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Short-Term Effects of Air Pollution on Daily Mortality in Athens: A Time-Series Analysis

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Touloumi G (Department of Hygiene and Epidemiology, University of Athens Medical School, 75 Mikras Asias Street, 11527 Athens [Goudi], Greece), Pocock S J, Katsouyanni K and Trichopoulos D. Short-term effects of air pollution on daily mortality in Athens: a time-series analysis. *International Journal of Epidemiology* 1994; **23:** 957–967.

Background. Athens has a serious air pollution problem which became evident in the early 1970s. Studies for the years 1975—1982 have indicated a positive association of sulphur dioxide (SO_2) with total daily mortality. Since 1983 the pollution profile in Athens has gradually changed but the levels of smoke, SO_2 and carbon monoxide (CO) remain relatively high.

Methods. The association of air pollution with daily all-cause mortality in Athens for the years 1984–1988 was investigated using daily values of SO_2, smoke and CO. Autoregressive models with log-transformed daily mortality as the dependent variable, were used to adjust for temperature and relative humidity (both lagged by 1 day), year, season and day of week, as well as for serial correlations in mortality.

Results. Graphic analysis revealed non-linear monotonically increasing relationships between total mortality and SO_2, smoke and CO, with steeper exposure-response slopes at lower air pollution levels. Air pollution data lagged by 1 day had the strongest association with daily mortality. In three separate autoregression models for $\log(SO_2)$, log(smoke) and log(CO) the regression coefficients for each were highly statistically significant ($P < 0.001$). Further multiple regression modelling showed that SO_2 and smoke are both independent predictors of daily mortality, though to a lesser extent than temperature and relative humidity. The inclusion of CO in the model did not further improve the prediction of daily mortality. The magnitude of association is small, for instance, a 10% reduction in smoke is estimated to decrease daily mortality by 0.75% (95% confidence interval [CI] : 0.51–0.99). However, it cannot be accounted for by climatic and seasonal effects, so that a causal influence of air pollution on daily mortality seems plausible.

Conclusions. These findings suggest that current air pollution levels in Athens (and many other industrialized cities) may be responsible for substantial numbers of premature deaths, and hence remain an important public health issue.

It is generally accepted that severe pollution episodes, such as in Donora, Pennsylvania in 1948 or London in 1952, can cause substantial excess mortality particularly among the elderly and in those already suffering from severe illness.[1] Over a period of several decades, efforts towards pollution control have led to marked reductions in air pollution levels in most developed countries. However, recent studies indicate that air pollution may have health effects even at levels lower than the air quality standards set by national and international organizations.[2-4]

In recent years, analyses of long time-series records have been used to explore the short-term effects of air pollution on daily mortality or morbidity. The time series is an appropriate design which avoids the confounding problems of geographical (ecologic) comparisons. However, the seasonal trends observed in mortality and pollution time series, as well as the presence of serial autocorrelation, can generate problems in analysis and interpretation. Such studies also need to take account of confounding factors such as meteorological variables and secular trends. In this paper, we illustrate a methodology for analysing such time series with data from Athens on the relation of daily total mortality to air pollution measures.

Athens has a serious air pollution problem which became evident in the early 1970s.[5] Hatzakis *et al.*[6] investigated the mortality effects of sulphur dioxide (SO_2) and smoke air pollution in Athens from 1975 to 1982, and found a statistically significant positive association of SO_2 with total daily mortality. Subsequently it was shown that this excess mortality was mainly due to respiratory causes among the elderly.[7] Since 1983 the pollution profile in Athens has gradually changed towards a more pronounced photochemical

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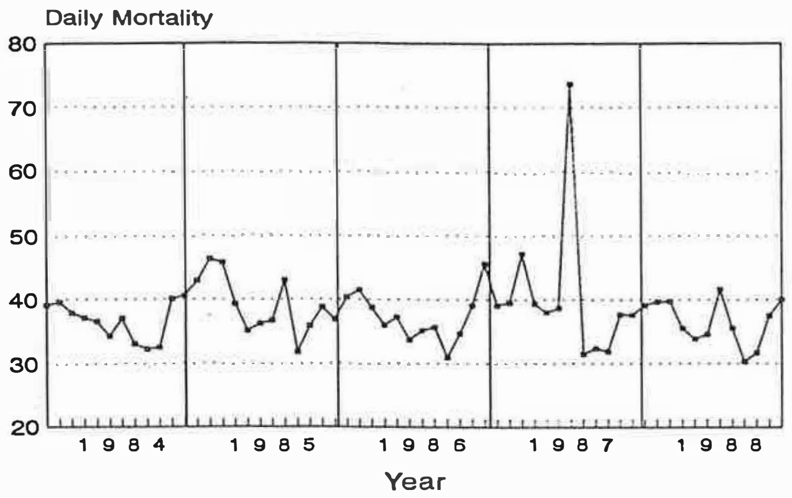


FIGURE 1 *Mean daily mortality in Athens by month, 1984–1988*

component, although the levels of smoke, SO_2 and carbon monoxide (CO) remain relatively high.[8]

Therefore, the study of adverse health effects of air pollution in Athens remains highly relevant. The present investigation assesses the short-term health effects of air pollution indices (black smoke, SO_2 and CO) on mortality from 1984 to 1988. The analytical approach we adopted enables control for confounding, adjustment for autocorrelation, estimation of lagged effects and dose-response curves, and exploration of the separate effect of each pollutant.

MATERIALS

Mortality

Mortality data for 1984–1988 were assembled from the Athens Town Registry and the registries of all contiguous towns. All deaths and burials occurring in these towns must be recorded in the town registries. The mortality data used here are the daily total number of deaths from all causes recorded in these registries. This daily mortality count has a daily mean of 37.8 deaths (standard deviation = 12.0).

In Figure 1 the mean daily total mortality during each month of the study period is presented. There is a seasonal cycle with a reliable peak in the winter months and a more erratic shorter-term peak during summer months. In July 1987 mortality more than doubled when a heat wave stuck Greece. The extreme temperatures as well as their possible synergistic effect with air pollution have been studied elsewhere.[9] This month is excluded from analysis as an obvious climatic outlier.

Meteorological Data

Mean daily temperature (°C) and relative humidity (%), recorded by the Institute of Meteorology and Physics of the Atmospheric Environment located on a hill in the centre of town, were used to summarize meteorological conditions.[10] The climate in Athens is typically Mediterranean. The minimum daily temperature rarely falls below 0°C during the winter while in the summer temperatures above 30°C are sometimes recorded.

Pollution Data

Sulphur dioxide, black smoke and CO were used as air pollution indicators. These pollutants are routinely monitored by a network of stations operated by the Ministry of the Environment, Planning and Public Works. Figure 2 shows the geographical locations of the air quality monitoring stations on a map of the Athens area. Sulphur dioxide is measured by the pulsed fluorescence method, smoke by the British smoke filter method and CO using an infra-red non-dispersive method. The values of SO_2 and smoke are 24-hour averages in $\mu g/m^3$, while for CO they are the maximum 8-hour moving average in mg/m^3. In the present study smoke measurements are taken from five monitoring stations located in Pireaus, Drapetsona, Ipourgio, Patision and Rentis, while for SO_2 the two stations used are located in Patision and Pireaus and for CO two stations in Patision and Botanicos. Note that all three pollutants are measured in the centre of Athens (Patision), where the highest levels of each pollutant are observed. The values of smoke and CO in Patision often exceed the WHO air quality guidelines (about 60% and 42% of days for smoke and CO respectively). The correlations between the daily measurements at different stations are reasonably strong (Pearson r between 0.6 and 0.8).

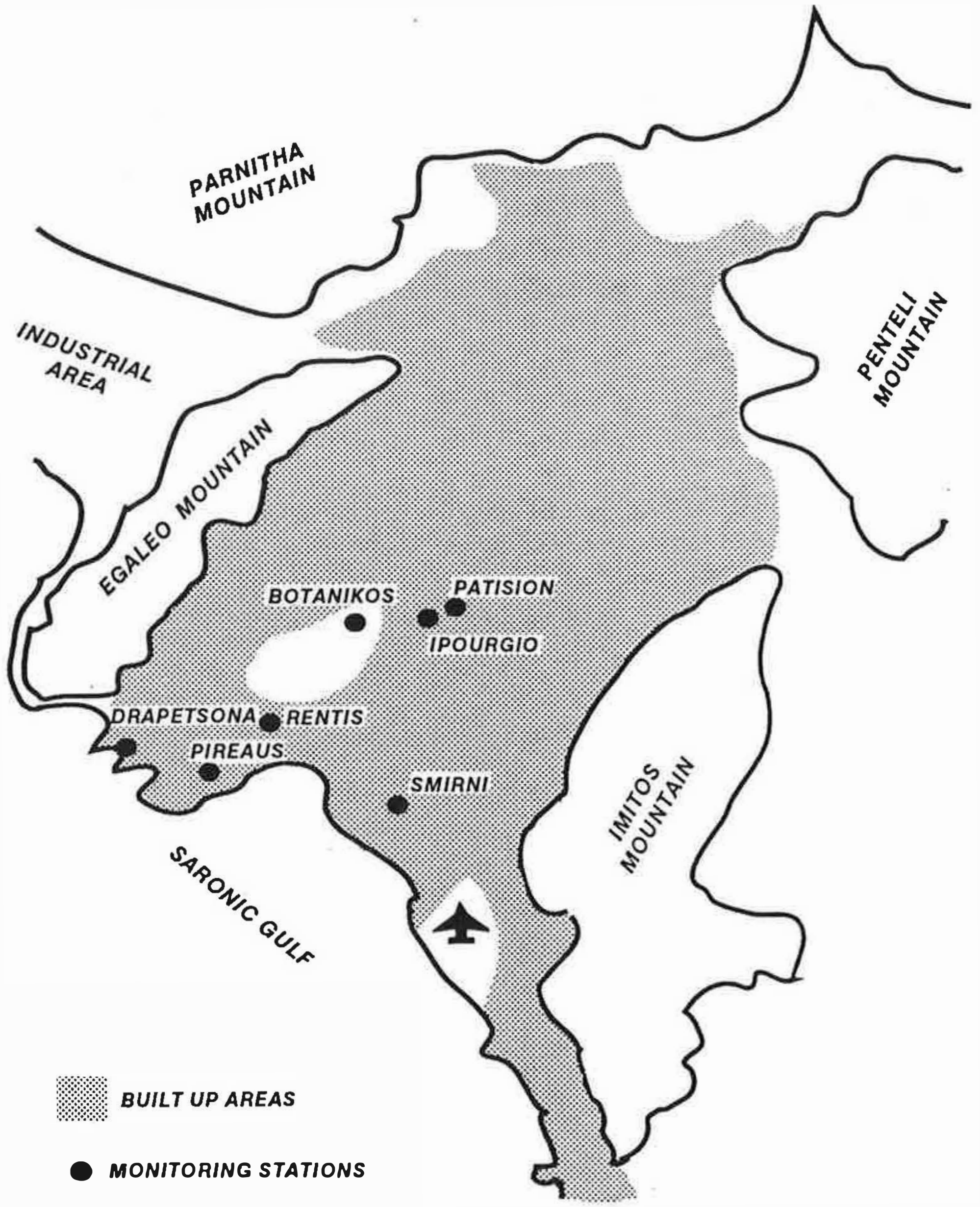


FIGURE 2 *Map of the Athens area with air quality stations*

For each pollutant, average daily values over all the monitoring stations were estimated. However, some values for particular dates in the pollution series were missing: SO_2 had missing values for 1.9% of days at Patision and 17.4% at Pireaus; smoke had missing values for 3.6% of days at Patision. 3.5% at Ipourgio, 9.3% at Pireaus, 10.8% at Rentis and 22.9% at Drapetsona; CO had missing values for 2.3% of days at Patision and 9.0% at Botanikos. For days when a pollutant had just one station's missing values, values

TABLE 1 *Levels of air pollution in Athens 1984–1988. Descriptive statistics*

Pollutant	Statistic	1984	1985	1986	1987	1988	1984–1988
SO_2[a]	Mean	38.48	37.21	38.04	38.77	71.46	44.92
($\mu g/m^3$)	SD[b]	21.90	21.48	25.21	20.70	40.34	30.16
Average over	Median	33.25	33.96	29.70	34.50	63.00	37.00
2 stations	No.[c]	363	354	351	357	365	1790
SO_2	Mean	54.63	47.49	46.75	55.25	82.45	57.47
Patision	SD	35.73	27.50	37.29	32.16	48.78	39.27
($\mu g/m^3$)	Median	47.00	42.00	36.00	51.00	74.00	49.00
	No.	363	354	351	357	365	1790
Smoke	Mean	98.57	92.11	68.77	83.67	73.62	82.93
($\mu g/m^3$)	SD	45.58	53.97	35.53	43.57	36.46	44.70
Average over	Median	89.80	76.00	58.20	69.49	64.80	70.38
5 stations	No.	309	331	344	349	351	1684
Smoke	Mean	191.73	172.22	139.24	164.59	147.14	162.68
Patision	SD	93.94	96.71	73.98	88.01	76.42	88.03
($\mu g/m^3$)	Median	190.00	160.00	126.00	143.00	140.00	150.00
	No.	346	344	362	355	356	1763
CO[d]	Mean	6.92	6.22	5.25	5.80	4.63	5.76
(mg/m^3)	SD	2.99	2.99	2.55	3.10	2.13	2.88
Average over	Median	6.7	5.9	4.75	5.10	4.38	5.25
2 stations	No.	359	343	361	356	364	1783
CO	Mean	11.85	10.80	8.68	9.54	7.43	9.57
Patision	SD	5.03	4.80	4.08	4.59	3.08	4.62
(mg/m^3)	Median	11.60	9.70	8.20	8.75	7.40	8.90
	No.	359	343	361	356	364	1783

[a] Sulphur dioxide.
[b] Standard deviation.
[c] Number of days with measurements.
[d] Carbon monoxide.

were substituted using a regression model based on the remaining stations' values.

Table 1 shows for each pollutant, the daily mean, standard deviation (SD) and median in each calendar year a) averaged over all the monitoring stations and b) for Patision in the centre of town. Subsequent analyses use the averages over all stations. Figure 3 shows monthly mean values of the three pollutants averaged over all the stations. There are seasonal trends for all three pollutants peaking in late autumn. Also the mean values of SO_2 were elevated in 1988.

Statistical Methods

As a first step, daily values of each of the five pollution and climatic variables were plotted against daily mortality to exhibit the shape of any dose-response relations, as described by Schwartz and Marcus.[11] For daily mortality, the geometric mean and log transformations are used throughout as standard procedures to stabilize the variance of such a Poisson random variable. For each variable the data were summarized by ranking the days according to the variable's magnitude. They were then formed in ranked groups of 20 days, for which means of both mortality and that variable were computed. If non-linearity was evident then appropriate transformations of that variable were employed.

Multiple regression models were then fitted, with log-transformed total daily mortality as the dependent variable. Potential explanatory variables were appropriate functions of daily pollutant levels, mean temperature and mean relative humidity as well as indicator variables for season, year (to control for any long-term trend), day of week and holidays. The three pollutants were, at this step, considered in three separate models because of their substantial correlation. The contribution of each additional variable in the model fit was assessed by an appropriate F-test. Two alternative ways were used to control for seasonal trend in mortality which were assumed to be the same in all years: a

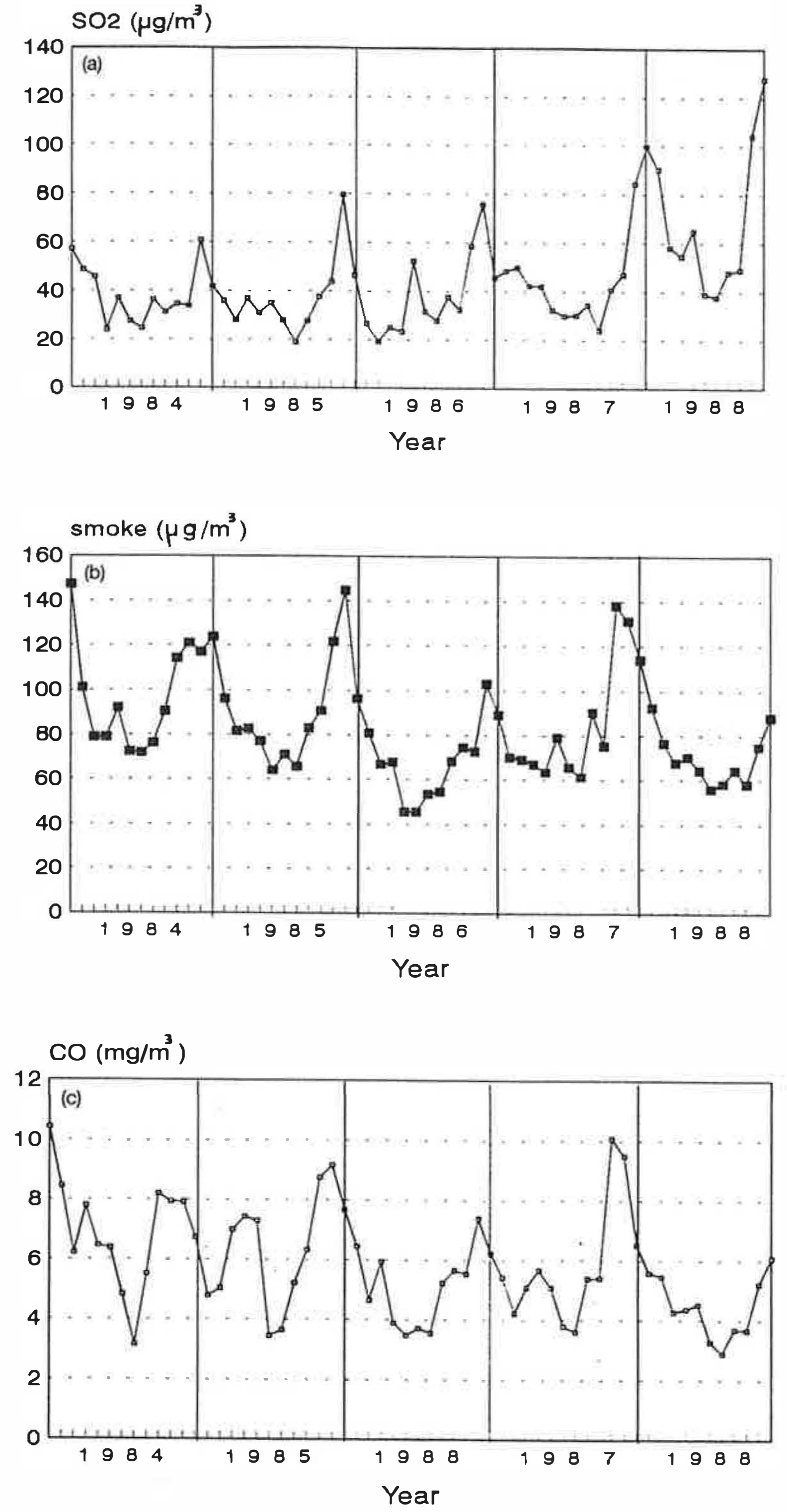
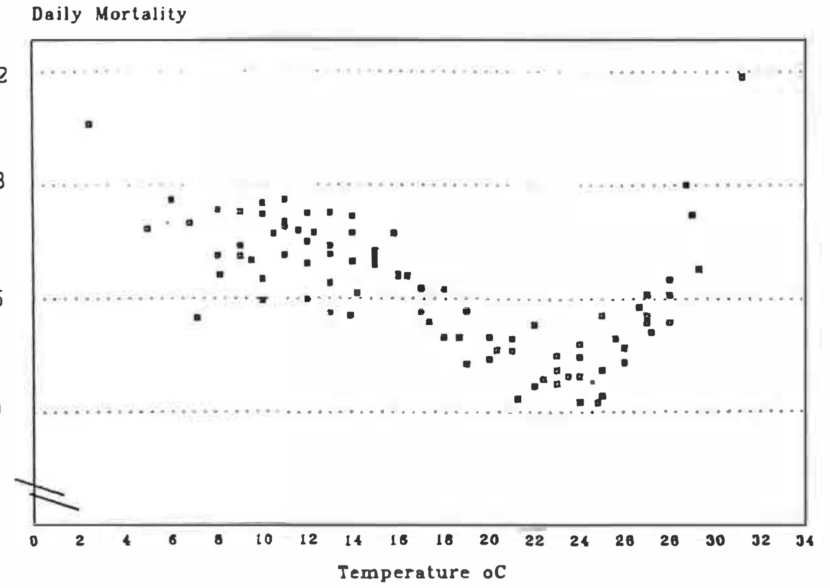


FIGURE 3 *Air pollution levels in Athens 1984–1988: (a) sulphur dioxide = mean values of two monitoring stations, (b) black smoke = mean values of five monitoring stations, (c) carbon monoxide = mean values of two monitoring stations*



Each point represents the mean of 20 ranked observations in increasing order of temperature, geometric mean daily mortality is plotted on a $\log_e$ scale

FIGURE 4 *Relation between daily mortality and daily temperature*

4-level nominal variable for calendar season, and a sinusoid curve of 1-year period. The effect of up to 7 days lagged values of air pollutants on daily mortality were also examined.

The use of ordinary least squares regression models on daily times series is likely to result in serially correlated errors. This violates the assumption of independent errors, and leads to a downward bias in the estimated standard deviations of regression coefficients. For this reason the residuals of the final ordinary least squares regressions were tested by the Durbin-Watson test of independence[12] and autoregressive models were then specified when necessary.

The underlying model for the dependent variable M (log of total daily mortality) is $M = X\beta + U$ where the disturbance U is assumed to be generated by a stationary autoregressive process of order p. That is:

$$U_t = e_t - a_1u_{t-1} - a_2u_{t-2} - \ldots\ldots - a_pu_{t-p}$$

where e_t is a sequence of independently and identically distributed random variables each with mean zero and variance σ^2 and a_i are the autoregressive parameters.

The generalized least squares method was used to estimate the regression parameters.[13] The Yule-Walker (Y-W) method described in Gallant and Goebel.[14] also called the two-step full transform method.[15] was applied to estimate the variance-covariance matrix of the disturbance vector $U = (u_1, u_2, \ldots, u_n)$. The plot of mean square error (MSE) versus the order p of the model as well as the Akaikes's (AIC) and Schwartz's Bayesian (SBC) Information Criteria[16,17] were examined to specify the required order p of the autoregressive process so as to obtain a parsimonious model.

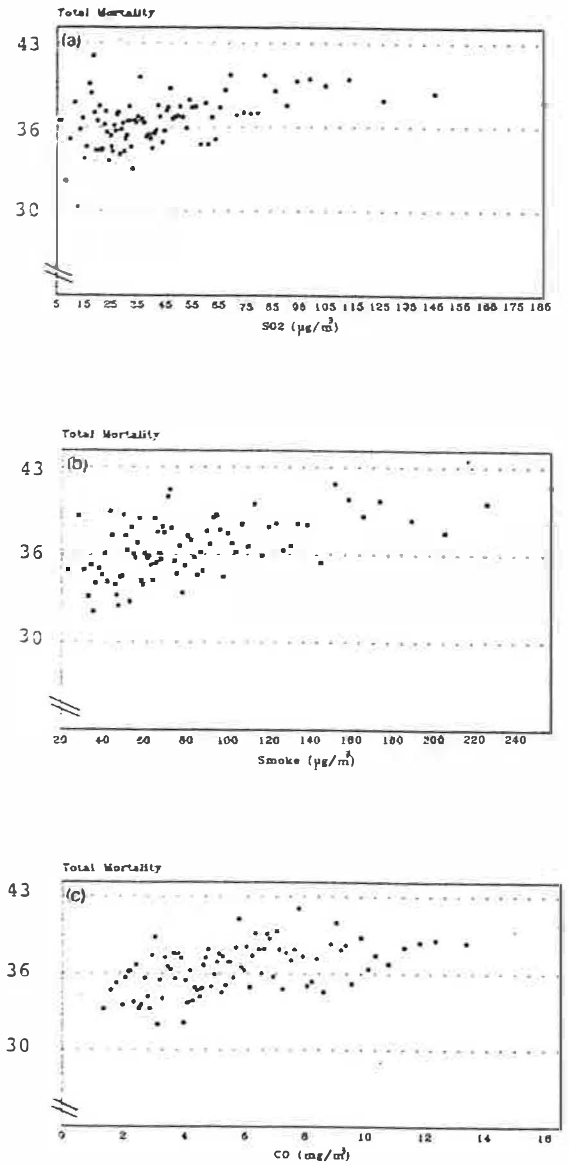
Autoregressive models using more than one pollution indicator as covariates were lastly fitted in order to assess whether one or more pollutants were independently predictive associates of daily mortality.

RESULTS

Preliminary Analysis

Figure 4 shows the scatter plot of daily mortality versus mean daily temperature. The relation appears J-shaped with lowest mortality when average daily temperature is about 23°C. The increase in mortality in hot weather is steeper than that for cold weather, and so it seems appropriate to model the mortality-temperature relation by a double quadratic curve with nadir at 23°C as follows.

Two complementary variables, h (hot) and c (cold) were therefore constructed to represent average daily temperature (T). So $h = 0$ if $T \leq 23°C$ and $T-23$ otherwise, while $c = 23-T$ if $T \leq 23°C$ and 0 otherwise. A regression model with log daily mortality as dependent variable and h^2 and c^2 as independent variables was fitted. This model gave a better fit than alternatives such as linear, simple quadratic or double quadratic with nadir at other temperatures.



Each point represents the mean of 20 ranked observations in increasing order of pollutant. geometric mean daily mortality is plotted on a $\log_e$ scale

FIGURE 5 *Relation between daily mortality and three air pollutants: (a) sulphur dioxide, (b) smoke, (c) carbon monoxide*

A similar plot of daily mortality against daily relative humidity showed a weak quadratic relationship between the two variables with the minimum number of deaths when relative humidity was about 53–55%. Scatter plots of daily mortality versus each air pollutant (Figure 5) revealed positive and curvilinear

TABLE 2 *Parameter estimates for pollution variables from ordinary least squares (OLS) and Yule-Walker (Y-W) autoregression*

	Pollutant[a]					
	SO_2[b]		Smoke		CO[c]	
	OLS	Y-W	OLS	Y-W	OLS	Y-W
Regression coefficient	0.060	0.062	0.076	0.071	0.060	0.053
Standard error	0.009	0.010	0.011	0.010	0.010	0.011
P-value	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Means of squared error	0.035	0.034	0.035	0.036	0.034	0.035
Estimated decrease in mortality for every 10% decrease in pollutant[d]		0.65%		0.75%		0.55%
95% confidence interval[e]		0.45–0.85		0.51–0.99		0.32–0.78

[a] Log transformations of all three pollutants at lag = 1 day, adjusted for temperature, humidity, year, season and day of week.

[b] Sulphur dioxide.

[c] Carbon monoxide.

[d] Derivation of % mortality reduction (1–r)*100 where r = exp (b* ln (0.9)).

[e] Derivation of its 95% confidence interval: {1–exp [log r ± (1.96 * ln (0.9) * se (b))]} * 100.

relationships, each with a reduced slope at higher pollution levels. A logarithmic transformation linearized the relation of each pollutant with mortality. All pollutants are positively correlated, the strongest association being between smoke and CO (r = 0.79). Daily temperature is inversely associated with air pollution (e.g. r = –0.29 with smoke) and with relative humidity (r = –0.62).

Multiple Regression Models

For each pollutant in turn, a sequence of ordinary least squares regression models were fitted, using a forward stepwise approach, in order to identify the subset of variables (including the pollutant of interest) which best predict total mortality. For example, a model with SO_2 and temperature (fitted as a double quadratic curve), explains 16% of the variance of log daily mortality variations. The additional contribution of humidity fitted as a simple quadratic curve is small but also significant. Further contributions of the indicator variables 'season', 'year', and 'day of week' were each significant but the indicator variable 'holidays' was not. It should be noted that the magnitude of the regression coefficient of each pollutant at lag = 1 was substantially higher compared to that at lag = 0, and hence the former has been adopted. However, when the pollutants' values were lagged by more than 1 day their regression coefficients became progressively smaller. In summary, the best models identified by this approach are those which include one of the 1-day lagged log-transformed pollutants (SO_2, smoke or CO), hot^2 and cold^2 lagged by 1 day, linear and quadratic terms of relative humidity lagged by 1 day and indicator variables of 'year', 'season' and 'day of week'.

In these ordinary least squares regression models the residual values were positively autocorrelated, as indicated by the Durbin-West (D-W) test ranges from 1.70 to 1.73. To allow for correlated errors, the above three best regression models were refitted using a second-order autoregressive error model for the residuals. The additional autoregressive coefficients for models containing more than two terms were small.

Table 2 shows the estimated regression coefficient from ordinary least squares (OLS) as well as from second-order autoregressive Yule-Walker (Y-W) models for each of the three pollutants: SO_2, smoke and CO. The error variances are reduced slightly by using the autoregressive error terms, while the standard error of the regression coefficients becomes slightly bigger, as expected. The coefficients for all three pollutants are highly significant and of similar magnitudes.

Since both mortality and pollutant are on a log scale, the coefficient can be re-expressed in proportionate mortality terms as follows: a 10% reduction in SO_2, smoke and CO is estimated to decrease mortality by 0.65%, 0.75% and 0.55% respectively with 95% confidence intervals (0.45–0.85%), (0.51–0.99%) and (0.32–0.78%) respectively.

TABLE 3 *Time series Yule-Walker (Y-W) autoregressions: Model for sulphur dioxide (SO_2) (lagged by 1 day) and other covariates*

	Y-W regression coefficient	Standard error	*P*
Constant	3.5333	0.1158	0.0001
Log (SO_2)	0.0622	0.0098	0.0001
Hot^2	0.0057	0.0007	0.0001
Cold^2	0.0005	0.0001	0.0001
Relative humidity	–0.0105	0.0036	0.0036
(Relative humidity)^2	0.0001	0.0000	0.0010
Season			
Winter	0.0744	0.0196	0.0001
Spring	0.1016	0.0163	0.0001
Summer	–0.0029	0.0188	0.8765
Year			
1984	0.0457	0.0188	0.0153
1985	0.0961	0.0190	0.0001
1986	0.0668	0.0191	0.0005
1987	0.0530	0.0193	0.0060
Days of week			
Tuesday	–0.0353	0.0156	0.0237
Wednesday	–0.0285	0.0158	0.0713
Thursday	–0.0317	0.0165	0.0546
Friday	–0.0453	0.0165	0.0062
Saturday	–0.0915	0.0158	0.0001
Sunday	–0.0573	0.0155	0.0002

Reference category for season—Autumn; for year—1988; and for day—Monday.

Table 3 shows more detailed results for the autoregressive model with SO_2. Among the other covariates, temperature is the most important predictor of daily mortality. The larger coefficient for hot weather confirms the more pronounced effect of hot compared to cold weather on increasing mortality.

Higher adjusted daily mortality is observed in both winter and spring. Presumably the excess in winter, even after allowing for temperature the day before, reflects a longer-term impact of the 'cold season' on any given day's mortality rate. Essentially similar results were derived when an alternative sinusoidal curve approach was used to allow for seasonal trends. The use of the sinusoid curve reduced sightly the levels of autocorrelation.

The significant contribution of 'day of week' is mainly due to an excess of mortality on Monday and a deficit during weekends.

The regression models for each pollutant have been repeated for each year separately. Despite the reduced power for each 1-year analysis due to the smaller number of observations, the regression coefficients were always positive for all three pollutants. For SO_2 they were also statistically significant, while for black smoke and CO they were statistically significant in all years except one.

TABLE 4 *Simultaneous modelling of two or more pollutants: Summary of several autoregressive models*

	Regression coefficient (SE)[a]	*P*
Model 1		
SO_2[b]	0.043 (0.014)	0.0019
Smoke	0.038 (0.016)	0.182
Model 2		
SO_2	0.057 (0.013)	0.0001
CO[c]	0.013 (0.014)	0.3823
Model 3		
Smoke	0.063 (0.017)	0.0003
CO	0.015 (0.017)	0.3661
Model 4		
SO_2	0.042 (0.014)	0.0032
Smoke	0.036 (0.019)	0.0581
CO	0.006 (0.018)	0.7404

[a] Standard error.

[b] Sulphur dioxide.

[c] Carbon monoxide.

Separating the Pollutants' Effects

Autoregression models including several combinations of the pollutants were fitted (Table 4). When SO_2 and smoke were included in the same model, their slopes although substantially reduced, were both significant (Model 1). Their interaction term was not significant, but synergistic effects would be difficult to detect due to the small numbers of observations at the extreme values. It appears that there are significant and independent effects of SO_2 and smoke on mortality, but CO does not seem to improve further the prediction of mortality. However, one should recall the high correlation between smoke and CO.

DISCUSSION

Public health measures have led to a substantial reduction in air pollution levels, particularly in countries where the problem has been severe for years. However, recently there has been widespread discussion about the shorter-term health effects of lower levels of air pollution (i.e. lower than the air quality standards set by national and international organizations).

In Athens, using a 5-year series of daily data, we have indicated significant positive associations between total daily mortality and air pollution. Multiple regression analyses were applied to allow for the confounding effects of several variables, such as temperature, relative humidity, season, year and day of week. In addition, autoregressive error terms were included in the models to allow for serial correlation in daily mortality. The results demonstrate that the observed relationship between daily mortality and air pollution cannot be explained by associated climatic conditions or seasonal patterns.

The curvilinear relations found for smoke, SO_2 and CO indicate a steeper slope at lower pollution levels than at higher levels. This is consistent with previously published results. Mazumdar *et al.*[18] in London using data from 1958 to 1972 found higher regression coefficients for smoke in the later years, when pollution was reduced somewhat. Ostro[19] reported a higher coefficient for smoke levels below 150 $\mu g/m^3$ than above 150 $\mu g/m^3$. Schwartz and Marcus[11] also found similar curvilinear relations for smoke and SO_2 in their analysis of the London winters of 1958–1972, while Shumway *et al.*[20] found curvilinear relations for CO, hydrocarbons and particulates in Los Angeles data.

Despite the colinearity problems which might arise from the substantial correlation among the pollutants, joint autoregressions including more than one pollutant showed that SO_2 and smoke have independent associations with mortality. The effect of CO became non-significant when SO_2 or smoke were included in the models indicating that it may be a surrogate marker of other pollutants. For instance, the source of CO (traffic) is also a major source of smoke.

In the present study the daily mortality from all causes and for all ages was used as the outcome. Since several studies have shown that the main health effects of air pollution concern the respiratory system and, to a lesser extent, the circulatory system,[21–24] total mortality is not the most specific outcome measure of the health effects of air pollution. In Athens, daily data on cause of death and age over the whole study period were not available and therefore the investigation of air pollution and cause, as well as age-specific mortality was impossible. However, one should note that total mortality is reliably reported, while there is often substantial error in recording cause of death. Furthermore, following an initial analysis which showed that total daily mortality for a previous period (1975–1982) increased with air pollution levels in Athens,[6] an in-depth analysis of the causes of death[7] demonstrated that the increase was mainly due to deaths from respiratory causes. Also, several recent papers have shown that air pollution affects total daily mortality and indicate comparable results with the present paper.[3,25]

Any predictive model for air pollution effects on mortality is dependent on the validity of the environmental measurements. The available data do not provide detailed geographical distributions, especially for SO_2 and CO and do not directly assess the total population exposure in Athens. In the analysis we tried to derive, as much as possible, citywide average levels of air pollution. An alternative 'population-weighted city average' was impossible due to insufficient data, but we are confident that the averages used are highly correlated with this unmeasurable ideal. Goldstein *et al.*[26] discuss the methodological problems associated with such choices of pollution summary measures. Overall, in using any such imperfect measure of pollution exposure we can expect that estimates of effect on mortality will therefore be diluted.

In several studies throughout the world significant relationships between air pollution levels and mortality or morbidity have been found consistently.[1–4,6,7,9,11,18–32] Thus, several authors[3,4,6,11,20,28,32] found significant effects of air pollution on mortality in Steubenville, Marseilles and Lyons, Athens, London, Los Angeles and Dublin respectively. Other workers[2,21,24,31] found significant effects of air pollution on hospital emergency admissions or lung function indices in different parts of the world. However, some of the above studies[6,11,21,24,31,32] are older and represent higher levels of air pollution and/or different air pollutant mixtures. In addition all studies except three,[2,4,6] are realized in Northern Europe or in the US where the emissions and the climate are substantially different from those in Mediterranean areas.

The challenge presented in current research is to determine whether the relatively low air pollution levels observed in many cities today have an effect on mortality. In the present study we have tried to control as effectively as possible for most of the known factors which could otherwise lead to artefactual relationships. The observed relationships cannot be attributed to confounding by climatic variables, autocorrelations or seasonal trends. Although one cannot exclude the possibility of some unmeasured confounder it seems plausible to infer that relatively low-level air pollution in Athens (and elsewhere) has a small but real effect on mortality.

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