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Short term effects of urban air pollution on respiratory health in Milan, Italy, 1980–89

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Abstract

***Study objective* – To investigate the association between daily urban air pollution and acute effects on respiratory health.**

***Study design* – Time series analysis following the procedure defined in the APHEA protocol.**

***Setting* – City of Milan, Italy, from 1980–89. Two air pollutants, total suspended particulates (TSP) and sulphur dioxide (SO_2), and two health outcomes, deaths and hospital admissions were considered. The last was analysed according to two age groups.**

***Subjects* – Daily deaths and general hospital admissions for respiratory causes in residents who died in Milan or were admitted to local hospitals in that city.**

***Main results* – There was an increased risk of respiratory death and of hospital admission associated with increased concentrations of SO_2 and TSP. The relative risks were similar for both pollutants, and were higher for respiratory deaths than for hospital admissions. No changes in relation to season were seen in the SO_2 effect on respiratory deaths, but there was a suggestion of a higher effect on hospital admissions in the cool months. The seasonal pattern of the TSP effect was inconsistent: for mortality it was higher in the warm period while for hospital admissions it seemed to be higher in the cool months. This last result might be due to chance, although some role could have been played by the hospital admission data on all general admissions for respiratory causes (ICD-9: 460–519) as these are a much less specific end point.**

***Conclusion* – In Milan, a positive association was found between the daily SO_2 or TSP concentrations and the number of deaths or hospital admissions for respiratory causes. This confirms results from other European and North American cities.**

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The episodes of very high pollution that occurred in the Meuse Valley in 1930,[1] in Donora, PA in 1948,[2] and in London in 1952[3] produced clear increases in the number of daily deaths. Since then, studies have reported smaller increases associated with much lower levels of air pollution.[4–13] Most of these studies have been conducted in North America, but more recently similar analyses have been reported in Europe,[14–20] South America, [21] and China.[22]

The principal associations have been reported with airborne particles and with sulphur dioxide (SO_2). It has generally been difficult to separate the contributions of the two pollutants because of their high correlation within a city. However, an analysis in Santa Clara, California[4] found an association between daily deaths and an optical measure of airborne particles in a town with essentially no SO_2 present. Studies have also been conducted that examine correlations between short term changes in air pollution and hospital admissions for respiratory diseases in North America.[23–31] This is also less well examined in Europe.[32–34]

The APHEA project, a multicentre study funded by the European Community, has examined these associations in a range of cities across both eastern and western Europe[35]; because these cities represent a range of co-pollutants, and of coincident weather patterns, this study offers the opportunity to examine some issues of potential confounding using cross study comparisons. Milan is one of the few cities in Italy where daily data on air pollutant concentrations and daily death and hospital admission counts have been available for an extended period. A study of the short term effects of air pollution on health in Milan[36] was started in 1991, with funding from the Italian National Research Council (CNR) and the Electric Power Authority (ENEL). The study joined the APHEA project in 1993. In this paper we report on the results obtained when analysing the short term associations between total suspended particulate matter (TSP) and SO_2 on the number of deaths and the number of hospital admissions due to respiratory disease.

Study design and methods

The municipality of Milan had a mean population of 1·5 million inhabitants during the study period. This population decreased slowly from 1981 (1·6 million) to 1989 (1·45 million). The population age structure showed the typical changes of most western European cities during that period: a reduction in the percentage of children (aged 14 and younger) from 4·1% to 3·2% of the population and an increase in the elderly population (aged 65 and older) from 14·1% to 16·2%. The study area included the central urban area; most of the industries are located north of the city itself.

AIR POLLUTION AND METEOROLOGICAL DATA

Air pollution data were provided by the interdistrict Defence Network for Health and Protection (PMIP) of Milan. During the years 1980–89 reliable data were available from four monitoring stations. These stations were located in different quadrants of the city, about 100 m within the Milan ring avenues. They were generally located in school yards. The 24 hour concentrations of TSP were measured by β attenuation method and the 24 hour SO_2 concentrations by coulometric method. The SO_2 mean hourly concentrations were computed from 15 second automatic measures, while the TSP values were acquired at the end of a two hour cycle of measurements. The 24 hour averages were computed if at least 75% of the measures were available. TSP concentrations were only available for two monitoring locations, and the correlation between their measurements was 0·81. SO_2 concentrations were available from all four stations, and the correlation among those stations ranged from 0·89 to 0·91. The correlation between the TSP and SO_2 was quite high (r= 0·63). Days with missing values were estimated following the APHEA protocol.[30] The TSP concentrations showed a slight upward trend during 1980s, increasing from an average of 132·2 μg/m³ in the years 1980–84 to an average of 142·5 μg/m³ in the years 1985–89. In contrast, SO_2 concentrations fell dramatically during the period – from 157 to 87 μg/m³. This was mainly because of national and local legislation requiring the use of lower sulphur fuel, the conversion of home heating in about half the residences to natural gas, and the transfer of industries outside of the city.

Daily mean temperature and relative humidity were drawn from the Brera-Dome monitoring station in the centre of the city. During the study period, the temperature ranged from an average of 23·6°C (range 11–31) in the summer to 4·3°C (range −6 to 13) in the winter. For relative humidity, the equivalent values were 56% (range 17–95) in summer and 67% (range 6–100) in winter. The distribution of pollution concentrations and meteorological variables are given in table 1.

HEALTH DATA

Anonymous death certificate data for the years 1980–89 were provided from the municipal statistics department. Causes of death were coded locally following the *International Classification of Diseases* (ICD) codes. Only residents of the city who died within the city were included in the analysis. During the study period, the mean number of daily deaths, excluding deaths from external causes (ICD–9:>799), was 31·9. Of these, an average of 2·9 deaths/ day were from respiratory causes (ICD–9:460–519). These deaths are the focus of this manuscript.

Hospital discharge records from all public and private hospitals for the entire region are routinary collected by the epidemiology department of Lombardia Region. Diagnoses were locally coded to ICD-8 codes up to year 1984, and to ICD-9 codes thereafter. This analysis was restricted to residents of Milan who were admitted to hospital in Milan, or to hospitals in the neighbouring local health units. This represents 92% of the admissions of Milan citizens during the period. An average of 11·3 admissions per day for respiratory disease occurred in residents aged 15–64 and an average of 8·8 hospital admissions for respiratory disease in older residents.

STATISTICAL METHODS

Mortality and morbidity were modelled using the APHEA protocol. Poisson regression analysis was used to model dependence of the daily count of deaths or admissions on weather and air pollution, after control for long term trend and season. Long term trend was modelled using dummy variables for years of study, a linear time trend term, and trigonometric functions of time, up to the 6th order, chosen to remove all significant patterns that were detected by spectral analysis. Because some

Table 1 Distribution of daily data on health indicators, meteorology, and air pollution – Milan, 1980–89.

	Period	*Mean*	*Minimum*	*Centile*						*Missing* %*
				5th	*25th*	*50th*	*75th*	*95th*	*Maximum*	
Air pollutants:										
SO_2–24 h (μg/m³)	All	117·7	3·0	15·0	34·0	65·5	162·5	376·3	827·8	14·9
	Winter	248·6	30·6	78·8	138·5	216·0	327·8	527.0	827·8	10·1
	Summer	30·5	3·0	9·1	18·5	27·8	39·2	62·7	113·8	20·4
TSP–24 h (μg/m³)	All	139·0	3·5	46·5	82·0	119·5	175·7	298·5	529·5	19·0
	Winter	193·0	33·5	77·5	128·0	174·5	246·0	355·0	529·5	12·6
	Summer	83·1	3·5	33·1	58·2	81·3	105·5	142.5	201·5	31·5
Meteorological variables:										
Temperature 24 h (C°)	All	14·0	−6	2	7	14	21	26	31	–
	Winter	4·3	−6	−1	2	4	6	9	13	–
	Summer	23·6	11	18	22	24	26	28	31	–
% Relative humidity–24 h	All	62·0	0	34	50	62	75	90	100	–
	Winter	67·0	6	30	52	69	82	95	100	–
	Summer	56·3	17	34	48	56	64	77	95	–
Respiratory diseases:										
No of deaths	All	2·2	0	0	1	2	3	5	12	–
	Winter	2·9	0	0	2	3	4	7	10	–
	Summer	1·7	0	0	1	1	2	4	10	–
Hospital admissions age: 15–64 y	All	11·3	0	3	7	11	15	22	35	–
	Winter	11·8	0	4	8	11	16	22	33	–
	Summer	9·0	0	2	5	8	12	19	33	–
Hospital admissions age: 65 + y	All	8·8	0	3	6	8	11	16	27	–
	Winter	10·5	0	4	8	10	13	18	27	–
	Summer	6·5	0	2	4	6	8	12	17	–

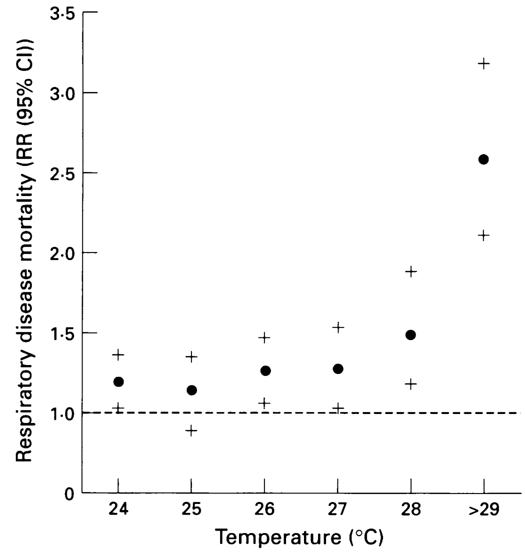
Winter = December to February; Summer = June to August
* % after estimation following the APHEA protocol

patterns can be aliased to several different frequencies when resolved into trigonometric spectra, plots of residuals of the models after the initial choice of trigonometric terms were examined, and any remaining patterns were dealt with. All diagnosis of long term trends was done in models that did not include air pollution. Other factors included in the models were: a dummy variable for months with influenza epidemics (defined as months when the daily admissions for influenza was twice the winter time average), dummy variables for day of the week, and 10 dummy variables for the major holidays.

Separate regression models were fitted for respiratory mortality and for respiratory hospital admissions. Because of the larger number of repiratory hospital admissions, there were sufficient counts to allow separate regressions by age category. Respiratory hospital admissions for children were not analysed because these were dominated by tonsillitis. The choice of weather model was allowed to vary for different outcomes. Exploratory graphical analysis was used to check for any non-linearities in the association with weather terms. If such effects were seen, they were incorporated in the model.

For respiratory *mortality*, the model included relative humidity, mean temperature of the day before, and six dummy variables for very hot days. These dummy variables were defined to represent 1°C temperature intervals from 24°C to 29°C and over. This approach was chosen because respiratory mortality increased non-linearly for very hot days. For *hospital admissions* of people aged 15–64, no effects of very hot days were seen, and the weather model included relative humidity and the same day's temperature. In people aged 65 or more, the weather model included relative humidity and temperature, and a dummy variable for days 29°C and hotter.

Once a baseline model had been developed, we examined the association between air pollution and respiratory outcomes. First, graphical analysis was used to determine whether the air pollution variables should be transformed in the regression analysis. Both SO_2 and TSP showed evidence of a curvilinear relationship, with a smaller slope at higher concentrations. Consequently, both pollutants were logarithmically transformed in our regression analyses. Because of the high degree of collinearity between the two pollutants, their associations with respiratory outcomes were assessed in single pollutant models. In sensitivity analyses, we examined the association of each pollutant with respiratory mortality and morbidity after stratification by high versus low concentrations of the other pollutant. High concentrations were defined as those above 100 μg/m^3. Finally Poisson regression models were fitted, including autoregressive terms of the 1st order for mortality and morbidity in the older age group, and terms up to the 2nd order for morbidity in the younger age group. The pollutant effect was tested for the exposure during a single day, the same day, or up to two days before (lags: 0,1,2) and for the cumulative exposure during consecutive days, up to three days before (lags: 0–1, 0–2, 0–3).



Relative risks, and 95% confidence intervals for dying of respiratory diseases in relation to °C of temperature over 23°C. Milan, 1980-89.

Results from the best fitted models for the single and the cumulative exposure are reported. The pollutants' effect modifications by season were assessed, including in the model a dummy variable for season (reference value: warm season, defined as the semester April–September) and its interaction term with the pollutant. The relative risks for the pollution results are presented for a 100 μg/m^3 increase from a concentration of 25 μg/m^3 to a concentration of 125 μg/m^3.

It has been observed[37] that the power of the statistical tests aimed to detect significant interactions may be very low. Given the very high number of observations in this study, we believe that power is not a problem in testing interactions in our analysis.

Results

WEATHER AND INFLUENZA EPIDEMICS

Hot summer days were associated with an increased risk of deaths when the 24 hour mean temperature reached 24°C (RR = 1·20, 95%Cl 1·04, 1·37) and the risk increased for each additional degree of temperature. If the temperature was 29°C or over the risk reached 2·58 (95%Cl 2·10, 3·17). The figure shows a plot of the relative risks and confidence intervals by degree of temperature above 23°C. Daily mean temperature of 29°C and higher was also associated with an increased risk of respiratory hospital admissions in the older age group (RR = 1·16, 95%Cl 1·01, 1·32). A significant effect of months with influenza epidemics was found for mortality (RR = 1·15, 95% Cl 1·06, 1·25) and hospital admissions in the older age group RR = 1·17 (95% CL 1·12, 22).

AIR POLLUTANTS AND MORTALITY DUE TO RESPIRATORY DISEASES

We found a statistically significant positive effect of SO_2 exposure on the number of deaths

Table 2 Hospital admissions for respiratory diseases (ICD-9: 460–519) in the age group 15–64 years. Effects of sulphur dioxide (SO_2) and total suspended particulate (TSP) levels (μg/m3) log transformed. Autoregressive Poisson models. Milan 1980–89

Lag	Exposure variable		RR*	(95% CI)
SO_2:				
0	Ln SO_2		1·05	1·00,1·10
0	Modification by season†	Warm	1·04	0·98,1·11
		Cool	1·06	1·00,1·13
0	Modification by TSP levels	<100	1·04	0·95,1·14
		≥100	1·03	0·97,1·09
0–3	Ln SO_2		1·09	1·01,1·17
0–3	Modification by season†	Warm	1·05	0·95,1·16
		Cool	1·12	1·03,1·22
TSP:				
2	Ln TSP		1·05	1·00,1·10
2	Modification by season†	Warm	1·08	1·00,1·17
		Cool	1·02	0·96,1·09
2	Modification by SO_2 levels	<100	1·04	0·97,1·12
		≥100	1·04	0·97,1·12
0–3	Ln TSP		1·05	0·98,1·13
0–3	Modification by season†	Warm	1·10	0·98,1·23
		Cool	1·03	0·94,1·12

* RR = relative risk at 125 μg/m^3 *v* 25 μg/m^2; † Warm season = April–September

Table 3 Hospital admissions for respiratory diseases (ICD-9: 460–519) in the age group over 64 years. Effects of sulphur dioxide (SO_2) and total suspended particulates (TSP) levels (μg/m^3) log transformed. Autoregressive Poisson models. Milan 1980–89

Lag	Exposure variable		RR*	(95% CI)
SO_2:				
0	Ln SO_2		1·04	1·00,1·09
0	Modification by season†	Warm	1·02	0·96,1·08
		Cool	1·05	1·00,1·11
0	Modification by TSP levels	<100	1·02	0·95,1·09
		≥100	1·05	1·00,1·11
0–3	Ln SO_2		1·07	0·99,1·15
0–3	Modification by season†‡	Warm	1·00	0·91,1·11
		Cool	1·09	1·01,1·19
TSP:				
1	Ln TSP		1·05	0·99,1·10
1	Modification by season†§	Warm	1·00	0·92,1·08
		Cool	1·07	1·01,1·14
1	Modification by SO_2 levels§	<100	1·02	0·95,1·10
		≥100	1·09	1·02,1·18
0–1	Ln TSP		1·05	0·99,1·12
0–1	Modification by season†	Warm	0·99	0·90,1·10
		Cool	1·07	1·00,1·15

* RR = relative risk at 125 μg/m^3 *v* 25 μg/m^3; † Warm season = April–September; ‡ Interaction term at p<0·10; § Interaction term at p<0·15

that occurred in the same day (RR = 1·12, 95%Cl 1·03, 1·23). The interaction term testing whether there was a seasonal difference in the association was not significant (p = 0·84). The average exposure to SO_2 on the same and the previous day had a slightly larger effect size (RR = 1·16, 95%Cl 1·05, 1·29); this was due to the smaller variance of the two day average pollution measures, and did not reflect any noticeable improvement in model fit. No relevant difference has been observed in the SO_2 effect when the level of particulate matters air concentration is below or over 100 μg/m^3.

TSP was also associated with an increased risk of respiratory mortality (RR = 1·12, 95%Cl 1·02, 1·23). The seasonal interaction term was marginally significant (p<0·10), suggesting a trend toward a stronger TSP effect in the warm season. The average TSP exposure over the same and previous day was also associated with an increased respiratory mortality (RR = 1·14, 95%Cl 1·02, 1·27), but again there was no improvement in fit versus the one day exposure variable. For cumulative exposure, the interaction term with season was significant (p<0·05) and showed a stronger effect of particles in the warm season (RR = 1·39; 95%Cl 1·15, 1·67) than in the cool season. There was no significant difference in the TSP association between low and high SO_2 days, but the effect estimate was larger during days with low SO_2.

AIR POLLUTANTS AND HOSPITAL ADMISSIONS FOR RESPIRATORY DISEASES

Tables 2 and 3 show the results observed for hospital admissions. In those aged between 15 and 64 years the best fitting model for the 24 hour SO_2 exposure (table 2) was the same day (lag 0), while for the cumulative exposure it was the average of four consecutive days (lag 0–3). The effect of SO_2 exposure, of the single day or the cumulative days, was more pronounced in the cool months, although the interaction term testing the seasonal difference was not significant. No evidence of interaction with different levels of TSP was found. The best fit in the TSP exposure models (table 2) were obtained with the concentration of two days before (lag 2) and the average of four consecutive days (lag 0–3). The TSP exposure of two days before showed a higher effect in the warm season (RR = 1·08, 95%Cl 1·00, 1·17), although the interaction term was not significant. There was no evidence of an interaction with SO_2 levels.

In the older age group, the best fit in the models for SO_2 exposure (table 3) was found at the same lags as the younger group. The associations were slightly weaker, however. Again, there was a suggestion that the effect was primarily during the cool months, although the interaction term was marginally significant only for the cumulative days exposure (p<0, 10). In the analyses of TSP effects on the elderly (table 3), the best fitted models were the previous day (lag 1) and the average of the same and previous day (lag 0–1). TSP air concentrations also seemed to have a greater effect in the cooler months. There was a little evidence of an interaction with SO_2 levels over 100 μg/m^3.

Discussion

We found that both SO_2 and TSP concentrations were associated with increased risks of respiratory deaths and hospital admissions. This confirms earlier findings. Dockery and Pope[12] summarised published reports. After converting their PM_{10} unit into a TSP unit, they found that a 100 μg/m^3 increase in TSP was associated with a relative risk of 1·17 for respiratory deaths. In this study, we found a relative risk of 1·12 which is quite consistent with their results.

We found an increase of 4–5% in hospital admissions for all respiratory causes for a 100 μg/m^3 increase in the TSP or SO_2 concentration. This is consistent with the effect, reported in the same review[12]: combining results from different studies the authors found that a 100 $\mu g/m^3$ increase in TSP was associated with a 4% increase in general hospital admissions for respiratory diseases. These results are also in the range of other estimates reported in a recent review.[13] Hospital admissions depend on cultural differences and national medical practices, as well as on health status. This can have substantial effects on the baseline number of admissions, and hence on the estimated relative increase. This may affect our findings.

For SO_2 the mortality association showed no effect in relation to season, but there was some evidence of such effect for hospital admission; the association seemed stronger in the winter. However, this may merely reflect the fact that non-urgent respiratory admissions form a larger percentage of total respiratory admissions in the warm months when infectious respiratory illness is at a minimum. The particulate matter association showed relatively immediate effects on the number of deaths and hospital admissions in elderly people, for both the single day and the cumulative days exposure (lag 0 or lag 1, and lag 0–1), while the effects were less immediate on hospital admissions in people aged between 15 and 64 years (lag 2 and lag 0–3). While some evidence of seasonal interaction for the TSP effects was also seen, this was inconsistent between mortality and hospital admissions. This suggests that the difference could be due to chance. The weak interactions with SO_2 seen for TSP exposure are indistinguishable from the seasonal ones. For mortality, the TSP effect was higher in the warm weather and on the days when SO_2 was low. For hospital admissions in the elderly the TSP effect was higher in the cool season and for high SO_2 days. However, SO_2 concentrations are highly seasonal, peaking in the winter, so it is difficult to determine whether these results hint at effect modification by season or SO_2, or, given their inconsistency, nothing.

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