the secondary nitrate) likely have less oxidative capacity due to these being aged particles, and therefore they may contribute less to the delivery of reactive oxygen species and oxidative stress. The observation that secondary nitrate was strongly associated with hospitalizations for influenza is supported by a recent study in Utah observing an increased risk of hospitalization (subset of all ED visits) for pneumonia associated with the gaseous nitrogen dioxide (NO$_2$). Since our ED visit group did not include the hospitalized patients, it is possible that the hospitalized patients in the study by Pirozzi et al. were driving the ED visit signal. The need for hospitalization may indicate an increased severity of illness related to either the oxidative potential of the gaseous species (NO$_2$), the SN particulate form as a vehicle for infection, or both, given the bidirectional redox reaction between NO$_2$ and SN. An increased burden of airborne bacteria and an increased virulence of bacteria have been observed in the setting of increased concentrations of particulate matter. Also, though more difficult to measure than airborne bacteria, the presence of viruses in aerosols also can put individuals at risk for infection. While detailing the risk of specific PM$_{2.5}$ sources is important, understanding the chemistry occurring between components of pollution mixtures and the interactions between pathogens and particles are two important areas for future research.

We observed decreased rates of influenza hospitalizations and ED visits associated with increased fresh sea salt (FSS). Periods of increased FSS contributions likely occurred when the prevailing winds were easterly (from the ocean) and therefore likely have a lower relative proportion of traffic and other source-specific particles. Although we adjusted for PM$_{2.5}$ mass from other sources in our analyses, this protective influenza/FSS association may be due to residual confounding by traffic PM sources.

We also observed differences in the effect estimates based on the timing of exposure. For influenza ED visits, which are presumably less severe infections than influenza hospitalizations, rate ratios were generally largest at the 0−3 and 0−6 lag days. For influenza hospitalizations, the effect estimates were largest at the 0 and 0−3 lag day(s). Patients with influenza infection generally become symptomatic within 2 days, and, depending on the severity of their illness, may seek medical care over the following several days. This pattern may indicate that patients exposed to elevated levels of source-specific particulate matter during an active infection (lag days 0−3) may have a more severe course (hospitalization rather than ED visit) than patients who were exposed to elevated levels of air pollution prior to an active infection (lag days 0−6).

A prior large time series analysis in Atlanta from 1999 to 2013 described modeled associations between changing pollution levels and ED visits for an aggregate outcome of respiratory diseases with a 3 day moving average. Similar to our suggestion that spark ignition (gasoline) emissions are the driver of the PM toxicity, the Atlanta study observed that greater reductions in ED visits for respiratory disease were associated with gasoline-related regulations than diesel-related regulations. However, due to the short lag time, it is difficult to directly compare their values to our study. Extending the included lag times of future source-specific studies to at least 6 days would help clarify the effect of exposure timing on the risk of respiratory infection.

The finding of a difference between ED visits and hospitalization may also simply represent a greater degree of exposure misclassification (and downward bias) for influenza ED visits than influenza hospitalizations. For example, there may just be a greater amount of error in using ED visit arrival date as an estimate of disease onset time (i.e., less severe disease may not spur the patient to seek care for several days) than when using date of influenza hospitalization (i.e., more severe disease may spur a patient to seek care soon after disease onset). Greater error in estimating disease onset time would likely produce more error in matching preinfluenza air pollutant concentrations to influenza ED visits than influenza hospitalizations, resulting in a greater degree of bias toward the null and underestimates of relative rates for influenza ED visits than influenza hospitalizations.

There are several additional limitations to consider when interpreting our results. Due to the use of ambient air pollution
levels for all patients within a 15 mile radius of each monitoring station, there is an element of exposure misclassification, which likely led to the underestimation of relative rates. Second, our source apportionment was designed to provide a continuous set of apportionments over the entire 12 year study period (2005–2016). However, this approach may have resulted in misspecification of the source-specific PM2.5 concentrations during time periods where composition and related pollutant concentrations were changing substantially and thus underestimation of relative rates. Also, although there is likely exposure error in our estimates of each source-specific PM concentration in our analyses, this error is not likely to be different on case days than control days, resulting in underestimates of excess rates associated with each source-specific PM. However, the amount of error and therefore the amount of underestimation of the excess rates by source category may differ, as there is likely more spatial variability in some source-specific PM concentrations (e.g., GAS) than others (e.g., SS). This exposure error would lead to more underestimation in excess rates for those sources with greater spatial variability (e.g., GAS). Given that our strongest findings were with GAS and DIE, sources with greater spatial variability, this exposure error was unlikely to change the pattern of our results. Our reporting of patterns of effects and mention of statistical significance as only one of the multiple descriptors (i.e., effect size, precision) for our results is consistent with the American Statistical Association statement on the appropriate use of p-values when making an inference. In our article, inference was made by the magnitude of the effect estimate, its precision, if it was consistent with our a priori hypothesis, and then finally by whether it was statistically significant.

Finally, there was a change in the ICD classification of diseases on Oct 1, 2015 that may have led to reduced counts of hospitalizations and ED visits during the study (due to increased numbers of diagnosis codes in the new ICD). This may have resulted in a reduction in the number of culture-negative pneumonia hospitalizations and ED visits after this time due to an increased granularity in the diagnosis codes available to clinicians (i.e., fewer patients placed in this general category). Outcome misclassification may be present for influenza as well given the possibility for IC9/10 diagnoses being made based on clinical assessment alone rather than in concert with the reverse transcriptase polymerase chain reaction (RT-PCR) or rapid influenza diagnostic tests. As little change in influenza classification occurred when moving from ICD9 to ICD10 coding, we were not able to subtype the influenza infections (i.e., H1N1 and H3N2) included in the study. For the benefit of air quality policy-making, further research on the inflammatory and immune responses to specific sources of PM is needed to help determine what aspects of traffic PM sources are responsible for the previously observed increase in toxicity per unit mass.

**Author Information**

**Corresponding Author**
*E-mail: daniel_croft@urmc.rochester.edu. Phone: 585 275 4161. Fax: 585 271 1171.*

**ORCID**
Daniel P. Croft: 0000-0002-1990-5542
Philip K. Hopke: 0000-0003-2367-9661

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The authors declare no competing financial interest.

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