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Short term effects of air pollution on mortality in the city of Lyon, France, 1985–90

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Abstract

***Objective* – The short term association between daily mortality and ambient air pollution in the city of Lyon, France (population, 410 000) between 1985 and 1990 was assessed using time series analysis.**

***Design* – This study followed the standardised design and statistical analysis (Poisson regression) that characterise the APHEA project.**

***Methods* – Four categories of cause of death were studied: total (minus external causes), respiratory, cardiovascular, and digestive causes (as a control condition).**

***Results* – No association was found with any cause of death for nitrogen dioxide (NO_2) and ozone (O_3), nor, for any pollutant, for digestive conditions. Sulphur dioxide (SO_2) and, to a much lesser degree, suspended particles (PM_{13}), were significantly related to mortality from respiratory and cardiovascular conditions. The relative risk (RR) of respiratory deaths associated with a 50 $\mu g/m^3$ increment of mean daily SO_2 over the whole period was 1·22 (95% CI 1·05, 1·40); the RR for cardiovascular deaths was 1·54 (1·22, 1·96). The corresponding RRs for PM_{13} were 1·04 (1·00, 1·09) for respiratory mortality and 1·04 (0·99, 1·10) for cardiovascular deaths.**

***Conclusions* – The effects of particulates were slightly increased during the cold season. When particulates concentrations were greater than 60 $\mu g/m^3$, the joint SO_2 effect was increased, suggesting some interaction between the two pollution indicators. These results agree with other studies showing an association between particulate pollution and daily mortality; however, they also suggest the noxious effect of SO_2.**

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Consistent results have accrued in the published reports, showing that ambient air pollution may be associated with mortality, even at levels lower than the current national or international standards.[1–11] Most of these studies dealt with daily mortality but there is also some growing evidence that long term exposure to polluted air reduces survival in the general population.[12–14] The environmental settings where these studies took place are diverse (old industrial towns, urban areas with prevailing automobile sources of emissions...), but the core of these data comes from the United States. In order to assess the generalisability of these findings and because the air pollution make up may be different in European countries, it was decided to launch a European collaborative study on air pollution and mortality and morbidity using time series data – the APHEA project (Air Pollution and Health; a European Approach).[15]

In this context, the city of Lyon, France, presented interesting features for such a study. It is the third largest town in the country (410 000 inhabitants) after Paris and Marseille, and its air pollution monitoring network has been working for a long time, showing that air pollution is still rather high compared with other French cities. The annual mean concentrations for sulphur dioxide (SO_2) and nitrogen dioxide (NO_2) in 1990 were 48 $\mu g/m^3$ and 70 $\mu g/m^3$ in Lyon, compared with 27 $\mu g/m^3$ and 53 $\mu g/m^3$ as averages of all urban networks in France. The SO_2 annual average concentrations are much higher (double) than in Paris and Marseille, due to the proximity of an important chemical industry site in the south of the city, while the values for NO_2 and particulates are similar between the three cities.[16–17] These average concentrations are also relatively high compared with the other western European cities involved in the APHEA project.[15] Using data collected in Lyon in 1974–76, a preceding paper had shown that daily mortality from respiratory conditions was significantly associated with SO_2, with a lag running up to 10 days, but not with suspended particulates, measured as black smoke.[18] Results of the recent short term mortality studies are, however, most consistent for particulates and specifically those indexed as inhalable particles (PM_{10}) or fine particles ($PM_{2.5}$).[1 2 6–11] Traditional industrial sources of SO_2 emissions have been efficiently controlled in France, as in most western European countries. By substituting other sources of energy for heavy fuels or coal and by building high stacks with filters, ambient SO_2 concentrations have been dramatically reduced over the past three decades. Particles and NO_2 have not shown such a positive evolution, due to the growing contribution of automobile emissions.[17 19] The physico-chemical nature of particulates has also changed over time, since their main sources have switched from industrial processes to transport emissions and, to a lesser degree, to urban heating. Therefore, the associations observed in 1974–76 may not hold true 10 to 15 years later.

Methods

The study period was 1985–90 inclusive. Air polution data were provided by the Laboratory of Hygiene, Lyon, which manages the met-

Table 1 Air pollution and meteorology characteristics in Lyon, 1985–90

Meteorology/pollutant	Period				
	Winter	Summer	Spring	Autumn	Whole period
Temperature (°C)					
Mean	3·32	10·86	20·06	12·35	11·69
Minimum	−13·86	0·05	9·89	−2.98	−13·86
Maximum	16·76	21·26	28·81	24·14	28·81
Humidity					
Mean	83·23	72·23	66·34	78·15	74·89
Minimum	54·25	39·25	38·63	44·50	38·63
Maximum	100·00	97·38	95·88	100·00	100·00
*SO_2 mean**					
Mean	76·76	42·22	26·39	42·10	46·76
Minimum	12·93	6·77	2·16	3·37	2·16
Maximum	314·57	157·96	86·65	149·99	314·57
SO_2 maximum					
Mean	148·33	93·83	61·22	98·50	100·22
Minimum	29·75	15·31	4·71	7·61	4·71
Maximum	635·69	509·50	436·68	504·38	635·69
PM_{13} mean†					
Mean	51·00	35·79	27·91	37·59	38·05
Minimum	6·48	3·82	4·81	2·67	2·67
Maximum	179·81	124·51	97·54	132·17	179·81
NO_2 mean‡					
Mean	67·08	71·70	67·46	75·60	70·17
Minimum	3·50	8·52	4·62	11·78	3·50
Maximum	323·75	226·40	194·74	193·86	323·75
NO_2 maximum					
Mean	117·72	147·18	133·48	132·83	132·73
Minimum	9·55	17·19	11·46	19·57	9·55
Maximum	716·25	737·26	485·14	428·28	737·26
O_3 mean§					
Mean	8·45	13·21	12·13	5·57	9·94
Minimum	0·0	0·0	0·0	0·0	0·0
Maximum	35·75	71·23	78·92	22·92	78·92
O_3 maximum					
Mean	11·85	19·55	20·10	9·29	15·23
Minimum	0·0	0·0	0·0	0·0	0·0
Maximum	44·0	98·0	152·0	52·0	152·0

* 5·1% missing data; † 10·0% missing data; ‡ 22·5% missing data; § 12·6% missing data.

ropolitan air quality monitoring network (COPARLY). In order to facilitate comparisons between results of APHEA cities, strict rules were set for the assessment of population exposure.[20] Daily mean or hourly maximum values for SO_2 (whole day), NO_2 (whole day) and ozone (O_3) (9 am to 5 pm for the mean and 6 am to 7 pm for the maximum) were used, along with daily means for particle concentrations. The measurement methods used by the Lyon monitoring network are ultraviolet fluorescence for SO_2, chemiluminescence for NO_2, ultraviolet absorption for O_3, and β-ray atomic absorption for particulates (with a cut off point about 13 μm, which gives results essentially identical to the more classical PM_{10} techniques). Means were calculated over all the relevant monitoring stations available within the limits of the city of Lyon (five sites for SO_2, three sites for PM, one for NO_2, and one for O_3). Maximums were taken as the averages of the higher one hour values over all the relevant monitoring stations. These stations were chosen in order to represent the background air quality levels. For this reason, one monitor was excluded. It was positioned in a place with a very high traffic density; its mean and maximum values for PM, NO_2, and even SO_2 (also associated with diesel sulphur emissions) were clearly outliers compared with the other sites (1985–89 average of daily means: 86 μg/m^3 for SO_2, 74 μg/m^3 for PM and 92 μg/m^3 for NO_2 in the central site).

In case one monitoring station had, for technical reasons, a missing value for one pollutant on a given day, this value was estimated using the average of the measurements of the other available stations. The ratio between the mean values of this station and the mean values of the other stations, for the same year and season, was used to correct for this substitution. When all stations had missing values, no substitution could be made. In the case of NO_2 (for which there was only one remaining station), the missing values were completed by using the measurements of the central station that had been discarded when available. For this substitution, the NO_2 values were also corrected using the ratio of the mean daily concentration of both sites, for the same year and season. With O_3, for which only one station was available, no substitution could be made for missing values. The location of this O_3 monitor, within the urban centre of Lyon, raises the question of its relevance to O_3 population exposure (due to scavenging by NO).

Table 1 provides descriptive daily data on air pollution and meteorology in Lyon over the period 1985–90 in relation to season.

Mortality data were also provided by the Laboratory of Hygiene, Lyon. Daily counts of total deaths minus deaths external causes (ICD-9 codes <800), total deaths from respiratory diseases (ICD-9 codes 460-519), total deaths from cardiovascular diseases (ICD-9 codes 390-429), and total deaths from digestive diseases (ICD-9 codes 520-579) were chosen for this analysis, based on the published reports. The latter was used as a control condition, for which no association with air pollution was expected. Table 2 gives descriptive daily data for these mortality categories during the study period. Only deaths occurring in Lyon to residents of the city were considered, excluding those registered in other cities of the country or the Lyon metropolitan area. The reason

*Table 2 Mortality in Lyon in relation to cause and season 1985–90 (number of daily events)**

Deaths	Period				
	Winter	*Spring*	*Summer*	*Autumn*	*Whole period*
Total deaths minus external causes					
Mean	7·63	6·69	5·97	6·20	6·43
Minimum	0	0	1	0	0
Maximum	18	15	15	15	18
Respiratory causes					
Mean	0·63	0·47	0·34	0·34	0·40
Minimum	0	0	0	0	0
Maximum	5	5	3	3	3
Cardiovascular causes					
Mean	2·45	2·09	1·68	1·93	2·04
Minimum	0	0	0	0	0
Maximum	8	9	6	8	9
Digestive causes					
Mean	0·41	0·39	0·34	0·36	0·38
Minimum	0	0	0	0	0
Maximum	3	3	4	3	4

*1·1% missing data (0%–2·7% according to season)

Table 3 Descriptive and confounding variables included in the final models

Total external causes	*Respiratory deaths*	*Cardiovascular deaths*	*Digestive deaths*
Trend (linear + quadratic)	Trend (linear)	Trend (linear + quadratic)	Trend (linear)
Years	Years	Years	Years
Sin 1	Sin 2	Sin 1	Sin 1
Cos 1	Cos 2	Cos 1	Cos 1
Sin 2	Sin 3	Sin 5	Sin 2
Cos 2	Cos 3	Cos 5	Cos 2
Sin 3	Days of week	Sin 6	Days of week
Cos 3	Hot season	Cos 6	Hot season
Days of week	Temperature	Days of week	Temperature (linear + quadratic)
Holidays	Humidity (lag 0–2)	Hot season	Humidity
Temperature (linear + quadric)	(linear + quadratic)	Temperature	Influenza epidemic
Humidity	Influenza epidemic	Humidity (lag 1)	
Autocorrelation		(linear + quadratic)	

for this selection was to provide a reasonable estimation of the true ambient air exposure of the population at risk.

The statistical analysis followed the time series protocol established by all the APHEA participants.[20 21] A Poisson time series regression was chosen because it yields directly relative risks which are easily comparable across the different APHEA cities, whose sizes vary a lot. The relation between air pollution and mortality was assessed after controlling for the best fit time patterns and weather factors. The descriptive and confounding variables that were used in the models are presented, for each pollutant, in table 3, including, when relevant, autocorrelation terms. Forward inclusion of descriptive and confounding variables was first done through linear regression modelling where the Wald statistic was the criteria for variable selection (the decision limit of the p value was set at 0·10, not to overlook some residual confounding). Some core variables (sinusoidal terms for long wave seasonality, week patterns, temperature, and relative humidity) were forced into the model in all cities irrespective of their statistical significance. Other variables could be included by each APHEA participant to fit local patterns of the data (year variables, holidays, influenza epidemics etc). Figure 1 shows the residuals of the final descriptive model for total mortality minus external causes in Lyon, before the inclusion of air pollution variables.

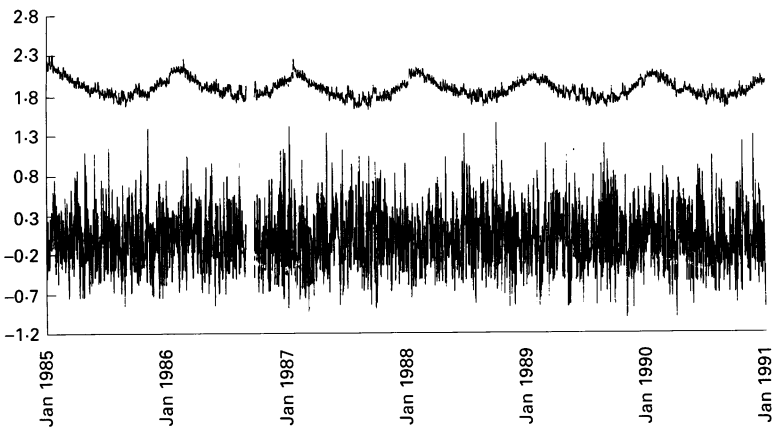

Figure 1 Predicted (log X+1) counts and residuals of the descriptive model for total mortality (minus external causes), including temporal and meteorological variables (variables in table 3).

Three models were tested for each pollutant: the crude concentrations and log or square transformations. The improvement in adjusted R^2 in the linear regression was used to choose the best transform. Also, for each exposure variable (daily mean or maximum hourly values), two types of lags were used: the best fitted one day lag (up to three days for SO_2, PM_{10}, or NO_2, up to four days for O_3) and the average of daily concentrations over several days (up to three to four days), representing some index of cumulative exposure. Furthermore, seasonal variations in the effect of the pollutants were assessed, introducing an interaction term for hot/cold season (for Lyon, "hot season" was defined as days between 1 March and 31 October). The interaction between pollutants that was the most interesting (SO_2 and PM_{13}) was studied by dividing the data set according to PM_{13} concentrations ("high", defined as values above 60 $\mu g/m^3$, and

Table 4 Relative risks of mortality in relation to cause (and 95% confidence interval) associated with a 50 μg/m³ increase in the level of pollutants over the whole 1985–90 period, in Lyon, France

Concentrations	*SO_2*		*PM_{13}*	*NO_2*		*O_3*	
	Mean	*Maximum*	*Mean*	*Mean*	*Maximum*	*Mean*	*Maximum*
Total minus external causes	1·06 (t-0)* (1·09, 1·02)	1·29 (t-0) (1·07, 1·55)	1·01 (t-0) (0·97, 1·05)	1·02 (t-1) (0·98, 1·06)	1·01 (t-1) (0·99, 1·02)	1·03 (t-0) (0·95, 1·12)	1·04 (t-0) (0·94, 1·16)
Respiratory deaths	1·05 (t-3) (1·02, 1·09)	1·02 (t-0-3)† (1·01, 1·03)	1·04 (t-0) (1·00, 1·09)	0·97 (t-2) (0·80, 1·17)	0·99 (t-2) (0·98, 1·01)	1·01 (t-2) (0·92, 1·10)	1·01 (t-1) (0·90, 1·13)
Cardiovascular deaths	1·08 (t-0-3)† (1·03, 1·12)	1·03 (t-1) (1·01, 1·05)	1·04 (t-2) (0·99, 1·10)	1·01 (t-1) (0·96, 1·05)	1·01 (t-2) (0·99, 1·03)	1·00 (t-1) (0·89, 1·12)	0·94 (t-1) (0·82, 1·09)
Digestive deaths	0·98 (t-0) (0·85, 1·13)	0·99 (t-0) (0·88, 1·11)	1·51 (t-0) (0·27, 8·50)	0·99 (t-1) (0·95, 1·02)	0·99 (t-1) (0·97, 1·00)	0·99 (t-0) (0·91, 1·07)	0·99 (-3) (0·89, 1·11)

*(t-x) indicates the lag (x) with the best fit.
†(t-0-3) indicates the average values of SO_2 (over lags 0 to 3 days) that best fit.

"low" values; this 60 μg/m³ limit was set because it represented the median value for several APHEA cities. In Lyon this cut-off point corresponded to the 85th centile of daily values, which actually is not "low"). The best model for SO_2 over the whole period was therefore rerun, after introducing an interaction term between SO_2 concentrations and this new binary variable for PM_{13}.[22]

Once the final model was fitted using linear regression, the corresponding variables (including lags and transforms) were input into a Poisson regression model whose results are presented below.

Results

As a general rule, the associations between mortality and air pollution were more significant using daily means or maximums, rather than averaging over many days' lag. Only these one day lag data will be presented, unless stated when averages over several days were more significant. This only occurs for SO_2. All the regression parameters were converted into relative risks (RR) for a 50 μg/m³ increase of the concentration of pollutants. Since only relatively "moderate to low" levels of pollution were observed during the study period, this computation is most valid in the range of 0–150 μg/m³. Typically, the RRs represent the relative increase in mortality counts when the levels of pollutants step from 25 to 75 μg/m³ (or 50 to 100 μg/m³). Table 4 presents RRs for each pairwise association between pollutant and mortality category, along with their 95% confidence intervals, both for daily means and hourly maximums. In addition, the lags that gave the best fit of the models are indicated.

SO_2 is the only pollutant that shows a clear association with mortality in the city of Lyon; it is associated with an increase in all causes of mortality except digestive conditions over the whole study period. The RRs linking SO_2 to deaths from cardiovascular conditions are the greatest. No effect of particles was apparent over the whole study period for total mortality, but this is of borderline significance for respiratory and cardiovascular deaths. As expected, no pollutant exhibited any association with digestive mortality.

Figure 2 suggests that these effects have weak seasonal patterns. The RRs of respiratory and cardiovascular deaths associated with mean particulate concentrations seemed a little greater during the hot season. The RR for a 50 μg/m³ increase in PM_{13} was 1·06 for respiratory mortality in the cold season and 0·98 in the hot season (p for season interaction = 0·22), while the respective RRs were 1·06 and 0·97 for cardiovascular mortality (p for season interaction = 0·20). The RRs were of borderline significance only during the cold season (p ranging from 0·04 to 0·07); the effect size was, however, always smaller than for the corresponding SO_2 effect, which did not exhibit a seasonal variation. The data also suggested an interaction between particulates and SO_2 whereby the RR of respiratory deaths associated with a 50 μg/m³ increase in daily mean of SO_2 was greater when joint particulates concentrations were "high" (RR of 1·27 (95% CI 1·09, 1·47) when PM_{13} were greater than 60 μg/m³ versus an RR of 1.19 (1·3, 1·37) when PM_{13} were less than 60 μg/m³; p for interaction = 0·03). No clear pattern is shown for cardiovascular mortality. The Pearson correlation coefficient between SO_2 and PM_{13} concentrations measured at the same monitoring site ranged between −0·08 to 0·76 according to season and location in Lyon, showing some independence between both pollutants that allow this pollutant interaction assessment.

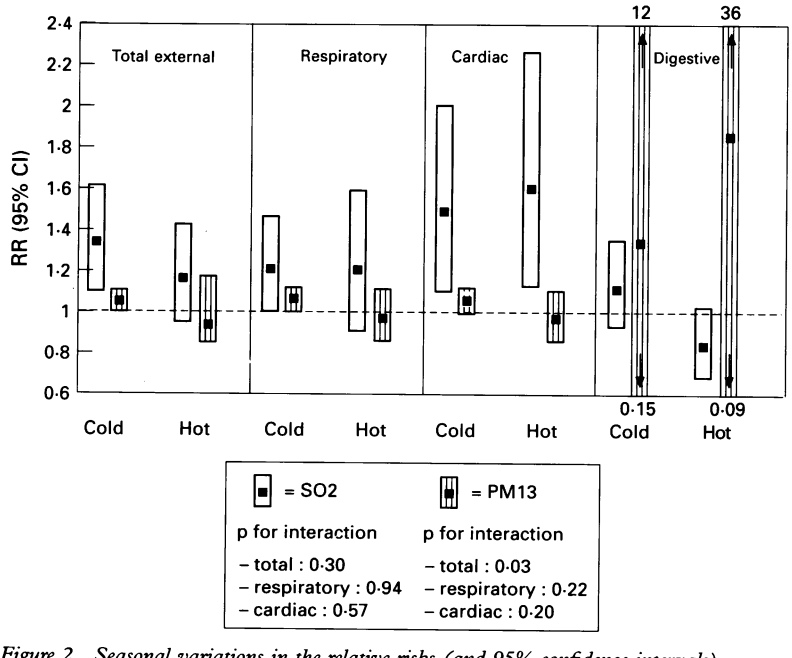

Figure 2 Seasonal variations in the relative risks (and 95% confidence intervals) associated with a 50 μg/m³ increase in SO_2 and PM_{13} in Lyon, France.

Discussion

The main results of this study are the following: (1) only SO_2 and suspended particles showed an association with index categories of mortality; NO_2 and O_3 concentrations were unrelated to mortality. (2) SO_2 was significantly associated with an excess risk of total deaths (minus external causes) and deaths from respiratory and cardiovascular conditions. The effect on respiratory mortality was increased when particulate concentrations were high; no seasonal modification or interaction with particulate pollution was noted for cardiovascular mortality. (3) Suspended particles were also associated with respiratory mortality and, although less clearly, with cardiovascular mortality; the regression coefficients were weaker than for SO_2. The size of these associations was slightly increased during the cold season.

These results should be discussed in the light of the limitations of this study. The variability of the regression parameters and, thus, the levels of significance, depend heavily upon the size of the population. It should be noted that Lyon is the smallest town in the APHEA project, and this affects the counts of daily mortality (0·1%, 65%, 14%, and 68% of days throughout the whole period had no mortality events, for total deaths minus external causes and deaths for respiratory, cardiovascular, and digestive conditions, respectively). This size limitation hampers a clear conclusion, on the subtle season or pollutants' combination effects.

As in all ecological type studies, exposure assessment is characterised by a high degree of misclassification. Indoor exposure to air pollutants cannot be controlled for with such a study design. Indoor air quality changes over time (people tend to open windows in summer and not in winter; indoor heating sources are used only during the cold season etc), and people spend more time outside in summer than in winter. The effect of this misclassification might be differential since, as a general rule, outdoor air tends to relate more closely to total personal exposure during the warm season than during the cold season, but its magnitude is difficult to assess. An effort was made to control for other factors that change over time, such as some meteorological variables and, of course, seasons and days of the week. However, the shape of the association with variables such as temperature and humidity might be more complex than can be modeled, and some residual confounding cannot be excluded. Other variables that characterise the population of Lyon, such as general housing conditions, age, gender, and smoking habits, do not change over time and thus should not confound the results since the time series approach utilises the population as its own control, without external unexposed population.

Another limitation concerns the configuration of the air quality monitoring network. The sites that were used were chosen in order to represent the background exposure to pollutants (and not extreme exposures such as the one indexed by the station located in a busy crossroad in the centre of Lyon). The ranges of concentrations are large enough for SO_2, PM_{13}, and NO_2, giving some power to the study. For O_3, however, whose only monitoring station during the study period was located downtown, the population of Lyon experienced very low exposures because of scavenging by the NO emitted by the traffic. Therefore, the lack of association between mortality and O_3 has no general significance.

NO_2 has been shown to be associated with respiratory symptoms and small reductions in pulmonary function, mostly in the context of indoor exposure and among children.[23 24] However, there is no evidence of an independent association with mortality in the epidemiological reports.

Suspended particles have been consistently related to short term mortality in different meteorological settings. The effect of SO_2 is less clear. Often associated with particulates, its association with mortality is generally considered weaker, at least in many studies conducted in the US. Where both pollutants were measured, the statistical association of SO_2 with mortality often decreased or disappeared where PM was also in the model.[2 9 25] In some European data, however, the effect of SO_2 persisted,[26 27] raising the question of the types of pollution blends indexed by the indicators PM and SO_2 that might differ across continental and urban settings according to the sources of air pollutants. SO_2 is one of many indicators of airborne acidity, along with acid aerosols whose untoward effects have been long established.[28 29] In Lyon, the effect of SO_2 on respiratory and cardiovascular mortality remained significant after adjustment for PM_{13} when both pollutants were kept in the model (data not presented). The interaction with season might also be explained by a change in such a complex pollution make up over time. In spite of the presence of seasonal terms in the models, some regression coefficients for PM_{13} still appeared greater in the cold than in the hot season. Both one day and "cumulative" exposure to air pollutants were considered in the data analysis because it had been suggested elsewhere[5 6] that longer exposure might show a stronger association with mortality than peak exposure. This hypothesis is still unproved, at least by our data, and warrants other studies.

People who died on "high" pollution days were on average a little older than those who died on other days. When SO_2 concentrations exceeded 100 $\mu g/m^3$, the proportion of people older than 70 among those who died (total mortality) was greater (72·0% versus 69·3%, $p = 0·09$); this difference did not hold for PM_{13} (70·2% versus 69·6%, $p = 0·80$). This result supports other findings showing that the elderly and those with acute or chronic respiratory and cardiac conditions are the sensitive population.[4 30 31] SO_2 and particulates per se may not be the primary agressors of the respiratory tract, but they can exacerbate preexisting conditions such as asthma, chronic bronchitis, and emphysema. This extra stress might thus trigger worsening of an existing disorder such as chronic cardiorespiratory

deficiency.[10 32 33] A clear indication of this harvesting effect was given by the data from Erfurt, in East Germany.[25]

In conclusion, this study along with many other APHEA data described in this supplement add to the findings of previous short term mortality studies on particulate air pollution. It also stresses some characteristics of western European urban air where SO_2 pollution still plays an important noxious role.

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