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Air pollution and mortality in Madrid, Spain: a time-series analysis

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Abstract Objective: To assess the relationship, if any, between air pollutant (sulfur dioxide and total suspended particulate) levels and mortality in the city of Madrid during the period 1986–1992, controlling for weather, season, and influenza epidemics. **Methods:** Daily death counts were obtained from the Regional Mortality Registry. Pollution data were supplied by the Municipal Monitoring Network. Time-series analysis methodology was used to assess the link between non-accidental as well as circulatory- and respiratory-disease mortality, on the one hand, and mean daily concentrations of SO_2 and total suspended particulate (TSP), on the other. Multivariate autoregressive integrated moving-average (ARIMA) models were used to adjust for season, temperature, relative humidity, and influenza. A sensitivity analysis was run to assess the robustness of the estimators. **Results:** Graphical analysis revealed a linear relationship between mortality and TSP. The relationship was logarithmic in the case of SO_2. TSP lagged 1 day and SO_2 lagged 3 days with an independent effect on mortality. This relationship was produced without the detection of a minimal threshold in emission values. **Conclusions:** These results support the hypothesis of an association between pollution levels and mortality between 1986–1992 in Madrid. Additional measures designed to reduce pollution levels without compromising thermal comfort should be implemented.

Key words Pollution · Mortality · ARIMA · Time series · Weather

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Introduction

Economic and technological growth have brought about a continual improvement in life expectancy, yet the use of fossil fuels as the economy's energy base has resulted in a mix of pollutants being emitted into the atmosphere as by-products of the combustion process.

Fossil-fuel consumption has increased 4-fold in the past 40 years [2], and this increase has in turn led to the appearance of periods of excess mortality linked to extremely high levels of air pollution (Mosa Valley [10], Donora [38], and London [25]). Legislation has successively lowered maximal permissible pollution levels, thereby achieving a considerable drop in pollutant emissions and, by extension, preventing episodic situations such as those described above. Nonetheless, subsequent studies have revealed a link between relatively low concentrations of pollutants and urban morbidity-mortality patterns [17, 19, 23, 26, 35]. The use of epidemiology studies rather than purely toxicology studies to detect this type of relationship has the advantage of reproducing the global environmental conditions to which populations are subject. However, it also has the disadvantage entailed in the difficulty of distinguishing between the effects of the various pollutants [8, 16, 30] and other external health-related atmospheric factors such as temperature, humidity, and wind [9, 27, 43]. To complicate matters even further, a correlation exists between atmospheric variables and pollutant concentrations [15, 18, 21, 22].

A possible way of trying to pinpoint the independent effect of each of the atmospheric variables vis-à-vis pollution is to conduct studies in areas with different concentrations of pollutants and specific climatic variables [8, 26, 41]. This study sought to analyze the association between SO_2- and total suspended particulate (TSP)-related air pollution and mortality in the city of Madrid, controlling for season, calendar year, temperature, and humidity. Madrid has a mesothermal Mediterranean type of climate characterized by cold winters,

hot summers, and, as a consequence, a marked seasonal fluctuation in ambient temperatures [31].

Methods

Mortality

Daily death counts for the period January 1986–December 1992 were taken from the Regional Mortality Register. To ensure the accuracy of the cause-effect relationship, all deaths of residents occurring outside the Madrid city limits were excluded. Daily deaths were analyzed by the following causes (all numbers refer to ICD-9 codes): non-accidental deaths (1–799), cardiovascular deaths (390–459), and respiratory deaths (460–519). Sex- and age-specific (65 years and over) analyses were also performed.

Atmospheric variables

Data were furnished by the National Meteorological Institute on the basis of readings at the Madrid-Retiro Observatory. The mean daily temperature was computed using daily recorded at 12 midnight, 6 a.m., 1 p.m., and 6 p.m. Dry- and wet-thermometer temperatures and barometric pressure were used to calculate the relative humidity at 7 a.m. The temperature was measured in tenths of a degree Celsius (°C).

Earlier papers had identified a V-shaped mortality-temperature relationship [27] in Madrid with a comfort temperature value in a maximal temperature of 30.8 °C. Thus, for the control of temperature effects, two series were created, Tcold and Twarm, defined as follows:

$$\text{Tcold} = 30.8 - \text{T if T} < 30.8$$

$$\text{Twarm} = \text{T} - 30.8 \text{ if T} > 30.8,$$

where T is the daily maximal temperature. The series was therefore divided into two periods: winter (November through March) and summer (June through August).

Air pollution

In an earlier cluster analysis of air pollution in Madrid [14], two areas showing a similar TSP and SO_2 pollution pattern were detected. Data from two representative stations in the municipal air pollution monitoring grid were used per pollutant, namely, stations 1 and 6 in the case of TSP and stations 1 and 18 in the case of SO_2. TSP was measured by attenuation of β-radiation and SO_2 was determined by ultraviolet fluorescence absorption. Daily mean SO_2 and TSP values, expressed in $\mu g/m^3$, were included in the analysis.

Descriptive statistics (mean, standard error) were obtained for each variable. A test for normality was performed. Where indicated by the plots, independent variable transformations (e.g., logarithmic, square-root) were studied. By spectral analysis, deterministic components (trend, season, and cycle) were identified. For the removal of these components, two methods were used: differentiation (simple or seasonal) or modeling by means of circular functions.

Scatterplots were used to detect the functional form of the relationship between the respective atmospheric variables and mortality. As a first step, pollution variables were sorted in ascending order. Equal intervals were obtained and the mean daily mortality for each interval was plotted. Similar plots were obtained for temperature and humidity. For investigation of the association between SO_2, TSP, and temperature, scatterplots were likewise employed.

The Box-Jenkins prewhitening method was used to detect significant lags and weights of the transfer function. Univariate models were constructed for the independent variables so as to obtain the goodness of fit required to yield white-noise residuals. Models constructed for each independent variable were then applied to the daily death series to obtain the residuals. The cross-correlation function (CCF) between the two sets of residuals was calculated.

To rule out the possibility of temperature's being a confounder for the effects of TSP and SO_2, an alternative approach was used. Mortality and pollution series were prewhitened separately. Independent univariate models were fitted to each series, white-noise residuals were obtained, and the CCF between these residuals was calculated. The transfer functions yielded by this method were similar to those obtained via the Box-Jenkins prewhitening method. Both annual and seasonal analyses were performed, and identical analyses were run for the pollution variables vis-à-vis temperature.

To control for the confounding effect of other independent variables, multivariate autoregressive integrated moving-average (ARIMA) models were constructed using a forward procedure. Variables and their respective lags were included in the model one by one, and all variables failing to attain significance were excluded. Once the final model had been obtained, residuals were analyzed and their autocorrelation function (ACF) and partial autocorrelation function (PACF) were used to identify the presence of structures that could bias estimator values. The autoregressive (AR) and moving-average (MA) components of the residuals were included in the final model. The model was considered complete when the ACF and PACF indicated white-noise residuals and the Box-Ljung Portomanteau test failed to reach significance at a lag greater than the span of seasonal components. Analysis was carried out using the SPSSWIN (Trends) 6.1, BMDP386 (1T, 2T) for extended memory, and SAS (ETS module) computer software packages.

Results

Annual and seasonal (winter-summer) descriptive statistics for pollutants (TSP, SO_2) are set out in Table 1. Total daily nonaccidental deaths and sex- and age-specific (all ages and over 64 years) daily deaths are shown according to cause in Table 2.

Spectral analysis of TSP and SO_2 revealed the same deterministic structure for each of the four monitoring stations, namely, a downward trend and statistically significant annual, weekly, and 3-day periodicities. The stationary part of the series was specific for each pollutant and monitoring station, with TSP models having a stationary ARMA (4,1) structure and differing in the cyclical 7-day MA component and SO_2 models sharing a common ARMA (1,1) structure for the 7-day cycle and differing in the stationary AR component.

Mortality registered a rising trend as well as a yearly and a 6-monthly seasonal component but no weekly cycle. In the case of temperature there was only a statistically significant annual cycle. The relationship between nonaccidental deaths and TSP was linear, whereas that observed for SO_2 was logarithmic.

The CCFs yielded by the above-mentioned two methods showed the same structure. Table 3 shows the lags at which statistically significant correlation coefficients were detected between the pollutants and mortality (annual and seasonal) as broken down by cause, sex, and age (over 64 years).

As a rule, TSP (Fig. 1a) registered an immediate positive effect on mortality on the same and the following day, with correlation coefficients being greater

Table 1 Descriptive statistics: independent variables, 1986–1992

	Annual				Summer				Winter			
	Mean	Standard error	Minimum	Maximum	Mean	Standard error	Minimum	Maximum	Mean	Standard error	Minimum	Maximum
Maximal temperature (°C)	19.8	8.8	0.8	39.4	30.4	4.7	16.0	39.4	12.2	4.1	0.8	28.8
Mean temperature (°C)	15.1	7.7	–0.9	32.2	24.5	4.2	11.3	32.2	8.4	3.5	–0.9	19.4
Minimal temperature (°C)	10.2	6.6	–4.3	27.2	18.0	3.6	9.1	27.2	4.6	3.3	–4.3	13.3
Relative humidity (%)	83	11	50	100	72	9	50	100	90	6	65	100
TSP1 (μg/m^3)	51.3	25.8	2	228	42.6	14.7	2	94	60.8	31.3	9	228
TSP6 (μg/m^3)	42.8	23.9	1	189	40.5	18.5	9	186	46.3	28.6	3	189
$SO_2$1 (μg/m^3)	70.5	52.2	4	479	39.9	18.6	7	97	105.4	61.1	13	479
$SO_2$18 (μg/m^3)	78.8	44.7	9	374	55.0	25.4	9	153	108.8	48.1	17	374

than those obtained for SO_2. In contrast, SO_2 exhibited different behavior patterns, depending on sex, age, and season. Nonaccidental deaths reached significance at lag 3 (Fig. 1b). On categorization by specific cause of death, circulatory and respiratory causes shifted up to lag 1. In the over-64-years age group the effect advanced to lag 1 for both sexes and for all-cause mortality. On a seasonal basis the association between circulatory-disease mortality and pollution was observed exclusively in summer, whereas that noted for respiratory diseases was in evidence throughout the year.

The correlation matrix for the environmental variables, displayed in Table 4, highlights the strong correlation between TSP and SO_2. The CCF between these two pollutants presented a statistically significant correlation on the same day and the day after, indicating a high degree of covariance. This poses problems due to multicollinearity in the multivariate regression model. Both pollutants were negatively related to minimal air temperature, a phenomenon that became even more marked in winter; a drop in temperature was associated with a rise in TSP on the same day and in SO_2 on the same and the following day. SO_2 registered a higher correlation coefficient with temperature than did TSP.

When the pollutants were introduced by means of the forward method into the ARIMA models for nonaccidental deaths, lag-0 and lag-1 TSP ranked first. The highest coefficient was yielded by TSP at lag 1. SO_2 showed increasing coefficients that reached significance only at lag 3, even when temperature was controlled for. Inclusion of influenza periods in the model led to a 50% fall in the magnitude of the cold-temperature coefficients. Influenza alone increased the number of daily deaths by 2.9 (Table 5). The pattern was similar for both sexes. Pollution, temperature, and influenza had their most pronounced effect on the over-64-years age group.

The pattern changed when summer and winter periods were analyzed separately. TSP remained in evidence throughout the same and the following day. When temperature was controlled for, the SO_2-induced effect disappeared in both winter and summer. Only TSP was related to mortality by cause (cardiovascular and respiratory), sex, and age. This model was completed by the addition of a stationary ARMA (1,1).

The ACF and PACF of final-model residuals showed a white-noise structure. The Box-Ljung Portmanteau test yielded a value of $P > 0.91$ at lag 390, indicating the absence of stationary or seasonal components in the residuals.

Discussion

The need to meet successive pollution-control standards (both national and European) has forced the Spanish authorities to place statutory limits on pollutant emissions. In the case of Madrid, the most significant of these measures has perhaps been the changeover from coal- and gas oil-based systems to heaters fired by natural gas.

Table 2 Descriptive statistics: causes of death expressed in deaths/day, 1986–1992

Mortality due to			Annual		Summer		Winter	
			Mean	Standard error	Mean	Standard error	Mean	Standard error
Nonaccidental causes	Total	All ages	60.3	11.3	54.4	9.41	66.9	10.6
		> 65 years	45.4	9.7	40.2	7.9	51.0	9.3
	Men	All ages	31.4	6.8	28.1	6.1	34.6	6.6
		> 65 years	21.2	5.6	18.5	4.9	23.7	5.5
	Women	All ages	29.0	6.8	26.3	6.0	32.3	6.7
		> 65 years	24.2	6.3	27.3	6.2	21.7	5.5
Cardiovascular causes	Total	All ages	23.7	6.5	20.1	5.3	27.4	6.1
		> 65 years	19.8	5.9	16.6	4.6	23.0	5.7
	Men	All ages	10.9	3.8	9.1	3.4	12.5	3.8
		> 65 years	8.0	3.2	6.6	2.8	9.3	3.2
	Women	All ages	12.9	4.3	11.0	3.6	14.9	4.3
		> 65 years	11.8	4.2	10.1	3.4	13.8	4.2
Respiratory causes	Total	All ages	5.8	3.1	4.7	2.4	7.0	3.4
		> 65 years	4.9	2.8	3.9	2.2	6.0	3.1
	Men	All ages	3.4	2.2	2.8	1.8	4.0	2.4
		> 65 years	2.7	1.9	2.2	1.6	3.2	2.2
	Women	All ages	2.4	1.8	1.9	1.4	2.9	2.0
		> 65 years	2.2	1.7	1.8	1.4	2.7	1.9

Table 3 Statistically significant lags, expressed in days, in the cross-correlation functions

Mortality		Annual	Summer	Winter
Nonaccidental	Total	SO_2 (3) TSP (0.1)	SO_2 (1) TSP (1)	SO_2 (2) TSP (1)
	Men	SO_2 (3) TSP (0.1)	SO_2 (2) TSP (1)	SO_2 (3)
	Women	SO_2 (3) TSP (0)	SO_2 (1) TSP (1)	
Cardiovascular	Total	SO_2 (1)	SO_2 (1) TSP (1)	
	Men	SO_2 (1)	SO_2 (1) TSP (0.1)	
	Women		SO_2 (3) TSP (1)	
Respiratory	Total	SO_2 (1) TSP (0)	SO_2 (1)	SO_2 (1) TSP (1)
	Men	SO_2 (0) TSP (0)	SO_2 (1) TSP (1)	
	Women	SO_2 (0) TSP (0)	TSP (1)	SO_2 (1) TSP (1)

Given that 49% of all SO_2 emissions and 38% of TSP [24] in Madrid are attributable to heaters, the shift to a cleaner fuel has lowered the levels of these contaminants over the study period. Yet despite this fall-off in pollutant emissions, anticyclone-induced temperature inversions during the winter months have the effect of trapping pollutants close to ground level. This has in turn caused emission indicators to breach WHO [44] guidelines on 60 different occasions during the study period and, at times, to exceed European Union (EU) limits [4, 5].

The point must be made, however, that mortality registered an upward trend due to aging of the population. The 12- and 6-month peaks detected in the periodogram were related to winter and summer excess mortality [1].

Fourier analysis detected three cyclical components in the pollution variables. Previous studies [12] have associated the annual cycle with climatic patterns, the 7-day cycle with anthropogenic activity, and the 3-day cycle with the persistence in Madrid latitudes of cyclonic situations that act as natural air-purifiers [13].

The results showed a statistically significant independent association throughout the year between TSP and SO_2, on the one hand, and mortality due to nonaccidental deaths, on the other. This relationship between relatively low levels of pollution (normal in cities throughout the developed world) and mortality is

consistent with different studies conducted in Europe and the United States [19, 22, 26, 28, 33, 42].

Furthermore, the linear (TSP) and logarithmic (SO_2) functional relationships with mortality indicate the nonexistence of a specific threshold above which the effect on mortality becomes detectable. Other authors have reported similar findings [7, 22, 23, 35, 42]. In the case of SO_2 the logarithmic relationship means that the highest regression coefficients are obtained when concentrations lie between 50 and 120 $\mu g/m^3$.

It is noteworthy that SO_2 showed an association with mortality for the whole year, but not when the winter and summer periods were analyzed separately. This might possibly be explained by the observation that the mean daily SO_2 concentration was 72 $\mu g/m^3$ for those months not included in said periods (i.e., September, October, April, and May), the segment with the steepest slope in the pollutant's logarithmic relationship with mortality. During the winter period, low-temperature episodes are associated with an increase in pollutant concentrations owing to the atmosphere's diminished pollution-dispersal capacity (temperature inversion) and an increase in the use of heating. The negative relationship between SO_2 and cold temperatures means that when this pollutant is introduced into the model, it is eliminated from lag 3 due to the high degree of collinearity. Similar results have been reported by Mackenbach et al. in The Netherlands [22].

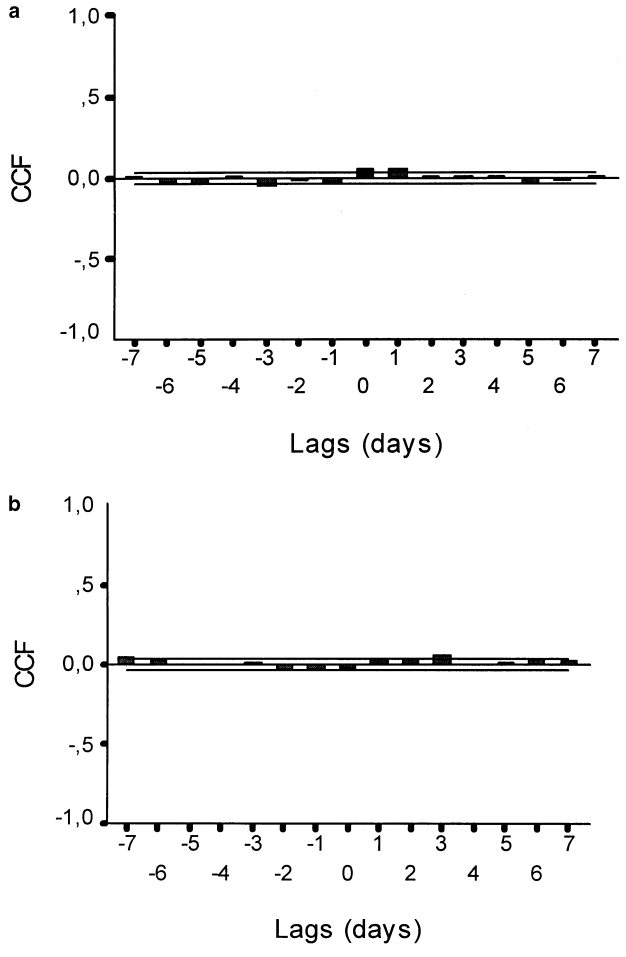

Fig. 1 a Correlation between nonaccidental deaths and TSP (station 6, annual). **b** Correlation between daily organic deaths and SO_2 (station 1, annual)

TSP remains in the model at lag 1 (where it usually has its greatest influence on mortality) throughout the summer period, even after the introduction of daily temperature, thus indicating an independent effect. Not only does TSP eliminate SO_2 from the univariate model on the same and the following day, but it also diminishes the coefficient value at lag 3 to a substantial degree. This displacement is observed for the whole year and for the winter and summer periods in both sexes and both age groups. The association persists even where autocorrelation, season, influenza epidemics, and weather variables are controlled for. This would support the hypothesis of there being a clear TSP/mortality effect, with SO_2 acting in a less obvious manner [7, 29, 35]. The increase of approximately 6% in mortality for every 100-$\mu g/m^3$ increase in TSP concentration is consistent with previous studies [33, 34, 39, 42].

Nonetheless, differences between SO_2 and TSP in functional relationship, lag structure, and magnitude of regression coefficients, along with the former's independent inclusion in the multivariate model for the whole year, argue in favor of SO_2's having an independent, albeit smaller, effect on mortality, possibly related to different physiological mechanisms. Whereas TSP would tend to act mechanically on the bronchi, producing bronchoconstriction – as evinced by the association detected between TSP and the increase in asthma, acute bronchitis, and emergency respiratory-related admissions [3, 32, 36, 40] – SO_2 would act by irritating the upper passages and lung tissue, reducing bronchial capacity, and changing the response to infection [11]. A change in response to infection is likewise found in the causal hypothesis accounting for cold-temperature behavior patterns [20], which would explain why both variables could be jointly responsible for the increase in mortality.

Earlier studies, cited above, have demonstrated that air-pollution-related deaths have primarily been due to an increase in respiratory-disease mortality. In our study the rise in respiratory-disease mortality was fundamentally associated with TSP. An association between TSP, SO_2, and cardiovascular mortality was thus established. The contribution of SO_2 was clearer in summer, conceivably due to an interaction between high temperatures and SO_2 [18]. The physiological mechanism underlying the pollution/cardiovascular relationship is not yet clearly understood. Some authors [37] point to the possibility of ultrafine acidic particles provoking alveolar inflammation, which would in turn lead to acute changes in blood coagulability and increased susceptibility to severe episodes of cardiovascular disease. Other authors make the point that in reports of the cause of death, "respiratory" might be reported as "cardiovas-

Table 4 Correlation coefficients between meteorological and air pollution variables[a]

	Maximal temperature	Mean temperature	Minimal temperature	TSP	SO_2
Maximal temperature	1.0000				
Mean temperature	0.9793	1.000			
Minimal temperature	0.8129	0.8378	1.0000		
TSP	−0.2061	−0.2198	−0.2019	1.0000	
SO_2	−0.4647	−0.4901	−0.4406	0.7060	1.0000

[a] Significance level (all cases): $P > 0.001$

Table 5 Final model regression coefficients

Independent variable (lag in days)[a]	Regression coefficient	Standard error	Statistical significance (P value)
Twarm (0)	0.06	0.02	0.008
Twarm (1)	0.10	0.02	< 0.001
Twarm (3)	0.06	0.02	0.002
Tcold (3)	0.020	0.006	< 0.001
Tcold (7)	0.017	0.005	0.002
Tcold (12)	0.021	0.005	< 0.001
Relative humidity (2)	−0.06	0.03	< 0.03
TSP (1)	0.029	0.009	< 0.001
$LnSO_2$ (3)	1.07	0.47	0.02
Influenza	2.88	0.98	0.003
N1	−0.018	0.004	< 0.001
AR 1	0.90	0.03	< 0.001
MA 1	0.83	0.03	< 0.001

[a] Change in daily mortality per unit increase in the explanatory variable: Twarm and Tcold (tenths of a °C), Relative humidity (%), TSP and SO_2 ($\mu g/m^3$)

cular," giving rise to a misclassification bias [6]. Nevertheless, the consistency of the mortality findings with the relevant morbidity studies suggests a real association rather than a mere certification error. The pronounced effect on the over-64-years age group would seem to indicate increased susceptibility and imbalance among patients with a clinical history of cardio-respiratory disease or regulatory mechanisms that have deteriorated through aging. There are no grounds for suspecting any age-related differential bias in certification.

Use of routinely collected mortality data poses problems inherent to death certification. Misclassification of the underlying cause of death could be a source of bias, but we are of the opinion that the use of broad categories of sex, age, and ICD coding reduces the likelihood of such an effect. Moreover, for such misdiagnosis to bias the estimated effect of air pollution, it must vary from day to day in a manner correlated with air pollution.

These results support the hypothesis of an association between TSP and mortality at the pollution levels currently prevailing in Madrid. Although the equivalent SO_2/mortality relationship has not been clearly established, its logarithmic nature indicates an even more striking effect for low concentrations. When temperature is controlled for, an independent and more marked effect on mortality is observed, in line with findings reported by other authors [22]. Additional measures designed to reduce pollution levels without compromising thermal comfort should thus be implemented, preferably via improvements in housing insulation rather than increases in the energy required to produce such comfort. Moreover, given that industries situated in and around Madrid represent 42% of overall SO_2 emissions and 44% of TSP emissions and that vehicle traffic emissions account for 8% and 18% of SO_2 and TSP emissions, respectively [24], it is clear that, aside from improved housing insulation, the situation calls for stricter legislation governing industrial emissions and tighter road traffic control.

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