Air pollution and cause specific mortality in Athens

K Katsouyanni, A Karakatsani, I Messari, G Touloumi, A Hatzakis, A Kalandidi, D Trichopoulos

Abstract

Study objective—The aim was to investigate the reported association between air pollution and cause specific mortality in the city of Athens.

Design—Cause specific mortality was contrasted between 199 d with high values of air pollution and 2*199 comparison days with low pollution, matched in a 1:2 ratio on the basis of various confounding factors. Statistical analysis was done, taking matching into account, using analysis of variance for randomised blocks.

Setting—The study was confined to the city of Athens, using data obtained between 1975 and 1982.

Participants—Cause of death was assessed in all 25 138 persons dying in the 3*199 d studied.

Measurements and main results—Causes of death were evaluated blindly by two medically qualified investigators on the basis of information in the death certificates. Mortality was generally higher during the high pollution days but the difference was more pronounced and more significant for respiratory conditions, even though the number of deaths in this category was smaller than the corresponding numbers in the other two categories examined (cardiac and "other" deaths).

Conclusion—The results show that the short term association between air pollution and overall mortality in Athens is likely to be causal, since it is particularly evident with respect to respiratory conditions, for which a biological air pollution link is more plausible.

$\mu\text{g}/\text{m}^3$.⁴ Between 1975 and 1982 a gradual reduction in the levels of SO_2 and to a lesser extent of smoke occurred as a result of several measures implemented to improve the quality of heating and car fuel.⁵ However, since 1982 pollution levels have stabilised, with an apparent change in pollutant profile towards a more pronounced photochemical component.⁶ The study of adverse health effects remains, therefore, relevant.

In a recently published paper⁵ the results of the study of short term effects of air pollution on total mortality were reported, using daily measurements of smoke and SO_2 as indicators of air pollution and daily number of all deaths in the Greater Athens area for the years 1975-82 as the health response variable. A positive statistically significant "effect" of high values of SO_2 on mortality was observed after controlling for the potential confounding effects of several variables (temperature, humidity, seasonal patterns, secular trends, monthly variation, day of the week, holidays etc), with a threshold at about the level of $150 \mu\text{g}/\text{m}^3$ SO_2 (geometric mean from measurements of five stations). In that study residual confounding by an unidentifiable or inadequately controlled factor could have been responsible for the results. One way to investigate the existence of such confounding is to use the specificity criterion to assess causality, ie, to explore whether the observed association concerns mainly deaths from respiratory causes, for which there is a more plausible a priori hypothesis. We report here the results of a study undertaken to investigate the association between air pollution and cause specific mortality for all ages as well as for specific age groups.

Methods

During the years 1975-1982 (inclusive) the total number of deaths reported to the Athens Town Registry and the Registries of all contiguous towns exceeded 100 000. Routine statistics on cause of death, age, sex, etc, are not available through the National Statistical Service or any other Authority on a daily basis, nor are the data of individual death certificates computerised. The information needed in order to study cause and age specific mortality had to be abstracted by us from the original death certificates. Since the amount of work involved in order to record information on all deaths during the study period was disproportionately high, we decided to change the study design in order to maximise cost-efficiency. A design contrasting high and low exposure was chosen where "index days" were all the days ($n = 199$) with high pollution levels (mean geometric value of SO_2 , as pollution indicator

The lethal short term effects of high levels of air pollution have been documented more than 30 years ago in studies of very severe episodes which occurred in the USA and Northern Europe.¹ Since that time, specific measures have been taken and air quality standards have been set, resulting in substantial lowering of the air pollution levels in most developed countries. However, more recent studies have demonstrated short term effects of air pollution on health even at relatively low levels, eg, when values of smoke are below $500 \mu\text{g}/\text{m}^3$.^{2,3}

Athens faces a serious air pollution problem which has probably existed for more than 20 years. Monitoring of pollutants, such as SO_2 and smoke, started in the mid-seventies and revealed that levels of smoke and SO_2 often exceeded 500

Department of Hygiene and Epidemiology, University of Athens Medical School, Goudi, 115 27 Athens, Greece
K Katsouyanni
A Karakatsani
I Messari
G Touloumi
A Hatzakis
A Kalandidi
Department of Epidemiology, Harvard School of Public Health, 677 Huntington Avenue, Boston, Massachusetts, USA
D Trichopoulos

Correspondence to:
Dr Katsouyanni

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from five monitoring stations, $> 150 \mu\text{g}/\text{m}^3$, ie, on or above the level of the estimated threshold for the study period),⁵ and “comparison days” were days ($n=398$) with low pollution levels ($\text{SO}_2 < 150 \mu\text{g}/\text{m}^3$) individually matched to the index days for all the previously established confounding factors.⁵ More specifically, each index day was matched with two comparison days using the following criteria: (1) index and comparison days should not differ in 24 h mean temperature by more than 4°C ; (2) index and comparison days should belong to the same, the previous or the following calendar year; (3) index and comparison days should belong to the same season of the year and not differ by more than 20 d; (4) comparison days should be the same week days as the corresponding index day; (5) if an index day was a holiday so should be the two comparison days.

For example, Tuesday, March 13, 1979 (temperature 14°) was matched with Tuesday, March 20, 1979 (temperature 16°) and Tuesday, March 4, 1980 (temperature 14°). Index days were either single days (about 50 days) or ran over two or three consecutive days. Index days were concentrated more in the early years of the study period and especially during the winter months. Information on age, sex, and cause of death concerning all deaths which occurred on the 199 index and 398 comparison days included in the study was abstracted from death certificates of the Athens Town Registry and the Registries of the contiguous towns. All deaths and burials occurring in these towns must be recorded in the Town Registries.

The information about the cause of death was photocopied from the death certificates and the deaths were blindly (as to the level of air pollution and the values of confounding factors) classified by two of us according to immediate and underlying cause of death using the ICD8.⁷ Three categories were used for the underlying, as well as for the immediate cause of death: cardiac deaths, deaths from respiratory causes, and “other”. Also, a descriptive parameter was calculated taking the difference of the percentage of deaths observed on index days from the expected percentage, ie, 33.33% . Statistical evaluation was done using goodness of fit χ^2 taking no account of the matching and ANOVA for randomised blocks, considering every set of one index and two comparison days as one block—a total of 199 blocks (this way of analysis preserves the matching of index and comparison days and increases statistical precision while allowing an assessment of the efficiency of “blocking”).⁸

Results

Table I shows the mean and maximum daily values of SO_2 and smoke (based on daily smoke filter observations, assessed by reflectance) by measurement site for the study period, and table II shows the mean values of the geometric mean of the five measurement stations by year. Table III shows the number of deaths which occurred on index and comparison days by underlying cause of death for all ages. The number of deaths from respiratory causes shows a statistically significant excess during index days ($p < 0.05$). The observed

number of deaths from respiratory causes during index days was 767, while only 723 would be expected under the null hypothesis. There were also more deaths from both cardiac and other causes on index days, but these excesses are smaller (as shown by the differences in expected and observed percentages on index days) although still statistically significant for “other” causes. Table IV shows the number of deaths which occurred on index and comparison days by immediate (proximate) cause of death. Deaths from respiratory causes show a similar excess to that observed when underlying causes were analysed. Deaths from other causes also show an excess, which again is proportionally smaller but still statistically significant. In Tables V and VI the number of deaths which occurred on index and comparison days is shown by underlying and immediate cause of death respectively, among persons aged 75 years or more. The number of deaths from respiratory causes was greater during the index days ($p < 0.10$ for underlying causes and $p < 0.005$ for immediate causes). The observed number of deaths from underlying respiratory causes was 472 while the expected was 443; and the corresponding figures with respect to immediate causes are 392 and 355. An analysis for infant mortality showed a similar pattern, but the number of deaths was too small to allow statistical substantiation.

Discussion

Public health measures have led to the reduction of air pollution levels, at least in countries where the problem has been acute for 20–30 years.⁹ However, in the last 10 years, there has been growing concern about the short term health effects of lower levels of air pollution (ie, lower than the air quality standards set by national and international organisations^{2,3}). The aggregate evidence, however, remains inconclusive.¹ The levels of some air pollutants monitored in Athens (particularly smoke, NO_2 and CO) are generally high, frequently exceeding the WHO air quality guidelines.^{10,11} For example, measurements of NO_2 (1 h) at the centre of town exceeded $400 \mu\text{g}/\text{m}^3$ on 12 d and $250 \mu\text{g}/\text{m}^3$ on 135 d during the five year period 1983–1987 and the value of smoke (24 h) was more than $250 \mu\text{g}/\text{m}^3$ on 313 d during the same period.⁶ Athens may, therefore, be considered as a city facing a serious air pollution problem. Furthermore, the pollution mixture in Athens may be different from that studied in other settings, since high levels of both smoke and photochemical pollutants are noted. Lastly, factors known to affect mortality, particularly high summer temperatures, are more common in this city¹² than in other cities where the interactive effects of air pollution and other environmental factors have been investigated.^{13,14}

The study reported here is a contribution towards the identification and measurement of the short term effects of moderate levels of air pollution on mortality. The short term effects of air pollution on mortality from respiratory and other diseases are investigated using an “extreme points” contrast in order to maximise the inherent power of the design.^{15,16} In addition, the comparative evaluation of the effects of air

Table I Mean and maximum daily values of SO₂ and smoke, by measurement site, in Athens 1975–82.

Measurement site	SO ₂ (µg/m ³)		Smoke (µg/m ³)	
	Mean	Maximum	Mean	Maximum
National Observatory	80.1	797.0	35.0	239.0
University Club	90.7	936.0	109.4	790.0
Agricultural School	98.8	392.0	43.8	440.0
School of Visiting Nurses	81.3	695.0	64.7	570.0
Student's Hostel	96.6	870.0	68.6	740.0

Table II Mean values (standard deviations) of the geometric mean of daily measurements, from five measuring stations, of SO₂ and smoke by year

Year	SO ₂ (µg/m ³) Mean (SD)	Smoke (µg/m ³) Mean (SD)
1975	126.5 (102.5)	73.3 (41.4)
1976	90.7 (55.5)	66.5 (33.0)
1977	92.8 (48.0)	56.5 (30.3)
1978	78.5 (33.1)	51.6 (28.5)
1979	80.9 (34.4)	54.3 (31.7)
1980	73.7 (32.3)	56.6 (29.7)
1981	76.0 (34.6)	53.6 (34.8)
1982	62.4 (17.5)	41.4 (23.7)

Table III Number of deaths which occurred on "index" and "comparison" days according to underlying cause of death (all ages)

Underlying cause of death	Number of deaths		Percent observed minus percent expected on index days	$\chi^2(p)^a$	$F(p)^b$
	Index days	Comparison days			
Cardiac	3952	7702	0.58	1.73 ^c	2.93(<0.10)
Respiratory	767	1404	1.99	3.83(0.05)	5.19(<0.03)
Other	3860	7433	0.85	3.67(<0.10)	8.32(<0.005)
Total	8579	16539	0.82	7.60(<0.01)	10.72(<0.005)

^a χ^2 goodness of fit^b F from ANOVA for randomised blocks^c $p > 0.10$

Table IV Number of deaths which occurred on "index" and "comparison" days according to immediate cause of death (all ages)

Immediate cause of death	Number of deaths		Percent observed minus percent expected on index days	$\chi^2(p)^a$	$F(p)^b$
	Index days	Comparison days			
Cardiac	5197	10 234	0.35	0.82 ^c	1.32 ^c
Respiratory	730	1315	2.37	5.07(<0.05)	8.43(<0.005)
Other	2652	4990	1.37	6.49(<0.05)	11.90(<0.005)
Total	8579	16 539	0.82	7.60(<0.01)	10.72(<0.005)

^a χ^2 goodness of fit^b F from ANOVA for randomised blocks^c $p > 0.10$

Table V Number of deaths which occurred on "index" and "comparison" days according to underlying cause of death (only persons aged 75 years or more)

Underlying cause of death	Number of deaths		Percent observed minus percent expected on index days	$\chi^2(p)^a$	$F(p)^b$
	Index days	Comparison days			
Cardiac	2191	4358	0.13	0.04 ^c	0.08 ^c
Respiratory	472	858	2.16	2.85(<0.10)	3.35(<0.10)
Other	1341	2701	-0.15	0.04 ^c	0.08 ^c
Total	4004	7917	0.26	0.34 ^c	0.95 ^c

^a χ^2 goodness of fit^b F from ANOVA for randomised blocks^c $p > 0.10$

Table VI Number of deaths which occurred on "index" and "comparison" days according to immediate cause of death (only persons aged 75 years or more)

Immediate cause of death	Number of deaths		Percent observed minus percent expected on index days	$\chi^2(p)^a$	$F(p)^b$
	Index days	Comparison days			
Cardiac	2726	5543	-0.36	0.49 ^c	1.10 ^c
Respiratory	392	674	3.44	5.78(<0.05)	8.10(<0.005)
Other	886	1700	0.93	1.00 ^c	1.95 ^c
Total	4004	7917	0.26	0.34 ^c	0.95 ^c

^a χ^2 goodness of fit^b F from ANOVA for randomised blocks^c $p > 0.10$

pollution on cause-specific mortality allows the utilization of the specificity criterion in order to assess the causal nature of the association of air pollution and overall mortality. Thus the untowards health effects of air pollution, if any, should be more pronounced for respiratory diseases, and weaker for the conditions which lack a strong respiratory or circulatory component. It should be noted that the matching approach used could be reserved in order to study temperature effects, controlling for air pollution levels.

As early as 1953 Logan¹⁷ reported that the increase of mortality in the 1952 London air pollution episode was mainly due to an eightfold increase in deaths from bronchitis and a threefold increase in deaths from pneumonia, while deaths from all other causes showed smaller relative increases. Similar conclusions were reported by Martin and Bradley¹⁸ from London; Greenburg *et al.*,¹³ Schimmel and Greenburg,¹⁹ and Schimmel and Muraski²⁰ from New York; and Mazumdar and Sussman²¹ from Pittsburgh. Results from studies focusing on various pollution and morbidity (rather than mortality) indicators have also supported the notion that the main health effects of air pollution concern the respiratory system and, to a lesser extent, the circulatory system. These studies have been undertaken in many cities and countries of the world including Nashville, Tennessee,²² Chicago,²³ London,^{24 25} New York,^{26–28} Los Angeles,^{29–31} Ontario,^{32 33} and Dublin.^{34 35}

Different studies have used various air pollution indicators depending on which pollutants were perceived as important and according to availability of measurements. It is not easy to specify the effects of each specific pollutant on health, since the exact composition of the polluted air is rarely known and the levels of most pollutants are highly correlated. In Athens, during the study period (1975–1982), only SO₂ and smoke levels were systematically measured, but it is highly likely that photochemical pollution was already considerable. In the present study, SO₂ was used to define high and low pollution days because the respective measurements were available throughout the study period in all five stations of the air pollution monitoring network and its distribution throughout the covered area was more uniform compared to that of smoke.^{5 36} Nevertheless SO₂ and smoke were highly correlated ($r = 0.73$) and correlations between other pollutants and SO₂ were also likely to be strong, making the latter an acceptable overall air pollution indicator. It follows therefore that SO₂ is only an "index" of air pollution, and the specific "threshold" used here to define high pollution days may not have the same meaning in a different context, ie, in a different area or time period.

The possibility of residual confounding and hidden biases can never be excluded in observational studies. It is therefore conceivable that the previously reported association between daily SO₂ and total daily mortality^{5 37} was not causal, even though great care was taken to control seasonal, weekly, and monthly variations as well as possible confounding relationships with extreme temperatures, humidity, and other meteorological factors. In the present study, the air pollution association with respiratory causes is

specifically strong, making causality a more plausible interpretation of the results.

In conclusion, air pollution in Athens during the study period appears to have definite short term effects on the mortality of the residents of the city. The association is not very strong but the results of the present study clearly indicate that it is causal since it is particularly evident with respect to respiratory conditions, thus satisfying the specificity criterion of causality.³⁸

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- 1 Ware JH, Thibodeau LA, Speizer FE, Colome S, Ferris BG. Assessment of the health effects of atmospheric sulfur oxides and particulate matter: evidence from observational studies. *Environ Health Perspect* 1981; 41: 255-76.
- 2 Mazumdar S, Schimmel H, Higgins IT. Relation of daily mortality to air pollution. An analysis of 14 London winters 50/59-71/72. *Arch Environ Health* 1982; 37: 213-28.
- 3 Ostro BD. A search for a threshold in the relationship of air pollution to mortality: a reanalysis of data on London winters. *Environ Health Perspect* 1984; 58: 397-9.
- 4 Bureau for Athens Environmental Pollution Monitoring. Technical Report, Vol 4, Athens: Ministry of Social Services, 1980.
- 5 Hatzakis A, Katsouyanni K, Kalandidi A, Day N, Trichopoulos D. Short-term effects of air pollution on mortality in Athens. *Int J Epidemiol* 1986; 15: 73-81.
- 6 Katsouyanni K, Kalandidi A, Trichopoulos D, Hatzakis A. Short-term effects of air pollution on mortality in Athens 1983-1987. Report to the Minister of Environment, Planning and Public Works. Athens, 1988.
- 7 World Health Organization. *International classification of diseases*. Eighth revision. Geneva: WHO, 1967.
- 8 Snedecor GW, Cochran WG. *Statistical methods*, 6th ed. Iowa: Iowa State University Press, 1967.
- 9 Waller RE. Control of air pollution: present success and future prospect. In: Bennett AE. *Recent advances in community medicine*. Edinburgh: Churchill Livingstone, 1978.
- 10 World Health Organization. *Air quality guidelines for Europe*. WHO Regional Publications, European Series No. 23. Geneva: WHO, 1987.
- 11 Trichopoulos D, Hatzakis A, Wynder E, Katsouyanni K, Kalandidi A. Time trends of tobacco smoking, air pollution, and lung cancer in Athens. *Environ Res* 1987; 44: 169-78.
- 12 Katsouyanni K, Trichopoulos D, Zavitsanos X, Touloumi G. The 1987 Athens heatwave (letter to the Editor) *Lancet* 1988; ii: 573.
- 13 Greenburg L, Field F, Erhardt CL, Glasser M, Reed JT. Air pollution, influenza and mortality in New York City. *Arch Environ Health* 1967; 15: 430-8.
- 14 Buechley RW, Riggan WB, Hasselblad V, Van Bruggen JB. SO₂ levels and perturbations in mortality. A study in New York-New Jersey Metropolis. *Arch Environ Health* 1973; 27: 134-7.
- 15 Miettinen OS. *Theoretical epidemiology*. New York: John Wiley, 1985.
- 16 Rothman KJ. *Modern Epidemiology*. Boston: Little, Brown and Co., 1986.
- 17 Logan WPD. Mortality in the London fog incident: 1952. *Lancet* 1953; i: 336-8.
- 18 Martin AE, Bradley WH. Mortality, fog and atmospheric pollution—an investigation during the winter of 58-59. *Monthly Bull Ministry of Health* 1960; 19: 56-72.
- 19 Schimmel H, Greenburg L. A study of the relation of pollution to mortality, NYC, 1963-68. *J Air Pollution Control Assoc* 1972; 22: 607-16.
- 20 Schimmel H, Murawski TJ. The relation of air pollution to mortality. *J Occup Med* 1976; 18: 316-33.
- 21 Mazumdar S, Sussman N. Relationships of air pollution to health: results from the Pittsburgh Study. *Arch Environ Health* 1983; 38: 17-24.
- 22 Zeidberg LD, Prindle RA, Landau E. The Nashville air pollution study. I. Sulfur dioxide and bronchial asthma. A preliminary report. *Am Rev Respir Dis* 1961; 84: 489-503.
- 23 Carnow BW, Lepper MH, Shekelle RB, Stamler J. Chicago air pollution study. SO₂ levels and acute illness in patients with chronic bronchopulmonary disease. *Arch Environ Health* 1969; 18: 768-76.
- 24 Martin AE. Mortality and morbidity statistics and air pollution. *Proc R Soc Med* 1964; 57: 969-75.
- 25 Lawther PJ, Waller RE, Henderson M. Air pollution and exacerbations of bronchitis. *Thorax* 1970; 25: 525-39.
- 26 Greenburg L, Field F, Reed JT, Erhardt CL. Air pollution and morbidity in New York City. *JAMA* 1962; 182: 161-4.
- 27 Glasser M, Greenburg L, Field F. Mortality and morbidity during a period of high levels of air pollution. *Arch Environ Health* 1967; 15: 684-94.
- 28 McCarroll J. Measurements of morbidity and mortality related to air pollution. *J Air Pollution Control Assoc* 1967; 17: 203-9.
- 29 Sterling TD, Pollack SV, Weikam J. Measuring the effect of air pollution on urban morbidity. *Arch Environ Health* 1969; 18: 485-94.
- 30 Korn EL, Whittemore AS. Methods for analyzing panel studies of acute health effects of air pollution. *Biometrics* 1979; 35: 795-802.
- 31 Schwartz J, Hasselblad V, Pitcher H. Air pollution and morbidity: a further analysis of the Los Angeles Student Nurses Study. *J Air Pollution Control Assoc* 1988; 38: 158-62.
- 32 Levy D, Gent M, Newhouse MT. Relationship between acute respiratory illness and air pollution levels in an industrial city. *Am Rev Respir Dis* 1977; 116: 167-73.
- 33 Bates DV, Sizto R. Relationship between air pollutant levels and hospital admissions in Southern Ontario. *Can J Public Health* 1983; 74: 117-22.
- 34 Kevany J, Rooney M, Kennedy J. Health effects of air pollution in Dublin. *Ir J Med Sci* 1975; 144: 102-15.
- 35 Bailey ML, Kevany JP, Walsh JJ. Air pollution and social welfare claims. *Ir J Env Sci* 1981; 1: 51-7.
- 36 National Observatory of Athens, Meteorological Institute. *Bulletin of air pollution*, Vol 6-13. Athens, 1975-1982.
- 37 Vatopoulos A, Hatzakis A, Tzonou A, Trichopoulos D. Daily variation of air pollution and total mortality in Athens. *Arch Med Soc* 1980; 7: 588-91.
- 38 US Department of Health, Education and Welfare. *Smoking and health*. Report of the Advisory Committee to the Surgeon General of the Public Health Service. Public Health Service Publication No 1103. Washington US Government Printing Office, 1964.