Vol. 161, No. 6 Printed in U.S.A. DOI: 10.1093/aje/kwi075

Seasonal Analyses of Air Pollution and Mortality in 100 US Cities

Roger D. Peng¹, Francesca Dominici¹, Roberto Pastor-Barriuso², Scott L. Zeger¹, and Jonathan M. Samet³

- ¹ Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.
- ² Epidemiology and Biostatistics Section, National Center for Epidemiology, Carlos III Institute of Health, Madrid, Spain.
- ³ Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

Received for publication May 19, 2004; accepted for publication September 10, 2004.

Time series models relating short-term changes in air pollution levels to daily mortality counts typically assume that the effects of air pollution on the log relative rate of mortality do not vary with time. However, these short-term effects might plausibly vary by season. Changes in the sources of air pollution and meteorology can result in changes in characteristics of the air pollution mixture across seasons. The authors developed Bayesian semiparametric hierarchical models for estimating time-varying effects of pollution on mortality in multisite time series studies. The methods were applied to the database of the National Morbidity and Mortality Air Pollution Study, which includes data for 100 US cities, for the period 1987–2000. At the national level, a $10-\mu g/m^3$ increase in particulate matter less than $10~\mu m$ in aerodynamic diameter at a 1-day lag was associated with 0.15% (95% posterior interval (PI): -0.08, 0.39), 0.14% (95% PI: -0.14, 0.42), 0.36% (95% PI: 0.11, 0.61), and 0.14% (95% PI: -0.06, 0.34) increases in mortality for winter, spring, summer, and fall, respectively. An analysis by geographic region found a strong seasonal pattern in the Northeast (with a peak in summer) and little seasonal variation in the southern regions of the country. These results provide useful information for understanding particle toxicity and quiding future analyses of particle constituent data.

air pollution; epidemiologic methods; models; statistical; mortality; seasons

Abbreviations: NMMAPS, National Morbidity, Mortality, and Air Pollution Study; PI, posterior interval; $PM_{2.5}$, particulate matter less than 2.5 μ m in aerodynamic diameter; PM_{10} , particulate matter less than 10 μ m in aerodynamic diameter.

Numerous time series studies have indicated a positive association between short-term variation in ambient levels of particulate matter and daily mortality counts (1–3). The models used in these studies have typically assumed that the association between particulate matter and daily mortality is constant over the study interval. However, the short-term effects of particulate matter on mortality might plausibly exhibit seasonal variation. Studies in a number of locations have shown that the characteristics of the particulate matter mixture change throughout the year and that the relative and absolute contributions of particular components to particulate matter mass may be different during different times of the year (see chapter 3 of Air Quality Criteria for Particulate Matter (4)). Patterns of human activity also change from season to season, so that a particular air pollution concentration in one season may lead to a different

exposure in another season. Other potential time-varying confounding and modifying factors, such as temperature and influenza epidemics, can also affect estimates of short-term effects of air pollution on mortality differently in different seasons. All of the issues described above indicate a need to extend current models for time series data on air pollution and health to incorporate time-varying pollution effects.

The composition of particulate matter is known to vary in the spatial domain as well, which suggests that seasonal patterns should be examined by geographic region (5). For example, in the Northwest, wood burning is a greater source of particulate matter in the colder seasons than in the warmer months. The particulate matter mixture in the eastern United States contains a large fraction of sulfates (almost 40 percent of total mass) originating from power

Correspondence to Dr. Roger D. Peng, Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, 615 North Wolfe Street, Baltimore, MD 21205 (e-mail: rpeng@jhsph.edu).

plants in the Midwest, while particulate matter in areas of the western United States, such as Southern California and the Pacific Northwest, contains more nitrates and organic compounds (approximately 30 percent of total mass) (4-6).

In this paper, we develop statistical methods for estimating seasonal patterns in the short-term effects of air pollution on mortality in multisite time series studies. We propose Bayesian semiparametric hierarchical models for estimating time-varying health effects within each city and for comparing temporal patterns across cities and geographic regions. Using data from the National Morbidity, Mortality, and Air Pollution Study (NMMAPS) (7), we estimate seasonal patterns in the short-term effects of particulate matter less than 10 µm in aerodynamic diameter (PM₁₀) on daily nonaccidental mortality. The data have been extended from the original study to include 100 US cities for the period 1987–2000, an addition of 10 cities and 6 years of data. The seasonal patterns are estimated for seven geographic regions and on average for the entire United States. We explore the sensitivity of estimated seasonal patterns to temperature adjustment, copollutants, exposure lag (in days), and adjustments for long-term mortality trends.

MATERIALS AND METHODS

The NMMAPS database contains daily time series of data on mortality, weather, and air pollution assembled from publicly available sources for the 100 largest cities in the United States. A full description of the construction of the database can be found in a paper by Samet et al. (7). The most recent data are available at the website of the Internet-based Health and Air Pollution Surveillance System (http://www.ihapss.jhsph.edu).

Within each city, we specify a semiparametric regression model for the time-varying log relative rate using a generalized additive model framework (8). More specifically, let Y_t^c be the total number t of nonaccidental deaths on day t in city c. The Y_t^c 's are Poisson-distributed with expectation μ_t^c and with possible overdispersion ϕ^c . The general form of the city-specific model is

$$\begin{split} & Y_t^c \sim \text{Poisson}(\mu_t^c) \\ & \text{Var}(Y_t^c) = \varphi^c \mu_t^c \\ & \log(\mu_t^c) = \beta^c(t) x_{t-l}^c + \text{confounders}, \end{split} \tag{1}$$

where x_{t-l}^c is the lag l PM₁₀ level for day t.

The function $\beta^{c}(t)$ in equation 1 represents the timevarying effect of PM₁₀ on mortality and is a yearly periodic function for estimating seasonal patterns. To estimate smooth seasonal patterns in the city-specific log relative rates, we use a sine/cosine model for $\beta^c(t)$ of the form

$$\beta^{c}(t) = \beta_{0}^{c} + \beta_{1}^{c} \sin(2\pi t/365)/c_{1} + \beta_{2}^{c} \cos(2\pi t/365)/c_{2},$$
(2)

where β_0^c , β_1^c , and β_2^c are estimated and c_1 and c_2 are known orthogonalizing constants. In this model, the effect of PM₁₀ is allowed to vary smoothly over the course of a year but is constrained to be periodic across years (9). While it is possible to include higher-frequency-basis terms for the

representation of $\beta^{c}(t)$ in equation 2, there is little reason to expect there to be much high-frequency variation in the seasonal effects of PM₁₀.

To allow for season-specific PM₁₀ log relative rates, we use a pollutant × season interaction model with indicator functions for each season:

$$\beta^{c}(t) = \beta_{W}^{c} I_{\text{winter}} + \beta_{Sn}^{c} I_{\text{spring}} + \beta_{Sm}^{c} I_{\text{summer}} + \beta_{F}^{c} I_{\text{fall}}, \quad (3)$$

where winter, spring, summer, and fall are defined as beginning on December 21st, March 21st, June 21st, and September 21st, respectively. Although these seasonal estimates serve as concise summaries, it is unlikely that the effect of PM₁₀ on mortality is discontinuous across seasons. Furthermore, the estimates depend on the specification of the season boundaries, which are artificial and can differ considerably across geographic regions.

Our main-effect model, which does not contain any adjustment for season, takes $\beta^{c}(t)$ to be constant across time—that is,

$$\beta^c(t) = \beta^c. \tag{4}$$

This model assumes a homogeneous log-linear effect of PM₁₀ on mortality, a condition that was found to be appropriate in previous NMMAPS analyses (10-13). Note that the main-effect model is nested within the interaction and sine/cosine models, so that if $\beta_W = \beta_{Sp} = \beta_{Sm} = \beta_F$ in equation 3 and $\beta_1^c = \beta_2^c = 0$ in equation 2, both models can be reduced to equation 4.

The potential confounders included in equation 1 are similar to those used in previous NMMAPS analyses (12, 13) and consist of indicators for the day of the week; agespecific intercepts corresponding to the categories of <65 years, 65–74 years, and ≥75 years; a smooth function of calendar time; and smooth functions of temperature and dew point temperature. In addition to the overall smooth function of time, two separate smooth functions of time are included for the older two age groups. All of the smooth functions are represented by natural cubic splines.

The complexity of each of the smooth functions of time and temperature is controlled by the numbers of degrees of freedom assigned to each function. We use 7 df per year for the overall smooth function of time, which removes any fluctuations in mortality at time scales longer than 2 months. The separate smooth functions of time for the older two age categories each receive 1 df per year to capture gradual trends specific to these age groups. For temperature we use 6 df, and for dew point we use 3 df. A somewhat larger number of degrees of freedom is necessary for temperature in order to capture the well-known "J-shaped" nonlinear relation between temperature and mortality. Other investigators have adjusted for temperature simply by conducting separate analyses of the data by season (7, 14-18).

All of the above models were fitted using quasilikelihood methods, as implemented in the R statistical software package (19). The data are available via the NMMAPS data package (20), and code for fitting the models is available on the World Wide Web at http://www.ihapss. jhsph.edu/data/NMMAPS/R/.

Minimum 25th percentile Median 75th percentile Maximum Average daily mortality (no. of deaths) 2.2 7.6 12.2 20.4 190.2 Average daily PM₁₀ (μg/m³) 13.2 24.7 27.1 32.0 48.7 Average daily temperature (°F) 37.0 51.8 58.1 64.7 77.8

TABLE 1. Summary statistics for average daily mortality, PM₁₀,* and temperature for 100 US cities, National Morbidity and Mortality Air Pollution Study, 1987–2000

Pooling information across cities

After fitting each of the city-specific models, we use a hierarchical normal model for pooling information and borrowing strength across cities (12, 16, 18). For a particular model, we have a city-specific maximum likelihood estimate $\hat{\beta}^c$, which is a scalar for the main-effect model in equation 4, a vector of length 4 for the pollutant \times season interaction model in equation 3, and a vector of length 3 for the sine/cosine model in equation 2. $\hat{\beta}^c$ is assumed to be normally distributed around the true city-specific log relative rates β^c with covariance matrix V^c , estimated within each city. In addition, the true rates are assumed to vary independently across cities according to a normal distribution—that is,

$$\hat{\beta}^{c}|\beta^{c} \sim \mathcal{N}(\beta^{c}, V^{c})$$

$$\beta^{c}|\alpha, \Sigma \sim \mathcal{N}(Z^{c}\alpha, \Sigma), \tag{5}$$

where Σ is the covariance matrix describing the betweencity variation of β^c and α is the overall mean for the cities. Z^c is a matrix of second-stage covariates for describing possible differences between cities. To characterize regional differences in seasonal patterns, we include as a secondstage covariate an indicator for the following seven regions (also used in the paper by Samet et al. (7)): Industrial Midwest (19 cities), Northeast (17 cities), Northwest (13 cities), Southern California (7 cities), Southeast (26 cities), Southwest (10 cities), and Upper Midwest (8 cities).

The final national average estimate α represents the combined information from all of the cities. The diagonal elements of Σ measure the heterogeneity across cities, and the off-diagonal elements represent the correlation of the estimates between cities. The hierarchical model is fitted using the two-level normal independent sampling estimation (TLNise) software of Everson and Morris (21), with uniform priors on α and Σ . This software provides a sample from the posterior distribution of Σ from which one can calculate posterior means and variances of the overall and city-specific pollution effects.

Evidence for seasonality in the log relative rates

To quantify the amount of evidence supporting the presence of a seasonal pattern in the national and regional averages, we examine the posterior distributions of the pooled log relative rate estimates. In particular, for the sine/cosine model in equation 2, we can check the posterior probability that the coefficients for the harmonic terms are

nonzero. While the values of the pooled coefficients β_1 and β_2 do not have meaningful interpretations, if either one of these coefficients is nonzero with high probability, there is strong evidence of a seasonal trend.

RESULTS

The daily mortality counts for the years 1987–2000 include approximately 10 million deaths. By city, the daily average ranged from two deaths per day in Arlington, Virginia, to 190 deaths per day in New York, New York. The daily mean of PM_{10} ranged from 13 $\mu g/m^3$ in Coventry, Rhode Island, to 49 $\mu g/m^3$ in Fresno, California. Summary statistics for the data set are shown in table 1.

Mortality and PM_{10} levels are known to vary considerably across seasons. Generally, mortality tends to be higher in the winter and fall and lower in the summer and spring. Figure 1 shows box plots of the square-root daily mortality counts for the 10 largest cities in the United States. Each city shows a clear decrease in mortality towards summer and a peak in the winter. Figure 2 shows the mean daily levels of PM_{10} by season for all cities in each of the seven regions of the United States. The Southern California, Northwest, and Southwest regions have their highest mean levels of PM_{10} in the fall, while other regions have their highest levels in the summer.

The national average estimates of the overall and seasonal short-term effects of PM₁₀ on mortality for lags of 0, 1, and 2 days are summarized in table 2. These estimates were obtained by pooling the city-specific maximum likelihood estimates from the main-effect and pollutant × season interaction models according to the hierarchical normal model. Across all seasons, we found that the national average estimate of the effect of PM₁₀ on mortality was largest at lag 1 and equal to an estimated 0.19 percent (95 percent posterior interval (PI): 0.10, 0.28) increase in mortality per 10-μg/m³ increase in PM₁₀. Previous NMMAPS analyses using data from the 8-year period 1987–1994 reported similar slightly higher national average estimates for PM_{10} log relative rates (11, 13). For example, the national average estimate reported by Dominici et al. (13) was a 0.22 percent (95 percent PI: 0.03, 0.42) increase in mortality for a 10- μ g/m³ increase in PM₁₀.

For PM_{10} at lag 1, the estimates for winter, spring, and fall are similar and equal to 0.15 percent (95 percent PI: -0.08, 0.39), 0.14 percent (95 percent PI: -0.14, 0.42), and 0.14 percent (95 percent PI: -0.06, 0.34), respectively. The estimate for summer is more than twice as large at 0.36

^{*} PM_{10} , particulate matter less than 10 μm in aerodynamic diameter.

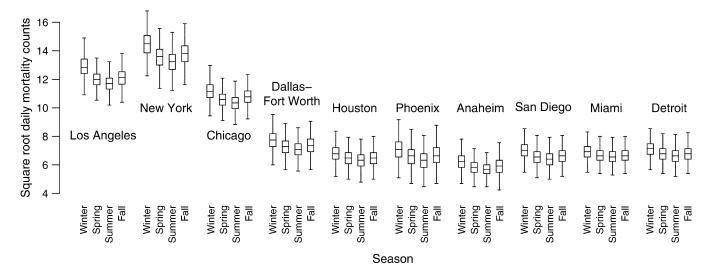


FIGURE 1. Box plots of square-root daily mortality for the 10 largest US cities, by season, National Morbidity and Mortality Air Pollution Study, 1987–2000. Horizontal line, median; edges of box, interquartile range (25th and 75th percentiles); bars, 1.5 times the interquartile range.

percent (95 percent PI: 0.11, 0.61). PM_{10} at lag 0 appears to have a larger effect in the spring and much smaller effects in the other seasons. In addition, estimates for lag 0 have a much larger between-season difference (e.g., spring and winter) than those for lag 1. The estimates for lag 2 are generally smaller than those for lag 0 or lag 1 and, given the size of the posterior intervals, do not vary much across seasons.

We explored regional differences in the seasonal patterns of the PM_{10} relative rates by including a region indicator variable in the second stage of the hierarchical model. For PM_{10} at lag 1, figure 3 shows the results of estimating separate seasonal trends from the sine/cosine model for the

seven regions of the United States. The Industrial Midwest and the Northeast have seasonal trends characterized as being lower in the winter and higher in the summer. In Southern California, there is a larger effect (a 0.5 percent increase in mortality per $10\text{-}\mu\text{g/m}^3$ increase in PM_{10}) that is constant all year. The effect of PM_{10} is close to zero year-round in the Northwest, Southeast, Southwest, and Upper Midwest, but the Northwest experiences a slight increase during the summer months. With the exception of Southern California, all regions have a smaller effect in the winter months. Seasonal analyses for mortality due to cardiovas-cular and respiratory diseases (not shown) provided results

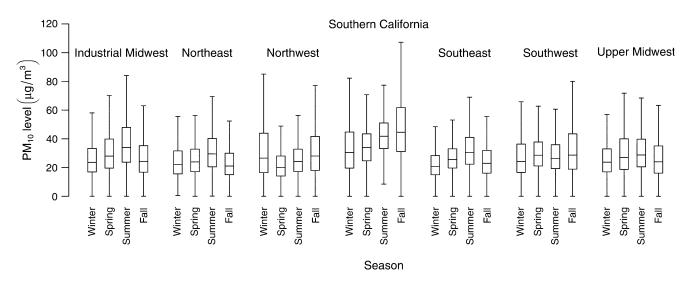


FIGURE 2. Box plots of regionally averaged daily levels of particulate matter less than 10 μ m in aerodynamic diameter (PM₁₀) for 100 US cities, by season, National Morbidity and Mortality Air Pollution Study, 1987–2000. Horizontal line, median; edges of box, interquartile range (25th and 75th percentiles); bars, 1.5 times the interquartile range.

Winter Spring Summer Fall All seasons Estimate 95% PI* Estimate 95% PI Estimate 95% PI Estimate 95% PI Estimate 95% PI Lag 0 -0.04-0.30, 0.210.32 0.08, 0.56 0.13 -0.11, 0.370.05 -0.16, 0.250.09 -0.01, 0.19 Lag 1 0.15 -0.08, 0.390.14 -0.14, 0.420.36 0.11, 0.61 0.14 -0.06, 0.340.19 0.10, 0.28 -0.27, 0.21Lag 2 0.10 -0.13, 0.330.05 -0.21, 0.32-0.030.13 -0.08, 0.350.08 -0.03, 0.19

TABLE 2. National average estimates of the overall and season-specific effects of PM₁₀* at lags of 0, 1, and 2 days for 100 US cities, National Morbidity and Mortality Air Pollution Study, 1987–2000†

that were qualitatively similar to those for total nonaccidental mortality, with larger summer effects in the Industrial Midwest and the Northeast, as well as overall for the entire United States.

Figure 4 shows samples from the joint posterior distributions of the regionally and nationally pooled harmonic coefficients β_1 and β_2 in the sine/cosine model for PM_{10} at lag 1. The region with the strongest evidence of a seasonal pattern is the Northeast: The marginal posterior probability of β_2 's being greater than 0, given the data, is 0.96 (Prob($\beta_2 > 0 | data) = 0.96$). There is moderate evidence of seasonality in the Industrial Midwest and the Northwest (Prob($\beta_2 > 0 | data) = 0.85$ and Prob($\beta_2 > 0 | data) = 0.74$, respectively). The joint distributions of the coefficients for the Southeast, the Southwest, the Upper Midwest, and Southern California are centered at zero, indicating a lack of any seasonal variation. At the national level, the marginal posterior probability of β_2 's being greater than 0, given the data, is 0.88 (Prob($\beta_2 > 0 | data) = 0.88$), while the marginal

distribution for β_1 is centered almost exactly around zero. PM_{10} at lag 0 shows slightly more evidence of seasonality for the national average. However, the overall short-term effect of PM_{10} at lag 0 is smaller on average, as indicated in table 2. There is little evidence of seasonal variation in the short-term effect of PM_{10} at lag 2.

Sensitivity analyses

We performed several additional analyses to explore the sensitivity of the estimated seasonal PM_{10} log relative rates to model specification. Specifically, we examined sensitivity to 1) adjustment for long-term trends and seasonality in mortality; 2) the inclusion of other pollutants; 3) the exposure lag; and 4) the specification of the temperature component.

Selecting the degrees of freedom of the smooth function of time used to control for long-term trends and seasonality is an important issue in time series models of air pollution

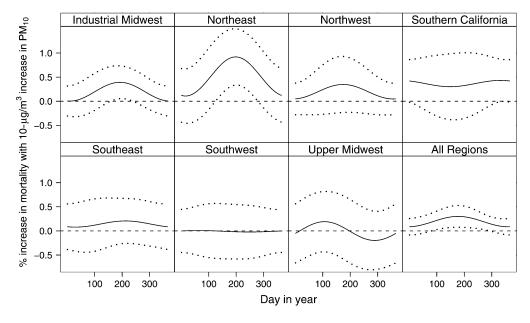


FIGURE 3. National and regional smooth seasonal effects of particulate matter less than 10 μ m in aerodynamic diameter (PM₁₀) at a lag of 1 day for 100 US cities, National Morbidity and Mortality Air Pollution Study, 1987–2000. Estimates were obtained by pooling city-specific coefficients from the sine/cosine model (equation 2). Dotted lines indicate pointwise 95% posterior intervals.

^{*} PM₁₀, particulate matter less than 10 μm in aerodynamic diameter; PI, posterior interval.

[†] Estimates were obtained by pooling city-specific coefficients from the main effect and pollutant \times season interaction models, respectively, and represent the percentage increase in daily mortality for a 10- μ g/m³ increase in PM₁₀.

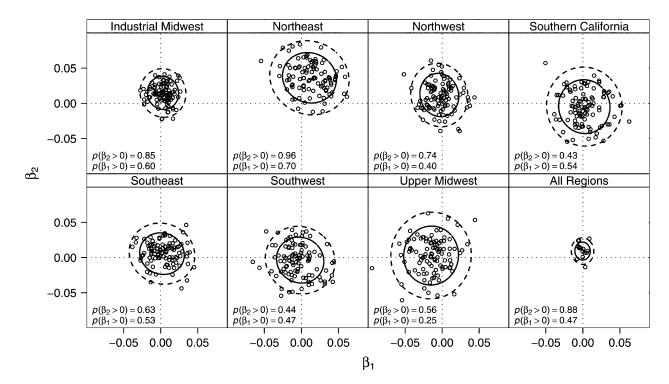


FIGURE 4. Samples from the national and regional joint posterior distributions of the pooled coefficients β_1 and β_2 from the sine/cosine seasonal model (equation 2) for particulate matter less than 10 μm in aerodynamic diameter (PM₁₀) at a lag of 1 day, National Morbidity and Mortality Air Pollution Study, 1987–2000. The solid and dashed lines indicate the 75% and 95% regions for the joint posterior distribution of β_1 and β_2 , given the data. Each panel includes the marginal posterior probabilities of each coefficient's being greater than 0. Posterior probabilities closer to 1 indicate stronger evidence of seasonal patterns.

and mortality, because estimates of pollution coefficients can change considerably depending on the specification of the number of degrees of freedom (22-24). Our original model used a natural cubic spline with 7 df per year of data. For PM₁₀ at lag 1, figure 5 shows the sensitivity of the sine/ cosine model to using 3, 5, 7, 9, and 11 degrees of freedom per year in the smooth function of time. With only 3 df per year, the curves deviate considerably from those in figure 3; for example, the estimate for Southern California exhibits much more seasonal variation. However, these deviations more likely reflect a lack of adjustment in the model rather than a real seasonal change. With more aggressive control for seasonality and long-term trends, the estimates appear to be stable.

Table 3 shows the sensitivity of the lag 1 PM₁₀ log relative rate as other pollutants are included in the pollutant \times season interaction model. The seasonal national average estimates exhibit the same pattern when current-day sulfur dioxide, ozone, or nitrogen dioxide is included as a copollutant in the model. With sulfur dioxide or nitrogen dioxide included, the summer effect for PM₁₀ increases slightly over the single pollutant estimate obtained with a restricted list of 45 cities. The inclusion of ozone appears to attenuate the effect somewhat. Note that the lack of data for the other pollutants reduced the number of cities available for the copollutant analyses.

Figure 6 shows the region-specific seasonal trends for PM₁₀ at lags 0, 1, and 2 with 95 percent posterior regions for lag 1. The lag 0 seasonal trend for each region has a pattern similar to that of the lag 1 trend but is lower in general. In the Northeast and the Industrial Midwest, the peak in the seasonal trend for lag 0 appears to come in late May, while the peak for lag 1 comes in mid-July. The Northwest, Southeast, and Upper Midwest exhibit small changes in seasonal patterns across lags but remain largely flat. Southern California and the Southwest appear to pick up slightly stronger seasonal patterns with lags 0 and 2.

To explore sensitivity to temperature and to control for temperature effects spread out over multiple days, we fitted separate models that included an additional interaction between the current-day temperature and the running mean of lags 1-3, as well as a running mean of lags 1-7. Neither addition to the model made a noticeable impact on the regional or overall seasonal patterns of the PM_{10} log relative rate.

DISCUSSION

In this paper, we have used a Bayesian semiparametric hierarchical model for estimating time-varying effects of air pollution on daily mortality. The model combines information across multiple cities to increase the precision of

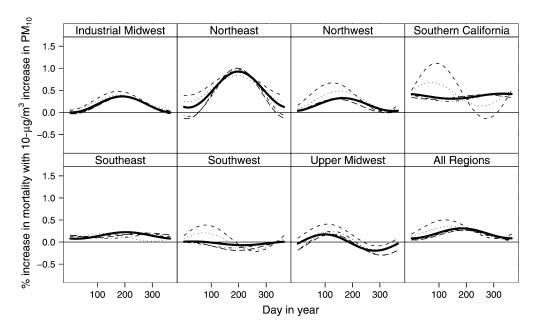


FIGURE 5. Sensitivity of national and regional estimates of smooth seasonal effects for particulate matter less than 10 μ m in aerodynamic diameter (PM₁₀) at a 1-day lag to the degrees of freedom assigned to the smooth function of time, National Morbidity and Mortality Air Pollution Study, 1987–2000. The degrees of freedom chosen were 3 df (short-dashed line), 5 df (dotted line), 7 df (solid line), 9 df (dotted-and-dashed line), and 11 df (long-dashed line) per year of data.

seasonal relative rate estimates. We found seasonal patterns for the national average effect of PM_{10} at both lag 0 and lag 1. Seasonal patterns varied by geographic region, with a strong pattern for lag 1 appearing in the Northeast. Equally interesting was the lack of seasonal variation in the southern regions of the country.

Understanding the health effects of particulate matter components is an increasingly important research problem, as the National Research Council noted (25). Exploration of the spatial-temporal variation of the short-term effects of particulate matter on mortality is essential to generating (or ruling out) specific hypotheses about the toxicity of particulate matter components. Data from the Environmen-

tal Protection Agency's $PM_{2.5}$ National Chemical Speciation Network are becoming available; these data contain detailed time series information on the composition of particulate matter (4). Knowledge of the spatial-temporal patterns of the short-term effects of particulate matter will be necessary for guiding future analyses of these particulate matter constituent data.

The modification of short-term effects of pollution by season has been explored previously in a number of single-city studies. Styer et al. (26) analyzed data from Cook County, Illinois, and Salt Lake County, Utah, and found (for Cook County) that the effect of PM₁₀ was higher in the spring and fall. In a review of research on particulate air

TABLE 3. National average estimates of season-specific lag 1 PM_{10}^* log relative rates adjusted for other pollutants, National Morbidity and Mortality Air Pollution Study, 1987–2000†

	Winter		Spring		Summer		Fall	
	Estimate	95% PI*	Estimate	95% PI	Estimate	95% PI	Estimate	95% PI
PM ₁₀ only (100 cities)	0.15	-0.08, 0.39	0.14	-0.14, 0.42	0.36	0.11, 0.61	0.14	-0.06, 0.34
PM ₁₀ only (45 cities)	0.15	-0.16, 0.45	0.13	-0.21,0.48	0.30	-0.10, 0.69	0.07	-0.23, 0.37
With sulfur dioxide (45 cities)	0.18	-0.16, 0.52	0.10	-0.30, 0.49	0.33	-0.14, 0.81	0.08	-0.25, 0.41
With ozone (45 cities)	0.13	-0.24,0.49	0.19	-0.18, 0.56	0.28	-0.13, 0.70	-0.01	-0.34, 0.31
With nitrogen dioxide (45 cities)	0.21	-0.18, 0.60	0.19	-0.17, 0.54	0.34	0.01, 0.68	0.13	-0.12, 0.39

^{*} PM₁₀, particulate matter less than 10 μm in aerodynamic diameter; PI, posterior interval.

[†] Estimates represent the percentage increase in daily mortality for a 10-µg/m³ increase in PM₁₀. Results for "45 cities" were obtained by pooling coefficients from the *same* list of 45 cities for which measurements for all copollutants were simultaneously available.

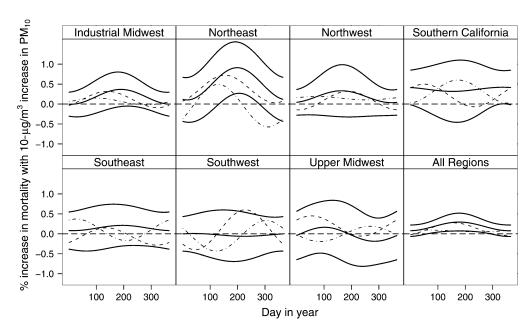


FIGURE 6. Sensitivity of national and regional estimates of smooth seasonal effects to particulate matter less than 10 μm in aerodynamic diameter (PM₁₀) exposure lag, National Morbidity and Mortality Air Pollution Study, 1987-2000. Solid black lines indicate the log relative rate estimate and pointwise 95% posterior intervals for PM₁₀ at a lag of 1 day. Also shown are the log relative rate estimates for PM₁₀ at lag 0 (shortdashed line) and lag 2 (dotted-and-dashed line).

pollution and mortality by Moolgavkar and Luebeck (27), analyses carried out in Steubenville, Ohio, Philadelphia, Pennsylvania, and Cook County, Illinois, indicated that the effects of pollutants are strongly modified by season. Kelsall et al. (28) examined data for Philadelphia and concluded that after adjustment for long-term variation in mortality and the effects of weather, there was little evidence of different effects by season. More recently, Moolgavkar (29) analyzed data from Cook County and Los Angeles County, California, and found between-season variation of the effects of numerous pollutants on daily mortality in both counties.

Estimation of short-term effects of air pollution on daily mortality for single cities is hampered by the inherent high variability of the resulting effect estimates. Estimation of seasonally varying effects poses an additional challenge, because it involves further stratification of the data. Since fewer data are available for estimating season-specific effects, the variability of such estimates increases, making it difficult to discern any meaningful seasonal pattern. Rather, a multisite approach in which information can be combined across neighboring cities can provide more precise city-specific log relative rates, as well as a natural framework for characterizing regional and national trends. For example, Moolgavkar (29) found an inconsistent relation between PM₁₀ and mortality in Los Angeles County when sulfur dioxide was included in the model. However, we find in table 3 that the seasonal pattern in the national average (as well as the Southern California regional average (data not shown)) is robust to the inclusion of copollutants.

Regional differences in the short-term effects of PM₁₀ have been explored in NMMAPS (12, 13) and in the APHEA Project [Air Pollution and Health: A European Approach] (30, 31). Both studies found regional modification of the effect of PM₁₀ on daily nonaccidental mortality. The results presented here are consistent with previous NMMAPS analyses with respect to regional average PM₁₀ effects. The estimated seasonal patterns for lag 1 appear to have two distinct shapes. The Industrial Midwest, the Northeast, and the Northwest all exhibit a larger effect during the summer months, while the other regions exhibit little seasonal variation. These patterns are somewhat sensitive to the pollution lag used. Therefore, an important question raised by this study is how the total effect of PM₁₀ in a distributed lag model would vary by season. Unfortunately, the US pollution database has daily particulate matter levels for a small fraction of cities, making it difficult to answer this question.

These analyses provide strong evidence that the PM₁₀ log relative rate is greater in the spring and summer in the northern regions, particularly in the Northeast. This result admits several competing hypotheses. First, the particulate matter constituents may vary by season in these regions, with the most toxic particles having a spring/summer maximum. A detailed analysis of the regional and seasonal variation in particulate matter constituents is needed to better understand these patterns. Data on particulate matter less than 2.5 µm in aerodynamic diameter (PM_{2.5}) and associated speciation data have only been collected regularly in the United States since 1999. Therefore, we expect multisite time series studies of PM_{2.5} speciation data to be carried out in the near future.

Second, even if the constituents do not vary substantially, it is possible that the higher short-term effect of ambient exposure to particulate matter estimated in spring and summer in the Northeast could be the result of more time spent outdoors and therefore less exposure measurement error. While there has been some work suggesting that differences between personal and ambient exposure to PM_{10} can vary across seasons (32), there are also data indicating that individual activity patterns are, on average, very similar across regions of the United States (33-35). If the seasonal variation in the PM₁₀ log relative rates were entirely attributable to activity patterns, we would expect to have estimated similar seasonal patterns of particulate matter effects across regions. However, Southern California exhibited a positive effect that did not vary by season.

A third possibility is that the particle effect may be swamped by the more powerful effect of winter infectious diseases, so that it can only be observed when infectious diseases are less prevalent. This hypothesis does not explain the absence of a PM₁₀-mortality association in the southern regions, where infectious disease incidence is also seasonal. Finally, this result may reflect seasonally varying bias from an as-yet-unidentified source. Having established the pattern of regional and seasonal variation in the PM₁₀ log relative rate, a more targeted investigation of possible sources of such bias is now possible.

ACKNOWLEDGMENTS

This research was supported in part by grant T32HL07024 from the National Heart, Lung, and Blood Institute, grant R01ES012054 from the National Institute of Environmental Health Sciences (NIEHS), and grant P30ES03819 from the NIEHS Center for Urban Environmental Health. Research described in this article was partially supported by a contract and a grant from the Health Effects Institute (Cambridge, Massachusetts), an organization jointly funded by the Environmental Protection Agency and automotive manufacturers. Dr. Roberto Pastor-Barriuso was supported in part by grant EPY 1261/02 from the Instituto de Salud Carlos III (Madrid, Spain).

The contents of this article do not necessarily reflect the views and policies of the Health Effects Institute, nor do they necessarily reflect the views and policies of the Environmental Protection Agency or of motor vehicle or engine manufacturers.

REFERENCES

- Pope CA, Dockery DW, Schwartz J. Review of epidemiological evidence of health effects of particulate air pollution. Inhal Toxicol 1995;7:1–18.
- Dockery DW, Pope CA. Epidemiology of acute health effects: summary of time-series studies. In: Wilson R, Spengler J, eds. Particles in our air. Cambridge, MA: Harvard University Press, 1996:123–47.

- Bell ML, Samet JM, Dominici F. Time-series studies of particulate matter. Annu Rev Public Health 2004;25:247–80.
- Office of Research and Development, National Center for Environmental Assessment, Environmental Protection Agency. Air quality criteria for particulate matter (fourth external review draft). (EPA publication nos. EPA/600/P-99/ 002aD and EPA/600/P-99/002bD). Research Triangle Park, NC: National Center for Environmental Assessment, 2003.
- 5. Spengler J, Wilson R. Emissions, dispersion, and concentration of particles. In: Wilson R, Spengler J, eds. Particles in our air. Cambridge, MA: Harvard University Press, 1996:41–62.
- Office of Research and Development, National Center for Environmental Assessment, Environmental Protection Agency. Air quality criteria for particulate matter. (EPA publication no. EPA/600/P-95/001aF). Research Triangle Park, NC: National Center for Environmental Assessment, 1996.
- Samet JM, Zeger SL, Dominici F, et al. 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.
- 8. Hastie TJ, Tibshirani RJ. Generalized additive models. New York, NY: Chapman and Hall, Inc, 1990.
- Stolwijk AM, Straatman H, Zielhuis GA. Studying seasonality by using sine and cosine functions in regression analysis. J Epidemiol Community Health 1999;53:235–8.
- Daniels MJ, Dominici F, Samet JM, et al. Estimating particulate matter-mortality dose-response curves and threshold levels: an analysis of daily time-series for the 20 largest US cities. Am J Epidemiol 2000;152:397

 –406.
- Dominici F, McDermott A, Zeger SL, et al. On the use of generalized additive models in time-series studies of air pollution and health. Am J Epidemiol 2002;156:193–203.
- Dominici F, Daniels M, Zeger SL, et al. Air pollution and mortality: estimating regional and national dose-response relationships. J Am Stat Assoc 2002;97:100–11.
- 13. Dominici F, McDermott A, Zeger SL, et al. Mortality among residents of 90 cities: revised analyses of time-series studies of air pollution and health. Cambridge, MA: Health Effects Institute, 2003:9–24.
- Moolgavkar SH, Luebeck EG, Hall TA, et al. Air pollution and daily mortality in Philadelphia. Epidemiology 1995;6:476–84.
- 15. Samet J, Zeger S, Kelsall J, et al. Does weather confound or modify the association of particulate air pollution with mortality? Environ Res 1998;77:9–19.
- Dominici F, Samet JM, Zeger SL. Combining evidence on air pollution and daily mortality from the twenty largest US cities: a hierarchical modeling strategy (with discussion). J R Stat Soc A 2000;163:263–302.
- Samet JM, Dominici F, Curriero FC, et al. Fine particulate air pollution and mortality in 20 US cities. N Engl J Med 2000;343:1742–9.
- Samet JM, Zeger SL, Dominici F, et al. The National Morbidity, Mortality, and Air Pollution Study, part I: methods and methodological issues. Cambridge, MA: Health Effects Institute, 2000.
- 19. R Development Core Team. R: a language and environment for statistical computing. (ISBN 3-900051-00-3). Vienna, Austria: R Foundation for Statistical Computing, 2004. (World Wide Web URL: http://www.R-project.org).
- Peng RD, Welty LJ. The NMMAPS data package. R News 2004;4:10–14. (World Wide Web URL: http://CRAN.Rproject.org/doc/Rnews/).
- 21. Everson PJ, Morris CN. Inference for multivariate normal hierarchical models. J R Stat Soc B 2000;62:399–412.

- Schwartz J. Nonparametric smoothing in the analysis of air pollution and respiratory illness. Can J Stat 1994;22:471–88.
- Schwartz J. Total suspended particulate matter and daily mortality in Cincinnati, Ohio. Environ Health Perspect 1994;102:186–9.
- 24. Touloumi G, Atkinson R, Le Tertre A, et al. Analysis of health outcome time series data in epidemiological studies. Environmetrics 2004;15:101–17.
- National Research Council, National Academy of Sciences. Research priorities for airborne particulate matter: IV. Continuing research progress. Washington, DC: National Research Council, 2004.
- Styer P, McMillan N, Gao F, et al. Effect of outdoor airborne particulate matter on daily death counts. Environ Health Perspect 1995;103:490–7.
- 27. Moolgavkar SH, Luebeck EG. A critical review of the evidence on particulate air pollution and mortality. Epidemiology 1996;7:420–8.
- 28. Kelsall JE, Samet JM, Zeger SL, et al. Air pollution and mortality in Philadelphia, 1974–1988. Am J Epidemiol 1997;146:750–62.
- Moolgavkar SH. Air pollution and daily mortality in two U.S. counties: season-specific analyses and exposure-response relationships. Inhal Toxicol 2003;15:877–907.
- 30. Katsouyanni K, Touloumi G, Samoli E, et al. Confounding and effect modifications in the short-term effects of ambient

- particles on total mortality: results from 29 European cities within the APHEA2 Project. Epidemiology 2001;12:521–31.
- Samoli E, Schwartz J, Wojtyniak B, et al. Investigating regional differences in short-term effects of air pollution on daily mortality in the APHEA Project: a sensitivity analysis for controlling long-term trends and seasonality. Environ Health Perspect 2001;109:349–53.
- 32. Keeler GJ, Dvonch JT, Yip FY, et al. Assessment of personal and community-level exposures to particulate matter among children with asthma in Detroit, Michigan, as part of Community Action Against Asthma (CAAA). Environ Health Perspect 2002;110:173–81.
- 33. Office of Research and Development, National Center for Environmental Assessment, Environmental Protection Agency. Descriptive statistics tables from a detailed analysis of the National Human Activity Pattern Survey (NHAPS) data. (EPA publication no. EPA/600/R-96/148). Research Triangle Park, NC: National Center for Environmental Assessment, 1996.
- 34. Klepeis NE, Nelson WC, Ott W, et al. The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. J Exposure Anal Environ Epidemiol 2001;11:231–52.
- 35. Wallace LA, Mitchell H, O'Connor T, et al. Particle concentrations in inner-city homes of children with asthma: the effect of smoking, cooking, and outdoor pollution. Environ Health Perspect 2003;111:1265–72.