A Time–Series Analysis of Acidic Particulate Matter and Daily Mortality and Morbidity in the Buffalo, New York, Region

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A component of particulate matter (PM) air pollution that may provide one biologically plausible pathway for the observed PM air pollution–health effect associations is aerosol acidity (H^+). An increasing number of observational studies have demonstrated associations between H^+ and increased adverse health effects in the United States and abroad. Although studies have shown significant H^+ associations with increased morbidity in the United States, similar associations have yet to be shown with daily mortality. We considered a 2.5-year record of daily H^+ and sulfate measurements (May 1988–October 1990) collected in the Buffalo, New York, region in a time–series analysis of respiratory, circulatory, and total daily mortality and hospital admissions. Other copollutants considered included particulate matter ≤ 10 μm in aerodynamic diameter, coefficient of haze, ozone, carbon monoxide, sulfur dioxide, and nitrogen dioxide. Various modeling techniques were applied to control for confounding of effect estimates due to seasonality, weather, and day-of-week effects. We found multiple significant pollutant–health effect associations—most strongly between SO_4^{2-} and respiratory hospital admissions (as indicated by its *t*-statistic). Additionally, H^+ and SO_4^{2-} demonstrated the most coherent associations with both respiratory hospital admissions [H^+: relative risk (RR) = 1.31; 95% confidence interval (CI), 1.14–1.51; and SO_4^{2-}: RR = 1.18, CI, 1.09–1.28] and respiratory mortality (H^+: RR = 1.55, CI, 1.09–2.20; and SO_4^{2-}: RR = 1.24, CI, 1.01–1.52). Thus, acidic sulfate aerosols represent a component of PM air pollution that may contribute to the previously noted adverse effects of PM mass on human health, and the associations demonstrated in this study support the need for further investigations into the potential health effects of acidic aerosols. *Key words*: **acid aerosols, air pollution, epidemiology, mortality, hospital admissions, particulate matter, time–series techniques.** *Environ Health Perspect* **108:125–133 (2000). [Online 30 December 1999]**

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In recent years, there has been growing concern about the adverse effects of particulate matter (PM) air pollution on human health. These concerns originally stemmed from historical air pollution episodes that were associated with increases in the indices of severe health outcomes, such as mortality and hospital admissions. The London smog episode of 1952 (*1*), probably the best documented of such incidents, resulted in a peak respiratory hospital admissions rate of 460/day, versus approximately 175/day just before the fog occurred. At the time, it was suspected that elevated levels of sulfuric acid from coal combustion played a role in these excess deaths (*1*). This and other historical air pollution episodes offer convincing evidence of the potential for adverse impacts on human health from extreme environmental exposures. However, the confirmation and quantification of air pollution health effects at more routine and much lower level exposures is not as straightforward.

Whereas various pollution measures, including PM mass [i.e., total suspended particulates, particulate matter ≤ 10 μm in aerodynamic diameter (PM_{10}), and/or particulate matter ≤ 2.5 μm in aerodynamic diameter ($PM_{2.5}$)], black smoke, sulfur dioxide, and ozone, are significantly correlated with increased morbidity and mortality, it is PM_{10} and $PM_{2.5}$ that have recently been the focus of the greatest interest (*2–4*). The Clean Air Act (*5*) currently regulates PM_{10} as a criteria pollutant and has established National Ambient Air Quality Standards (NAAQS) for a 24-hr (150 μg/m^3) and an annual (50 μg/m^3) averaging period (*5*). In 1997, the U.S. Environmental Protection Agency (EPA) issued revised NAAQS (*5*), in which a new fine particle standard ($PM_{2.5}$) was added. Despite these standards, there is still concern that specific unregulated PM components may cause adverse health effects.

Some have argued that future research efforts should focus specifically on those chemical components of PM that are most responsible for the noted effects (*6*). In addition, the identification of harmful chemical components would help provide further biologic plausibility evidence supportive of the causality of the observed PM/health effect associations. This in turn would help direct PM control measures at those sources of greatest health consequence.

Among the PM components that may elicit harmful toxicologic responses are sulfates and strong aerosol acidity (H^+) (*7–9*). Sulfate concentration has traditionally been interpreted as an indicator of the acidic content of the PM. However, the SO_4^{2-} ion represents the sum of various forms of sulfate: H_2SO_4, $(NH_4)HSO_4$, and $(NH_4)_2SO_4$, which range from strongly to weakly acidic, respectively. The distribution of each component within the total sulfate content is highly variable, as is the overall level of acidity. A more direct measurement of acid aerosol exposure is the strong H^+ concentration of a PM sample, but this is more difficult to measure accurately at low ambient levels, and has not been widely measured to date, thus limiting analyses that directly assess the potential health effects of strongly acidic aerosols.

The biologic plausibility of the acid aerosol component as a causal agent in the PM/adverse health effect associations is supported by a growing body of evidence from both animal toxicity and controlled human exposure studies. Short-term sulfuric acid exposures between 0.1 and 1.0 mg/m^3 have produced lung clearance function and pulmonary mechanical effects in normal and asthmatic human subjects (*10,11*). Animal studies have also shown adverse effects from exposure to acid aerosols such as clearance abnormalities (*12*), airway hyperresponsiveness and secretory cell hyperplasia (*13*), and changes in pulmonary function (*14*). However, the potential for neutralization of acidic aerosols by endogenous respiratory tract ammonia plays a complex and uncertain role in the toxicity of acidic aerosols (*15,16*). Thus, although an exact mechanism of acidic aerosol toxicity is not yet clear, controlled exposure studies generally offer support to acid-aerosol associations with health effects.

Observational epidemiologic evidence of increased health effects due to acid aerosol

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exposures has also begun to accumulate. Some studies in London, England, indicate stronger associations between aerosol acidity and increases in mortality and morbidity than other PM measures (*17,18*). In North America, summertime levels of H^+ and SO_4^{2-}, in combination with O_3, have been significantly associated with acute increases in respiratory hospital admissions (*4,19,20*). Additionally, H^+ was more consistently associated with asthma symptoms than other environmental factors considered in a study of asthmatics in Denver, Colorado (*21*). More recently, a study of 24 communities by Dockery et al. (*22*) showed that white children between 8 and 12 years of age living in communities with the highest strong aerosol acidity levels were more likely to have one or more episodes of bronchitis than those living in the least polluted communities.

Relatively few observational studies of acid aerosols and mortality have been conducted in North America. Dockery et al. (*23*) examined the influence of acid aerosol levels on mortality in an evaluation of various particulate measures in two of the cities from the Harvard Six Cities Study but were unable to detect significant associations. In a combined analysis of the entire Six Cities Study data, Schwartz et al. (*24*) again found a nonsignificant association between H^+ and daily mortality. However, the relatively short period of daily acid observations for this pollutant (~ 9 months in each city) limited the power of these analyses to detect associations for H^+ relative to the other PM measures considered. Overall, the limited nature of these results indicates a need to further investigate the potential acid-aerosol mortality association.

Thus, the objectives of this research were to first evaluate the hypothesis that acid aerosols are a harmful component of PM for a North American city with a more extensive database, and then to determine if observed pollutant/health effect associations are coherent across both morbidity and mortality outcomes. To evaluate these objectives, a unique comprehensive environmental/health outcome database was constructed for the Buffalo and Rochester, New York, region.

Table 1. Health outcome categories according to *ICD-9* codes.

Classification	*ICD-9* categories and codes
Respiratory	Acute bronchitis/bronchiolitis: 466
	Pneumonia: 480–486
	COPD and asthma: 490–493, 496
Circulatory	Hypertensive disease: 401–405
	Ischemic heart disease: 410–414
	Disease of pulmonary circulation: 415–417
Total	Total minus accident: 800

COPD, chronic obstructive pulmonary disease.

Materials and Methods

Hospital admissions data. We used hospital admissions as an indicator of morbidity within the combined Buffalo and Rochester area (Erie, Niagara, Monroe, Orleans, Genesee, and Wyoming counties) populations. This ensured that a physician deemed each patient ill enough to require hospital admission. Daily hospital admissions data were obtained for the years 1988–1990 from the Statewide Planning and Research Cooperative System (SPARCS), a division of the New York State Department of Health (Albany, NY). SPARCS is a comprehensive health care database that compiles hospital admissions records for all of the general hospitals in New York State. This period of time was selected because daily samples of acidic aerosols were collected by the New York University School of Medicine (NYUSM; Tuxedo, NY) during those years (*25*). Daily unscheduled hospital admissions for residents of the Buffalo–Rochester metropolitan area were considered according to their primary diagnoses, as classified according to the *International Classification of Diseases, 9th Revision* (*ICD-9*; World Health Organization, Geneva). For the purpose of these analyses, the hospital admissions data were grouped into three general classifications: total, circulatory, and respiratory. The *ICD-9* codes used to construct these categories are shown in Table 1.

Mortality data. Daily mortality counts for residents of the Buffalo and Rochester metropolitan area were obtained from the National Center for Health Statistics (Hyattsville, MD) mortality tapes for the same years (1988–1990). These data were classified according to the *ICD-9* codes listed for the hospital admissions category. Accidental deaths and deaths occurring outside of the designated areas were excluded from this dataset.

Environmental data. We used daily measurements of air pollution and weather variables for environmental data. Daily aerosol acidity and sulfate ion measurements were made in Buffalo by the NYUSM from 19 May 1988 to 10 October 1990. These measurements were made using the sequential acid aerosol system developed at the NYUSM (*25*). The NYUSM monitor was located in the residential neighborhood of Amherst, New York, within the Buffalo metropolitan area. Direct comparisons with daily H^+ and SO_4^{2-} measurements made for 2 months in Rochester (60 miles east of Buffalo) confirmed that the site was regionally representative for these pollutants (H^+, $r = 0.95$; SO_4^{2-}, $r = 0.95$) (*9*).

Daily measurements for the EPA's criteria air pollutants were procured for multiple sites in the area for this period from the EPA Aerometric Information Retrieval System (AIRS) (*26*); these pollutants included SO_2, nitrogen dioxide, O_3, carbon monoxide, and PM_{10}. Monitoring sites were selected from the AIRS network based on their population exposure relevance, and were averaged to obtain regional mean daily values for each city. These values were then used to obtain a population-weighted mean for the Buffalo–Rochester metropolitan area. Additionally, correlations among individual sites were calculated to assess intersite variability. Daily mean coefficient of haze (CoH) measurements were obtained from the new York State Department of Environmental Conservation (*27*). Daily weather data were collected at the Buffalo International Airport. Table 2 provides summary statistics for the important environmental and health variables. The intercorrelations among the

Table 2. Summary statistics for environmental and health outcome variables for the Buffalo/Rochester, New York, area, 1988–1990.

Variable	No.	Minimum	25th percentile	Mean	75th percentile	Maximum
Total mortality (deaths/day)	1,096	29.0	43.0	49.0	54.0	75.0
Total hospital admissions (adm/day)	1,096	317.0	437.0	499.4	557.0	693.0
Respiratory mortality (deaths/day)	1,096	0.0	2.0	3.7	5.0	12.0
Respiratory hospital admissions (adm/day)	1,096	15.0	43.0	56.3	67.0	123.0
Circulatory mortality (deaths/day)	1,096	6.0	13.0	16.3	19.0	32.0
Circulatory hospital admissions (adm/day)	1,096	28.0	67.0	83.0	101.0	141.0
H^+ (nmol/m^3)	859	0.63	15.7	36.4	42.2	381.9
SO_4^{2-} (nmol/m^3)	856	0.78	23.5	61.7	74.6	390.5
PM_{10} (μg/m^3)	175	6.88	14.8	24.1	29.2	90.8
Filled PM_{10} (μg/m^3)	812	6.88	17.5	24.9	28.4	90.8
Mean daily O_3 (ppb)	1,095	2.38	17.3	26.2	32.1	87.6
Mean daily SO_2 (ppb)	1,094	1.63	8.4	12.2	15.4	37.7
Mean daily CO (ppm)	1,095	0.30	0.53	0.73	0.86	2.33
Mean daily NO_2 (ppb)	1,090	4.0	15.5	20.5	24.5	47.5
Mean daily CoH/1,000 ft	992	0.0	0.1	0.2	0.3	0.9
Mean daily temperature (°F)	1,096	3.35	34.5	48.4	64.3	83.9
Mean daily relative humidity (%)	1,096	36.3	64.5	72.0	79.6	98.3

adm, admissions.

pollutant indices used in the analysis are given in Table 3.

PM_{10} was monitored only every sixth day; therefore, to have comparable numbers of observations across pollutants, missing PM_{10} observations were estimated using a PM_{10} prediction regression model. Daily measurements of SO_4^{2-}, CoH, and a winter/summer indicator variable to account for differing seasonal background concentrations were used to estimate missing PM_{10} values. These two measures are indices of each of the two major components of fine particulate matter: CoH is an indicator of primary (carbonaceous) particulate emissions and SO_4^{2-} is an indicator of secondary particulate matter formed in the atmosphere. PM_{10} values were well predicted by this model ($r = 0.9$), as shown in Figure 1.

Modeling approach. Mortality and hospital admissions are considered relatively rare occurrences. The number of occurrences (counts) of admissions or deaths per day are generated by a Poisson process, where the probability distribution is given by:

$$\Pr(Y = y) = \frac{e^{-\mu}\mu^{y}}{y!};\ y = 0, 1, 2, \mathrm{K}\ ,$$

The Poisson distribution is determined solely by the mean, μ, which must be positive. Because of this restriction, log-linear models, a family of generalized linear models (GLMs), are used to model Poisson distributed count data. GLMs use a link function that relates a linear predictor η to the expected value μ. In the case of the Poisson model, the link function is $\eta = \log \mu$, thus $\mu = e^{\eta}$, and it is η rather than μ that follows the assumptions of linear model, thereby ensuring a nonnegative mean estimate (*28*).

Despite the usefulness of the log-linear model in handling count data, there are still some concerns about its appropriateness for time–series analyses, such as in this work. One concern is that the variance may exceed the mean, leading to overdispersion (*28*). This may be due to the influence of some unmeasured factor on the health outcome variable. If left unaddressed, overdispersion can lead to the underestimation of coefficient standard errors. The degree of dispersion relative to the Poisson model can be estimated by the overdispersion parameter:

$$\phi = \sum \frac{(y_i - \mu_i)^2}{\mu_i} \Big/ (n - p),$$

where n is the number of observations and p is the number of parameters in the model. When $\phi = 1$ the assumptions of the Poisson model have been met. The model is overdispersed when $\phi > 1$. Therefore, the variance of the Poisson model is $\mathrm{var}(Y) = \phi\mu$.

For the mortality data series, we were able to remove overdispersion by including seasonal and day-of-week terms; however, this was not sufficient for the hospital admissions series. To accommodate the remaining overdispersion that we found in the hospital admissions data (as indicated by the model dispersion parameters), we used the negative binomial (NB) model to analyze the admissions data. The NB model is sometimes referred to as a mixed Poisson model because γ_t follows a Poisson distribution, but it is conditional on the latent process, ε_t. When the distribution of ε_t is gamma, with mean 1 and variance a, the NB model applies. The NB probability function is

$$\Pr(Y = y|x) = \frac{\Gamma\left(y + a^{-1}\right)}{y!\,\Gamma\left(a^{-1}\right)} \left(\frac{a\mu(x)}{1 + a\mu(x)}\right)^{y} \times \left(\frac{1}{1 + a\mu(x)}\right)^{a^{-1}},\ y = 0, 1, \mathrm{K}\ ,$$

where x is the vector of explanatory variables and a is called the index or dispersion parameter (*29*) and represents the degree of extra-Poisson variation. When $a = 0$ in the above equation (i.e., when no overdispersion is present), the negative binomial reduces to a Poisson distribution. The variance of the NB model is $\mathrm{Var}(Y|x) = \phi[\mu(x) + a\mu(x)^2]$. When $\phi = 1$, the negative binomial model holds; otherwise, the distribution is over- or underdispersed (*30*). We estimated the regression coefficients and a using maximum likelihood methods (*31*).

Exploratory analyses and model development. Our overall modeling approach was to consider several modeling specifications and then choose the model that best fit the data, while minimizing overdispersion. The basic model was therefore constructed so that the known potential confounders, such as season, day-of-week, holidays, and weather were addressed within the model. If not adequately controlled, these confounders might lead to spurious associations, overdispersion, and/or autocorrelated residuals, potentially producing biased results.

We applied several alternative approaches to control for seasonal cycles in the data. These included multiday weighted moving average filters (WMAF) (*32*), inclusion of sine/cosine waves (*33*), and loess and spline smoothers (*34*). Periodograms of each of the health effect outcomes indicated that strong long-wave variations on the order of 1 month were present in the data series. Scatterplots and periodograms of the residuals from the models using each of the long-wave control approaches for a 1-month cycle were examined for any remaining systematic variations. Additionally, the AIC and dispersion parameters from each model were computed and intercompared to determine the model that best fit the data while retaining the assumptions of the Poisson model. Figure 2 provides examples of the seasonal fits for the total mortality outcome for each alternative method. Based on this evaluation of the model diagnostics, a 31-day WMAF similar in design to the 19-day filter used by Shumway (*32*) was chosen as the method to control seasonal cycles in this analysis.

Day-of-week and holiday influences were also noted in the periodograms of the outcomes and were therefore addressed in the

Table 3. Cross-correlations of pollutant indices for Buffalo and Rochester, New York.

	H^+	SO_4^{2-}	O_3	SO_2	NO_2	CO	M_PM_{10}[a]	F_PM_{10}[b]	CoH	Temp
H^+	1.00	0.87	0.57	0.06	0.22	0.15	0.73	0.79	0.24	0.48
SO_4^{2-}	–	1.00	0.66	0.19	0.36	0.24	0.87	0.95	0.43	0.51
O_3	–	–	1.00	0.02	0.06	-0.23	0.68	0.66	0.11	0.56
SO_2	–	–	–	1.00	0.36	0.11	0.19	0.15	0.29	-0.25
NO_2	–	–	–	–	1.00	0.65	0.44	0.42	0.72	0.00
CO	–	–	–	–	–	1.00	0.23	0.28	0.62	-0.01
M_PM_{10}	–	–	–	–	–	–	1.00	1.00	0.53	0.60
F_PM_{10}	–	–	–	–	–	–	–	1.00	0.54	0.60
CoH	–	–	–	–	–	–	–	–	1.00	0.15
Temp	–	–	–	–	–	–	–	–	–	1.00

Temp, temperature.
[a]Unfilled PM_{10} index, which consists of PM_{10} values measured every sixth day. [b]Filled PM_{10} index, which consists of PM_{10} values measured every sixth day and predicted values from the regression model.

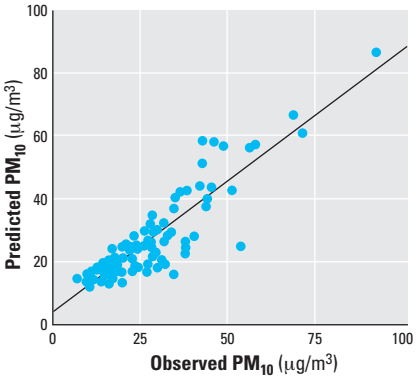

Figure 1. Predicted versus observed PM_{10} values for Buffalo and Rochester, New York (1988–1990). Missing PM_{10} values were predicted from a regression of PM_{10} on SO_4^{2-} and CoH. $Y = 0.81x + 4.67$; $r^2 = 0.81$.

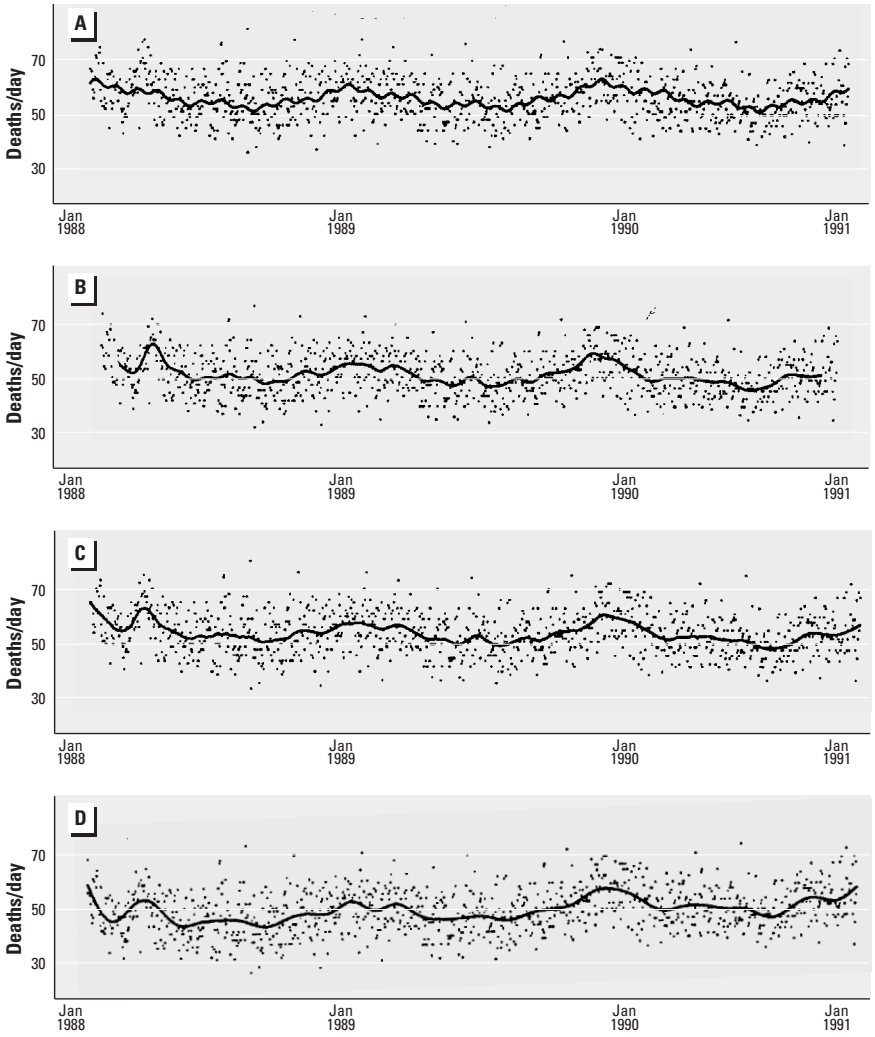

Figure 2. Various approaches used to control for total mortality seasonal variations in the Buffalo–Rochester region (1988–1990). Abbreviations: AIC, Akaike information criteria; disp, dispersion parameter. (*A*) Sine–cosine fitted values (1 month): AIC = 1,196.9; disp = 1.09. (*B*) Thirty-one-day WMAF fitted values; AIC = 1,120.3, disp = 1.02. (*C*) Loess smooth fitted values (span = 0.05); AIC = 1,107.4, disp = 1.01. (*D*) Natural spline (degrees of freedom = 35); AIC = 1,201.7, disp = 1.06.

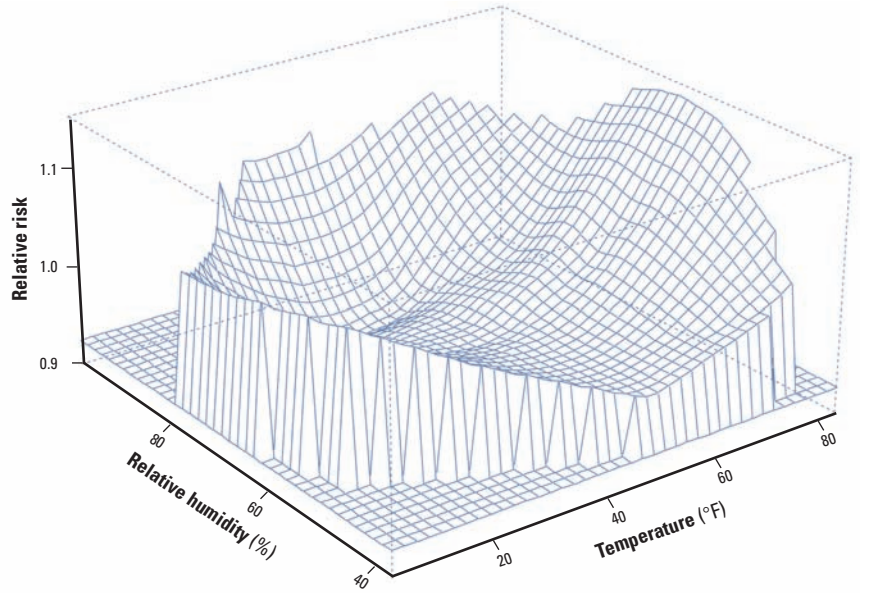

Figure 3. Relative risk of respiratory mortality due to variations in same-day temperature and relative humidity.

model specification. These consistent day-of-week variations can result from generally lower numbers of admissions over the weekends and holidays (when fewer people go to the hospital and when hospitals are not as well staffed) versus higher admissions during the week, especially on Mondays. Thus, indicator variables were constructed for each day of the week and each of the nine federal holidays. Once these indicator variables were included in the model, the periodograms of the residuals and the dispersion parameter were again examined for unaddressed systematic variations. Despite these added controls, the dispersion parameter for all of the hospital admissions categories remained high (~ 2.0). Therefore, the NB model was used for the hospital admissions categories to address the remaining overdispersion in those data series.

After these steps were taken to control the various systematic temporal variations in each health outcome data series, we investigated the nonlinear effects of weather on human health. To elucidate the relationship between weather and the various health outcome variables, we examined exploratory plots of temperature, relative humidity, and dewpoint versus the health outcome variables. We used locally weighted regression (loess) methods to fit smooths to the data to better visualize relationships between the variables. Additionally, three-dimensional loess surfaces of the health outcome variables versus temperature and relative humidity were examined for any synergistic effects between these two weather variables. Figure 3 shows the 3-dimensional relationship between respiratory mortality, temperature, and relative humidity.

Several possible weather specification models were then selected for further investigation, including linear temperature terms, quadratic functions of deviations from a central focal (minimum effect) temperature (chosen based on examination of plots), loess fitted functions of the health effect outcome on temperature, and loess fitted functions of the health effect outcome on both temperature and relative humidity simultaneously. Based on visual inspection of the loess plots of temperature versus each health effect at various lags, the same-day and 2-day lags of each temperature specification were included to account for the strongest hot and cold effects of weather on human health, respectively. We used generalized additive models, which further expand on the classic linear model (*35*), to allow for the inclusion of these nonparametric functions in the regression models.

Once the optimal basic model was selected, the 0–3 day lagged concentrations for each pollutant were added individually

into the basic regression model to evaluate any remaining associations between air pollution and the various morbidity and mortality outcomes considered in this analysis. Figure 4 illustrates the relationship between the respiratory hospital admissions category and each of the pollutant variables, adjusted for monthly and day-of-week variations. The curve superimposed on the data is a loess function of the pollutant/respiratory hospital admissions relationship. Although several of the curves appear somewhat nonlinear, we used a linear function to represent the relationship between the health outcomes and the various pollutants so that the resulting regression coefficients can be more readily interpreted.

Risk estimation. For each health outcome, we computed the relative risk (RR) and 95% confidence interval (CI) using the most significant lag of each pollutant as follows:

$$RR = \exp(\Delta Conc \times \beta_{pollutant})$$

$$LL = \exp[\Delta Conc \times (\beta_{pollutant} - 1.96 \times se_{pollutant})]$$

$$UL = \exp[\Delta Conc \times (\beta_{pollutant} + 1.96 \times se_{pollutant})],$$

where ΔConc is an increment in pollutant concentration. We chose the maximum concentration of a pollutant minus its mean concentration as the primary ΔConc metric because it provides an indication of the effect of an episode day versus the average day, thereby providing a physically meaningful, and directly intercomparable, exposure increment for each pollutant. The interquartile range was also used for ΔConc to provide a more statistically robust alternative metric.

Multipollutant models. To investigate the robustness of the derived PM effect estimates (i.e., RRs), we also included each of the gaseous pollutants in the model simultaneously with each of the PM indices for each health effect outcome, and the pollutant RRs were then reestimated. The RRs from multipollutant models were compared with those of the single pollutant models in terms of absolute size and statistical power. The most robust risk estimates were considered to be those that were least affected by the inclusion of other pollutants. More than two pollutants were not modeled simultaneously to minimize the chance of model overspecification (i.e., excessive intercorrelations among the *x* terms), which could result in biased RR estimates.

Results

The basic model included one of the four alternative sets of temperature specifications, a 31-day WMAF (included for seasonal cycles), indicator variables for day-of-week and holidays, a linear trend term, and each pollutant included individually. The resulting pollutant coefficients and standard errors from each of the four models were then evaluated to assess the impact of the various weather specifications on the pollutant estimates. Additionally, we evaluated the intercorrelations of the coefficients for each pollutant and temperature term to assess the degree of collinearity between these model variables.

The pollutant risk estimates were not greatly affected by the choice of temperature specification in this work. For example, O_3 and SO_2 coefficients, standard errors, intercorrelations with the temperature terms, and *t*-statistics using each of the four models are shown in Table 4. Overall, models that used the loess fits of temperature–relative humidity achieved better fits and produced lower intercorrelations between the β of the weather and pollutant terms. Based on these exploratory results, we chose a loess surface of temperature and relative humidity to control for weather in all analyses.

We computed RRs for each pollutant's most significant lag (as indicated by the *t*-statistic) using the maximum minus mean increment as well as the interquartile range. Single pollutant RRs, based on the maximum minus mean increment, are shown in Figure 5 for the hospital admissions and mortality categories. Tables 5–7 give the pollutant coefficient, standard error, *t*-statistic, and RR for each health effect outcome. Simultaneous pollutant RRs (based on the maximum minus mean increment) for each of the PM indices are presented in Figure 6A–C.

Respiratory mortality and hospital admissions. All pollutants considered, except CO, CoH, and NO_2, yielded significant associations with respiratory hospital admissions, whereas only H^+ and SO_4^{2-} were

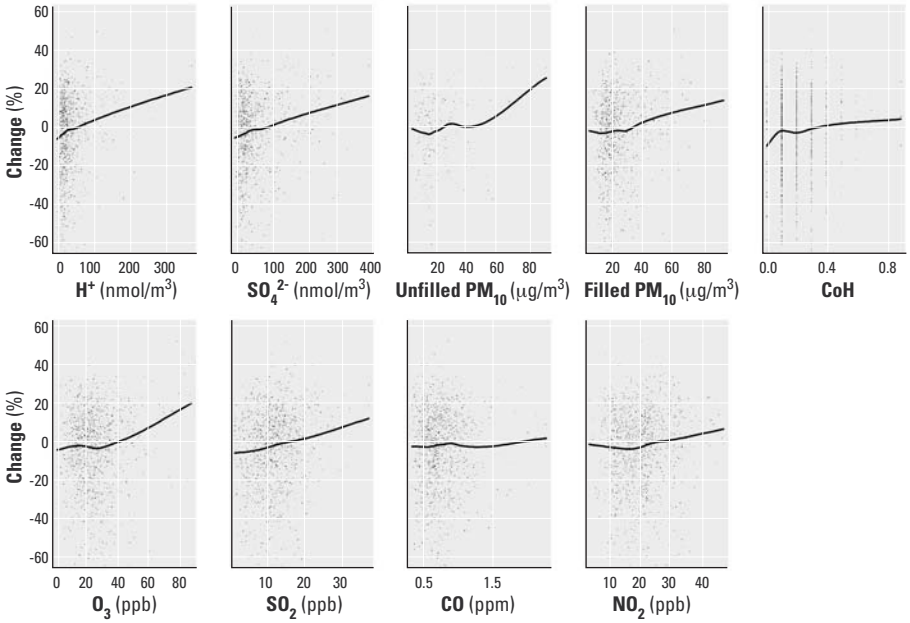

Figure 4. The nonparametric loess fit of the pollutant-respiratory hospital admissions relationship. The *y*-axis represents the percent change in respiratory hospital admissions, adjusted for seasonal and day-of-week variations.

Table 4. Regression coefficients, SE, and correlation of the βs between the temperature and pollutant terms from the four weather models for respiratory mortality.

Pollutant, temperature	β	SE	*t*-Value	Correlation With hot term[a]	Correlation With cold term[b]	Weather *t*-value Lag 0	Weather *t*-value Lag 2
O_3							
Linear	0.0020	0.0015	1.30	-0.364	-0.026	0.97	-0.60
Quadratic	0.0019	0.0018	1.05	-0.657	0.179	0.22	-0.24
Loess temperature	0.0030	0.0014	2.07	-0.476	0.108	-0.49	0.62
Loess temp and relative humidity	0.0024	0.0013	1.84	-0.304	0.034	0.54	2.22
SO_2							
Linear	0.0063	0.0032	1.96	-0.126	0.285	1.27	0.02
Quadratic	0.0063	0.0033	1.91	-0.174	-0.392	0.83	-1.14
Loess temperature	0.0050	0.0031	1.61	-0.181	-0.086	0.23	0.29
Loess temp and relative humidity	0.0050	0.0030	1.65	-0.078	0.015	1.00	2.16

temp, temperature.
[a]Intercorrelation of βs for temperature term (lag 0) and pollutant. [b]Intercorrelation of βs for temperature term (lag 2) and pollutant.

significantly associated with respiratory mortality. The pollutants that were most strongly associated with respiratory hospital admissions were SO_4^{2-} (t = 4.10), H^+ (t = 3.76), and O_3 (t = 3.70). Similarly, SO_4^{2-} (t = 2.10) and H^+ (t = 2.50) were among the pollutants most strongly associated with respiratory mortality. Simultaneous regressions of the gaseous and PM pollutants produced only small changes in the PM pollutant risk estimates for respiratory hospital admissions and mortality. Overall, the inclusion of O_3 tended to produce the largest reduction of the PM risk estimates for both respiratory hospital admissions and mortality outcomes.

Circulatory mortality and hospital admissions. Although no pollutants considered in these analyses were significantly associated with circulatory hospital admissions, the H^+ coefficient did approach statistical significance (t = 1.64). In contrast, unfilled PM_{10} was significantly associated with circulatory mortality. Although the other PM coefficients were marginally significant, the strongest individual association was observed between unfilled PM_{10} and circulatory mortality (t = 2.05), despite the reduced number of observations considered. Simultaneous copollutant regressions for the circulatory categories showed only very small changes in the various RR estimates. However, the inclusion of CO, NO_2, and SO_2 did reduce the unfilled PM_{10} estimate to nonsignificance.

Total mortality and hospital admissions. The pollutants that demonstrated significant associations with total hospital admissions included H^+, NO_2, O_3, and SO_4^{2-}, whereas CO, filled PM_{10}, unfilled PM_{10}, H^+, and SO_4^{2-} were significantly associated with total mortality. However, all of the RRs for total hospital admissions were very close to 1, indicating relatively small morbidity impacts on high-pollution days. This is to be expected because the total admissions category also includes causes unlikely to by affected by air pollution. Simultaneous inclusion of gaseous pollutants caused only minimal changes in the risk estimates for total hospital admissions and mortality. The unfilled PM_{10} estimate for total mortality was most affected by the inclusion of O_3. However, the significance level of the unfilled PM_{10}/total mortality effect estimate was increased, not reduced, by the inclusion of gaseous pollutants.

Discussion and Conclusions

In these analyses, significant associations were observed between several air pollutant indices and the various health-effect outcomes considered, making it difficult to clearly discriminate the influence of a single pollutant. This is likely a result of the relatively high intercorrelations among the various air pollutants, as well as the possible interactive role of several pollutants in the reported air pollution/health effects associations. Overall, although no single pollutant was significant across all health effect outcomes, H^+ and SO_4^{2-} demonstrated consistent significant associations with the respiratory outcomes.

The unfilled PM_{10} index demonstrated significant associations with the total and circulatory mortality, but not with respiratory mortality. The lack of a statistically significant association between the unfilled PM_{10} index and respiratory mortality may indicate that the total mortality PM_{10} RR estimate was driven by the association between unfilled PM_{10} and circulatory mortality. However, the RR of total mortality based on

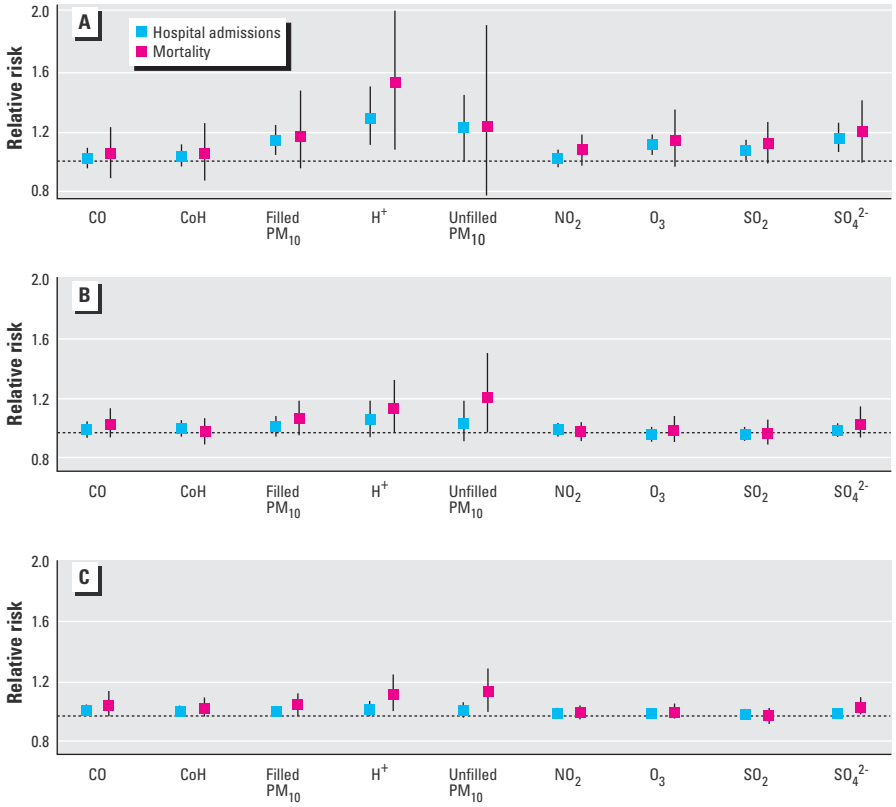

Figure 5. Cause-specific hospital admissions and mortality relative risks and their CI from basic regression model. Relative risks computed based on a maximum minus mean increase in pollutant concentration: (*A*) respiratory outcomes, (*B*) circulatory outcomes, and (*C*) total outcomes.

Table 5. Pollutant coefficients and SE from final respiratory regression models.

Outcome, pollutant	Coefficient	SE	*t*-Value	RR (max - mean)	RR (IQR)
Respiratory hospital admissions					
CO (lag 2)	0.016620	0.021274	0.78	1.027	1.005
CoH (lag 0)	0.060206	0.050515	1.19	1.042	1.012
Filled PM_{10} (lag 0)	0.002083	0.000683	3.05	1.147	1.023
H^+ (lag 0)	0.000782	0.000208	3.76	1.310	1.021
Unfilled PM_{10} (lag 1)	0.003186	0.001563	2.04	1.237	1.047
NO_2 (lag 1)	0.001201	0.000913	1.32	1.033	1.011
O_3 (lag 1)	0.001950	0.000527	3.70	1.127	1.029
SO_2 (lag 0)	0.003594	0.001178	3.05	1.096	1.025
SO_4^{2-} (lag 0)	0.000498	0.000122	4.10	1.178	1.026
Respiratory mortality					
CO (lag 0)	0.032466	0.053802	0.60	1.053	1.011
CoH (lag 3)	0.080642	0.134999	0.60	1.057	1.016
Filled PM_{10} (lag 0)	0.002511	0.001749	1.44	1.180	1.028
H^+ (lag 0)	0.001266	0.000506	2.50	1.549	1.034
Unfilled PM_{10} (lag 0)	0.003291	0.003322	0.99	1.245	1.048
NO_2 (lag 1)	0.003121	0.002244	1.39	1.088	1.028
O_3 (lag 0)	0.002420	0.001314	1.84	1.160	1.037
SO_2 (lag 0)	0.005024	0.003036	1.65	1.137	1.036
SO_4^{2-} (lag 0)	0.000648	0.000308	2.10	1.237	1.034

Abbreviations: IQR, interquartile range; max, maximum.

a 100-μg/m^3 increase in PM_{10}, using the unfilled PM_{10} index, is 1.26 (CI = 1.05–1.52). This risk estimate is 2- to 6-fold higher than previously published results. This unusually large risk estimate may result from instability in the regression model that results from the low number of observations for this pollutant. The filled PM_{10} index yielded a more typical total mortality risk estimate (a 100-μg/m^3 increase in PM_{10} gives RR = 1.11, CI = 1.00–1.24). This instability was also demonstrated by the large fluctuations in the unfilled PM_{10} estimate when gaseous pollutants were simultaneously included. However, the large PM_{10} health-effect association remains significant even after the addition of the gaseous copollutants.

A more comprehensive strategy to assess the impacts of the various pollutants is to evaluate the coherence of the observed associations across similar health endpoints. As discussed by Hill (*36*), the coherence of an observed association among similar health end points strengthens arguments of the causality of the association. Bates (*37*) also discussed the importance of coherence in epidemiologic investigations in his evaluation of the health indices used in the many air pollution investigations, and he stressed the need for internal coherence.

Several of the pollutants considered in these analyses demonstrated coherence across similar health-effects categories. H^+ and SO_4^{2-} demonstrated significant associations with both the respiratory hospital admissions and respiratory mortality categories. Additionally, these risk estimates were similar in magnitude and were generally larger than effects estimated for the other health categories considered. No pollutant was significantly associated with both circulatory outcomes, although those that were significant associated with both total mortality and total hospital admissions categories included filled PM_{10}, H^+, and SO_4^{2-}. Thus, H^+ and SO_4^{2-} were the only pollutants that demonstrated coherence across both the respiratory and total outcomes.

Although the total hospital admissions risk estimates were positive and significant for several pollutants, they were closer to the baseline (RRs = ~ 1.0) than those for total mortality. This could be in part because total hospital admissions and total mortality are not directly comparable with respect to the distribution of underlying causes contributing to their respective overall total category counts. For example, 33% of the total mortality category is composed of deaths attributed to circulatory causes, whereas only 17% of the total hospital admissions category can be attributed to circulatory causes. Additionally, total hospital admissions includes causes that would not necessarily result in death. As a result, analyses on the total categories may not be very useful in testing coherence in air pollution/health effect associations.

The significant associations of H^+, SO_4^{2}, and O_3 with respiratory hospital admissions lend support to the theory of a summertime haze effect contributed by both O_3 and acidic particles (*20*). However, the association between acidic aerosols and respiratory hospitalization, as indicated in these analyses, has not been always been demonstrated in other analyses. Burnett et al. (*38*) reported that the association between aerosol acidity and respiratory hospital admissions in Toronto, Ontario, Canada, was nonsignificant once it was adjusted for gaseous pollutant exposures. One possible explanation for the lack of association in Toronto is the relatively low levels of H^+ observed in Toronto during that study period (the summers of 1992–1994) as compared to those of this 1988–1990 Buffalo analysis (1992–1994 Toronto mean/maximum H^+ = 5.0/75 nmol/m^3; 1988–1990 Buffalo mean/maximum H^+= 36.4/381.9 nmol/m^3). During an overlapping period (the summers of 1986–1988), Thurston et al. (*39*) found a significant association between H^+ and hospital admissions in Toronto that remained significant even after adjusting for O_3 (1986–1988 Toronto summer mean/maximum H^+ = 29.0/391 nmol/m^3. Thus, peak H^+ levels > 75 nmol/m^3 may be required to provide a signal large enough to detect

Table 6. Pollutant coefficients and SE from final circulatory regression models.

Outcome, pollutant	Coefficient	SE	*t*-Value	RR (max - mean)	RR (IQR)
Circulatory hospital admissions					
CO (lag 1)	0.013616	0.016926	0.80	1.022	1.004
CoH (lag 1)	0.042619	0.041016	1.04	1.030	1.009
Filled PM_{10} (lag 1)	0.000619	0.000499	1.24	1.042	1.007
H^+ (lag 0)	0.000252	0.000154	1.64	1.091	1.007
Unfilled PM_{10} (lag 3)	0.001107	0.000906	1.22	1.077	1.016
NO_2 (lag 0)	0.000975	0.000686	1.42	1.027	1.009
O_3 (lag 0)	0.000114	0.000383	0.30	1.007	1.002
SO_2 (lag 0)	0.000245	0.000917	0.27	1.006	1.002
SO_4^{2-} (lag 1)	0.000098	0.000088	1.12	1.033	1.005
Circulatory mortality					
CO (lag 3)	0.039216	0.026544	1.48	1.065	1.013
CoH (lag 2)	0.012160	0.064438	0.19	1.008	1.002
Filled PM_{10} (lag 2)	0.001444	0.000816	1.77	1.100	1.016
H^+ (lag 1)	0.000453	0.000243	1.87	1.169	1.012
Unfilled PM_{10} (lag 2)	0.003281	0.001604	2.05	1.245	1.048
NO_2 (lag 2)	0.000634	0.001074	0.59	1.017	1.006
O_3 (lag 0)	0.000557	0.000674	0.83	1.035	1.008
SO_2 (lag 3)	0.000493	0.001521	0.32	1.013	1.003
SO_4^{2-} (lag 1)	0.000246	0.000142	1.72	1.084	1.013

Abbreviations: IQR, interquartile range; max, maximum.

Table 7. Pollutant coefficients and SE from final total regression models.

Outcome, pollutant	Coefficient	SE	*t*-Value	RR (max - mean)	RR (IQR)
Total hospital admissions					
CO (lag 0)	0.011622	0.007105	1.64	1.019	1.004
CoH (lag 0)	0.025448	0.017011	1.50	1.018	1.005
Filled PM_{10} (lag 0)	0.000374	0.000200	1.88	1.025	1.004
H^+ (lag 0)	0.000143	0.000061	2.33	1.051	1.004
Unfilled PM_{10} (lag 1)	0.000580	0.000382	1.52	1.039	1.008
NO_2 (lag 0)	0.000719	0.000287	2.50	1.020	1.006
O_3 (lag 0)	0.000324	0.000156	2.08	1.020	1.005
SO_2 (lag 0)	0.000764	0.000383	1.99	1.020	1.005
SO_4^{2-} (lag 0)	0.000090	0.000036	2.53	1.030	1.005
Total mortality					
CO (lag 3)	0.040214	0.015205	2.64	1.066	1.013
CoH (lag 3)	0.070013	0.037043	1.89	1.049	1.014
Filled PM_{10} (lag 0)	0.001076	0.000536	2.01	1.073	1.012
H^+ (lag 1)	0.000410	0.000146	2.80	1.152	1.011
Unfilled PM_{10} (lag 2)	0.002326	0.000935	2.49	1.168	1.034
NO_2 (lag 3)	0.001050	0.000622	1.69	1.029	1.009
O_3 (lag 2)	0.000585	0.000376	1.56	1.037	1.009
SO_2 (lag 0)	–0.000088	0.000902	–0.10	0.998	0.999
SO_4^{2-} (lag 1)	0.000218	0.000088	2.48	1.074	1.011

Abbreviations: IQR, interquartile range; max, maximum.

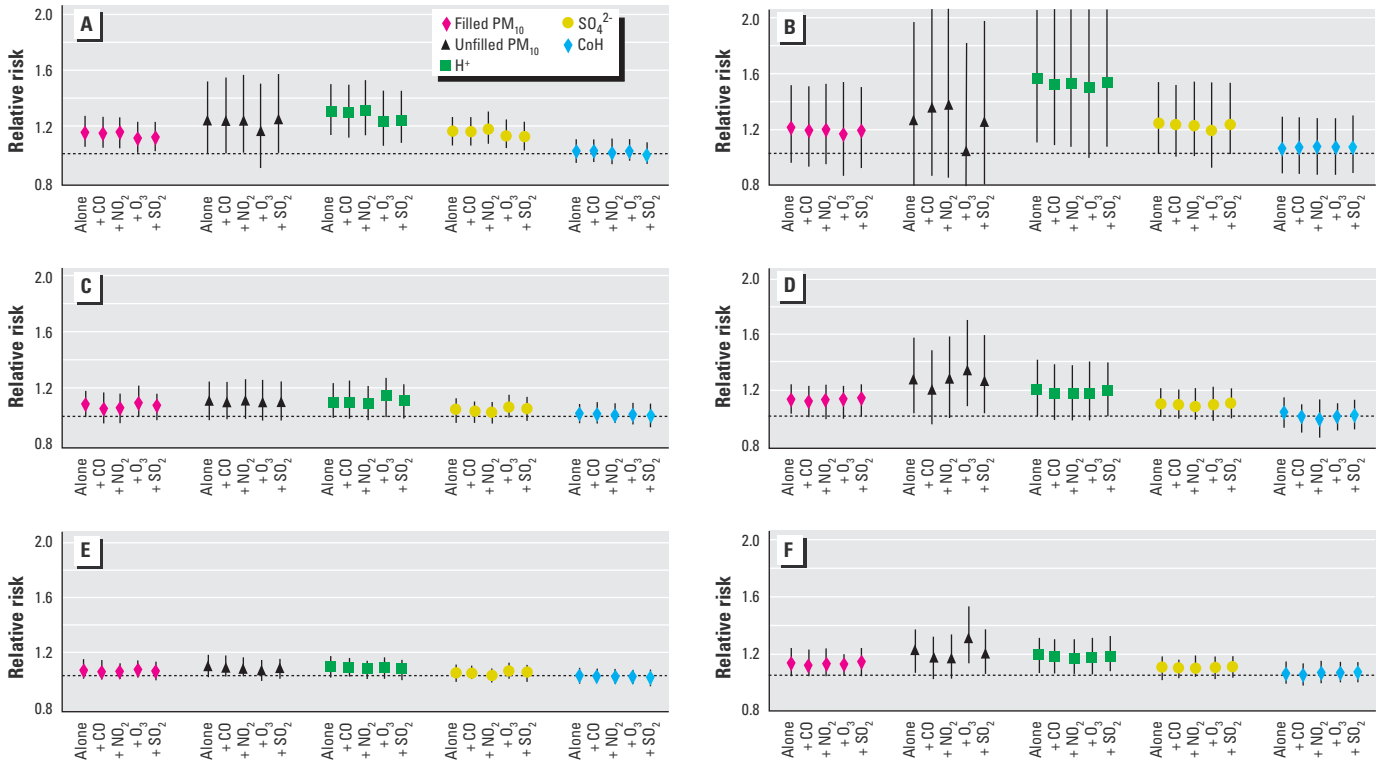

Figure 6. The effect of the inclusion of gaseous pollutants on PM cause-specific relative risk estimates. (*A*) Respiratory hospital admissions, (*B*) respiratory mortality, (*C*) circulatory hospital admissions, (*D*) circulatory mortality, (*E*) total hospital admissions, and (*F*) total mortality.

associations using present H^+ measurements and time–series methods.

In addition to the coherence observed across complementary health end points, the relative magnitudes of the risk estimates observed across the different health end points are also biologically plausible: the respiratory outcome risk estimates are generally greater in magnitude than those of the total outcomes. These results indicate that air pollution has a greater impact on the respiratory system, which is the initial target site. The risk estimates for the total categories are diluted by the inclusion of health outcomes not likely to be directly affected by air pollution levels, thereby resulting in lower risk estimates, as expected based on biologic grounds.

Unlike other criteria pollutants regulated by the EPA, PM is not a single pollutant, but rather a class of pollutants. As regulatory policy moves toward regulating fractions of PM_{10}, such as $PM_{2.5}$, it may be more prudent to identify one or more of the most harmful components of PM, then focus control efforts on the specific sources that are responsible for their production. These results indicate that acidic aerosols, as represented by SO_4^{2-} and H^+, may significantly contribute to the observed PM health effects.

Although the exact mechanism behind these H^+/health effect associations is not yet known, several have been suggested. Seaton et al. (*10*) proposed the hypothesis that acidic ultrafine aerosols provoke alveolar inflammation, causing the release of mediators that might induce attacks of acute respiratory illness in susceptible individuals. Winchester (*40*) suggested that sulfuric acid coatings on particles lead to the solubilization of aluminum, iron, and other metals, resulting in lung injury when inhaled. The toxicologic findings of Dreher et al. (*41*) provide some support for this mechanism. They instilled rats with a leachate of residual oil fly ash (ROFA) containing primarily iron, nickel, vanadium, calcium, magnesium, and acidic sulfate, which produced similar lung injury as that of the original ROFA suspension, suggesting that the acidic metal solution is the casual component.

Other mechanisms have also been proposed from animal studies that demonstrated adverse effects from acidic aerosol. A suggested mechanism for observed changes in airway responsiveness is the interference with the normal contractile/dilatory homeostatic process through the modulation of airway receptors (*42*). Clearance abnormalities may result from changes in viscosity in acidic mucous versus alkaline mucous (*43*). Changes in lung function and airway hyperresponsivity observed in guinea pigs (*44,45*), suggest that the number concentration of acidic particles may be more important than the H^+ mass concentration in eliciting adverse respiratory responses. Although these proposed mechanisms provide some insight into the potential toxicologic impacts of acid aerosol exposure, further research into the possible mechanism(s) of acid aerosol toxicity is needed.

In summary, we observed multiple pollutant/health effect associations in this analysis. The serial correlations among the various pollutants did not allow for the unambiguous identification of a single causal pollutant via epidemiologic methods. Furthermore, the lack of daily PM_{10} data in this work limits the statistical interpretation of the two PM_{10} mass indices used. However, the observed associations of SO_4^{2-} and H^+ with both respiratory hospital admissions and mortality indicate coherence of effects and suggest a need for comparable long-term, multiple health outcome investigations in other cities with PM_{10} chemical compositions different from those considered in this work.

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