Air pollution and daily mortality in Rome, Italy

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Abstract

Objectives— To assess the relation between several daily indicators of air pollution (particulates and gases) and daily mortality in the metropolitan area of Rome and in the central part of the city.

Methods—Time series analysis. The associations between daily concentrations of pollutants (particles, SO₂, NO₂, CO, O₃) recorded by five fixed monitors and daily total mortality in the period from January 1992 to June 1995 were evaluated. The analysis included examination of the pollution effect on mortality by place of residence within the metropolitan area, by season, age, place of death (in and out a hospital), and cause of death (cardiovascular and respiratory disease). The Poisson model included loess smooth functions of the day of study, mean temperature, mean humidity, and indicator variables for day of the week and holidays.

Results—The mean daily number of deaths was 56.9 (44.8 among people ≥65 years old). A mean of 36.3 deaths occurred in the city centre; 37.3 deaths a day were recorded in a hospital. Total mortality was significantly associated with a 10 µg/m³ increase in particles (0.4%) on that day (log 0), and with a 10 µg/m³ increase in NO₂ at lag 1 (0.3%) and lag 2 (0.4%) (1 and 2 days before, respectively). The effect of particles (lag 0) and of NO₂ (lag 2) on total mortality was higher among those living in the city centre (0.7% and 0.5%, respectively). The risk estimates were higher in

the warmer season (1.0% and 1.1%, respectively), whereas no difference was found for those dying in or out of the hospital. The effect of particles was robust to a sensitivity analysis and to the inclusion of NO₂ in the regression model.

Conclusions—Increase in particulates and NO₂, generated by the same mobile combustion sources, is associated with a short term increase in mortality in Rome. The effect is more evident among residents in the city centre, where the levels of exposure to pollutants recorded by fixed monitors are probably more reliable indicators of personal exposure.

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Keywords: air pollution; time series; smoothing

Epidemiological studies conducted in the United States and Europe have provided evidence that serious health effects, including premature mortality, are associated with exposure to ambient particles found in urban environments, even at concentrations below current standards.¹ Most studies evaluating the short term effects of pollutants on daily mortality have found a similar level of increase of risk per unit increase in particle concentration (total suspended particulates, or particulate matter with mean aerodynamic diameter of 10 µm (PM₁₀)) across various geographical and climatic conditions. Ambient exposure to fine particles, PM_{2.5}, may be primarily responsible for the association found²; yet the association between particle exposure and daily mortality has been questioned.³

The association between air pollution and daily mortality has been studied in Europe, mostly within the air pollution and health: a European approach (APHEA) initiative,^{4,5} a unique project aimed at evaluating the short term effect of pollution in 10 countries. In most European cities—for example, London⁶ and Birmingham⁷ in the United Kingdom—an association between particulates and total mortality is clear. In the recent pooled analysis of 12 APHEA cities, both SO₂ and particulate matter were found to be associated more or less equally with daily mortality.⁵

Few studies have been conducted within the Mediterranean area, and none in cities with low concentrations of SO₂. In Rome, the main source of pollution is traffic that generates medium to high concentrations of airborne particles and NO₂. By contrast with other western European areas where time series studies have been conducted, SO₂ concentrations in Rome are low. We examined the association between daily concentration of various pollutants (particles, SO₂, NO₂, CO,

Table 1 Summary of environmental variables in Rome 1992–5

Variable	Mean*	SD	Percentiles		
			25	50	75
Temperature (°C)	16.5	6.8	11.0	15.7	22.2
Humidity (%)	61.5	12.3	53.0	63.0	71.0
Particles (µg/m ³)	84.2	26.1	65.7	82.7	100.3
SO ₂ (µg/m ³)	16.2	9.8	9.4	13.3	20.7
NO ₂ (µg/m ³)	99.2	22.8	83.8	96.2	111.0
CO (mg/m ³)	4.1	1.6	3.1	3.9	5.0
O ₃ (µg/m ³)	25.9	19.6	10.3	21.0	36.0

* 24 h mean for all except O₃ which is 8 h mean.

Table 2 Summary of daily mortality data in Rome 1992–5

Variable	Metropolitan area		Central area	
	Mean	SD	Mean	SD
Whole year	57.0	10.5	36.3	8.4
Cold period	60.5	9.3	38.6	7.5
Warm period	53.4	10.4	33.9	8.6
Among elderly people (≥65)	44.8	9.4	29.8	7.6
Deaths in hospital	37.3	7.7	18.8	5.4
Deaths out of hospital	19.4	5.3	17.5	5.3
Cardiovascular mortality	23.3	6.4	15.3	5.1
Respiratory mortality	3.2	2.0	2.1	1.6

Table 3 Pearson correlation coefficients among daily environmental variables, Rome 1992–5

	Temperature	Humidity	Particles	SO ₂	NO ₂	CO	O ₃
Temperature	1.000						
Humidity	-0.300	1.000					
Particles	0.247	-0.152	1.000				
SO ₂	-0.621	0.132	0.267	1.000			
NO ₂	0.058	-0.100	0.507	0.409	1.000		
CO	-0.440	0.448	0.238	0.646	0.282	1.000	
O ₃	0.604	-0.437	0.223	-0.263	0.237	-0.479	1.000

(A) Loess smoothing (span=0.03) of daily mortality in Rome. (B) Loess smoothing (span=0.11) of the relation between daily mean temperature (°C) and daily mortality. (C) Loess smoothing (span=0.30) of the residuals from the basic Poisson model including smoothing of time, mean temperature (lag 1), relative humidity (lag 1), and indicators for day of the week and holidays.

O₃) and daily total mortality in Rome in the period 1992–5. Detailed data were available on the specific area of residence within the metropolitan area, as well as on the place of death

(hospital *v* other dwellings) of the people who died during the study period. It was thus possible to evaluate whether the effects of pollution on mortality are actually higher among residents in the central city than among those living in the outskirts, and whether the effects are similar among people who die in a hospital and those who die at home.

Methods

AIR POLLUTION AND WEATHER DATA

The metropolitan area of Rome has a population of about three million inhabitants and covers an area of 1495 km². About 65% of the population live in the city centre, which has been defined by the local authorities as the area of concern for air pollution control. The city centre (about 320 km²) includes archeological and historical sites, business areas, and residential neighbourhoods. A network of fixed air quality monitoring stations has been operating in Rome since January 1992 under the Regional Department of Environment. Five stations, located in densely populated areas within the central city, continuously collect hourly data on concentrations of SO₂ (ultraviolet fluorescence), NO₂ (chemiluminescence), and CO (infrared photometry); three of the five monitors also collect hourly data on O₃ (ultraviolet photometry) and 2-hourly data on particles. Counts for PM₁₀ were not available for the period under study. Suspended particles are continuously monitored with a low volume air sampler with an open face inlet and β ray atomic absorption. Investigations in Rome with a gravimetric method to measure PM₁₀ and total suspended particulates showed a higher ratio of PM₁₀ to total suspended particulates (0.70–0.80) than the ratios detected in North America.⁸ This is presumably due to both the low volume sampling and to the peculiar geometry of the open face inlet which produced a higher efficiency for small size particulate fractions. Furthermore, detailed examinations with electron microscopy of the relative size of the particles sampled with the Italian instrument indicated that the particle fraction actually measured is <13 μ m.

We collected the daily air pollution data (24-hour integrated measure for particles, SO₂, NO₂, and CO; the mean O₃ concentration between 800 am and 400 pm) from the five population oriented fixed monitors. For each day, we averaged the data from the available monitors to compute a city mean to match the daily mortality data. During the study period (1 January 1992 to 30 June 1995) data were available from all the monitors for 72.3% of the days for particles, 91.5% for SO₂, 90.6% for NO₂, 99.8% for CO, and 75.6% for O₃. As some values for a particular monitor and a particular pollutant were missing, before computing city means we imputed missing data with regression models based on the other monitors' values; the estimated values were used only if the goodness of fit (R^2) of the regression models was >0.60. After this procedure, the percentage of missing values was 2.6% for particles, 0.2% for SO₂, 0.2% for NO₂, 0.1% for

Table 4 Increase (%) in daily mortality for 10 µg/m³ increase in particles, SO₂, NO₂, O₃, and for 1 mg/m³ increase in CO in the entire metropolitan area of Rome and in the central city (results from Poisson regression models, * Rome 1992–5)

Pollutant	Lags	Metropolitan area		Central area	
		Increase (%)	95% CI	Increase (%)	95% CI
Particles	0	0.38	0.09 to 0.68	0.66	0.31 to 1.02
	1	0.26	−0.03 to 0.56	0.45	0.10 to 0.81
	2	0.07	−0.20 to 0.34	0.23	−0.12 to 0.58
	3	−0.02	−0.29 to .25	0.07	−0.28 to 0.42
SO ₂	4	0.08	−0.19 to 0.36	0.13	−0.22 to 0.48
	0	−0.77	−1.66 to 0.13	−0.98	−2.02 to 0.08
	1	−0.69	−1.56 to 0.19	−0.67	−1.69 to 0.37
	2	−0.54	−1.43 to 0.36	−0.85	−1.89 to 0.21
NO ₂	3	−0.53	−1.40 to 0.35	−0.95	−1.99 to 0.11
	4	−0.42	−1.29 to 0.46	−0.73	−1.77 to 0.33
	0	0.23	−0.10 to 0.56	0.45	0.04 to 0.87
	1	0.34	0.01 to 0.68	0.48	0.07 to 0.90
CO	2	0.43	0.10 to 0.77	0.54	0.13 to 0.96
	3	0.38	0.05 to 0.72	0.40	−0.01 to 0.81
	4	0.25	−0.08 to 0.58	0.14	−0.27 to 0.55
	0	0.29	−0.22 to 0.81	0.52	−0.11 to 1.15
O ₃	1	0.30	−0.23 to 0.83	0.47	−0.18 to 1.12
	2	0.19	−0.35 to 0.73	0.24	−0.41 to 0.89
	3	0.28	−0.24 to 0.81	0.07	−0.57 to 0.71
	4	0.18	−0.35 to 0.70	0.09	−0.54 to 0.73
	0	0.07	−0.34 to 0.48	0.21	−0.28 to 0.70
	1	0.38	−0.03 to 0.79	0.45	−0.06 to 0.96
	2	0.28	−0.13 to 0.69	0.36	−0.13 to 0.85
	3	0.29	−0.12 to 0.70	0.32	−0.17 to 0.81
	4	0.28	−0.13 to 0.69	0.33	−0.16 to 0.82

* The basic model predicting daily mortality includes smoothed time (span=0.03), mean temperature (lag 1; span=0.11), and relative humidity (lag 1; span=0.35), indicators for days of the week and holidays. Each pollutant was entered as a continuous variable.

CO, and 4.6% for O₃. Mean daily temperature (°C) and relative humidity (%) were available from the local weather station in the central area.

DEATHS

We collected information on all deaths of residents in Rome during the study period, retrieved from the Regional Register of Deaths. Individual information on sex, age, census block of residence, date of death, municipality of death, place of death, and cause of death was available. Deaths due to accidents (international classification of diseases ninth revision (ICD-9 800–999)) and those occurring outside Rome were excluded from the analysis. The daily number of deaths was computed by place of residence within the metropolitan area (central area, outskirts) on the basis of the census block of residence, by age (<65 years, ≥65 years), place of death (inside or outside a hospital; dead on arrival at a hospital is usually

coded as dead outside a hospital), and by cause (cardiovascular and respiratory disease).

DATA ANALYSIS

We used Poisson regression to estimate the association between pollutants at different lags and mortality in the entire metropolitan area and in the central area. The analysis was conducted in stages. Firstly, we developed the basic model to allow for time trends and weather variables (and possible serial correlation). Secondly, we tested the effect of the pollutants by adding continuous variables (with lags from 0 to 4, on the same day to 4 days before) to the basic model. We then conducted a sensitivity analysis to evaluate the robustness of our findings to time trend and weather modelling. Finally, regressions in various subgroups were estimated and multipollutant models were evaluated.

To build the basic model, we used a Poisson regression replacing some of the covariates of a particular day with non-parametric smoothed data.^{2 9 10} The locally weighted (loess) smoothing technique¹¹ can accommodate non-linear and non-monotonic patterns between the covariate and mortality, offering a flexible non-parametric tool.^{12 13} We used loess smoothed data of time, mean temperature (at lag 1), and mean relative humidity (at lag 1). The choice of the appropriate span was based on the generalised cross validation criterion.¹⁴ To smooth daily total mortality against time, we chose to use 3% of the data (38 days), whereas 11% and 35% of the data were used to smooth temperature and humidity, respectively. We fitted separate smoothed data for each end point, although total, elderly, cardiovascular, and respiratory mortality showed similar patterns. The basic model also included indicator variables for day of the week and holidays.

For comparability with other studies, the results of our analysis were expressed as percentage increase in daily mortality with each increment of 10 µg/m³ in the pollutant (1 mg/m³ for CO). However, additional analysis was conducted with particles and NO₂ divided into quartiles (indicator variables were considered) to evaluate the linearity of the effects as well as multipollutant models. Analysis was

Table 5 Increase (%) in daily mortality for 10 µg/m³ increase in particles (lag 0) and in NO₂ (lag 2) in the entire metropolitan area of Rome and in the central city, by season, age, place of death, and cause of death, Rome 1992–5

Variable	Pollutant	Metropolitan area		Central area	
		Increase (%)	95% CI	Increase (%)	95% CI
Whole year	Particles	0.38	0.09 to 0.68	0.66	0.30 to 1.02
	NO ₂	0.43	0.10 to 0.77	0.55	0.14 to 0.95
Cold period	Particles	0.02	−0.33 to 0.37	0.20	−0.25 to 0.66
	NO ₂	0.07	−0.32 to 0.46	0.32	−0.19 to 0.83
Warm period	Particles	0.96	0.49 to 1.44	1.32	0.72 to 1.93
	NO ₂	1.10	0.48 to 1.71	0.97	0.21 to 1.73
Among elderly people(≥65)	Particles	0.42	0.11 to 0.74	0.74	0.34 to 1.13
	NO ₂	0.42	0.07 to 0.78	0.59	0.14 to 1.04
Dead in hospital	Particles	0.40	0.05 to 0.76	0.58	0.09 to 1.08
	NO ₂	0.38	−0.01 to 0.77	0.59	0.02 to 1.15
Dead out of hospital	Particles	0.37	−0.12 to 0.86	0.69	0.18 to 1.21
	NO ₂	0.35	−0.20 to 0.90	0.44	−0.15 to 1.03
Cardiovascular mortality	Particles	0.37	−0.07 to 0.82	0.69	0.13 to 1.24
	NO ₂	0.39	−0.11 to 0.89	0.54	−0.08 to 1.15
Respiratory mortality	Particles	0.29	−0.90 to 1.47	0.34	−1.12 to 1.80
	NO ₂	−0.29	−1.61 to 1.04	−0.02	−1.63 to 1.59

Table 6 Increase (%) in daily mortality for 10 µg/m³ increase and for quartiles of particles (lag 0) and NO₂ (lag 2) in the entire metropolitan area of Rome and in the central city, in single, and two pollutant models, Rome 1992–5

Variable	Pollutant	Metropolitan area		Central area	
		Increase (%)	95% CI	Increase (%)	95% CI
Single pollutant model:					
Linear term (10 µg/m³)	Particles	0.38	0.09 to 0.68	0.66	0.30 to 1.20
	NO ₂	0.43	0.10 to 0.77	0.55	0.14 to 0.95
Quartiles	Particles				
II		1.00	−1.11 to 3.20	2.80	0.10 to 5.60
III		1.80	−0.40 to 4.00	3.30	0.60 to 6.20
IV		3.80	1.70 to 5.90	5.80	3.10 to 8.60
Quartiles	NO ₂				
II		−1.80	−3.90 to 4.70	−0.20	−2.80 to 2.50
III		2.50	0.30 to 4.70	5.00	2.30 to 7.90
IV		2.25	0.10 to 4.50	3.70	0.90 to 6.50
Two pollutant model:					
Linear term (10 µg/m³)	Particles	0.29	−0.03 to 0.61	0.58	0.18 to 0.98
	NO ₂	0.29	−0.07 to 0.65	0.25	−0.21 to 0.70
Quartiles	Particles				
II		0.90	−1.20 to 3.10	2.50	−0.10 to 5.40
III		1.90	−0.90 to 3.50	2.60	−0.20 to 5.50
IV		3.10	0.90 to 5.30	4.70	1.90 to 7.70
Quartiles	NO ₂				
II		−2.20	−4.24 to 0.00	−0.74	−3.30 to 2.00
III		1.80	−0.40 to 4.00	4.00	1.20 to 6.90
IV		1.20	−1.10 to 3.50	2.10	−0.74 to 5.09

conducted with STATA¹⁵ and SAS.¹⁶ The S-Plus package¹⁷ was used to run robust Poisson regression to correct for overdispersion.

Results

Tables 1 and 2 summarise the environmental variables and daily mortality for the whole study period. Particles and NO₂ did not follow a specific seasonal pattern. The SO₂ and CO tended to be higher in winter than in summer, whereas O₃ was higher in the warm season. There was a certain degree of collinearity among the environmental variables (table 3), especially between SO₂ and CO ($r=0.646$), and between NO₂ and particles ($r=0.507$).

Rome had an average of 56.9 daily deaths during the 1277 days of the study. An average of 36.2 deaths occurred in the central area (tables 1 and 2). A strong seasonal pattern in mortality was evident (figure A), with excess deaths in winter. However, mortality peaked also in two of the three summers in the study period. There was a non-linear dependence of mortality on temperature (figure B), with a steep increase above 26°C. After having considered all the time and weather variables, the distribution of the residual did not follow a particular pattern (figure C). Partial autocorrelation coefficients for the residuals of the basic model were inspected, and no residual autocorrelation was found up to seven days.

Table 4 shows the results from the Poisson regression analysis. Daily mortality in the metropolitan area was significantly associated with same day particle concentration (0.38% increase per 10 µg/m³), and with NO₂ at lag 1, lag 2, and lag 3, with the highest effect at lag 2 (0.43% increase per 10 µg/m³). A borderline significant association was found for O₃ at lag 1, whereas no association was found for CO and SO₂. When the analysis was restricted to the deaths occurring among residents of the central area, higher coefficients were found for particles (0.66% at lag 0) and for NO₂ (0.55% at lag 2). No effect of CO, SO₂, or O₃ was

detected. The analysis of daily mortality only in the outskirts of Rome did not show a single significant association with pollution levels, and the coefficients for particles (0.02%, 95% CI –0.47% to 0.51%) and NO₂ (–0.21%, 95% CI –0.78 to 0.36) were significantly different from those estimated for the central area ($p=0.04$ and $p=0.04$, respectively).

The results for particles and NO₂ were robust to changes in the modelling technique. The regression coefficients for the pollution effects were stable for a wide range of less stringent time spans (the same results were obtained up to a time span of 0.1). Small changes were found when indicator variables for hot and cold days (highest and lowest 10% of the temperature distribution) were included in the model (particles 0.38% at lag 0, 95% CI 0.09 to 0.68; NO₂ 0.36% at lag 2, 95% CI 0.03 to 0.70). The 95% CI of the particles effect (0.08 to 0.69) and of the NO₂ effect (0.09 to 0.78) changed only slightly when overdispersion was taken into account.

The results of the subgroup analysis are shown in table 5. The association of particles and NO₂ with total mortality in the metropolitan area was significantly stronger in the warmer season ($p=0.04$ and $p=0.02$, respectively). Slightly higher risk estimates for particles were consistently found among elderly people. There was no substantial difference in the effect for those dying in or out of a hospital. Cardiovascular mortality, but not respiratory mortality, was significantly associated with particles in the central area; however, the coefficients were not higher than those found for total mortality.

Considering the high degree of correlation between pollutants, especially between particles and NO₂, it is difficult to determine the role of a single factor (table 6). However, when multipollutant models were run, the risk estimates decreased for both particles and NO₂, but particles remained of borderline significance in the metropolitan area and significantly associated with mortality in the

city centre. When concentrations of particles and NO₂ were divided into quartiles, in single pollutant models, mortality increased by 3.8% (and by 5.8% in the central area) in the highest quartile of particles compared with the first quartile, and by 2.3% (3.7% in the central area) in the highest quartile of NO₂. In the multipollutant model with quartiles of both particles and NO₂, the effect of particles remained and an exposure-response relation was found. The results for NO₂ were less consistent and not significant.

Discussion

We found that both particles and NO₂ are associated with the daily count of deaths in Rome. The risk estimates were higher among citizens living in the city centre, as they probably more directly experienced the pollution levels recorded by the fixed monitors. No differences were found between those dying in the hospital and those at home. In the multipollutant models, the results for particles were more stable than those obtained for NO₂. The body of evidence from the United States indicates an increase in daily mortality ranging from 0.5%–1.6% per 10 µg/m³ particle concentration.^{1–18} Studies conducted in western Europe have yielded slightly lower risk estimates of mortality associated with particle levels than those reported by United States time series analyses.^{5–6, 19–23} However, in most of the European cities that have been studied, other pollutants had a stronger effect on mortality. For example, SO₂ was found to be associated with mortality in all cities with moderate to high concentrations of SO₂ (Athens,¹⁹ Barcelona,²⁰ Lyon²¹). In London, O₃ was a stronger determinant of mortality than black smoke.⁶

Our risk estimates of the effect of particles are similar to what has been found in the recent APHEA meta-analysis (0.4%–0.5% increase per 10 unit increase).⁵ Our findings add weight to the general tendency of risk in Europe to be lower, and suggest that the detected effect varies according to the area investigated (from 0.38% in the entire metropolitan area to 0.66% when considering only the central area). There has been concern in the scientific literature over the use of fixed monitors in time series analysis, as they may not represent personal exposure. We interpret the stronger effect of particles found in the central area as an indication that refinement in the exposure assessment in time series may yield higher risk estimates. As all the pollution monitors in the metropolitan area of Rome are located within the central city, it is likely that they represent more the daily exposure to pollution of the citizens in the city centre than of those living in more suburban areas. Time series analyses in other European settings have usually considered the entire metropolitan area (although in some situations the distribution of fixed monitors is wider).

The effect of air pollution on mortality in Rome was clearly stronger in the warmer months. Other studies in Europe^{6, 19–23} also have found an increased effect of air pollution in

summer. There are three possible, non-mutually exclusive interpretations of the findings. Firstly, during the warmer period, other stronger determinants of daily mortality (such as acute respiratory infections) are less influential. Secondly, in the warmer period, people spend more time outdoors or tend to live with the windows left open so that exposure to air pollutants is higher and closer to what is being measured by the fixed monitors. Finally, temperature affects mortality through various mechanisms,²⁴ and a biological interaction between air pollution and high temperature may exist, increasing the pollution effect, as has been shown for SO₂ and high temperature in Athens.²⁵

The biological mechanism underlying the association between exposure to particles and daily mortality and the population subgroups possibly more susceptible to the pollutant effects are still under debate. Our risk estimates due to particles were significant for cardiovascular disease, and the results are of interest because of the recent findings that relate particulate pollution to an increased plasma viscosity,²⁶ and to electrocardiographic changes in a canine animal model.²⁷ However, contrary to some studies,¹⁸ yet in agreement with others,⁶ we did not find a significantly increased risk for respiratory mortality, possibly as a result of insufficient power.

It has been proposed that the increase in particulate pollution precipitates deaths in already ill patients whose cardiorespiratory system is compromised.²⁸ Following this assumption, people already in hospital should be a sensitive subgroup to the acute effects of air pollution, although in several instances air filtration or air conditioning reduces the exposure of hospital patients. In Rome, most hospitals do not have air filtration systems in the wards, and especially during summer, the air is changed through open windows. With the exception of hospital intensive care units, indoor and outdoor particle concentrations tend to be similar in the warm period. It is thus not surprising that we did not find a difference in the risk estimates between those dying in and out of a hospital. This comparison, however, has an unavoidable limitation in time series analysis, namely, the lack of information regarding the precise place at the time of the pollution increase. To date, this issue has not been systematically evaluated, although an increase in deaths outside hospital during high pollution days was noted in Philadelphia.²⁸

Some studies have indicated short term effects of NO₂ on hospital admissions and visits to emergency departments.^{29–30} Positive findings of NO₂ on daily mortality have been reported from Los Angeles,³¹ and in the APHEA meta-analysis.⁴ However, from the studies available, the independent role of NO₂ on mortality is difficult to separate from that of particles³² as often, as in Rome, both originate from the same sources, and NO₂ may be a surrogate of the unmeasured concentration of fine particles. Moreover, as NO₂ is converted to nitrates, it also contributes to the

fine particle mass. We found the strongest association between NO₂ and mortality at lag 2, whereas the association with particles was maximum at lag 0; in the multipollutant models the effect of particles was more robust than that of NO₂. These findings lead us to conclude that the association between NO₂ and mortality may be mediated by a particulate effect.

Ozone is a pollutant of concern in the entire Mediterranean area,²⁵ and an association with daily mortality has been reported in London.⁶ We found only slight evidence of an association with mortality in Rome: an increase in mortality of borderline significance was noted at lag 1 in both the metropolitan area and the city centre. However, our study may have been insufficiently sensitive to the O₃ effects as a result of the position of the O₃ monitors. It is known that O₃ tends to be higher in the outskirts of cities, because of the scavenger effect of primary gases in the city centre, but the pollution monitors in Rome record only central city values.

In conclusion, the present study found an association between particulate pollution and daily total mortality in Rome. Unlike many cities in North America, where particulate pollution has many sources, mostly of industrial origin, pollution in Rome derives mostly from car traffic. Our findings emphasise the importance of considering transportation in cities as a public health issue.³⁵

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- 1 US Environmental Protection Agency. *Air quality criteria for particulate matter*, Vol III of III. Washington, DC: EPA Office of Research and Development, 1996. (EPA/600/P-95/001cF US.)
- 2 Schwartz J, Dockery DW, Neas LM. Is daily mortality associated specifically with fine particles? *Journal of the Air and Waste Management Association*, 1996;46:927–39.
- 3 Moolgavkar SH, Luebeck EG. A critical review of the evidence on particulate air pollution and mortality. *Epidemiology* 1996;7:420–8.
- 4 Touloumi G, Katsouyanni K, Zmirou D, et al. Short term effects of ambient oxidant exposure on mortality: a combined analysis within the APHEA project. *Am J Epidemiol* 1997;146:177–85.
- 5 Katsouyanni K, Touloumi G, Spix C, et al. Short term effects of ambient sulphur dioxide and particulate matter on mortality in 12 cities: results from time series data from the APHEA project. *BMJ* 1997;314:1658–63.
- 6 Anderson HR, Ponce de Leon A, Bland JM, et al. Air pollution and daily mortality in London: 1987–92. *BMJ* 1996;312:665–9.
- 7 Wordley Jo, Walters S, Ayres JG. Short term variations in hospital admissions and mortality and particulate air pollution. *Occup Environ Med* 1997;54:108–16.
- 8 Brook JR, Dann, TF, Burnett RT. The relationship among TSP, PM₁₀, PM_{2.5}, and inorganic constituents of atmospheric particulate matter at multiple Canadian locations. *Journal of the Air and Waste Management Association* 1997;47:2–19.
- 9 Schwartz J. Air pollution and hospital admissions for respiratory disease. *Epidemiology* 1996;7:20–8.
- 10 Schwartz J, Spix C, Touloumi G, et al. Methodological issues in studies of air pollution and daily counts of deaths or hospital admissions. *J Epidemiol Community Health* 1996;50(suppl 1):S3–11.
- 11 Cleveland WS, Devlin SJ. Robust locally-weighted regression and smoothing scatterplots. *Journal of the American Statistical Association* 1988;74:829–36.
- 12 Schwartz. Non-parametric smoothing in the analysis of air pollution and respiratory illness. *Canadian Journal of Statistics* 1994;22:471–87.
- 13 Hastie T, Tibshirani R. *Generalized additive models*. London: Chapman and Hall, 1990.
- 14 Efron B, Tibshirani R. *An introduction to bootstrap*. New York: Chapman and Hall, 1993.
- 15 StataCorp. *Stata statistical software: release 5.0* College Station, TX: Stata Corporation, 1997.
- 16 SAS Institute. *SAS/STAT, Version 6, 4th ed*. Cary, NC: SAS Institute, 1989.
- 17 StatSci. *S-Plus*. Seattle, Washington: StatSci, 1993.
- 18 Schwartz J. Air pollution and daily mortality: a review and meta analysis. *Environ Res* 1994;64:36–52.
- 19 Touloumi G, Pocock SJ, Katsouyanni K, et al. Short-term effects of air pollution on daily mortality in Athens: a time-series analysis. *Int J Epidemiol* 1994;23:957–67.
- 20 Sunyer J, Castellsague J, Saez M, et al. Air pollution and mortality in Barcelona. *J Epidemiol Community Health* 1996;50(suppl 1):S76–80.
- 21 Zmirou D, Barumandzadeh T, Balducci F, et al. Short term effects of air pollution on mortality in the city of Lyon, France, 1985–90. *J Epidemiol Community Health* 1996;50(suppl 1):S30–5.
- 22 Ballester F, Corella D, Perez-Hoyos S, et al. Air pollution and mortality in Valencia, Spain: a study using the APHEA methodology. *J Epidemiol Community Health* 1996;50:527–33.
- 23 Verhoeff AP, Hoek G, Schwartz J, et al. Air pollution and daily mortality in Amsterdam. *Epidemiology* 1996;7:225–30.
- 24 Khaw K-T. Temperature and cardiovascular mortality. *Lancet* 1995;345:337–8.
- 25 Katsouyanni K, Pantazopoulou A, Touloumi G, et al. Evidence for interaction between air pollution and high temperature in the causation of excess mortality. *Arch Environ Health* 1993;48:235–42.
- 26 Peters A, Doring A, Wichmann H-E, et al. Increased plasma viscosity during an air pollution episode: a link to mortality. *Lancet* 1997;349:1582–7.
- 27 Godleski JJ, Sioutas C, Verrier RL, et al. Inhalation exposure of canines to concentrated ambient air particles. *Am J Resp Crit Care Med* 1997;155:A246.
- 28 Schwartz J. What are people dying of on high air pollution days? *Environ Res* 1994;64:26–35.
- 29 Castellsague J, Sunyer J, Saez M, et al. Short-term association between air pollution and emergency room visits for asthma in Barcelona. *Thorax* 1995;50:1051–6.
- 30 Pantazopoulou A, Katsouyanni K, Kourea-Kremastinou J, et al. Short-term effects of air pollution on hospital emergency out patient visits and admissions in the greater Athens, Greece area. *Environ Res* 1995;69:31–6.
- 31 Kinney PL, Ozkaynak H. Associations of daily mortality and air pollution in Los Angeles County. *Environ Res* 1991;54:99–120.
- 32 Anderson HR, Limb ES, Bland JM, et al. Health effects of an air pollution episode in London, December 1991. *Thorax* 1995;50:1188–93.
- 33 Godlee F. Transport: a public health issue. *BMJ* 1992;304:45–50.