ENVIRONMENTAL RESEARCH 54, 99–120 (1991)

# Associations of Daily Mortality and Air Pollution in Los Angeles County

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Received May 15, 1990

We report results of a multiple regression analysis examining associations between aggregate daily mortality counts and environmental variables in Los Angeles County, California for the period 1970 to 1979. Mortality variable included total deaths not due to accidents and violence (*M*), deaths due to cardiovascular causes (CV), and deaths due to respiratory causes (Resp). The environmental variables included five pollutants averaged over Los Angeles County—total oxidants ($O_x$), sulfur dioxide ($SO_2$), nitrogen dioxide ($NO_2$), carbon monoxide (CO), and KM (a measure of particulate optical reflectance). Also included were three meteorological variables measured at the Los Angeles International Airport—temperature (Temp), relative humidity (RH), and extinction coefficient ($B_{ext}$), the latter estimated from noontime visual range. To reduce the possibility of spurious correlations arising from the shared seasonal cycles of mortality and environmental variables, seasonal cycles were removed from the data by applying a high-pass filter. Cross-correlation functions were examined to determine the lag structure of the data prior to specifying and fitting the multiple regression models relating mortality and the environmental variables. The results demonstrated significant associations of *M* (or CV) with $O_x$ at lag 1, temperature, and $NO_2$, CO, or KM. Each of the latter three variables were strongly associated with daily mortality but also were highly correlated with one another in the high-frequency band, making it impossible to uniquely estimate their separate relationships to mortality. The results of this study show that small but significant associations exist in Los Angeles County between daily mortality and three separate environmental factors: temperature, primary motor vehicle-related pollutants (e.g., CO, KM, $NO_2$), and photochemical oxidants.

## INTRODUCTION

The well-known London fog of 1952 demonstrated convincingly the deadly potential of very high levels of urban air pollution (Martin and Bradley, 1960), particularly for the elderly and for those already suffering from severe illness. Concerted efforts toward pollution control, motivated in part by this and other early episodes of severe pollution, have led to significant declines in urban pollution levels in most developed countries over the past 20 years. As pollution levels have come down, periods of increased mortality that can be directly attributed to air pollution episodes have largely disappeared.

However, concern remains about the possibility of less obvious, but still meaningful, effects of contemporary pollution episodes on the mortality experience of sensitive members of urban populations. In recent years, analyses of long-time

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0013-9351/91 $3.00

series records from London and New York City have demonstrated small but statistically significant associations between daily mortality counts and levels of British Smoke, Coefficient of Haze, and other indicators of urban air pollution, at exposure levels more typical of those experienced today (Schimmel, 1978; Shumway *et al.,* 1983; Schwartz and Marcus, 1990). These studies have used linear regression methods in conjunction with other more elaborate time-series approaches to detect small air pollution associations against the substantial background variability in daily mortality counts.

Unfortunately, the interpretation of results from aggregate-level epidemiological studies of the health effects of air pollution may be hindered by several issues. Of particular note is the problem of inadequate data on population exposures. Pollution concentrations are usually measured only outdoors, which may be a poor surrogate for human exposure. Individual exposures will vary as a result of outdoor spatial variations, variations in penetration of pollutants indoors, and differential activity patterns of individuals. While the time-series design avoids many of the problems associated with studies of cross-sectional design (e.g., confounding by geographical covariates), there are problems unique to this design which must be dealt with analytically. In most locations, mortality, and pollution variables possess annual cycles that comprise a substantial fraction of their variance. The resulting correlation between mortality and pollution at this frequency is unlikely to arise from a casual mechanism directly linking those variables, but rather reflects the underlying influence of weather and other factors on both variables. Failure to control for seasonal cycles may lead to confounding. In addition, mortality counts often possess day-of-week cycles, and also may exhibit correlations with temperature, such as during summer heat waves. Since short-term pollution variations also may correlate with day-of-week and changes in weather, these factors, if left uncontrolled, may lead to confounding.

Beginning in the late 1950's, a series of studies have addressed the relationship between daily mortality counts and pollution levels in Los Angeles. Mills (1960) analyzed total daily deaths from respiratory and cardiac causes for the years 1956–1958 in relation to daily maximum oxidant and temperature levels. In an effort to avoid confounding due to temperature, analysis was restricted to days on which maximum temperature was less than 97°F. Seasonal variability was removed prior to analysis by reexpressing all data as deviations from monthly means. Significant associations between mortality and ozone were reported. This same data set was subsequently reanalyzed using more elaborate statistical methods by Hechter and Goldsmith (1961) after data on daily carbon monoxide concentrations was added. Care was taken to remove seasonal cycles from all data prior to analysis by subtracting one or more trigonometric function from each variable. Lagged partial cross correlations between mortality and environmental variables were examined. These cross correlations were positive but not statistically significant for lags 0, 1, and 2 in all cases. In contrast to Mills (1966), these authors concluded that there was no association between mortality and pollution.

Total daily mortality for the years 1962–1965 was analyzed in relation to oxidants, CO, and temperature using multiple regression methods (Hexter and Goldsmith, 1971). Control for seasonality was accomplished by including several sine and cosine functions of time as covariates in the regression models, along with several functions and lags of the environmental variables. Identification of the "best" model was approached through a stepwise backward elimination process. The final model included eight temperature variables and log CO. The CO coefficient was positive and significant at $P < 0.002$. The authors did not report model results for oxidants, but state that models that included oxidants instead of CO had higher mean squared errors. Mosher *et al.*, (1971) subsequently cautioned that CO should be viewed as a surrogate for primary automotive emmissions in Los Angeles, and that CO is highly correlated with other pollutants, such as $NO_2$, which were not included in the analysis.

Using modern time-series methods, Shumway *et al.* (1988) analyzed a series of data for the period 1970 to 1979 from Los Angeles. This study was unique in the sophistication of the statistical methods which were brought to bear on the problem of identifying relationships between mortality and environmental variables. The analysis was also unique in focusing primarily on long-wave periodicities in the data. This was accomplished by filtering the data to exclude periods shorter than 11 days, followed by weekly subsampling, yielding a final data set of 508 observations per variable for analysis. Thus, in contrast to previous studies which specifically excluded or controlled for seasonal cycles, this analysis specifically addressed relationships among variables in the long waves, including the seasonal cycle. The authors reported statistically significant slopes of total mortality regressed on pollution (CO, hydrocarbons, or KM), and temperature, with or without control for autocorrelation among regression residuals.

In the present paper, we report results of a new analysis of daily death counts and levels of environmental variables in Los Angeles County, CA during the period 1970–1979. We analyzed both total and cause-specific deaths reported to have occurred in L.A. County. Environmental variables included measures of gaseous and particulate pollution as well as weather-related variables. Pollution variables were available from up to eight monitoring stations throughout L.A. County. In the principal analyses reported here, we used the multiple regression model to estimate slopes relating short-term fluctuations in mortality and environmental variables. The confounding effect of seasonal cycles was eliminated by prefiltering all data prior to regression analysis. However, the robustness of results obtained by this approach was checked using alternative prefilters and by season-specific regressions. We present further supplementary analyses addressing the consistency and robustness of the regression results, including the issues of functional form, the degree of influence of statistical outliers, the consistency of the regression slopes over time, the role of day-of-week as a possible confounder, and the influence of correlation among regression residuals.

## DATA

Pollution data measured by the South Coast Air Quality Management District were obtained for the years 1970 through 1979. A subset of eight air monitoring stations in L.A. County were chosen to be used in the analysis, providing good coverage of the L.A. County air-shed (Fig. 1).

Data on five pollutants and three meteorological variables were included in the analysis. Pollution variables were chosen to cover a range of criteria pollutants of both primary and secondary nature (i.e., emitted directly or formed via reactions in the atmosphere). The pollution variables included total oxidants ($O_x$), sulfur dioxide ($SO_2$), nitrogen dioxide ($NO_2$), carbon monoxide (CO), and KM (defined below). Daily values of the variables $SO_2$, $NO_2$, and KM consisted of the 24-hr average of the hourly concentrations. For $O_x$, the maximum daily 1-hr average was chosen to represent daily exposures. This metric was chosen because it corresponds to the form of the current ambient air standard and, in addition, is highly correlated with multihour averages. Photometrically measured ozone data were routinely collected beginning only in 1979. For prior years, data were collected on total oxidants by a potassium iodide method. KM is measure of particulate loading based on optical reflectance of a sample tape (Hall, 1952) and is similar in principle to the well-known British Smoke and Coefficient of Haze measurements. KM has been shown to be closely related to the elemental carbon content of the atmosphere in Los Angeles (Conklin *et al.*, 1981). The carbon monoxide series was obtained from Dr. Robert Shumway. It represented the mean of the daily maxima measured at six sites in L.A. County (Shumway *et al.*, 1988).

Both pollution and mortality data were aggregated across L.A. County. In the case of pollution, the average of each pollutant parameter was computed across the eight stations for each study day (except for CO, as noted above). Not all pollutants were available for each station and year. Prior to computing the averages, missing values were estimated using the mean computed across available stations, along with a station-specific offset (Appendix). The daily eight-station

FIG. 1. Los Angeles County monitoring stations used in analysis.

average pollution variables computed in this way contained no missing data, except for KM, which had a short gap in 1974.

Daily meteorological data were obtained from the Los Angeles International Airport. The variables used in our analysis were mean temperature, mean relative humidity, and the extinction coefficient ($B_{\text{ext}}$). Extinction coefficient was derived from noontime visual range measurements using the Koschmeider formula, with relative humidity correction (Patterson *et al.*, 1981). $B_{\text{ext}}$ has been related both theoretically and empirically to fine particle concentrations in many locations (Özkaynak *et al.*, 1985). In Los Angeles, light extinction has been shown to significantly relate to both the sulfate and the non-sulfate fraction of the aerosol mass (Cass, 1979; White and Roberts, 1977). Thus $B_{\text{ext}}$ represented an alternative KM as an estimate of airborne fine particulate matter concentrations.

Los Angeles County death certificate data were obtained from the L.A. Department of Health Services. The death certificates were aggregated by day and by cause to produce a data set containing cause-specific death counts for each day from 1970 through 1979. The cause-specific categories included in the present analysis were total deaths not due to accidents or violence ($M$), cardiovascular deaths (CV), and deaths due to respiratory causes (Resp). The eighth revision ICD codes used to define these categories were: $M$, less than 800; CV, 390–459; Resp, 460–519. All deaths which *occurred* in Los Angeles County were included in the analysis.

## ANALYTICAL METHODS

To eliminate the possibility of confounding resulting from the shared seasonal cycles of mortality and environmental variables, a filter designed to remove seasonal cycles was applied to the data prior to model fitting. A filter introduced by Shumway *et al.* (1983) was used that consisted of subtracting a weighted 19-day moving average of each variable from the variable itself. The filter coefficients are listed in Table 1. This operation was performed on each of the 10 variables in the analysis, resulting in substantial reduction in the variance contributed by annual and other long-period cycles while leaving intact short-term, day to day variations. The filtered variables had means of zero. The filter used here achieves a smoother and more precise frequency cut than is achieved by the unweighted 15-day moving average filter that has been used in some previous studies (e.g., Schimmel, 1978). It should be noted that when a linear filter is applied to both the predictor and predicted variables prior to regression analysis, linear regression relationships among variables are preserved and can be estimated without bias. Thus, it was appropriate to apply the filter to both mortality and environmental variables.

Descriptive statistics were computed from the unfiltered and filtered data. Temporal structure in the filtered variables was examined by computing autocorrelation functions. Simple Pearson product moment correlations among the 10 variables were computed both before and after filtering. The functional form of the relationship between $M$ and each environmental variable was examined visually using condensed scatterplots of the type described by Schwartz and Marcus

TABLE 1
FILTER WEIGHTS[a]

| Lag | Weight |
|---|---|
| −9 | 0.0123081 |
| −8 | 0.0200389 |
| −7 | 0.0295593 |
| −6 | 0.0403846 |
| −5 | 0.0518010 |
| −4 | 0.0629365 |
| −3 | 0.0728599 |
| −2 | 0.0806902 |
| −1 | 0.0857055 |
| 0 | 0.0874320 |
| 1 | 0.0857055 |
| 2 | 0.0806902 |
| 3 | 0.0728599 |
| 4 | 0.0629365 |
| 5 | 0.0518010 |
| 6 | 0.0403846 |
| 7 | 0.0295593 |
| 8 | 0.0200389 |
| 9 | 0.0123081 |

[a] These weights were used to compute a moving average of each variable. The moving average was then subtracted from the variable value at lag 0 to produce the filtered time series. Filter was developed by Shumway *et al.* (1983) and weights were obtained from Robert Shumway via personal communication.

(1990). The data were condensed by first ranking in order of the environmental variable in question and then computing means of both $M$ and that variable across consecutive sets of 40 observations.

To explore the temporal structure of any associations between mortality and the environmental variables, cross-correlation functions (CCF) were computed following a prewhitening procedure, as recommended by Box and Jenkins (1976). Prewhitening consists of transforming both the input and output series using a filter designed to remove all autocorrelation in the individual variables. Only in this way can the cross correlation (correlation of two variables as a function of lag) be estimated without bias. A 365-day difference and two-term autoregressive function was applied to each unfiltered variable, yielding residuals that possessed no autocorrelations.

Following the descriptive analyses, multiple regressions were fit, with the three mortality variables as alternative "outcome" variables and the five pollutants and three meteorological parameters as potential "explanatory" variables. Initial regressions included all eight explanatory variables. An informal backward elimination procedure was then used to eliminate variables with little explanatory power from the models. Results of these reduced models represent the basic results of our analysis.

Additional analyses were performed to assess the consistency and robustness of the basic results. The degree to which outliers and influence points affected the regression for total mortality was analyzed using regression diagnostic procedures (Belsley *et al.*, 1980). The total mortality regression model was fit to data from each of the 10 years (1970–1979) to evaluate the consistency of slope estimates across years. Day-of-week effects were examined by including day-of-week dummy variables in the regression model. Sensitivity of the regression results to autocorrelation among the residuals was assessed by performing regressions that included up to a four-term autoregressive error model. We also examined the sensitivity of the results to alternative filters that varied in their degree of long-cycle removal. This latter assessment was performed in the frequency domain, which enabled construction of various high-pass filters with frequency cuts at exact points on the frequency spectrum (Shumway, 1988). Regressions were run after applying five alternative filters that selectively removed all cycles from the original data with periods greater than 7, 14, 30, 90, or 365 days. A regression was also fit with no prefiltering.

Statistical analyses were performed on an IBM mainframe and Compaq 386 computer using the Statistical Analysis System (SAS) (SAS Institute, 1982).

## RESULTS

Means and standard deviations of the 11 basic variables are presented in Table 2. Daily mortality counts trended downward slightly from 1970 to 1979, in spite of the fact that the population of L.A. County increased roughly 6% over this period. Pollution levels either remained steady or tended downward over this same period. The pollutant with the biggest percentage drop was $SO_2$, which fell about 50%.

In addition to these long-term trends, most of the variables possessed cyclic behavior with a period of 1 year. This is illustrated by time series plots of $M$, $O_x$, and Temp for the years 1973 through 1975 (Fig. 2, top panel). Mortality exhibited regular variation across seasons (seasonality), with levels highest in winter and lowest in summer. There was also a high degree of variation from day to day in the mortality counts. Most of the seven environmental variables showed some degree of seasonality, with the pattern strongest for temperature, ozone, and KM.

Figure 2 (bottom panel) shows the filtered data for the same time period. Filtered variables are referred to in this paper by appending "*_F*", e.g., *M_F* for filtered total mortality.

The autocorrelation functions of the filtered variables were examined. For the three mortality variables, autocorrelations were small in absolute terms and decreased rapidly with lag. The autocorrelations for pollution and weather variables were somewhat larger, decreased more slowly, and exhibited some cyclic behavior. This indicates that some temporal structure still remained in these variables following the filtering operation.

The Pearson correlations among the 11 unfiltered variables are presented in Table 3 (top panel). These correlations were largely dominated by the shared annual cycles of the variables. For example, $M$ and $O_x$ were negatively correlated ($r = -0.26$, $P < 0.01$) as a result of their out-of-phase annual cycles.

The correlation matrix for the filtered variables is presented in Table 3 (bottom panel). The correlations among the three mortality variables ranged from 0 for

TABLE 2

MEANS AND (STANDARD DEVIATIONS) OF 10 VARIABLES

| Year | *M* (No./day) | CV (No./day) | Resp (No./day) | $O_x$ (ppb) | $SO_2$ (ppb) | $NO_2$ (ppb) | CO (ppm) | KM | $B_{ext}$ ($km^{-1}$) | Temp (°F) | RH (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1970 | 156 (16) | 90 (12) | 8 (3) | 90 (52) | 19 (5) | 73 (29) | 11.2 (5.2) | 26 (11) | 0.40 (0.32) | 62 (5) | 71 (15) |
| 1971 | 158 (18) | 93 (13) | 9 (4) | 78 (47) | 17 (5) | 76 (29) | 9.5 (4.9) | 27 (11) | 0.37 (0.36) | 61 (7) | 71 (15) |
| 1972 | 154 (18) | 90 (13) | 8 (4) | 71 (41) | 19 (6) | 70 (28) | 8.8 (4.3) | 26 (11) | 0.34 (0.33) | 62 (7) | 72 (14) |
| 1973 | 155 (23) | 92 (15) | 9 (6) | 69 (43) | 18 (6) | 67 (25) | 7.6 (3.9) | 24 (10) | 0.38 (0.32) | 61 (5) | 73 (14) |
| 1974 | 152 (15) | 90 (11) | 7 (3) | 73 (43) | 16 (4) | 66 (27) | 7.9 (4.5) | 23 (10) | 0.34 (0.27) | 62 (6) | 75 (14) |
| 1975 | 150 (19) | 86 (14) | 8 (4) | 71 (40) | 17 (5) | 65 (30) | 8.0 (4.3) | 24 (12) | 0.37 (0.34) | 61 (6) | 74 (16) |
| 1976 | 149 (17) | 84 (12) | 9 (4) | 79 (44) | 12 (5) | 69 (28) | 7.4 (3.7) | 23 (11) | 0.30 (0.25) | 63 (6) | 72 (16) |
| 1977 | 146 (14) | 81 (11) | 8 (3) | 72 (39) | 14 (6) | 72 (33) | 6.9 (3.5) | 25 (11) | 0.36 (0.36) | 62 (5) | 76 (14) |
| 1978 | 150 (17) | 82 (12) | 9 (4) | 75 (48) | 10 (4) | 66 (26) | 6.5 (3.2) | 26 (10) | 0.30 (0.30) | 63 (6) | 76 (14) |
| 1979 | 149 (15) | 83 (11) | 9 (3) | 77 (48) | 9 (4) | 65 (25) | 6.1 (3.0) | 26 (11) | 0.27 (0.28) | 62 (7) | 71 (15) |
| All years: | 152 (18) | 87 (13) | 8 (4) | 75 (45) | 15 (6) | 69 (28) | 8.0 (4.4) | 25 (11) | 0.34 (0.32) | 62 (6) | 73 (15) |

CV_F and Resp_F to 0.77 for CV_F and *M_F*. The high correlation of the latter pair was not surprising since cardiovascular deaths comprise a large fraction of total deaths. Correlations between the mortality and pollution variables were small but positive. Note that the correlation between *M* and $O_x$ after filtering was positive ($r = 0.11$, $P < 0.01$). Small positive correlations also were seen between mortality and temperature. Relative humidity was not correlated with mortality. Correlations between pollutants were moderate to high, ranging from 0.42 to 0.88, with most less than 0.6. The highest correlations were between $NO_2$, KM, and CO, which ranged from 0.79 to 0.88. Correlations between pollution and temperature were small, ranging from $-0.16$ for $B_{ext}$_*F* to 0.19 for $O_x$_*F*. Thus, mortality and pollution were related in the plausible (positive) direction after removing annual cycles from the variables.

Cross-correlation functions between *M* and each environmental variable were examined following a prewhitening procedure as noted above. For all variables except $O_x$, the only statistically significant cross correlation with total mortality occurred at lag 0. In contrast, the only significant cross correlation between total mortality and $O_x$ occurred at lag 1 (i.e., *M* on day *k* correlated with $O_x$ on day *k*-1).

Filtered mortality was analyzed in multiple regressions on the eight filtered environmental variables. On the basis of the CCF results noted above, $O_x$ was introduced as a 1-day lag, while all other variables were introduced coincident with mortality. The first model tested included all eight variables in a regression with *M_F* (Table 4). The variable with the strongest association with mortality was temperature, with a slope of 0.595 deaths/degree *F* ($P < 0.0001$). The next most important variable was $O_x$_*F*, with a slope of 0.030 deaths/ppb ($P = 0.0005$). No other slopes were statistically significant although two (CO_*F* and $NO_2$_*F*) were nearly so. As noted in Table 3, $NO_2$_*F*, CO_*F*, and KM_*F* were highly correlated. Dropping any two of these variables from the model resulted in a positive statistically significant slope for the remaining variable.

Three alternative models were evaluated which included $O_x$_*F*, Temp_*F*, and either $NO_2$_*F*, CO_*F*, or KM_*F* (Table 5). The regression slopes for $O_x$_*F* and Temp_*F* did not change markedly in these reduced models, reinforcing the consistency of the relation of *M* with $O_x$_*F* and Temp_*F*. The model which included $NO_2$_*F* provided a slightly better fit and, for this reason, we selected this as the "basic" model for further analyses. However, because of their high correlations, CO_*F* or KM_*F* could have been substituted for $NO_2$_*F* without any substantial change in the results.

To evaluate the adequacy of the basic model, we computed diagnostic statistics recommended by Belsley *et al.* (1980) that assess model fit and influence points (not shown). There was no evidence that the linear regression was poorly fit or that the results were unduly influenced by a small number of extreme data points. The distribution of standardized regression residuals was examined; it appeared to be normally distributed, both visually and by statistical test. There was no excess of extreme values over that which would be expected due to chance alone in a data set of this size. Diagonal values of the "hat" matrix, which measure the degree of leverage that the independent variables have on the vector of slope estimates as a function of date, were also unremarkable.

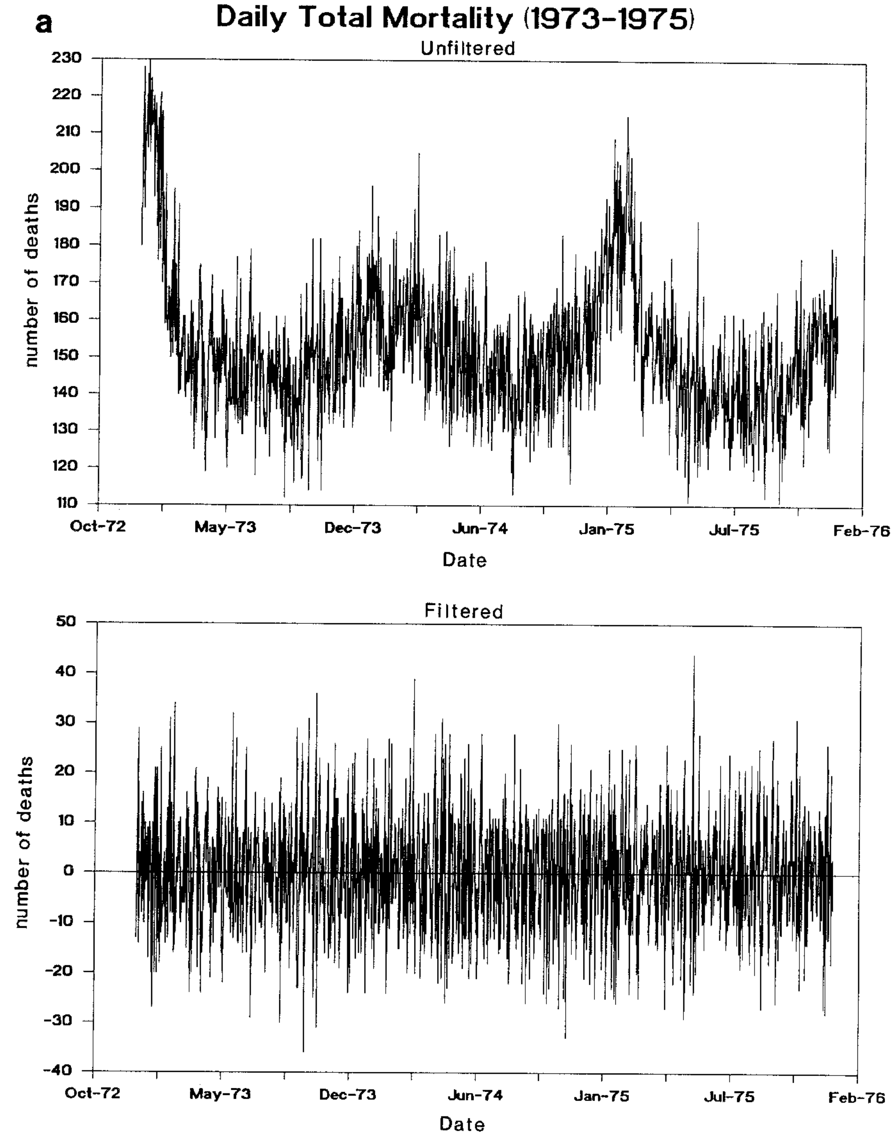

FIG. 2. 1973–1975 daily data for (a) total mortality, unfiltered and filtered, (b) oxidants, unfiltered and filtered, (c) temperature, unfiltered and filtered.

The regression model we utilized assumed a linear functional form relating mortality and the explanatory variables. Condensed scatterplots of the type described by Schwartz and Marcus (1990) were examined to evaluate the linearity of the relationships between *M_F* and each of the three variables included in the basic model. No evidence for nonlinearity was detected in the scatterpots.

The multiple regression approach described above was repeated for filtered cardiovascular (CV_*F*) and respiratory (Resp_*F*) mortality. Initial "exhaustive" models were fit that included the entire set of seven explanatory variables. Re-

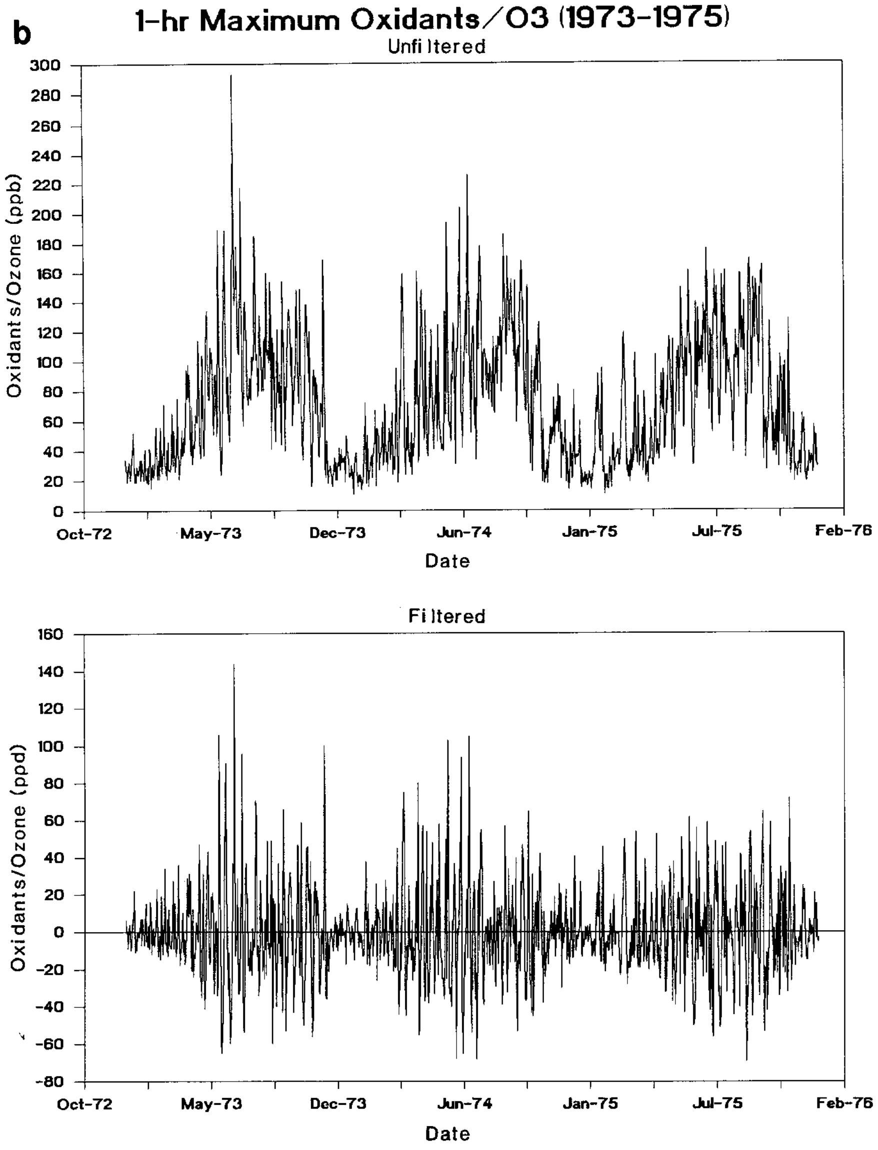

FIG. 2.—*Continued*

duced models were then run that included lag 1 $O_x$_*F*, $NO_2$_*F*, and Temp_*F*. The results of the reduced model regressions for CV_*F* and Resp_*F* are shown in Table 6. In the case of cardiovascular deaths, the results were similar to those observed for *M_F*. $O_x$_*F*, $NO_2$_*F*, and Temp_*F* were all strongly associated with CV_*F*. The results for Resp_*F* were quite unique. The only significant variable in this regression model was Temp_*F*.

In a second set of supplemental regressions, we assessed the stability of the slope estimates for the basic total mortality model from year to year (Table 7). As

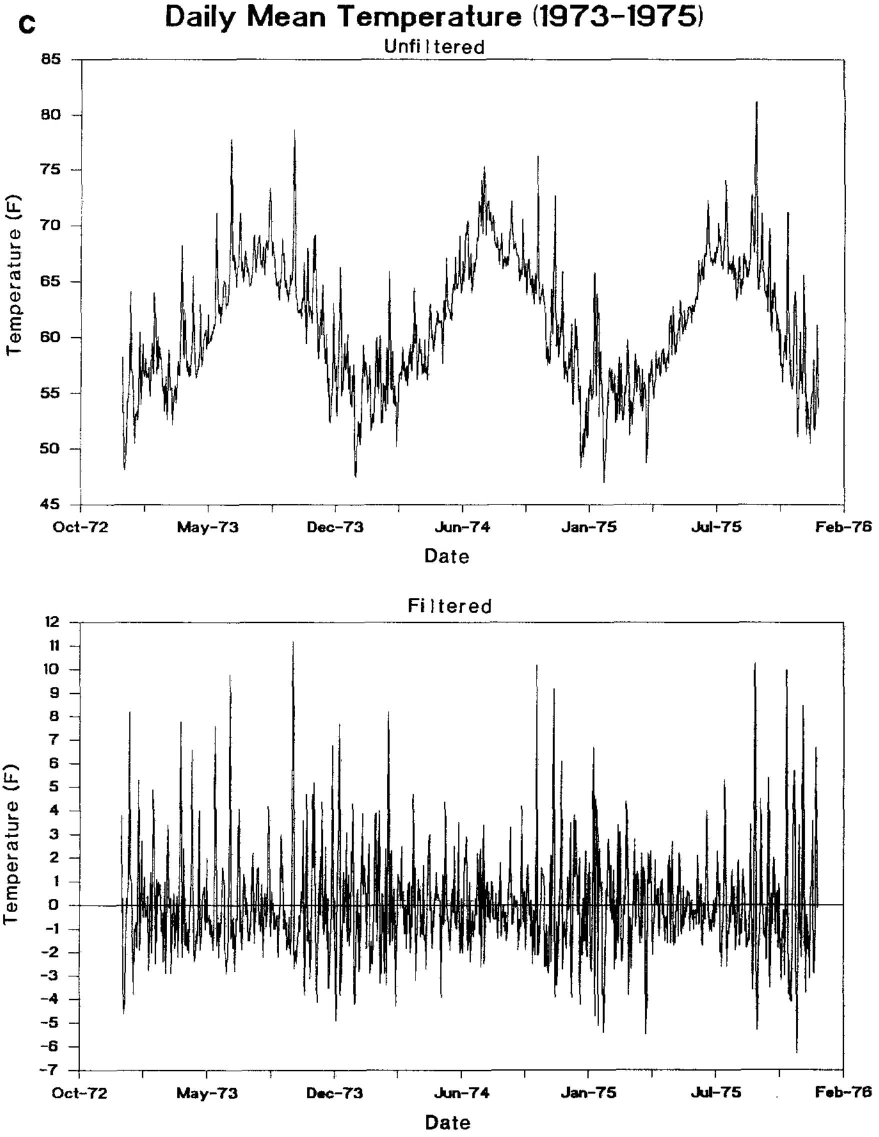

FIG. 2.—*Continued*

expected, the annual slopes were, in general, smaller in relation to their standard errors (i.e., lower *t* statistics) than was the case for the overall regression. Statistical variation increased as the sample size went down. However, the slopes for $O_x$_*F*, $NO_2$_*F*, and Temp_*F* were nearly always positive and often were statistically significant. Further, there were no obvious trends in these slopes over time.

Another issue we examined in supplemental regression analyses was the influence of day-of-week as a possible confounder of the association between pollution and mortality. Since there are regular day-of-week variations in both mortality and pollution that are to some extent unrelated to any hypothesized causal model,

TABLE 3

Correlations among 10 Unfiltered Variables

| | $M$ | CV | Resp | $O_x$ | $SO_2$ | CO | $NO_2$ | KM | $B_{ext}$ | Temp | RH |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $M$ | — | | | | | | | | | | |
| CV | 0.86 | — | | | | | | | | | |
| Resp | 0.52 | 0.33 | — | | | | | | | | |
| $O_x$ | −0.26 | −0.26 | −0.22 | — | | | | | | | |
| $SO_2$ | 0.12 | 0.19 | −0.03* | 0.39 | — | | | | | | |
| CO | 0.28 | 0.28 | 0.12 | −0.30 | 0.17 | — | | | | | |
| $NO_2$ | 0.18 | 0.17 | 0.06 | 0.29 | 0.64 | 0.21 | — | | | | |
| KM | 0.30 | 0.28 | 0.16 | 0.01* | 0.47 | 0.36 | 0.85 | — | | | |
| $B_{ext}$ | 0.03* | 0.02* | −0.02* | 0.36 | 0.50 | 0.07 | 0.56 | 0.43 | — | | |
| Temp | −0.39 | −0.39 | −0.27 | 0.64 | 0.12 | −0.29 | 0.01* | −0.19 | 0.01* | — | |
| RH | −0.21 | −0.21 | −0.11 | 0.23 | 0.08 | −0.21 | 0.02* | −0.14 | 0.33 | 0.02* | — |
| | $M\_F$ | CV_$F$ | Resp_$F$ | $O_x\_F$ | $SO_2\_F$ | CO_$F$ | $NO_2\_F$ | KM_$F$ | $B_{ext}\_F$ | Temp_$F$ | RH_$F$ |
| $M\_F$ | — | | | | | | | | | | |
| CV_$F$ | 0.77 | — | | | | | | | | | |
| Resp_$F$ | 0.23 | 0.00* | — | | | | | | | | |
| $O_x\_F$ | 0.11 | 0.11 | 0.00* | — | | | | | | | |
| $SO_2\_F$ | 0.11 | 0.11 | 0.01* | 0.56 | — | | | | | | |
| CO_$F$ | 0.13 | 0.12 | 0.03* | 0.43 | 0.57 | — | | | | | |
| $NO_2\_F$ | 0.13 | 0.12 | 0.01* | 0.58 | 0.76 | 0.79 | — | | | | |
| KM_$F$ | 0.11 | 0.11 | 0.02* | 0.47 | 0.68 | 0.82 | 0.88 | — | | | |
| $B_{ext}\_F$ | 0.05 | 0.03 | 0.00* | 0.42 | 0.48 | 0.27 | 0.51 | 0.45 | — | | |
| Temp_$F$ | 0.13 | 0.12 | 0.07 | 0.19 | 0.11 | 0.25 | 0.10 | 0.08 | −0.16 | — | |
| RH_$F$ | −0.02* | −0.02* | −0.02* | 0.08 | 0.20 | −0.03* | 0.22 | 0.14 | 0.37 | −0.48 | — |

*Note.* All correlations are significant at $P < .01$ except those indicated by an asterisk.

TABLE 4

EXHAUSTIVE MULTIPLE REGRESSION MODEL FOR TOTAL MORTALITY[a]

$N = 3591$
$R^2 = 0.036$

| Regressor variable | Slope | SE (slope) | $P$ |
|---|---|---|---|
| Intercept | −0.006 | 0.197 | 0.97 |
| Lag 1 $O_x$ | 0.030 | 0.009 | 0.0005 |
| $SO_2$ | 0.005 | 0.088 | 0.95 |
| CO | 0.287 | 0.156 | 0.07 |
| $NO_2$ | 0.040 | 0.026 | 0.12 |
| KM | −0.063 | 0.069 | 0.36 |
| $B_{ext}$ | 0.454 | 0.966 | 0.64 |
| Temp | 0.595 | 0.105 | <0.0001 |
| RH | 0.014 | 0.023 | 0.55 |

*Note.* All variables filtered.

[a] Units given in Table 2.

the regression slopes for pollution might be biased if such variations were not accounted for. We supplemented the basic three-variable regression model for *M_F* by adding day-of-week indicator variables. The only indicator variable whose slope reached statistical significance was that for Monday; the positive sign indicated death reports were highest on Monday. However, there was very little change in the regression slopes for $NO_2$*_F*, $O_x$*_F* or Temp*_F* when the indicator variables were present in the model, indicating that the basic model we have employed was not confounded by day-of-week effects.

When analyzing time series data using regression methods, there is concern that the regression residuals may be temporally correlated, thus violating a basic assumption of the regression model and typically leading to a positive bias in the estimates of the regression slope standard deviations. Prefiltering the data with a high-pass filter should have reduced this problem, but may not have eliminated it entirely. To examine the effects of correlated errors in our data set, we refitted the basic regression model while simultaneously fitting a four-term autoregressive error model to the residuals. The regression slopes and *P*-values for the variables of interest—$O_x$*_F*, $NO_2$*_F*, and Temp*_F*—did not change markedly.

The regression analyses described above all were performed following a filtering operation designed to remove potentially confounding long-period cycles from the data. It was of interest to test how the regression results would change if alternative filters were applied. Specifically, we were interested in evaluating the changes in regression slope estimates and their standard errors that would result following varying degrees of long-cycle removal, from no removal, to removal of all cycles with periods longer than 7 days. This analysis was performed using the basic regression model involving *M* regressed on lag 1 $O_x$, $NO_2$, and Temp. The results (Table 8) showed that the regression estimates for $O_x$, $NO_2$, and Temp were relatively stable for filters with cut points at cyclic periods of 7, 15, 30, and 90 days, and were consistent with the results reported above in Table 5. The regression results changed markedly when periods up to and including the annual

TABLE 5

REDUCED MODEL REGRESSION RESULTS FOR TOTAL MORTALITY[a]

(a) $NO_2$

$N = 3634$
$R^2 = 0.036$

| Regressor variable | Slope | SE (slope) | $P$ |
|---|---|---|---|
| Intercept | −0.006 | 0.196 | 0.98 |
| Lag 1 $O_x$ | 0.030 | 0.008 | 0.0002 |
| $NO_2$ | 0.054 | 0.010 | <0.0001 |
| Temp | 0.578 | 0.085 | <0.0001 |

(b) CO

$N = 3633$
$R^2 = 0.034$

| Regressor variable | Slope | SE (slope) | $P$ |
|---|---|---|---|
| Intercept | −0.005 | 0.196 | 0.98 |
| Lag 1 $O_x$ | 0.038 | 0.008 | <0.0001 |
| CO | 0.399 | 0.082 | <0.0001 |
| Temp | 0.504 | 0.087 | <0.0001 |

(c) KM

$N = 3590$
$R^2 = 0.034$

| Regressor variable | Slope | SE (slope) | $P$ |
|---|---|---|---|
| Intercept | −0.008 | 0.197 | 0.97 |
| Lag 1 $O_x$ | 0.036 | 0.008 | <0.0001 |
| KM | 0.127 | 0.029 | <0.0001 |
| Temp | 0.615 | 0.086 | <0.0001 |

*Note.* All variables filtered.

[a] Units given in Table 2.

cycle remained in the data, and when regression was performed with no filtering. Those regressions were dominated by the annual cycle. Both $NO_2$ and daily deaths followed cycles which peaked in winter, while the cycles for oxidants and temperature peaked in summer. The latter two regressions in Table 8 reflected these correlated cycles, and were markedly different than the previous results. These results illustrate the importance of controlling for seasonal cycles in regression analysis using time series data. More importantly, they demonstrate that our results were not an artifact of a particular prefiltering method.

## DISCUSSION

Using a 10-year record of daily data from Los Angeles County, we have demonstrated associations between short-term variations in total mortality (excluding accidents and suicides) and pollution, controlling for temperature. These results were obtained by fitting multiple linear regression models with mortality as the outcome variable and up to eight environmental variables as regressors. A parsimonious three-variable model ($NO_2$, 1-day lagged $O_x$, and temperature) explained

TABLE 6

BASIC MULTIPLE REGRESSION RESULTS FOR CARDIOVASCULAR AND RESPIRATORY MORTALITY[a]

(a) CV

$N = 3634$
$R^2 = 0.026$

| Regressor variable | Slope | SE (slope) | $P$ |
|---|---|---|---|
| Intercept | 0.003 | 0.149 | 0.99 |
| Lag 1 $O_x$ | 0.023 | 0.006 | <0.0001 |
| $NO_2$ | 0.039 | 0.008 | <0.0001 |
| Temp | 0.368 | 0.065 | <0.0001 |

(b) Resp

$N = 3591$
$R^2 = 0.008$

| Regressor variable | Slope | SE (slope) | $P$ |
|---|---|---|---|
| Intercept | −0.002 | 0.046 | 0.96 |
| Lag 1 $O_x$ | 0.002 | 0.012 | 0.26 |
| $NO_2$ | −0.001 | 0.002 | 0.67 |
| Temp | 0.085 | 0.020 | <0.0001 |

*Note.* All variables filtered.
[a] Units given in Table 2.

4% of the short-term variation in total mortality. Temperature and $O_x$ had the strongest association with mortality in these models, followed by $NO_2$, CO, or KM (which were difficult to separate due to their high correlation). Systematic evaluation of the adequacy of the linear regression model detected no violations of the basic assumption of independent, normally distributed errors. Annual regressions demonstrated the consistency of the results over time.

Ozone is a well-established acute pulmonary toxicant. Brief exposures of humans to ozone levels which occur frequently in Los Angeles (i.e., 120–200 ppb)

TABLE 7

SLOPES AND $R^2$ FROM ANNUAL REGRESSIONS FOR TOTAL MORTALITY[a]

| Year | Lag 1 $O_x$ | $NO_2$ | Temp | $R^2$ |
|---|---|---|---|---|
| 1970 | 0.031 | 0.078[b] | 0.745[b] | .06 |
| 1971 | 0.006 | 0.106[b] | 0.644[b] | .06 |
| 1972 | 0.039 | 0.023 | 0.557[b] | .02 |
| 1973 | 0.026 | 0.026 | 0.752[b] | .03 |
| 1974 | 0.025 | 0.084[b] | 0.619 | .03 |
| 1975 | 0.047 | −0.002 | 0.443 | .02 |
| 1976 | 0.023 | 0.041 | 0.657[b] | .03 |
| 1977 | 0.024 | 0.048 | 0.536 | .02 |
| 1978 | 0.007 | 0.099[b] | 0.306 | .04 |
| 1979 | 0.071[b] | 0.038 | 0.546[b] | .06 |

*Note.* All variables filtered.
[a] Units given in Table 2.
[b] $P < 0.05$.

TABLE 8

REGRESSION RESULTS FOR TOTAL MORTALITY USING ALTERNATIVE FILTERS[a]

| Cycle periods removed (days) | $R^2$ | Variable | Slope | SE | $P$ |
|---|---|---|---|---|---|
| >7 | .01 | Lag 1 $O_x$ | 0.033 | 0.012 | 0.005 |
| | | $NO_2$ | 0.058 | 0.017 | 0.0005 |
| | | Temp | 0.438 | 0.144 | 0.002 |
| >15 | .03 | Lag 1 $O_x$ | 0.030 | 0.009 | 0.0007 |
| | | $NO_2$ | 0.057 | 0.012 | <0.0001 |
| | | Temp | 0.576 | 0.097 | <0.0001 |
| >30 | .04 | Lag 1 $O_x$ | 0.029 | 0.008 | 0.0002 |
| | | $NO_2$ | 0.054 | 0.010 | <0.0001 |
| | | Temp | 0.606 | 0.080 | <0.0001 |
| >90 | .04 | Lag 1 $O_x$ | 0.031 | 0.008 | <0.0001 |
| | | $NO_2$ | 0.046 | 0.010 | <0.0001 |
| | | Temp | 0.420 | 0.073 | <0.0001 |
| >365 | .18 | Lag 1 $O_x$ | −0.037 | 0.008 | <0.0001 |
| | | $NO_2$ | 0.134 | 0.010 | <0.0001 |
| | | Temp | −0.874 | 0.057 | <0.0001 |
| None | .19 | Lag 1 $O_x$ | −0.033 | 0.008 | <0.0001 |
| | | $NO_2$ | 0.131 | 0.010 | <0.0001 |
| | | Temp | −0.934 | 0.056 | <0.0001 |

[a] Units given in Table 2.

result in increased lung permeability and reactivity, decreased forced expiratory lung volumes and flows, and the development of an inflammatory response (Lippmann, 1989). However, there are very few past data demonstrating a relationship between mortality and ozone. Analyzing 3 years of data from the 1950's, Mills reported a significant relationship (Mills, 1960). However, a later and more thorough analysis of this same data set detected no associations between mortality and pollution (Hechter and Goldsmith, 1961). Mahoney (1970) showed that age-, sex-, and income-adjusted mortality rates increased monotonically with oxidant concentrations across five regions of L.A. County with differing oxidant levels. If real, these cross-sectional results could represent a mix of both acute and chronic effects of ozone exposure (Evans *et al.*, 1984).

Based on ozone's known acute pulmonary effects, one can speculate about a possible mechanism linking ozone with mortality. It is possible that exposure to high ozone levels would increase pulmonary permeability and hence induce pulmonary edema in an individual with a compromised left ventricle. Or, the full spectrum of acute reactions might lead to a life-threatening pulmonary compromise in persons with severe chronic lung disease.

The results of the cross-correlation analysis suggested that the associations of $NO_2$ and Temp with $M$ were immediate, while the $O_x$ association involved a 1-day lag. This result is consistent with the hypothesis that late-afternoon peaks or multihour elevated oxidant levels result in excess mortality which appears the following day. While this is the first study to report a lagged relationship between mortality and $O_x$, there have been several studies demonstrating delayed ozone effects on morbidity. Bates and Sizto (1989) have shown in southern Ontario that hospital admissions for respiratory diseases are related to 1- or 2-day lagged $O_3$. Pulmonary function declines resulting from ambient ozone exposures have been related to previous as well as same-day exposures (Spektor *et al.*, 1990). Controlled exposures of healthy human volunteers to low-level ozone concentrations result in a pulmonary inflammatory response measured 18 hr later (Seltzer *et al.*, 1986; Koren *et al.*, 1989). While the relevance of these findings to the mortality associations we have demonstrated is uncertain, they do establish that delayed health effects occur following ambient level ozone exposures.

$NO_2$_*F*, CO_*F*, and KM_*F* were highly correlated in this data set. High correlation between covariates in a regression setting leads to instability (i.e., high variance) in the corresponding slope estimates. $NO_2$ is a quasiprimary pollutant formed rapidly from NO emitted directly by motor vehicles and other combustion sources. CO is a primary pollutant emitted predominantly by motor vehicles in the Los Angeles basin. KM is a measure of particulate opacity which has been shown in Los Angeles to be related closely to elemental carbon concentrations (Conklin *et al.*, 1981). All of these variables may reflect primary mobile source emissions. $NO_2$_*F* was slightly more correlated with total mortality than were CO_*F* or KM_*F* in the present study, and thus was included in the basic model used for analyzing model robustness and consistency.

Insight into the possible roles of these three pollutants in acute mortality may be sought from a review of known acute toxicity. $NO_2$ exposure causes acute pulmonary toxic responses similar to those produced by ozone, but at higher than ambient concentrations. There have been no previous studies implicating $NO_2$ as a causative agent in acute mortality. KM is a specialized measure of particulate matter concentration for which no experimental health data are available. Two similar particulate measures, British Smoke (BS) and Coefficient of Haze (COH), have been related to daily mortality in London and New York City, respectively (Schwartz and Marcus, 1990; Schimmel, 1978). It has been suggested that in London, BS may represent a surrogate for sulfuric acid aerosol concentrations (Thurston *et al.*, 1989). This is not likely to be the case in Los Angeles, where $SO_2$ emissions are much lower. In a recent analysis of Los Angeles data, Shumway *et al.* (1988) reported that long-wave variations in KM (among other variables) correlated with long-wave mortality. Because seasonal cycles would have dominated these correlations, they are unlikely to reflect acute casual relationships among the variables. The health effects of CO exposure are well established. Exposure to CO reduces the level and biological availability of oxygen in the blood, thus putting a strain on tissues with high oxygen demand, such as the heart. A large body of data exists demonstrating that CO exposure results in cardiac abnormalities in people with chronic cardiovascular disease (e.g., Allred *et al.*, 1989). People with chronic lung disease are also particularly susceptible to CO effects, since their lungs are already less efficient at oxygenating the blood (CARB, 1989). A previous time series study in Los Angeles observed a strong acute relationship between CO and mortality (Hexter and Goldsmith, 1971).

Consistent multiple regression results were obtained for total deaths and deaths due to cardiovascular causes. In contrast to these results, no significant pollution slopes were observed for respiratory deaths. Note that cardiovascular deaths comprised a substantial fraction of total daily deaths (87/152, or 57%, on average), while respiratory death counts were much lower (8/day). The few numbers of deaths due to respiratory causes may have limited our ability to detect small pollution associations. Assuming Poisson variability in mortality counts, it follows that the ratio of the error standard deviation to the mean number of deaths increases as the mean number of deaths decreases. This phenomenon results in a higher coefficient of variation in daily respiratory deaths than in cardiovascular deaths (50% versus 15%). Furthermore, deaths associated with pollution exposures would not necessarily be classified as respiratory. A variety of advanced disease states might predispose individuals to heightened susceptibility to premature death due to air pollution exposure; cause-of-death determinations by attending physicians would reflect this variability. As MacMahon and Pugh (1970) have noted, during the London Fog of 1952, all major causes of death except auto accidents were elevated. These authors suggest that total deaths may be the most appropriate outcome measure in studies of health effects of noxious agents.

We filtered all variables to be used in the regression analysis in order to remove seasonal cycles from the data. This use of high-pass prefiltering was chosen to avoid spurious correlation due to shared seasonality. However, prefiltering reduces the variability in the data, thus reducing statistical power. Also, with filtering there is a risk of removing more than just the assumed spurious correlation. That is, a true casual relationship may be involved to some extent in the long cycles that have been removed. In spite of these potential difficulties, we chose to filter our data prior to performing regression analyses, in order to avoid analyzing biologically meaningless seasonal correlations among variables. As Hexter and Goldsmith (1971) have noted, the seasonal nature of mortality results in its being correlated with such variables as the price of hogs in Quebec and maximum daily temperature in Buenos Aires. The sensitivity analysis demonstrated that the fitted regression coefficients were relatively insensitive to a range of high-pass filters with different cut-points, as long as the annual cycle was removed. This was especially evident for $O_x$. In the full range of frequencies up to but not including the annual cycle, $O_x$ possessed a statistically significant positive association with daily mortality. When the annual cycle was included, or in the absence of prefiltering, the association became strongly negative.

Prefiltering has been used to remove seasonal cycles prior to analyzing mortality/air pollution relationships in New York City (Schimmel, 1978), London (Shumway *et al.*, 1983; Schwartz and Marcus, 1990), and Los Angeles (Hechter and Goldsmith, 1961). Other methods for controlling seasonality are available and have been used as well. Cyclic variables, such as sine waves or daily temperature, can be included in the multiple regression models to capture the seasonal component of mortality (Hexter and Goldsmith, 1971). Alternatively, data can be analyzed separately for each season (Lebowitz, 1973) or after seasonal or monthly means have been subtracted (Mills, 1960). The latter method is really a special case of prefiltering (i.e., a monthly unweighted moving average).

As a further check on the robustness of results in the present study, the unfiltered data were reanalyzed separately for the winter (December–February) and summer (June–August) seasons, using the basic three-variable regression model. In the winter regression, only temperature was a significant predictor of mortality. In the summer regression, lag 1 $O_x$, $NO_2$, and temperature all were significantly associated with mortality. The regression slope for lag 1 $O_x$ (0.032 deaths/ppb) was very similar to the slope obtained using prefiltering (0.030 deaths/ppb). These results provide further confirmation of the robustness of our basic results.

As noted above, a recent paper by Shumway *et al.* (1988) has reported an alternative analysis of Los Angeles County mortality data. The data set used in that analysis was very similar to the present one; it covered the period 1970–1979 and included a similar set of mortality, pollution, and weather variables. However, the two analyses differ markedly in their approaches to data analysis. Shumway and colleagues analyzed principally long-period (low-frequency) fluctuations in the data, while our approach yielded an analysis of short-period (high-frequency) fluctuations. Statistically, the approach used by Shumway and colleagues can be viewed as being complimentary to the one we and others have employed. Shumway *et al.* demonstrated that in the lower frequencies, mortality and environmental variables are all highly correlated with one another. CO, hydrocarbons, and KM had the highest correlations with mortality. However, we believe that our approach, in removing the influence of annual cycles, yields results that are more likely to represent biologically meaningful relationships among the variables analyzed.

It is important to emphasize that, although statistically significant associations have been detected among mortality and environmental variables, one can never conclude with complete confidence that such associations are casual based on results from an observational study. Support for a casual hypothesis may be sought by assessing evidence for both internal and external validity (Kleinbaum *et al.*, 1982). Measures of internal validity include the strength of the association, evidence for a dose response, and temporal plausibility. External validity assessment involves comparison of results with other studies and evaluation of biological plausibility. We have evaluated several measures of internal and external validity in our analyses and discussion. None of these evaluations have yielded evidence that contradicts the causal hypothesis. Thus we tentatively conclude that there is a reasonable likelihood that the results we have obtained do represent causal relationships among the variables analyzed. It is noteworthy that in every large mortality series examined thus far (in London, New York, and Los Angeles), statistically significant associations of pollution and temperature with mortality have been demonstrated (Schimmel, 1978; Shumway *et al.*, 1983; Schwartz and Marcus, 1990). This consistency across different locations and investigators lends further support to the notion that day to day fluctuations in both pollution and temperature have a real impact on daily mortality.

Future studies should be directed at providing insight into the mechanisms underlying a possible causal relationship between pollution exposures and mortality. Of particular interest is the question of whether the putative pollution effects consist mainly of 1- or 2-day hastening of deaths that would have occurred anyway, or some other phenomenon. Analyses directed at age-specific death counts might shed light on this issue.

## APPENDIX

Method used to fill in missing pollution data ($\hat{X}ijk$) for station $i$, on day $j$, in year $k$.

$$\hat{X}ijk = \overline{X}.jk \frac{\overline{X}i.k}{\overline{X}..k}$$

where,

$\overline{X}.jk$ = daily mean of other stations present on day $j$.
$\overline{X}i.k$ = annual mean for station $i$ and year $k$.
$\overline{X}..k$ = annual mean across stations for all stations present on day $j$.

## ACKNOWLEDGMENTS

This work was supported by EPA Cooperative Agreements No. CR-812667-02-0 and CR-813526-01-2. We acknowledge the contributions of Peter Matthews (Purdue University) and Bettina Burbank for assistance in developing the statistical methodology, Paul Switzer (Stanford University) for data set development, Paul Gaffney for computer work, and Janet Garrison and Cheryl Brandwein for their diligent help in preparing the manuscript. We also thank R. H. Shumway (University of California—Davis) for providing the carbon monoxide series used in this analysis. Those data were compiled by R. H. Shumway and A. S. Azari under contract A5-152-33 with the California Air Resources Board. Finally, we are grateful to the anonymous reviewers for their helpful comments.

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