

Hospital Admissions and Chemical Composition of Fine Particle Air Pollution

Michelle L. Bell¹, Keita Ebisu¹, Roger D. Peng², Jonathan M. Samet³, and Francesca Dominici²

¹School of Forestry and Environmental Studies, Yale University, New Haven, Connecticut; ²Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; and ³Keck School of Medicine, University of Southern California, Los Angeles, California

Rationale: There are unexplained geographical and seasonal differences in the short-term effects of fine particulate matter (PM_{2.5}) on human health. The hypothesis has been advanced to include the possibility that such differences might be due to variations in the PM_{2.5} chemical composition, but evidence supporting this hypothesis is lacking.

Objectives: To examine whether variation in the relative risks (RR) of hospitalization associated with ambient exposure to PM_{2.5} total mass reflects differences in PM_{2.5} chemical composition.

Methods: We linked two national datasets by county and by season: (1) long-term average concentrations of PM_{2.5} chemical components for 2000–2005 and (2) RRs of cardiovascular and respiratory hospitalizations for persons 65 years or older associated with a 10- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} total mass on the same day for 106 U.S. counties for 1999 through 2005.

Measurements and Main Results: We found a positive and statistically significant association between county-specific estimates of the short-term effects of PM_{2.5} on cardiovascular and respiratory hospitalizations and county-specific levels of vanadium, elemental carbon, or nickel PM_{2.5} content.

Conclusions: Communities with higher PM_{2.5} content of nickel, vanadium, and elemental carbon and/or their related sources were found to have higher risk of hospitalizations associated with short-term exposure to PM_{2.5}.

Keywords: air pollution; particulate matter; carbon; vanadium; nickel

Statistically significant associations between short-term exposure to airborne particulate matter (PM) and mortality and morbidity have been reported in numerous multicity studies (1–6). Several studies also found that health effect estimates vary substantially across communities and seasons (4, 7, 8). The findings of these studies support the hypothesis that geographical and seasonal heterogeneity of community-specific relative rates could be explained by differences in the chemical composition of PM_{2.5} (PM with aerodynamic diameter $\leq 2.5 \mu\text{m}$). Animal and human toxicological studies support this hypothesis (9–12). However, empirical population-based evidence supporting this hypothesis is lacking. Understanding the basis of the variation in PM effects is critical to further characterize the biological mechanisms of toxicity and to move toward more focused regulatory approaches for PM (13).

We investigated whether particular PM_{2.5} chemical components are responsible for observed geographical and seasonal

(Received in original form August 7, 2008; accepted in final form March 18, 2009)

Supported by U.S. Environmental Protection Agency grant RD-83241701 (M.L.B., R.D.P., J.M.S., F.D.), the National Institute for Environmental Health Science grant P30 ES03819 (R.D.P., F.D.), and Health Effects Institute New Investigator Award 4720-RFA04-2/04-16 and NIEHS Outstanding New Environmental Scientist (ONES) Award 5R01ES015028 (M.L.B., K.E.).

Correspondence and requests for reprints should be addressed to Michelle L. Bell, M.D., Yale University, 195 Prospect St., New Haven, CT 06511. E-mail: michelle.bell@yale.edu

This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org

Am J Respir Crit Care Med Vol 179, pp 1115–1120, 2009

Originally Published in Press as DOI: 10.1164/rccm.200808-1240OC on March 19, 2009
Internet address: www.atsjournals.org

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Although airborne particulate matter (PM) has been linked to adverse human health effects, the chemical constituents that cause harm are unknown. The relationship between PM and health varies seasonally and regionally, as does the particle's chemical composition.

What This Study Adds to the Field

This work provides evidence that the chemical composition of PM affects its toxicity. In places and during seasons when PM had higher fractions of nickel, vanadium, and elemental carbon, the risks of hospital admission associated with PM with aerodynamic diameter $\leq 2.5 \mu\text{m}$ were higher.

variation in the short-term association of PM_{2.5} with hospital admissions (4, 7). We also performed a similar analysis based on effect estimates for PM₁₀ and mortality (see online supplement).

METHODS

We analyzed whether community-specific estimates of the impact of PM on health risk (cardiovascular and respiratory hospital admissions and mortality) were higher or lower in communities or seasons with particular PM_{2.5} chemical composition, as indicated by the fraction of PM_{2.5} total mass that is a particular component (e.g., elemental carbon [EC]). We estimated county- and season-specific relative risks (RR) of cardiovascular and respiratory hospitalization associated with a 10- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} total mass on the same day for 106 U.S. counties for the years 1999 through 2005 (Figures 1 and 2). Counties were selected based on data availability for PM_{2.5} total mass and chemical components and on having a population of 200,000 or more persons to allow for sufficient sample size and to allow a distribution of counties across the United States. The population criterion results in more urban counties. We conducted similar analysis for PM₁₀ and total nonaccidental mortality in 100 U.S. communities for 1987 through 2000 (see Figure E1 in the online supplement) (8). All county- and season-specific effect estimates were adjusted for day of the week, seasonality, and long-term trends based on a smooth function of a variable representing time by including these variables in the county-specific regression models. We adjusted for daily temperature and dew point temperature and for the previous 3 days' temperature and dew point temperature. Details of the methods are provided elsewhere (4, 7, 8).

We generated a national database of PM_{2.5} chemical component concentrations from February 2000 to December 2005 based on data obtained from the U.S. Environmental Protection Agency (USEPA) (14). We calculated county- and season-specific averages of PM_{2.5} chemical components that were demonstrated to contribute a substantial fraction of PM_{2.5} total mass (14) or to have been implicated as potentially toxic in earlier research (11, 15–18) (Table 1). Detailed information on the spatial and temporal variation of the PM_{2.5} chemical components is provided elsewhere (14). We then calculated the fraction of PM_{2.5} total mass for each component by season and county. Chemical composition data were available for 106 of the 200

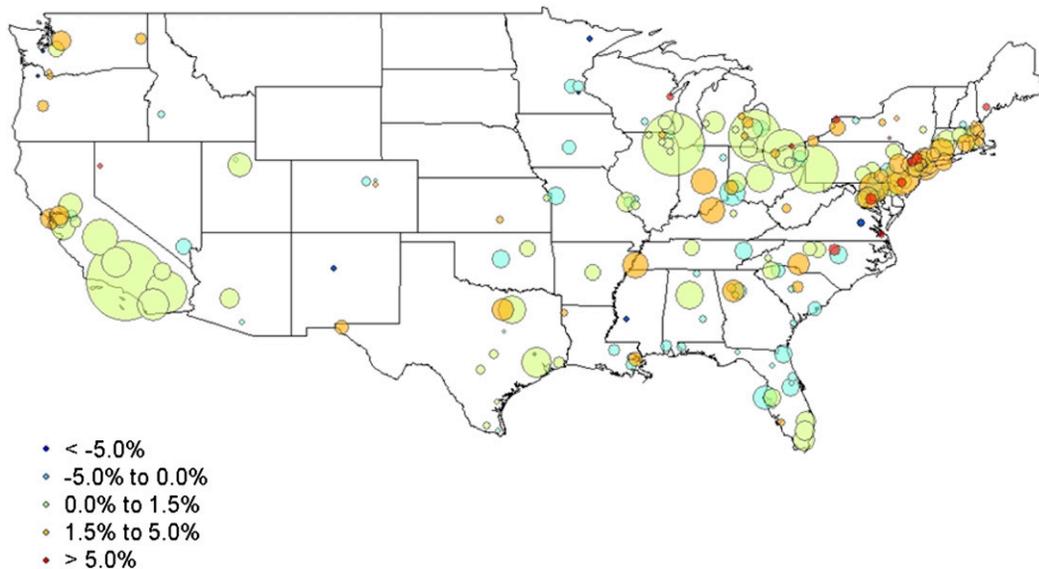


Figure 1. Percent increase in cardiovascular hospital admissions per $10 \mu\text{g}/\text{m}^3$ increase in lag 0 particulate matter with aerodynamic diameter $\leq 2.5 \mu\text{m}$ ($n = 200$). The values are based on estimates from our previous work (7). The size of the circle is proportional to the inverse of the estimate's variance. In other words, more certain estimates are shown with larger circles.

U.S. continental counties with available $\text{PM}_{2.5}$ and hospital admissions RRs. The air pollution monitors for $\text{PM}_{2.5}$ total mass and $\text{PM}_{2.5}$ chemical composition were sited by the USEPA for regulatory compliance purposes and to represent populations' exposures.

We applied Bayesian hierarchical regression modeling (19, 20) to estimate the association between county- and season-specific RRs of hospitalizations and county- and season-specific fractions of $\text{PM}_{2.5}$ chemical constituents in relation to the $\text{PM}_{2.5}$ total mass. This approach accounts for the statistical uncertainty of the county-specific health effect estimates. In other words, county-specific results that are less certain contribute less evidence to the overall estimate. Results are provided as the percent increase in the RR associated with an interquartile range increase in the component's fraction of $\text{PM}_{2.5}$ total mass. Estimates were considered statistically significant if the 95% posterior interval did not overlap zero.

We examined whether key results were robust to: (1) adjustment by other chemical components in the regression analysis, (2) exclusion of individual communities, and (3) lag selection. We also performed analysis to evaluate an alternative hypothesis that other community factors explained variability among PM effect estimates including: (1) socioeconomic conditions, (2) racial composition, and (3) degree of urbanization. Similar analysis was applied to examine variability in ozone mortality estimates (21).

Analysis based on socioeconomic conditions, racial composition, or degree of urbanization used yearly health effect estimates because these variables are unlikely to change by season. This analysis examines variability in health effect estimates across locations only, as opposed to the chemical component analysis that incorporates variation across seasons. County-specific variables were based on data from the 2000 U.S. census (22, 23) for analysis of $\text{PM}_{2.5}$ and hospitalizations and time-weighted values from the 1990 and 2000 U.S. censuses for PM_{10} and mortality (22–25).

RESULTS

Table 1 summarizes the $\text{PM}_{2.5}$ chemical components data and the contribution of each constituent to $\text{PM}_{2.5}$ total mass. Ammonium, EC, organ carbon matter, nitrate, and sulfate comprise the majority of $\text{PM}_{2.5}$ total mass.

Figure 3 shows the percent increases in the $\text{PM}_{2.5}$ risk estimates for cardiovascular and respiratory admissions per interquartile range increase in the fraction of each $\text{PM}_{2.5}$ component to the $\text{PM}_{2.5}$ total mass. We found statistically significant evidence that $\text{PM}_{2.5}$ RRs for cardiovascular and

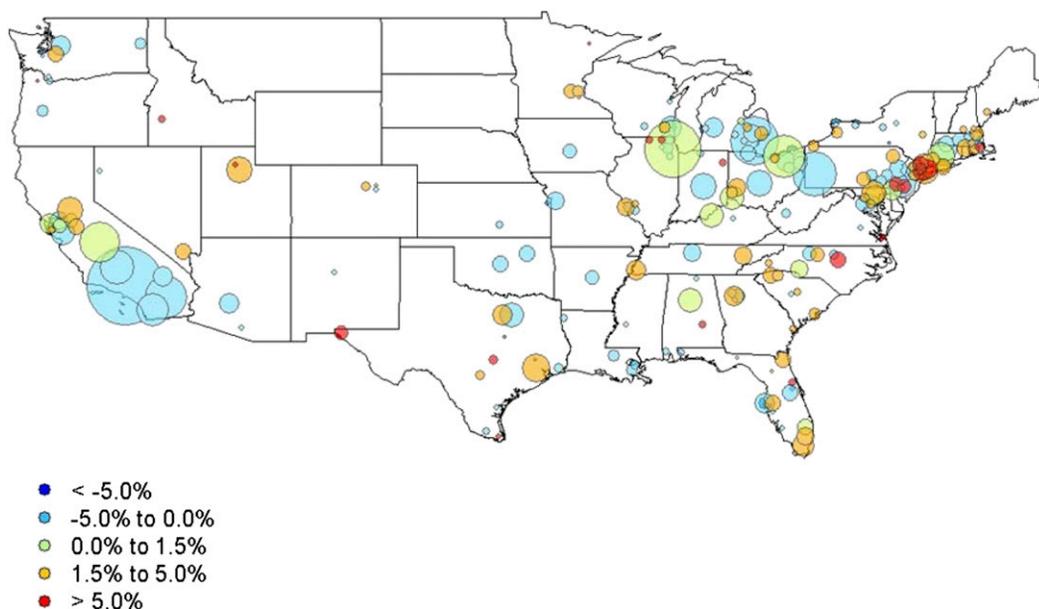


Figure 2. Percent increase in respiratory hospital admissions per $10 \mu\text{g}/\text{m}^3$ increase in lag 0 particulate matter with aerodynamic diameter $\leq 2.5 \mu\text{m}$ ($n = 200$). The values are based on estimates from our previous work (7). The size of the circle is proportional to the inverse of the estimate's variance. In other words, more certain estimates are shown with larger circles.

TABLE 1. SUMMARY STATISTICS FOR COUNTY-LEVEL PM_{2.5} CHEMICAL COMPONENT CONCENTRATIONS ON AVERAGE FOR 106 US COUNTIES (2000–2005)

	Mass of component (μg/m ³)			Percent of PM _{2.5} total mass (interquartile range of percents)
	Average	Range	Interquartile Range	
Aluminum	0.031	0.010–0.135	0.013	0.11
Ammonium	1.60	0.338–3.86	0.794	3.8
Arsenic	0.002	0.0006–0.004	0.0006	0.005
Calcium	0.060	0.017–0.441	0.036	0.32
Chlorine	0.033	0.006–0.305	0.030	0.20
Copper	0.005	0.001–0.023	0.003	0.02
Elemental carbon	0.715	0.309–1.73	0.245	1.7
Organic carbon matter	4.04	2.19–8.34	1.13	9.0
Iron	0.101	0.037–0.437	0.048	0.32
Lead	0.005	0.002–0.024	0.002	0.02
Magnesium	0.016	0.007–0.066	0.004	0.05
Nickel	0.002	0.0003–0.021	0.001	0.01
Nitrate	1.93	0.415–9.95	1.53	9.7
Potassium	0.073	0.036–0.275	0.021	0.19
Silicon	0.111	0.038–0.458	0.053	0.42
Sodium ion	0.141	0.037–0.521	0.063	0.53
Sulfate	3.66	0.650–5.62	1.85	9.3
Titanium	0.006	0.003–0.016	0.002	0.02
Vanadium	0.003	0.001–0.010	0.001	0.01
Zinc	0.017	0.004–0.130	0.011	0.07

Definition of abbreviation: PM_{2.5} = particulate matter with aerodynamic diameter 2.5 μm or less.

respiratory hospitalizations are higher in counties and seasons with higher EC, nickel, or vanadium PM_{2.5} content. County- and season-specific PM₁₀ RRs of all-cause mortality were higher in counties and during seasons with higher PM_{2.5} nickel content (Figure E2).

In multiple pollutant models, for cardiovascular hospitalizations, the relationship between the PM_{2.5} RR and nickel was robust to adjustment by EC or vanadium. The association between the PM_{2.5} RR and vanadium was robust to adjustment

by EC. All other associations lost statistical significance but remained positive with the inclusion of another component. Table 2 summarizes multipollutant models' results. Table 2 shows how the health effect estimate for PM_{2.5} total mass is affected by the fraction of PM_{2.5} total mass that is a given component. The unexplained heterogeneity of county- and season-specific PM_{2.5} RRs for cardiovascular hospitalization was reduced by 37% when the model included nickel and vanadium content, 32% with nickel and EC, and 11% with EC and vanadium. The between-community variance of PM_{2.5} respiratory hospitalization RRs was not greatly reduced by including multiple components into the model. The only association that remains statistically significant when adjusted for other co-pollutants is the relationship between nickel and PM_{2.5} effect estimates for cardiovascular hospital admissions adjusted for EC and vanadium. We found this association to be robust to the inclusion of these two co-pollutants as well as each of the five community-level variables reflecting indicators of socioeconomic conditions, racial composition, or urbanization (Table E1). The association between the PM_{2.5} RR for respiratory hospitalizations and nickel loses statistical significance when Queens County or New York County are excluded. Effect modification by other components was robust to the exclusion of any other single community (Figures E3 and E4), and the association with vanadium loses statistical significance when Queens County is excluded.

Our primary results were based on the lag structure most strongly associated with the health response; we also conducted sensitivity analyses of the main results to other lags (Table E2). Higher effect estimates for PM_{2.5} and cardiovascular hospitalizations were observed in communities with higher nickel or vanadium PM_{2.5} content under all lag structures; however, results were only statistically significant for the lag of the primary analysis (same-day health effect estimates). Results for associations between components and effect estimates for PM_{2.5} and respiratory hospitalizations decreased dramatically with consideration of additional lag structures. However, the sensitivity analyses are based on lag structures for which the community-

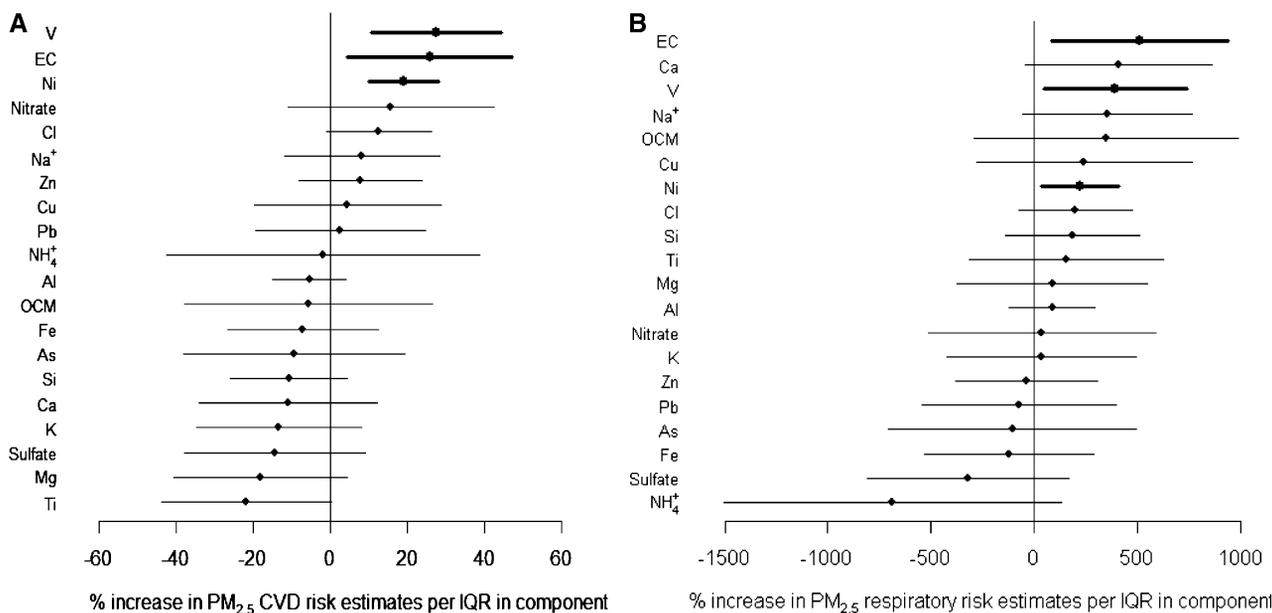


Figure 3. Percent increase in health effects estimates for particulate matter with aerodynamic diameter 2.5 μm or less (PM_{2.5}) lag 0 and risk of cardiovascular hospitalizations (A) and respiratory hospitalizations (B) per IQR increase in the fraction of PM_{2.5} total mass for each component. The points reflect the central estimate and the horizontal line represents the 95% posterior interval. Statistically significant associations are shown in bold. CVD = cardiovascular disease; EC = elemental carbon; IQR = interquartile range; OCM = organ carbon matter.

TABLE 2. PERCENT INCREASE IN HEALTH EFFECTS ESTIMATES FOR PM_{2.5} LAG 0 AND RISK OF CARDIOVASCULAR HOSPITALIZATIONS AND RESPIRATORY HOSPITALIZATIONS PER INTERQUARTILE RANGE INCREASE IN THE FRACTION OF PM_{2.5} TOTAL MASS FOR EACH COMPONENT, WITH AND WITHOUT COPOLLUTANT ADJUSTMENT (95% POSTERIOR INTERVAL)

	Co-pollutant Adjustment	PM _{2.5} and CVD Hospital Admissions*	PM _{2.5} and Respiratory Hospital Admissions
Elemental carbon (EC)	None	25.8 (4.4 to 47.2) [†]	511 (80.7 to 941)
	Nickel	14.0 (-7.6 to 35.5)	399 (-45.1 to 843)
	Vanadium	14.9 (-7.8 to 37.6)	386 (-74.8 to 846)
	Nickel and vanadium	11.9 (-10.4 to 43.2)	362 (-98.0 to 823)
Nickel	None	19.0 (9.9 to 28.2)	223 (36.9 to 410)
	EC	17.3 (7.7 to 26.9)	176 (-18.7 to 370)
	Vanadium	15.5 (4.1 to 26.9)	151 (-78.4 to 381)
	EC and vanadium	14.9 (3.4 to 26.4)	136 (-94.9 to 368)
Vanadium	None	27.5 (10.6 to 44.4)	392 (46.3 to 738)
	EC	23.1 (4.9 to 41.4)	279 (-93.2 to 651)
	Nickel	10.9 (-9.6 to 31.5)	230 (-193.7 to 853)
	EC and nickel	8.1 (-13.3 to 29.5)	140 (-300 to 579)

Definition of abbreviations: CVD = cardiovascular disease; EC = elemental carbon; PM_{2.5} = particulate matter with aerodynamic diameter ≤ 2.5 μm.

* The correlation between the fractions of PM_{2.5} for each pair of components is 0.48 for nickel and vanadium, 0.33 for vanadium and EC, and 0.30 for nickel and EC.

[†] Values in parentheses are interquartile ranges.

specific health effects estimates do not collectively provide the strongest evidence of an association between particles and health. The association observed between risk estimates for same-day PM₁₀ and mortality and nickel PM_{2.5} content remained when lag 2 risk estimates were used and was similar with same-day estimates, although results were less certain (Table E3).

Yearly PM health effect estimates were related to community-specific variables for socioeconomic status, racial composition, and degree of urbanization (Table E4). No statistically significant associations were observed between any of these variables and PM_{2.5} effect estimates for cardiovascular or respiratory hospital admissions or for PM₁₀ effect estimates for mortality.

DISCUSSION

A large fraction of the geographical and seasonal variation in the short-term effects of PM on mortality and morbidity is explained by differences in PM chemical composition. Specifically, we found that nickel and vanadium content explain 37% of the heterogeneity in cardiovascular PM_{2.5} hospitalization estimates. For example, county- and season-specific PM_{2.5} RRs of cardiovascular hospitalizations were 26% higher in counties and seasons with a nickel fraction of PM_{2.5} in the 75th compared with the 25th percentile. In some cases, results for one pollutant were robust to adjustment by another component, but in other cases they were not (Table 2). In general, results for nickel for PM_{2.5} and cardiovascular hospital admissions were most robust to co-pollutant adjustment. There are several potential reasons for this, although our analysis cannot definitively provide a single explanation. Possibilities include that nickel PM_{2.5} is causal for the health outcome resulting in or contributing to the PM_{2.5} total mass health effect estimates, that nickel levels exacerbate the short-term effects of PM_{2.5} on cardiovascular hospital admissions, that long-term nickel levels might act as a surrogate for other pollution that is not captured by vanadium or EC, and that nickel is measured with less error than the other two pollutants. We did explore whether the effect is driven by one or a few of the counties.

Vanadium, EC, or nickel could be markers for other components with similar sources. For example, PM_{2.5} with nickel and vanadium is generated by oil combustion, whereas EC in PM_{2.5} comes from vehicles, biomass burning, and oil combustion. Each component has multiple sources, and each source generates multiple components. Nickel, for example, has been linked to emissions from vehicles, oil combustion, road dust, and metal plating industry (26–28). The biological mech-

anisms by which these and other particle components affect health are not fully understood. Studies have linked various particle components to human physiological responses, such as nickel and changes in heart rate variability (29) and vanadium and oxidative DNA damage (30).

EC contributes approximately 5% to total PM_{2.5} mass on average across the United States, whereas vanadium and nickel each contribute an average of less than 1% (14). Detection limits for these components are an important limitation of any analysis of PM components. In particular, some components' measurements are likely to be more accurate than others based on detection limit and measurement error issues (31). Another limitation of this work is uncaptured spatial variability of PM_{2.5} component concentrations within a given community; the degree of variability may vary by the component (32–34). Thus, overall, there is likely to be varying uncertainty for the estimated exposures to the various PM components. Although we performed various sensitivity analyses, we did not perform exhaustive analyses of all possible combinations of various components and pollutant mixtures, which would include many of the components investigated here as well as others.

We found evidence of effect modification of PM health effects by several PM_{2.5} chemical components and did not identify relationships with socioeconomic conditions, racial composition, or degree of urbanization. However, other county-specific characteristics could explain such heterogeneity. For example, exposure patterns, population characteristics, air conditioning use, and socioeconomic conditions vary across cities, and this variation may modify air pollution health associations (21, 35–39). In a recent study, we found that communities with a higher prevalence of air conditioning had lower health effect estimates for PM, especially for cardiovascular hospital admissions and central air conditioning (40). County averages of PM_{2.5} components may be affected by different degrees of measurement error because some components are more spatially homogeneous than others (41).

Although information on how specific PM components affect health is limited, several other studies have indicated differential toxicity by components or sources. A study of six California counties examined the risk of cardiovascular mortality and multiple components including EC, organic carbon, nitrate, sulfate, calcium, chlorine, copper, iron, potassium, sulfur, silicon, titanium, and zinc (15, 16). Higher mortality risk was associated with several components in particular groups based on sex, race, and education level. Same-day component levels were associated with higher cardiovascular mortality risk for non-high school graduates for nitrate, sulfate, and sulfur and for men for sulfur

and zinc (16). Lead used as a marker for traffic pollution and selenium as a marker for coal combustion were linked with daily mortality in six U.S. cities (42). Poisson regression analysis of mortality data in the Southwestern U.S. found a decrease in mortality during a period of a strike at copper smelters, implying a link between sulfate and PM health risks (43).

Two earlier studies examined whether PM health effect estimates are modified by chemical components. One study compared PM₁₀ mortality effect estimates with PM_{2.5} nickel, vanadium, EC, zinc, sulfate, copper, lead, organic carbon, selenium, chromium, manganese, iron, arsenic, nitrate, aluminum, or silicon using health effect estimates generated by the National Mortality, Morbidity, and Air Pollution Study (11, 44). Concentrations of nickel or vanadium PM_{2.5} were significantly associated with PM₁₀ mortality effect estimates. However, subsequent analysis found that the results were highly sensitive to the New York City community (17). This study also found higher PM₁₀ mortality effect estimates associated with higher nickel PM_{2.5} content, with results sensitive to the New York City community (Figure E5).

The variation in the effect estimates for cardiovascular hospitalization associated with PM_{2.5} and levels of nickel, EC, and vanadium PM_{2.5} content were robust to the exclusion of any single county. The variation in effect estimates for respiratory hospitalization with nickel and vanadium PM_{2.5} content lost statistical significance with the exclusion of some New York counties; however, the central association (i.e., the relationship between RR and PM component) did not decrease dramatically (Figures E3–E5).

Community-specific PM_{2.5} mortality effect estimates for 25 U.S. communities were higher in the communities where PM_{2.5} content was higher for aluminum, arsenic, sulfate, silicon, and nickel (3). Our research identified a link between nickel and PM₁₀ mortality effect estimates or PM_{2.5} hospitalizations but did not find strong associations with other components identified in the 25-city study (aluminum, arsenic, sulfate, and silicon). Our study differs from the 25-city study in several ways, including the cities considered, PM metrics and health outcomes used, and lag structures of the models: same-day PM in ours and a cumulative lag structure in the 25-city study.

The range of chemical components and sources linked to various health responses supports the hypothesis that no single component is responsible for the harmful nature of PM. Although some sources, such as vehicle traffic, have received particular attention, understanding the relative toxicity of different sources contributing to ambient PM requires substantial investigation (5, 45). Associations between particles and health outcomes in epidemiological studies may be the result of multiple components acting on different physiological mechanisms. We found that the spatial and temporal variation in the risk of PM is partially explained by chemical composition. The evidence presented here indicates that the chemical composition of PM_{2.5} contributes to between-community and seasonal heterogeneity in PM health effects, particularly the EC, nickel, and vanadium contents.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

References

- Bell ML, Samet JM, Dominici F. Time-series studies of particulate matter. *Annu Rev Public Health* 2004;25:247–280.
- US EPA. Air quality criteria for particulate matter. Research Triangle Park, NC: US Environmental Protection Agency, Office of Research and Development; 2004.
- Franklin M, Zeka A, Schwartz J. Associations between PM_{2.5} and all-cause and specific-cause mortality in 27 US communities. *J Expo Sci Environ Epidemiol* 2007;17:279–287.
- Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, Samet JM. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. *JAMA* 2006;295:1127–1134.
- Pope CA, Dockery DW. Health effects of fine particulate air pollution: lines that connect. *J Air Waste Manag Assoc* 2006;56:709–742.
- Samoli E, Analitis A, Touloumi G, Schwartz J, Anderson HR, Sunyer J, Bisanti L, Zmirou D, Vonk JM, Pekkanen J, *et al.* Estimating the exposure-response relationships between particulate matter and mortality within the APHEA multicity project. *Environ Health Perspect* 2005;113:88–95.
- Bell ML, Ebisu K, Peng RD, Walker J, Samet JM, Zeger SL, Dominici F. Seasonal and regional short-term effects of fine particles on hospital admissions in 202 US counties, 1999–2005. *Am J Epidemiol* 2008;168:1301–1310.
- Peng RD, Dominici F, Pastor-Barriuso R, Zeger SL, Samet JM. Seasonal analyses of air pollution and mortality in 100 US cities. *Am J Epidemiol* 2005;161:585–594.
- Riediker M. Cardiovascular effects of fine particulate matter components in highway patrol officers. *Inhal Toxicol* 2007;19:S99–S105.
- Chuang KJ, Chan CC, Su TC, Lin LY, Lee CT. Associations between particulate sulfate and organic carbon exposures and heart rate variability in patients with or at risk for cardiovascular diseases. *J Occup Environ Med* 2007;49:610–617.
- Lippmann M, Ito K, Hwang JS, Maciejczyk P, Chen LC. Cardiovascular effects of nickel in ambient air. *Environ Health Perspect* 2006;114:1662–1669.
- Gilmour MI, McGee J, Duvall RM, Dailey L, Daniels M, Boykin E, Cho SH, Doerfler D, Gordon T, Devlin RB. Comparative toxicity of size-fractionated airborne particulate matter obtained from different cities in the United States. *Inhal Toxicol* 2007;19:S7–S16.
- NRC Committee on Research Priorities for Airborne Particulate Matter Board on Environmental Studies and Toxicology. Research priorities for airborne particulate matter IV: continuing research progress. Washington, DC: National Academy Press; 2004.
- Bell ML, Dominici F, Ebisu K, Zeger SL, Samet JM. Spatial and temporal variation in PM_{2.5} chemical composition in the United States for health effects studies. *Environ Health Perspect* 2007;115:989–995.
- Ostro B, Feng WY, Broadwin R, Green S, Lipsett M. The effects of components of fine particulate air pollution on mortality in California: results from CALFINE. *Environ Health Perspect* 2007;115:13–19.
- Ostro BD, Feng WY, Broadwin R, Malig BJ, Green RS, Lipsett MJ. The impact of components of fine particulate matter on cardiovascular mortality in susceptible subpopulations. *Occup Environ Med* 2008;65:750–756.
- Dominici F, Peng RD, Ebisu K, Zeger SL, Samet JM, Bell ML. Does the effect of PM₁₀ on mortality depend on PM nickel and vanadium content? A reanalysis of the NMMAPS data. *Environ Health Perspect* 2007;115:1701–1703.
- Franklin M, Koutrakis P, Schwartz J. The role of particle composition on the association between PM_{2.5} and mortality. *Epidemiology* 2008;19:680–689.
- Everson P. Two-Level Normal Independent Sampling Estimation (TLNISE). Swarthmore, PA: Swarthmore College; 2000.
- Everson PJ, Morris CN. Inference for multivariate normal hierarchical models. *J Roy Stat Soc Ser B* 2000;62:399–412.
- Bell ML, Dominici F. Effects modification by community characteristics on the short-term effects of ozone exposure and mortality in 98 US communities. *Am J Epidemiol* 2008;167:986–997.
- US Census Bureau. Census 2000, summary file 1. Washington, D.C.: US Census Bureau; 2000.
- US Census Bureau. Census 2000, summary file 3. Washington, D.C.: US Census Bureau; 2000.
- US Census Bureau. Census 1990, summary file 3. Washington, D.C.: US Census Bureau; 1990.
- US Census Bureau. Census 1990, summary file 1. Washington, D.C.: US Census Bureau; 1990.
- Buzcu-Guven B, Brown SG, Frankel A, Hafner HR, Roberts PT. Analysis and apportionment of organic carbon and fine particulate matter sources at multiple sites in the midwestern United States. *J Air Waste Manag Assoc* 2007;57:606–619.
- Okuda T, Nakao S, Katsuno M, Tanaka S. Source identification of nickel in TSP and PM_{2.5} in Tokyo, Japan. *Atmos Environ* 2007;41:7642–7648.
- Thomaidis NS, Bakeas EB, Siskos PA. Characterization of lead, cadmium, arsenic and nickel in PM_{2.5} particles in the Athens atmosphere, Greece. *Chemosphere* 2003;52:959–966.
- Cavallari JM, Eisen EA, Fang SC, Schwartz J, Hauser R, Herrick RF, Christiani DC. PM_{2.5} metal exposures and nocturnal heart rate

- variability: a panel study of boilermaker construction workers. *Environ Health* 2008;7:36.
30. Sørensen M, Schins RP, Hertel O, Loft S. Transition metals in personal samples of PM_{2.5} and oxidative stress in human volunteers. *Cancer Epidemiol Biomarkers Prev* 2005;14:1340–1343.
 31. Pun B, Seigneur C, Edgerton E. Creation of an air pollutant database for health effects studies: Phase I report—collection of Pm speciation and related data. San Ramon, CA: Atmospheric and Environmental Research, Inc. report submitted to Health Effects Institute; 2004.
 32. Ivy D, Mulholland JA, Russell AG. Development of ambient air quality population-weighted metrics for use in time-series health studies. *J Air Waste Manag Assoc* 2008;58:711–720.
 33. Kim E, Hopke PK, Pinto JP, Wilson WE. Spatial variability of fine particle mass, components, and source contributions during the Regional Air Pollution Study in St. Louis. *Environ Sci Technol* 2005;39:4172–4179.
 34. Ito K, Xue N, Thurston G. Spatial variation of PM_{2.5} chemical species and source-apportioned mass concentrations in New York City. *Atmos Environ* 2004;38:5269–5282.
 35. Medina-Ramón M, Zanobetti A, Schwartz J. The effect of ozone and PM₁₀ on hospital admissions for pneumonia and chronic obstructive pulmonary disease: a national multicity study. *Am J Epidemiol* 2006;163:579–588.
 36. O'Neill MS, Jerrett M, Kawachi I, Levy JI, Cohen AJ, Gouveia N, Wilkinson P, Fletcher T, Cifuentes L, Schwartz J, with input from participants of the Workshop on Air Pollution and Socioeconomic Conditions. Health, wealth, and air pollution: advancing theory and methods. *Environ Health Perspect* 2003;111:1861–1870.
 37. Zeka A, Zanobetti A, Schwartz J. Short term effects of particulate matter on cause specific mortality: effects of lags and modification by city characteristics. *Occup Environ Med* 2005;62:718–725.
 38. Zanobetti A, Schwartz J. Race, gender, and social status as modifiers of the effects of PM₁₀ on mortality. *J Occup Environ Med* 2000;42:469–474.
 39. Gwynn RC, Thurston GD. The burden of air pollution: impacts among racial minorities. *Environ Health Perspect* 2001;109:S501–S506.
 40. Bell ML, Ebisu K, Peng RD, Dominici F. Air conditioning use lowers particulate matter's adverse health effects: results from national United States studies on hospital admissions and mortality. *Epidemiology* (In press).
 41. Athanassiadis GA, Rao ST. Spatial and temporal variation in the trace elemental data over the northeastern United States. *Environ Pollut* 2003;123:439–449.
 42. Laden F, Neas LM, Dockery DW, Schwartz J. Association of fine particulate matter from different sources with daily mortality in six US cities. *Environ Health Perspect* 2000;108:941–947.
 43. Pope CA, Rodermund DL, Gee MM. Mortality effects of a copper smelter strike and reduced ambient sulfate particulate matter air pollution. *Environ Health Perspect* 2007;115:679–683.
 44. Samet JM, Zeger SL, Dominici F, Curriero F, Coursac I, Dockery DW, Schwartz J, Zanobetti A. The National Morbidity, Mortality, and Air Pollution Study, part II: morbidity and mortality from air pollution in the United States. Cambridge, MA: Health Effects Institute; 2000.
 45. Grahame TJ, Schlesinger RB. Health effects of airborne particulate matter: do we know enough to consider regulating specific particle types or sources? *Inhal Toxicol* 2007;19:457–481.