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Associations of London, England, Daily Mortality with Particulate Matter, Sulfur Dioxide, and Acidic Aerosol Pollution

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ABSTRACT. During the extreme pollution episodes of 1952 and 1962 in London, England, excesses in daily mortality were clearly evident. In this study, we examined daily British Smoke, sulfur dioxide, acid aerosols, and weather variables for their short-term associations with daily mortality in the more typical (nonepisodic) winters of 1965–1972. Consideration of the acid aerosol data was of special interest because this chemical component has been suspected as a causal agent in past episodes. Temporal lag structures between the variables were examined after removal of long-term components from each series in order to obtain "rational" cross-correlations. Significant associations between same-day and lagged pollution variables and mortality were found. Alternative regression models with pollution and weather variables were also developed. The coefficients obtained were applied to the 1962 pollution episode to examine the continuity of the estimated slopes. The pollution-predicted deaths fit the observed deaths well, which supports the applicability of such deviation-derived coefficients to the absolute scale. These models were also employed to estimate mean excess daily deaths attributed hypothetically to air pollution. On average, mean effect ranged from 2–7% of all deaths during the nonepisodic winters in Greater London, but the 95% confidence intervals of these estimates overlapped for all model specifications examined. This estimated pollutant mixture "effect" cannot be attributed to a particular pollutant because of a lack of quantitative information on the relative downward biases caused by both analytical errors and errors in the spatial representativeness of each respective pollution index.

IN DOCUMENTS that described the December, 1952, London, England, smog episode, the overall excess in daily deaths (estimated to be 3 500–4 000) was obviously associated with air pollution.[1,2] The average daily concentrations of particulate matter, British Smoke and sulfur dioxide (SO_2), in Greater London reached 1.4 mg/m^3 and 0.7 ppm, respectively. The excess deaths were reported to have occurred primarily among the people who had respiratory or cardiovascular problems. Whereas strong evidence of the potential lethality of air pollution is provided, a more generalizable exposure/human health response relationship is not extrapolated easily from such an isolated extreme incident.

More recent extended series of daily pollution and mortality observations in London during more usual (i.e., nonepisodic) pollution levels have allowed researchers to explore and estimate the possible exposure/response relationships more systematically. A summary table of 21 past London weather/pollution/mortality studies can be found in another study by Ito.[3] Despite

the variety of approaches taken by the various data analysts to date, those studies on London data have generally shown significant associations between health effects and more routine levels of London air pollution. However, in terms of the effects attributed to individual pollutants (i.e., British Smoke versus SO_2), different analyses of the same data sets sometimes produced different conclusions, depending on the statistical approach employed. For example, in the case of the various analyses of the 1958–1972 London winter pollution-mortality data, Mazumder, Schimmel, and Higgins[4] concluded that an association was found with British Smoke, but not with SO_2; Shumway, Tai, Tai, and Pawitan[5] reported that British Smoke and SO_2 predicted mortality equally well and appeared to be acting identically; and Schwartz and Marcus concluded that British Smoke was more strongly associated with mortality, but both British Smoke and SO_2 were significant when regressed separately. Roth et al.,[7] however, concluded that the high correlations between British Smoke and SO_2 in the 1958–1972 winter data (correlations of raw data ranging from 0.788–0.962, with a median of 0.910) made it impossible to determine what portion of association may result from British Smoke or SO_2. Whereas these results all support a pollution effect on mortality, small differences among collinear pollutants in their respective strengths of association with the health effects have resulted in quite different pollutant-specific conclusions, depending on the particular model specification and study period chosen by the modeler.

The day-to-day temporal variations of pollutants in London are driven largely by varying overall weather conditions, such as the occurrence of air stagnations resulting from temperature inversions on cold, clear nights, which create collinearity among the pollutant variables. Three pollutants are examined in this analysis: British Smoke, SO_2, and aerosol acidity (H^+). The aerosol acidity analyses are especially of interest because aerosol acidity is presently under consideration by the U.S. Environmental Protection Agency (EPA) as a possible new Criteria Pollutant. These three pollutants were likely to have been either emitted directly from the same sources (e.g., domestic coal burning), or were the secondary products thereof. The physicochemical characteristics of the three pollutants are quite different, however; British Smoke is an index of black particulate matter which, in general, can be insensitive to changes in individual chemical constituents. In England, British Smoke has been shown, in practice, to be a good index of carbon concentration, but is a somewhat less reliable metric of total particulate matter mass concentration.[8] Sulfur dioxide—a reactive vapor—can have a different dispersion pattern from that of particulate matter. Chemical reactions may cause conversions to other (nongaseous) species and may, therefore, lead to a reduction in levels over time, even without a dispersion influence. Conversely, London particulate aerosol acidity is thought to result largely from sulfates, either from primary emission or heterogeneous reaction.[9,10] Such reactions might depend on the availability of both British Smoke (a reaction catalyst) and SO_2 concentrations (a reaction precursor). Acid neutralization by basic gases or alkaline particles is also possible during collection and analysis of these samples, although the investigators took precautions to minimize this effect.[9] These various pollutants' differing physicochemical characteristics may also help create unique temporal variations, but in another way, as in the case of aerosol acidity's potential relationship to both British Smoke and SO_2, may also result in further pollutant collinearities.

An important additional complication in the separation of pollutant effects is that some of the unique variation of each pollutant may be caused by measurement errors, rather than by true fluctuation. Furthermore, different pollutants may have different spatial variabilities over the area of interest, and the temporal fluctuations of pollutants at a given site, or average of multiple sites, are likely to have "errors" in spatial representativeness. As a result, any true associations, as well as regression coefficients, between the pollutant and health effects will be necessarily biased *downward*,[11] especially for the pollutants with the greatest errors. If the influence of such measurement errors is to be assessed quantitatively, signal-to-noise variance ratios of each pollutant are required, but such information is not available for this dataset. Compilations of available information on these three pollutants, such as the EPA criteria document on Particulate Matter and SO_2[12] or the EPA Acid Aerosol Issue Paper,[13] have, therefore, been unable to separate unambiguously the relative attribution of each pollutant as a single causal agent.

Given the above considerations, the primary goal of the research reported in this paper was to utilize time-series methods to evaluate the associations between each of the three pollutants studied and daily mortality. These models were employed to estimate a range of mortality "effects," if any, attributable to air pollution when each measured pollutant was used as an index of the London air pollution mixture. Finally, the regression coefficients obtained from the nonepisodic period were applied to the 1962 episode data to examine the continuity of the hypothetical mortality/pollution slope.

Materials and methods

The methods of collection and analysis and descriptive statistics for the pollution and mortality data analyzed here are detailed elsewhere.[3,14] Briefly, the daily means of pollution at seven sampling sites in Greater London and at a single central London site are available for British Smoke and SO_2. In contrast, the daily aerosol acidity data analyzed here was available for the single central London site only. The analytical method of the aerosol acidity determination was reported in detail by Commins.[9] The particulate matter in the air was collected by filtration, and the filter was subsequently immersed in a known excess of sodium tetraborate and titrated back to pH 7 with sulfuric acid. The procedure allows the sodium tetraborate to neutralize the acid before the potentially interfering insoluble bases do. It is important to note that the sampling interval for the mean of 7 sites British Smoke and SO_2 data began 12–15 h prior to the midnight-midnight mortality record collection period, whereas the sampling period for the central London pol-

lutant data coincided exactly with the mortality record collection period. The nonepisodic time period 1965–1972 was analyzed because all the three pollutants showed relatively stable levels during this period. Time-series plots of these pollutant, weather, and mortality data are shown in Figure 1. Prominent features include (1) a strong seasonal component in all the series, (2) larger variations of pollutants in the winter than in the summer, (3) broad mortality peaks that resulted from winter influenza epidemics, and (4) a similarity of shapes among the three pollution series and in their inverse relationship to the temperature series.

Power spectral analyses. The strong seasonal components in the data can dominate apparent association between variables, masking their short-term relationships and, in almost all the past London correlation/regression analyses, it has been customary to use a 15-d moving average, or its equivalent, to first estimate the slowly moving (long-wave) components of each series. This component was then subtracted from the original series to obtain the "high-frequency" (short-wave) deviations for subsequent analysis. Although this filter does eliminate the seasonal component and the broad influenza peaks, its frequency cutoff point is rather arbitrary, and its appropriateness has not been evaluated previously. Therefore, the power spectrum of each time series was examined to gain insight into how much the choice of prefiltering influences the subsequent health effects analyses. Power spectrum decomposes univariate series' variance into contributions from each frequency region.

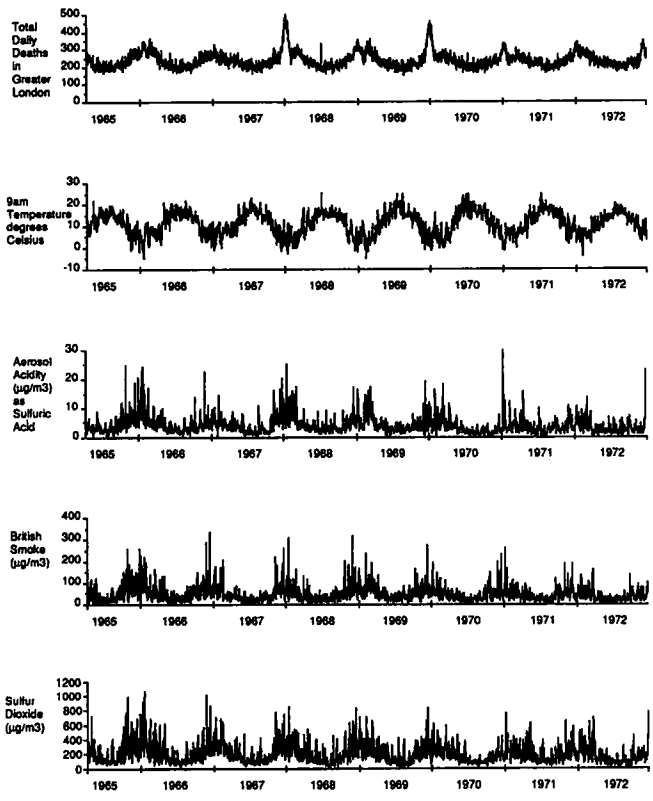

Fig. 1. Time series plot of daily mortality, pollution, and temperature in London, England (1965–1972).

Spectra for winter periods (November through February) were obtained by averaging the periodograms in each frequency band for the multiple years, as suggested by Shumway.[15] Each winter's series was centered and detrended prior to analysis. It should be noted that any cycles that exceeded the 120-d season data length (e.g., multi-year effects) will not be detected in this pooled data because any such long waves will be detrended out.

Cross-correlation function (CCF) analysis/regression models. One cannot assume in modeling such serial data that a day's mortality is influenced solely by that day's pollution or weather alone. Possible lag associations with prior days must also be investigated via cross-correlation analyses to develop appropriate *distributed lag* regression models that account for any such lagged associations. Cross-correlation is a series of correlation coefficients between a pair of time series evaluated at different lags. Given that each series contains strong seasonal fluctuations, cross-correlations among the raw data series would be influenced strongly by these low-frequency components, and such raw cross-correlations would not be appropriate for the development of "short-term" models. Our preliminary approach was, therefore, to apply a high-pass filter prior to CCF analysis.[14] The resulting filtered mortality series were essentially of random appearance, but the temperature and pollution series showed significant autocorrelation. Thus, evaluation of the lagged associations between such series was still confounded by correlation over time within the temperature and pollution series.

An alternative approach was, therefore, used to remove the significant nonrandom structures (such as autoregressive [AR] or moving average [MA] structure) in each original series. This was accomplished by first developing an AR-MA model, followed by using the residuals of that model in the health effects analyses. This "prewhitening"[16] of both series prior to CCF was first suggested by Haugh and Box[17] as "rational cross-correlation." The advantage of this approach is that, unlike raw or arbitrarily filtered CCF analyses, meaningful confidence intervals can be drawn (because of the lack of autocorrelation), and the significance of cross-correlation can be assessed quantitatively. The approximate error variance of these CCFs at each lag is simply the inverse of the number of observations minus the number of lags. Another feature of this approach is that both the seasonal cycles and the influenza mortality peaks, exhibited as significant positive autocorrelations, are eliminated from the analysis. Despite the statistical desirability, a possible disadvantage of this step is the potential elimination of any real long wave or autocorrelated relationships that may be causal, but this is also a threat when conducting conventional filtering with a frequency cut-off point.

Thus, each series' structure was modeled after the prior examination of autocorrelation and partial autocorrelation, and after the development of autoregressive models within each winter. The residuals from the models were then calculated for subsequent CCF analysis. First-order autoregressive models were adequate to model the temperature and pollution series, but the more autocorrelated mortality series required up to

fourth-order autoregressive models. The residuals from the estimated time-dependent models were then examined to ensure there were not remaining significant autocorrelations. When more than one model was possible, the result with the smallest Akaike Information Criteria was chosen.[18] Pooled cross-correlations could be obtained by connecting the consecutive winters' residual series with as many intervening "missing values" as the number of lags for calculation of cross-correlation in between (i.e., ± 15 d in this case). Autocorrelations of each of these combined series were also calculated to assure that there was still no autocorrelation. These CCFs were also obtained for logarithm and square-root transformed pollution data (prior to elimination of long-wave components) in order to observe the effects of transformations. Given these CCF results, mortality regression model specifications were developed with all significant lagged pollution/weather variables.

Results

Shown in Figure 2 are the power spectra for the pollution, weather, and total mortality series. Each series was centered and detrended prior to power spectrum calculation, but was not filtered or prewhitened. Periodograms were smoothed, using a rectangular frequency window with 6 degrees of freedom (*df*) for each winter, resulting in 42 *df* for the seven winters. There is a contrast between the shape of the spectra for pollution/temperature versus that for mortality. Whereas the pollution and temperature spectra show a gradual increase in power toward the lower frequencies (i.e., long wave), mortality has a narrow range in which low-frequency power dominates (i.e., for cycles that exceed approximately 4 d, or for frequencies less than approximately 0.025 cycles/d). The implication of using the 15-d moving average filter or its equivalent to these series is, therefore, that the pollution and temperature series would then appear to have cycles at periods longer than 10–20 d, but the mortality series would appear to be very nearly random. There were also apparent weekly cycles (1/7 d or approximately 0.14 cycles/d) in the British Smoke and SO_2 spectra, especially in central London series. Weekly cycles were not present for aerosol acidity, temperature, humidity, or mortality.

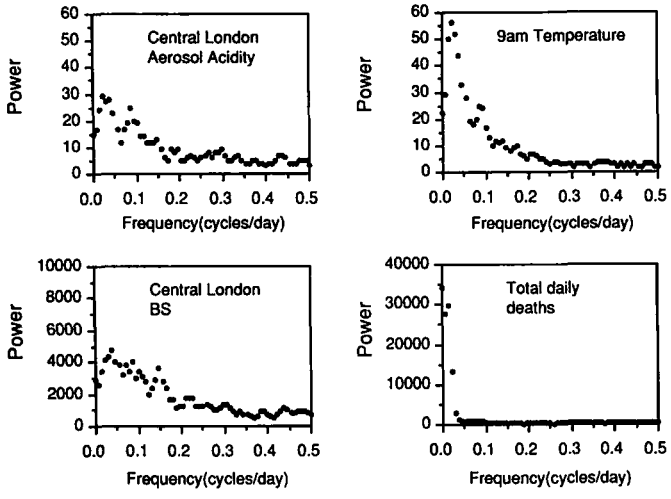

Fig. 2. Power spectra of weather, pollution, and total mortality for the pooled winter data (1965–1966 to 1971–1972).

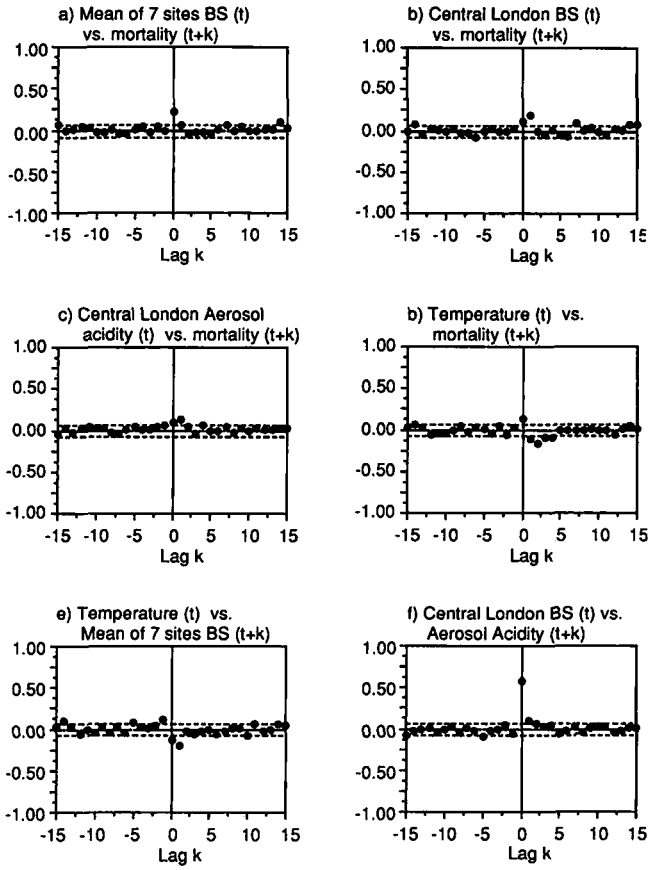

Fig. 3. Cross-correlation function of pollutant (t) and weather (t) versus total deaths (t + k), all prewhitened by winter and pooled (1965–1966 to 1971–1972). *Dotted lines* **are upper and lower 95% confidence intervals.**

In Figure 3 is shown the CCFs among the key variables. The CCF results for total deaths versus the logarithm and square-root transformed data did not show significant differences, both in terms of lag structures and their strengths of association; therefore, the results for only the untransformed pollution variables are shown. It can be seen that the mean of seven sites British Smoke has the largest positive correlation with mortality among the pollution and weather variables, and this occurs without lag. However, the impact of British Smoke from the day before is nonsignificant, whereas the result of the pollutant variables have significant coefficients on both the same day and the day before. As expected, the weekly lags at 7 and 14 d were often significant because of weekly autocorrelation of pollution indices, but these lagged variables were not included in the final regression because they cannot be causal, and several intervening coefficients were clearly nonsignificant. The CCFs for cardiovascular deaths and respiratory deaths with pollution and weather variables (not shown) were also obtained, displaying essentially the same lag structure as is shown in Figure 3, but with somewhat weaker associations.

Comparison of the mean of seven sites' data coefficients versus the central London site data coefficients indicates that, for both the British Smoke and SO_2, the mortality association with pollution on the prior day is larger than that of the same day at the central site, but the reverse is true for the mean of seven sites. This is consistent with the fact that both mortality and central London values were recorded from midnight to midnight, whereas the mean of seven sites' values were recorded between approximately noon of the previous day to noon of the same day. Thus, if there is both a same-day and a 1-d lag, as suggested by the central London values, then the (partially lagged) mean of seven sites' data will be less likely to reveal it. However, if there is actually a 12–15 h lag in effects, the mean of seven sites' data might well give a better model fit than the midnight-to-midnight data.

Temperature also showed a significant lagged association with mortality. However, it had a positive coefficient for the same day and significant negative coefficients (as expected) for up to 4-d lags. The reported positive temperature correlation with total mortality on the same day is not plausible biologically. Warmer temperatures during a winter day in London are unlikely to cause adverse health effects, and colder winter temperatures are also unlikely to influence health positively. The results are, however, consistent with the results reported by Shumway et al.[5] for the 14 winters (obtained from multiple-input frequency domain regression) indicating that total mortality was a positive 2-d differential function of the temperature. Furthermore, the negative correlations of temperature up to 4-d lags are also consistent with Bull and Morton's[19] findings on England and Wales data that the temperature occurring 5 d before deaths is most important for respiratory infections, temperature 3–4 d prior to death is most important to stroke deaths, and temperature 1–2 d prior to death is critical with respect to myocardial infarcts.

In an attempt to investigate further the time sequence of London's weather/pollution/mortality data, CCFs of temperature versus pollution variables were obtained (Figure 3e). It can be seen that the pollution is associated negatively with temperature of the same day and of the previous day. This seems reasonable in that a high-pressure cold-weather cell (anti-cyclone) often causes radiative cooling during clear nights, which causes very low temperatures at the surface, and a resultant surface-based temperature inversion. This, in turn, causes stagnation of air at the surface with attendant pollution buildups, which is further exacerbated by increased pollution emissions during the cold weather. As reported by Brazell,[20] this pollution may then provide the nuclei for the development of a pollution fog over the city. Notice, however, that temperature exhibits a positive correlation with pollution of the previous day. This phenomenon was seen clearly in the past London smog episodes of 1952, 1955–1956, 1957, and 1962.[2,21] A sharp drop of temperature is followed by a sharp rise in pollution. Then, however, a sharp rise of temperature follows that sharp rise in pollution. One possible explanation for this sequence is that the stagnant air mass, initially created by the cold temperature inversion, becomes filled with pollution, which then acts like a "blanket" over the city, trapping its heat under an elevated inversion.[22] Thus, it is possible that the apparent (and counter-intuitive) positive correlation of same-day temperature and mortality is actually driven by the positive correlation of the prior day's pollution with both the temperature and mortality.

Such complexities in the weather/pollution/mortality inter-relationships inhibit the development of a single definitive causal pathway model via purely statistical criteria. Therefore, the mortality regression was conducted for three alternative models, using the prewhitened series; the total mortality was regressed on (1) each of the pollution variables, with significant lags only; (2) lagged significant pollution variables with the same-day temperature; and (3) lagged pollution variables, with humidity and temperature variables with significant lags, to observe any effects from inclusion of further controlling variables. These models' respective pollution coefficients are summarized in Table 1. Overall, all of the pollutant variables were associated significantly with total daily mortality. Adding only the same-day temperature (model 2) actually increased the pollution coefficients for the same day in all cases, but this was likely the result of the pollution-temperature confounding on the same day. Controlling for both temperature and humidity for all the significant lags generally tended to decrease the significance of the lagged pollution coefficients, as expected, but all three pollution variables remained significant in this model.

Given the differences in scale among the pollution indices, a comparison of their absolute regression coefficients is not very meaningful, and comparisons of the significance of coefficients do not depict the total health effects impact from each pollutant (i.e., they are not additive). An estimate of excess (premature) deaths at the mean pollution level has been employed in past studies to provide direct comparisons among independent variables (e.g., for New York City[23–25]). This index, called *mean effects*, is calculated by multiplying the individual pollutant coefficients (obtained here from AR-MA filtered analyses) by their respective mean concentration values during the study period. Such an index is convenient in the comparison of the "effects" estimated via the different pollutant indices, but it must be remembered that this calculation makes the inherent assumption that the regression coefficients obtained from the adjusted variables (i.e., deviations at the mean) also apply to the absolute values. Thus, the calculation of this index is provided here primarily for the purposes of allowing more direct comparisons of the reported regression coefficients. The mean effects were calculated for the same-day plus the 1-d lagged pollution, as these lags generally had the most significant coefficients.

When the linear model's excess premature deaths are expressed as a percentage of mean winter deaths during the period (mean = 278 deaths/d), the largest mean effect estimate was 6.7%, using SO_2, with control only for the same-day temperature. The various estimated mean effects do not vary significantly among the five pollution indices. Indeed, the 95% confidence intervals of the combined same-day and 1-d lagged mean effects of pollution all overlapped each other. The combined (same

Table 1.—Distributed Lag Coefficients (*t* Ratios) for Total Daily Deaths on Pollution with and without Control for Temperature and Humidity, Winter Data (1965–1972)

Pollutant	Model 1: pollution only	Model 2: model 1 plus the same day temperature	Model 3: model 1 plus full control with temperature and humidity
7__BS			
No lag	0.107 (6.65)	0.117 (7.31)	0.100 (6.19)
Lag 1	0.029 (1.78)	0.019 (1.20)	−0.008 (−0.51)
C__BS			
No lag	0.058 (3.14)	0.079 (4.17)	0.060 (3.19)
Lag 1	0.096 (5.22)	0.090 (4.97)	0.062 (3.27)
7__SO_2			
No lag	0.047 (5.33)	0.060 (6.63)	0.050 (5.43)
Lag 1	0.032 (3.61)	0.026 (3.02)	0.010 (1.10)
C__SO_2			
No lag	0.017 (2.96)	0.023 (3.92)	0.018 (2.99)
Lag 1	0.028 (4.92)	0.024 (4.07)	0.014 (2.31)
C__Acidity			
No lag	0.746 (2.96)	1.115 (4.27)	0.701 (2.62)
Lag 1	1.075 (4.25)	0.984 (3.92)	0.497 (1.86)

Notes: BS = British Smoke, SO_2 = sulfur dioxide; 7____ = mean of seven sites, C____ = central London.

and previous day) mean effects were also calculated for the central London pollution indices and are shown in Figure 4. Again, there is no appreciable difference among the three pollutants' estimated mean effects on mortality, with the mean pollution effect results with full temperature and humidity controls ranging from 2.4–3.3% excess deaths/d.

It was of interest to compare the mortality/pollution slopes obtained from the nonepisodic period to that from an episode. The 1962 London pollution episode was measured at the same sites as in the nonepisodic data, and the pollution levels were an order of magnitude higher than the nonepisodic levels. No similar attempt was made for the 1952 episode because the 1952 pollution was measured at 12 stations that were different from the 7 stations in this dataset, and the levels at the 12 stations varied more than an order of magnitude from site to site. The actual 1962 episode concentrations were applied to the coefficients from the 3 models for both British Smoke and SO_2, resulting in the excess mortality estimates shown in Figure 5. Prior to the rise in pollution levels, the "pollution-attributed" deaths for the 3 models averaged approximately 20 deaths, which is slightly higher than the "mean effects" calculated for the nonepisodic period. However, the models' estimates of attributable deaths at the peak levels of pollution averaged at approximately 200 deaths. This corresponds well to the difference between the observed peak daily deaths (approximately 470) and the pre-episode death levels (approximately 260). Thus, in this episodic event, the hypothetical mortality/pollution slopes obtained from nonepisodic periods appear to be consistent with the apparent slope of this episode.

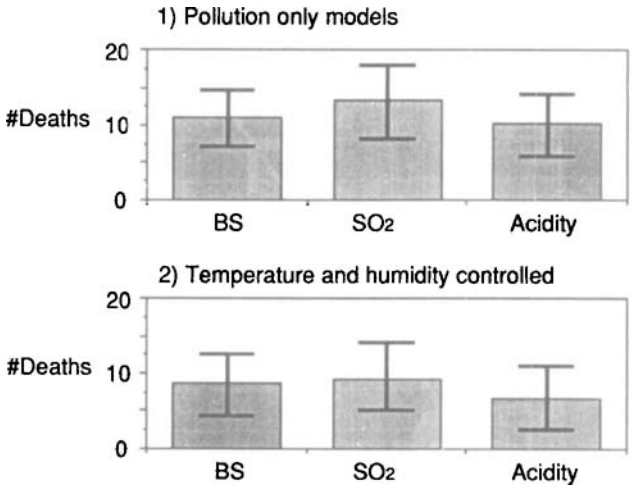

Fig. 4. Estimated hypothetical mean effects attributed to pollution with 95% confidence intervals.

Discussion

A distributed lag model was examined, using shortwave pollution and mortality series of nonepisodic periods. Air pollution on the same day and on the previous day showed significant associations with daily mortality. Longer prolonged effects seen in the 1952 London fog episode (i.e., up to 2 wk after the pollution peak), were not apparent in this nonepisodic data. This is likely the result of the much lower concentrations involved, which caused the longer lag effects to be indiscernible from random fluctuations because they are much smaller than the short-lag effects. With regard to the

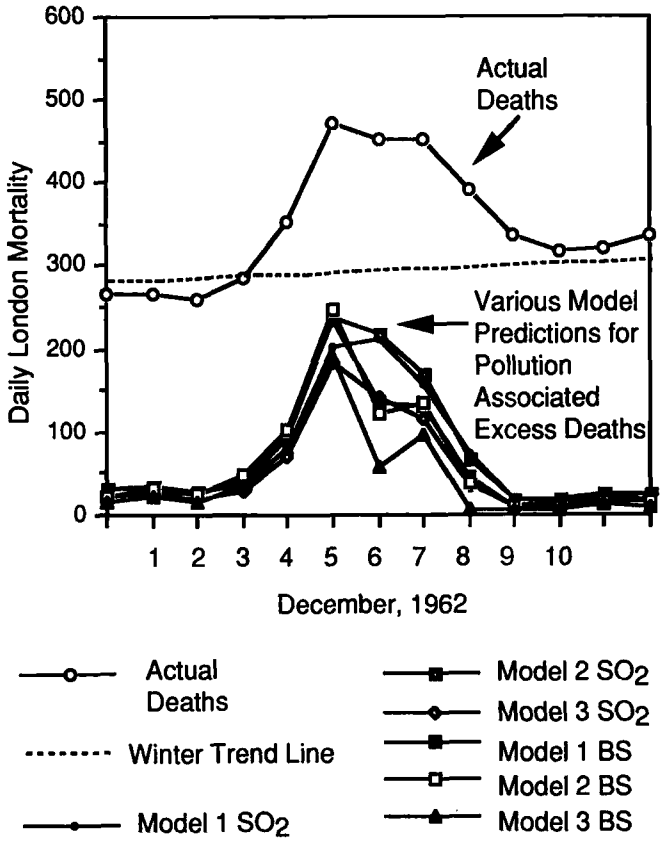

Fig. 5. Actual deaths during the episode period versus the model predicted deaths attributed to pollution (December 1962, London).

1962 episode, the extent of excess deaths appears to be fit well by the model developed in this research. This supports the linear extrapolation of slopes obtained from such "low-level" short-wave analyses. However, it is not appropriate to apply such London, England, regression coefficients to other locations without first considering the possible influences of the prevailing population age distribution, mixture of pollutants, and pre-existing sensitive populations (e.g., individuals with chronic respiratory illness). These regression coefficients are acute premature death estimates only, because long-wave (chronic) components were eliminated from consideration at the initial data analysis step due to statistical analyses considerations.

All pollutants measured daily were found to be associated significantly with mortality effects. It is not appropriate, however, to interpret the small (nonsignificant) differences in strength of association among the three pollutants considered as indicative of their respective importance to mortality. This is because of the pollutants' collinearity and the lack of quantitative information on their relative measurement errors. These errors include not only analytical errors (e.g., during pH measurements), but also errors in the spatial representativeness of the samples in relation to the distribution of the exposed population. Despite the potential importance of their errors to the regression results (as they determine the extent of downward bias of the correlation and regression coefficients for each pollutant), discussion on this matter is virtually nonexistent in past literature wherein attempts were made to "separate" the effects of London's collinear pollutants. A quantitative analysis of this factor is very difficult because (a) the representativeness of different pollution indices for the area in question can be determined empirically only with multiple stations, and (b) because measurement errors are usually expressed as a plus-minus percentage of a particular concentration at an analytical process, or of a collected sample, whereas the actual required information for a statistical adjustment for these errors is instead the ratio of the variance of errors to the variance of "true" signals. This ratio is expected to be concentration-dependent unless the percent relative error is constant over the entire range of concentrations for a given analytical method. As such, the available analytical relative errors for each pollutant[12] cannot be compared quantitatively on a variance basis, and we cannot know the extent to which apparent differences in pollutant coefficient significances result from differences in our ability to accurately measure the respective pollutant exposure. If these factors are considered qualitatively, however, it is not surprising that H^+ is generally found to have slightly smaller significances than the other two pollutants in these analyses, in that the H^+ analytical measurement errors are thought to be higher than for British Smoke or SO_2, and limited data from six London sites in 1957 and 1958 indicate a somewhat lower site-to-site correlation for H^+ than for British Smoke.[3]

The fact that the mean of seven sites' pollutants showed higher associations with mortality than central London values would appear to indicate the advantage of using the averaged values, as opposed to a single site, i.e., errors resulting from spatial representativeness may have been reduced by averaging over the seven sites. However, the differences in strength of mortality associations are not remarkable. Furthermore, it may merely be that the 12- to 15-h lag in the mean of seven sites happens to coincide better with the actual lag time between pollution exposure and effects.

We did not attempt to discriminate the mortality effects of individual pollutants for the reasons discussed above. It is also possible that some other unmeasured pollutants, including indoor air pollutants whose levels would have increased during cold air inversions, were responsible for the mortality/pollution association. The pollutants coexisted as a pollutant mixture. For example, as has been observed in a separate experiment in London,[25] carbonaceous particulate matter was coated with acid. Furthermore, differing size distributions of British Smoke and acid aerosols during different weather conditions may have played a role in varying actual doses of toxic chemical components received by the deep lung. It was reported that, in foggy weather, the acid occurred as larger droplets, which may not be inhaled as deeply into the lungs as British Smoke.[26,27] Although the sample holder inlet for aerosol acidity sample collection was inverted to avoid collection of larger particles, the cut-off size of particles collected could have been larger than that for British Smoke, whose sampling train had additional tubing that prevents penetration of larger particles (50% cut-off diameter is approximately 4.5 μm).[28] Fine

particles as a carrier of acid is also a possibility. For example, a recent animal study[29] indicated that fine aerosol (zinc oxide) coated with sulfuric acid caused much greater response in guinea pigs than the same concentration of sulfuric acid alone. In a study in which hamsters were used,[30] the mixture of carbon particulates and sulfuric acid produced larger cytotoxic effects than sulfuric acid or carbon alone. It is, therefore, possible that acid aerosol had to be delivered on fine aerosols, which are expected to have been correlated with levels of British Smoke. If the relative strength of associations among the different pollution indices and health effects are to be evaluated quantitatively, the nature of such errors (both measurement and exposure) need to be investigated further. In particular, conducting precision studies to characterize error-to-signal variance ratios for different pollution indices are needed. Such studies may be used to estimate the bias or attenuation of any real exposure/response relationship and to adjust retrospectively for such undesirable effects. In addition, such error estimates should also be employed during the design phase of future studies to minimize these adverse statistical problems in advance.

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