Human health risks of airborne particles: Historical perspective [1]

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1. INTRODUCTION

The historical overview is limited to the past 125 years on the basis that this is the period whose experience with particulate matter (PM) pollution remains relevant to contemporary concerns. A landmark event was the London smog of 9-11 December 1873, which produced a significant excess of human mortality, as well as mortality and pathological changes in show cattle that were on exhibit at that time. A similar smog episode of 5-9 December 1952 caused similar responses, and led to remedial action in the UK during the 1950's and 1960's that greatly reduced both black smoke concentrations and their public health impacts.

In the post coal-smoke era, epidemiological studies in the U.S. showed close associations between the sulfate (SO4=) concentrations in PM and annual mortality, hospital admissions for respiratory and cardiovascular diseases, lost-work time, and respiratory symptoms. With the introduction of monitoring networks for thoracic particulate matter (PM10) in the mid 1980's, many investigators began to show significant correlations between PM10 and daily mortality for a large number of urban areas that differed greatly in climate and in their proportions of other air pollutants. In the relatively few studies

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that also had access to data on the mass concentrations of particles smaller than 2.5 μm in aerodynamic diameter (PM2.5), the associations with health effects were generally comparable to the associations with SO4=, and stronger than those with PM10, leading the EPA Administrator to propose new National Ambient Air Quality Standards (NAAQS) for PM2.5. This paper reviews these historical developments.

2. HIGHLIGHTS OF THE COAL-SMOKE ERA

Quantitative information on adverse health effects associated with particulate matter dates back to the London episode of 1873. A summation of bronchitis mortality during and following the 9-11 December 1873 fog episode was tabulated in the Ministry of Health (1954) report of the 5-9 December 1952 episode. As shown in Table 1, various 19th Century fog episodes produced excesses in bronchitis deaths that were comparable to that reported for the more famous 1952 episode. Also, it is important to note the higher baseline bronchitis mortality for London in the late 19th Century, when the population was below 3 million (compared to about 8 million in 1952), and at a time when that cigarette smoking could not have been a contributory cause.

Table 1

Excess Bronchitis Deaths Associated with Historic London Fogs

Dates of Fog*	Av. Weekly Bronchitis Mortality in Previous 10 Years*	Excess Bronchitis Deaths in Week of Fog and During Succeeding Three Weeks*				Total 4 Week Excess in Bronchitis Deaths
9-11 Dec. 1873		7-13 Dec.	14-20 Dec.	21-27 Dec.	28 Dec.-3 Jan.	
	228	133	424	129	102	788
26-29 Jan. 1880		25-31 Jan.	1-7 Feb.	8-14 Feb.	15-21 Feb.	
	294	258	939	453	167	1817
2-7 Feb. 1882		29 Jan.-4 Feb.	5-11 Feb.	12-18 Feb.	19-25 Feb.	
	357	14	324	186	31	555
21-24 Dec. 1891		20-26 Dec.	27 Dec.-2 Jan.	3-9 Jan.	10-16 Jan.	
	375	35	583	333	437	1388
28-30 Dec. 1892		25-31 Dec.	1-7 Jan.	8-14 Jan.	15-21 Jan.	
	451	-55	208	154	2	309
26 Nov.- 1 Dec. 1948		21-27 Nov.	28 Nov.-4 Dec.	5-11 Dec.	12-18 Dec.	
	65	14	84	33	20	151
5-9 Dec. 1952		1-6 Dec.	7-13 Dec.	14-20 Dec.	21-27 Dec.	
	86	-3	621	308	92	1018

* Source: Ministry of Health (1954). Report # 95 on Public Health and Medical Subjects. MORTALITY AND MORBIDITY DURING THE LONDON FOG OF DECEMBER 1952. London, H.M. Stationery Office.

The first scientific literature citation on the health effects of London smog was also related to the December 1873 episode. Some excerpts from this paper follow:

Excerpts from: The Veterinarian XLVII (JAN. 1874)

THE EFFECTS OF THE LONDON FOG ON CATTLE IN LONDON

Our readers will have heard a good deal already about the terrible disturbance which was caused at the last show of the Smithfield Club by the sudden occurrence of a dense fog during a sharp frost....The atmosphere became dense and pungent on the second day of the Show of 1873....

Before the fog had continued for many hours some of the cattle in the Agricultural Hall evinced palpable signs of distress.

On Tuesday, the first day of the fog, as early as eleven o'clock in the morning several animals were marked as affected with difficult breathing. No abatement of the fog took

place during the day; on the contrary, towards evening it became rather worse, and the majority of the cattle in the Hall showed evidence of suffering from its influence.

Sheep and pigs did not however experience any ill effect from the state of the atmosphere either then or during the remaining time of the Show.

During Wednesday night ninety-one cattle were removed from the Hall for slaughter. On Thursday the atmospheric conditions were improved, and no fresh attacks were recorded. On Friday, the air was comparatively clear, and all the animals which remained in the Hall were in good sanitary condition.

The post-mortem appearance were indicative of bronchitis; the mucous membrane of the smaller bronchial tubes was inflamed, and there was also present the lobular congestion and emphysema which belong to that disease.

While we have no air concentration data for the late 19th Century episodes, we do have visual impressions of air quality of that era. Figure 1 is a Gustave Dore woodblock print of 1872 of a downtown London street showing a plume from a coal-fired locomotive, as well as horse drawn traffic and smoke from domestic furnaces. Figures 2 and 3 shows Claude Monet paintings of the Thames River at London in 1871. Figure 4 is an 1884 watercolor by James McNeil Whistler of Piccadilly. Monet was so entranced by the varying colors of the coal smoke that he encountered during his residence in London in the early 1870's that he returned for a 3-year visit at the turn of the Century and produced about 100 oil paintings of London and vicinity. Figure 5 is one of these paintings of the Houses of Parliament.

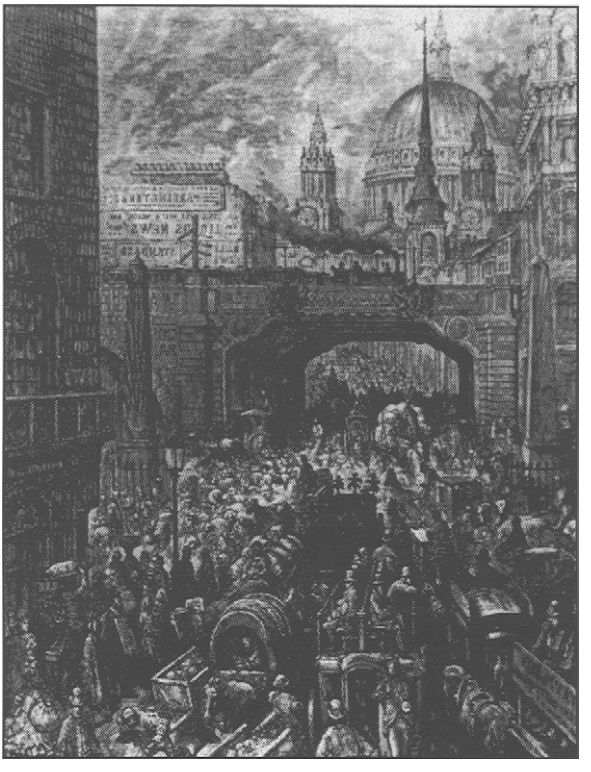


Figure 1. Ludgate Hill - A Block in the Street. Gustave Dore - 1872.

Figure 2. 1871 painting by Claude Monet entitled 'Boats on the Thames, London'. Private Collection.

Figure 3. 1871 painting by Claude Monet entitled 'Westminster Bridge'. The National Gallery, London.

Figure 4. 1884 watercolor by James McNeil Whister entitled 'Nocturne in Grey and Gold-Picadilly'. National Gallery of Ireland, Dublin.

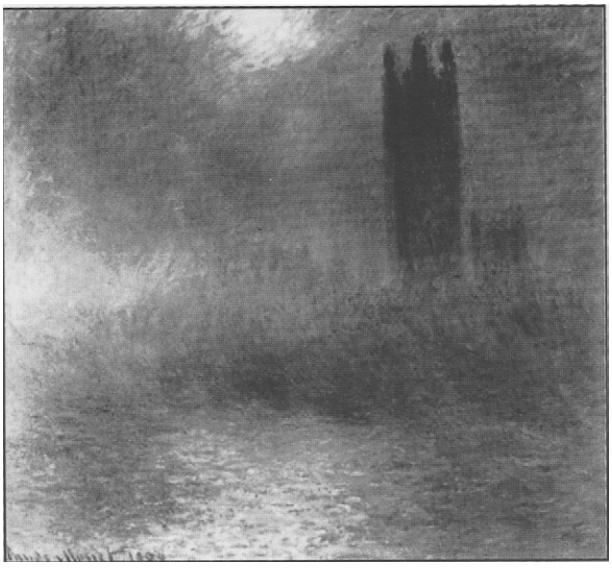


Figure 5. 1904 painting by Claude Monet entitled 'Houses of Parliament, London, Sun Breaking through the Fog'. Musee d'Orsay, Paris.

As shown in Figure 6, the daily death rate rose rapidly with the onset of the fog on December 5, 1952, and peaked one day after the peak of pollution, as it was indexed by the measured pollutants, i.e., black smoke (BS) and sulfur dioxide (SO2). There was also a rise in hospital emergency bed admissions, which peaked two days after the pollutant peaks. Both the deaths and hospital bed admissions remained elevated for several weeks after the fog lifted (see Tables 1-3). Note also that hospital admissions exhibited declines on Sundays, a finding consistent with the known practices for hospital admissions.

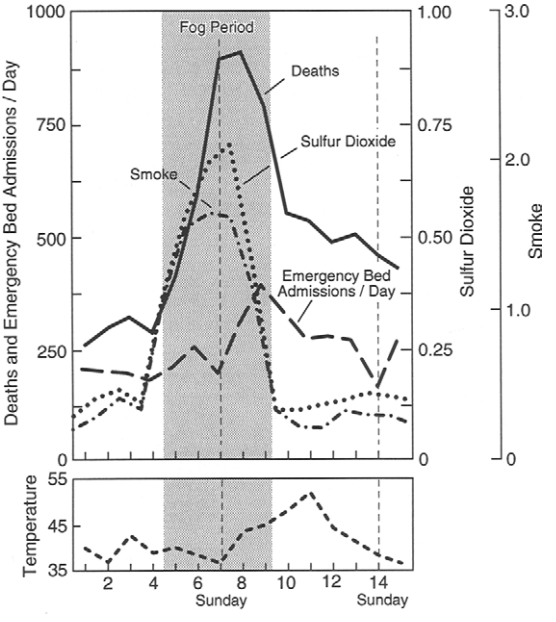


Figure 6. Metropolitan London total mortality and emergency bed admissions during the 1952 pollution episode in relation to black smoke, expressed as mg/m3, and sulfur dioxide, expressed as parts per million by volume.

The Ministry of Health (1954) report attributed an excess of ~ 4,000 deaths from all causes to the exposures during the 1952 episode, and Table 2 shows the deaths, by week, divided according to cause. Deaths peaked in the first full week, and were still above baseline levels two weeks after that. The specific cause with the greatest number of excess deaths over the four weeks was bronchitis (1,156 excess deaths) and it had the

greatest relative risk (RR=6.67). The next greatest increase, for heart disease (737 excess deaths), had an RR of only 1.82. The all cause relative risk was somewhat higher (1.96). Table 3 shows that most of the excess deaths occurred in individuals over 55 years of age (2,616 excess deaths over the four weeks), but there was an excess for all age groups beyond 4 weeks of age. Overall, the excess mortality was concentrated among the elderly with pre-existing disease.

It is of particular interest to current concerns that while recent daily mortality studies show much lower absolute risk levels from the much lower peaks in PM pollution, the elevated relative risks among the very young and oldest cohorts and the risk rankings among causes of death are quite similar today to those of December 1952.

Table 2
Greater London Deaths Divided According to Cause - Nov. and Dec. 1952

Cause	Av. Number of deaths in weeks ending 8th, 15th, 22nd, 29th Nov.	Number of deaths registered in week ending 6th, 13th, 20th, 27th Dec.				For weeks ending Av. No. of deaths	RR
		6th Dec.	13th Dec.	20th Dec.	27th Dec.		
Pulmonary Tuberculosis	17	14	77	37	21	37.25	2.19
Lung Cancer	34	45	69	32	36	45.50	1.34
Heart Disease	226	273	707	389	272	410.25	1.82
High Blood Pressure	14	19	47	36	21	30.75	2.20
Other Circulatory	22	26	46	31	32	33.75	1.53
Influenza	2	2	24	9	6	10.25	5.13
Pneumonia	31	45	168	125	91	107.25	3.46
Bronchitis	51	76	704	396	184	340.00	6.67
Other Respiratory	6	9	52	21	13	23.75	3.96
Ill-defined Causes	20	25	79	35	37	36.50	1.83
All Other Causes	340	411	511	412	316	412.50	1.21
All causes	763	945	2,484	1,523	1,029	1,495	1.96

From: Comm. on Air Pollution: Interim Report, Cmd 9011, London. H.M. Stationery Office (Dec. 1953).

Table 3

Greater London Deaths Divided According to Age - Nov. and Dec. 1952

Age	Av. Number of deaths in weeks ending 8th, 15th, 22nd, 29th Nov.	Number of deaths registered in week ending				For weeks ending 6th, 13th, 20th, 27th Dec. Av. No. of deaths	RR
		6th Dec.	13th Dec.	20th Dec.	27th Dec.		
Weeks:							
0-4	20	16	28	19	12	18.75	0.94
4-52	8	12	26	15	11	16.00	2.00
Years:							
1-4	7	6	7	13	7	8.25	1.18
5-14	4	4	6	6	2	4.50	1.18
15-24	7	9	7	14	7	9.25	1.32
25-34	11	16	28	17	11	18.00	1.64
35-44	26	36	64	29	34	40.75	1.57
45-54	70	80	204	96	83	115.75	1.65
55-64	133	157	448	251	167	255.75	1.92
65-74	211	254	717	444	258	418.25	1.98
75 and over	266	355	949	619	437	590.00	2.22
All ages	763	945	2,484	1,523	1,029	1,495.00	1.96

From: Comm. on Air Pollution: Interim Report, Cmd 9011, London, H.M. Stationery Office (Dec. 1953).

The Ministry of Health (1954) report also noted that there was a clear association between chronic air pollution and the incidence of bronchitis and other respiratory diseases. The death rate from bronchitis in England and Wales (where coal smoke pollution was very high) was much higher than in other northern European countries (with much lower levels of coal smoke pollution). The very high chronic coal smoke exposure in the U.K., associated with a high prevalence of chronic bronchitis, appears to have created a large pool of individuals susceptible to "harvesting" by an acute pollution episode.

The December 1962 London fog episode was the last to produce a clearly evident acute harvest of excess deaths, albeit a much smaller one than that of December 1952. Commins and Waller (1963) developed a technique to measure H2SO4 in urban air, and made daily measurements of H2SO4 at St. Bartholomew's Hospital in Central London during the 1962 episode. As shown in Figure 7, the airborne H2SO4 rose rapidly during the 1962 episode, with a greater relative increase than that for black smoke (BS).

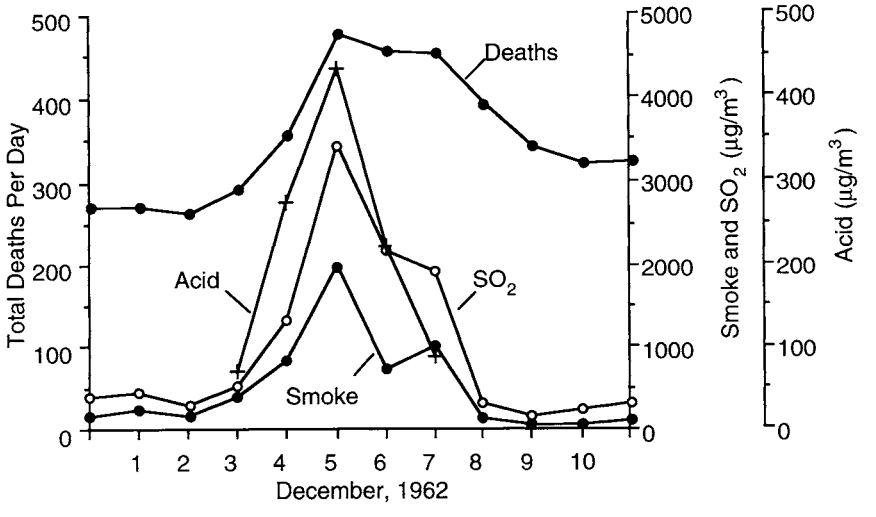


Figure 7. December 1962, London pollution episode.

The U.K. Clean Air Act of 1954 had led to the mandated use of smokeless fuels and, as shown in Figure 8, annual mean smoke levels had declined by 1962, to about one-half of

the 1958 level. The annual average SO2 concentrations had not declined by 1962, but dropped off markedly thereafter, along with a further marked decline in BS levels. For the period between 1964 and 1972, the measured levels of H2SO4 followed a similar pattern of decline.

During the later part of the coal smoke era in the U.K., researchers begin to study the associations between long-term daily records of mortality and morbidity and ambient air pollution. In the first major time-series analysis of daily London mortality for the winter of 1958-1959, Martin and Bradley (1960) and Lawther (1963) used the readily available BS and SO2 data. They estimated that both pollutants were associated with excess daily mortality when their concentrations exceeded about 750 μg/m3. However, additional analyses of this data set led to different conclusions. For example, Ware et al. (1981) concluded that there was no demonstrable lower threshold for excess mortality down to the lowest range of observation (BS ≈ 150 μg/m3), as illustrated in Figure 9. Although 150 μg/m3 is now near the upper end of observed concentrations rather than at the lower end, time-series analyses still indicate an increasing slope as concentrations decrease.

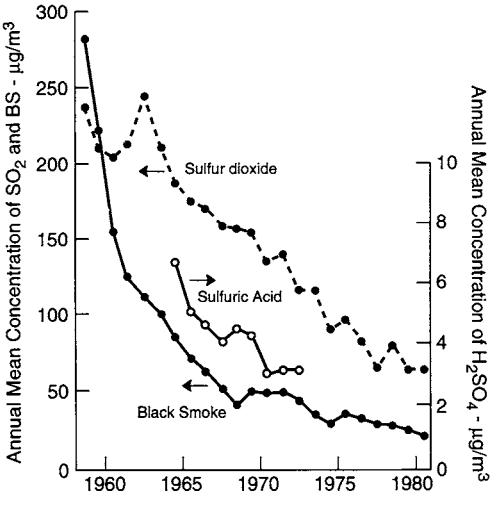


Figure 8. Long-term trends in annual mean atmospheric concentrations of black smoke (BS) and sulfur dioxide (SO2) at seven stations in Greater London, and annual mean concentration of sulfuric acid (H2SO4) at St. Bartholomew's Hospital in Central London.

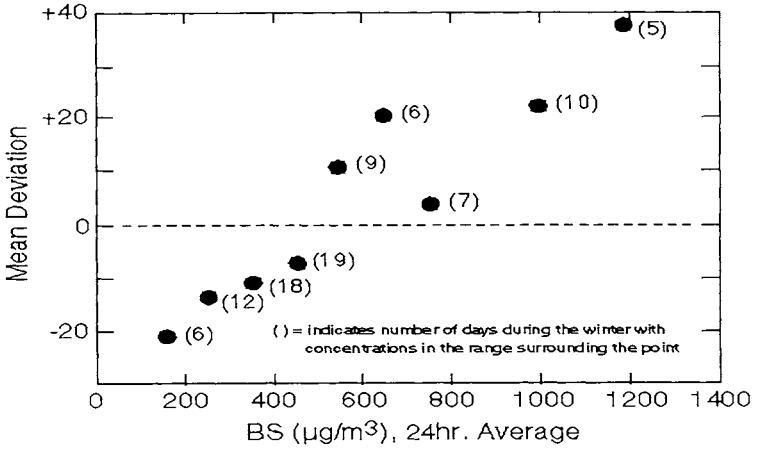


Figure 9. Martin and Bradley (1960) data for winter of 1958-9 in London as summarized by Ware et al. (1981), showing average deviations of daily mortality from 15-day moving average by concentration of black smoke (BS).

In terms of time-series analyses of morbidity, a study by Lawther (1970) reported the daily symptom scores of a panel of patients with chronic bronchitis in relation to the daily concentrations of BS and SO2. As shown in Figure 10, there was a close correspondence between symptom scores and both pollutant indices.

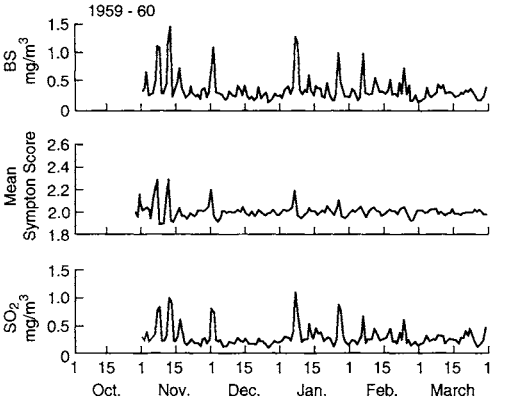


Figure 10. Results from 'diary' studies in London, winter 1959-60, showing day-to-day variations in the illness score for bronchitic subjects together with mean daily concentrations of black smoke (BS) and sulfur dioxide (SO2).

Chronic coal smoke exposure also affected baseline lung function. Holland and Reid (1965) analyzed spirometric data collected on British postal workers in 1965. By that time, pollution levels were well below their peaks, but the postal workers had been exposed out-of-doors for many years when pollution levels were higher. As shown in Figure 11, the London postal workers had lower forced expiratory volumes in one second (FEV1) and peak expiratory flow rates (PEFR) than their country town counterparts. As indicated in Figure 11, the deleterious effects of smoking were accounted for in these analyses. Within each smoking category, the differences between the London and country town means were attributed to pollution on the basis that pollution levels were, on average, twice as high in London as in the country towns.

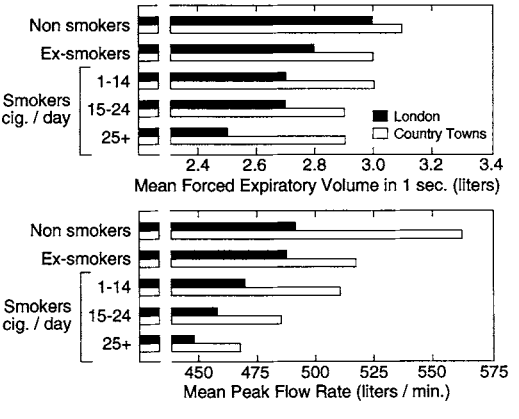


Figure 11. Cross-sectional study of lung function in British Postal Workers in 1965 standardized to age 40. Adapted from: Holland, W.W. and Reid, D.D. (Lancet 1:445-448, 1965) SO2 and smoke levels in the country towns were about half those in London.

The marked reduction in U.K. smoke pollution levels during the 1960's was shown to be associated with a marked reduction in annual mortality in County Boroughs by Chinn et al. (1981). As shown in Table 4, mortality rates in middle-aged and elderly men and women for the 1969-1973 period were no longer associated with an index of smoke pollution. By contrast, for both the 1948-1954 and 1958-1964 periods, the index of smoke exposure correlated strongly with annual mortality rates for both chronic

bronchitis and respiratory tract cancers. On the basis of such evidence of improved health status, our U.K. colleagues considered air pollution to be a problem solved, and essentially halted further investigations for the next several decades.

Table 4

Standardized Annual Mortality Rate Regression Coefficients on Smoke* for 64 UK County Boroughs (From: Chinn, S. et al., J. Epid. Comm. Health 35: 174-179, 1981)

Sex	Ages	Mortality in	Cancer of Trachea, Bronchus & Lung	Chronic Bronchitis
Males	45-64	1969-1973	0.07	0.02
		1958-1964	0.53++	0.32+
		1948-1954	0.71+++	0.48+++
	65-74	1969-1973	0.15	-0.06
		1958-1964	0.68+++	0.31
		1948-1954	0.87+++	0.37+
Females	45-64	1969-1973	-0.02	-0.02
		1958-1964	-0.64++	0.33+
		1948-1954	0.49+	0.49++
	65-74	1969-1973	0.07	0.03
		1958-1964	0.25	0.40+
		1948-1954	0.61++	0.31

* Based on index of black smoke pollution 20 years before death of Daly (Br. J. Prev. Soc. Med. 13: 14-27, 1959).
\+ $p < 0.05$
++ $p < 0.01$
+++ $p < 0.001$

Coal smoke pollution affected acute mortality and morbidity in the U.S. and in other countries as well as in the U.K., but there was much less documentation and quantitative analyses prior to the mid 1960's. Among the notable non-U.K. reports are those of Firket (1936) on the December 1930 fog episode in the Meuse Valley in Belgium, and the reports on the October 1948 Donora, PA fog episode.

The December 1930 fog in the Meuse Valley was associated with 60 deaths from a population of ~ 6,000, but the pollutant concentrations were not measured.

In Donora, a valley town of about 10,000 people at a bend in the Monongahela River

south of Pittsburgh, there were steel mills, wire mills, zinc works and a sulfuric acid plant along the river bank for the entire length of the town. As reported by Schrenk et al. (1949), a persistent valley fog was associated with 20 excess deaths as well as acute morbidity among 43% of the population. About 10% were reported to have severe effects requiring medical attention. In a ten-year follow-up of the affected population, Ciocco and Thompson (1961) reported greater mortality rates and incidences of heart disease and chronic bronchitis among the residents who had reported acute illness in 1948 in comparison to residents who did not report such illness.

3. EXPERIENCE WITH SULFATE (SO4=) AS AN INDEX OF PM EXPOSURE AND RISK

With the phasing out of bituminous coal as a fuel for domestic heating, the use of the optical density of smoke samples as an index of the health risk associated with ambient particulate matter became increasingly problematic. It has also become clear that total suspended particulate matter (TSP), the standard index of PM pollution in the U.S. prior to 1987 was also far from ideal. Under high wind conditions, gravimetric TSP concentrations are dominated by PM too large to penetrate into the human thorax, even during oral inhalation. Some U.S. investigators chose the sulfate (SO4=) content of TSP samples as an alternate index of PM associated health risk. Because of the nature of its sources, essentially all of the SO4= in the ambient air is on fine particles below 2.5 μm in aerodynamic diameter (PM2.5).

As discussed by Lippmann and Thurston (1996). Sulfate is often a relatively large fraction of PM2.5, it is non-volatile, it is stable on filters used for air sampling, it can be easily extracted from the filters, and it can be accurately analyzed with relatively simple and inexpensive procedures. Furthermore, it generally correlates better with mortality and indices of morbidity in populations than do other frequently measured PM indices, such as TSP, BS, CoH, and PM10. An early example of a health effect closely associated with ambient SO4= concentration, i.e., incidence of protracted respiratory disease among female workers is illustrated in Figure 12.

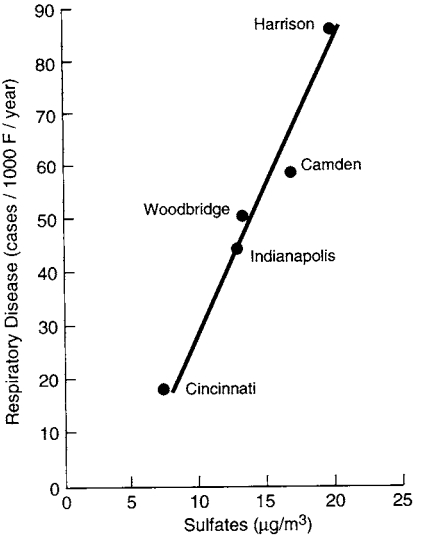


Figure 12. Incidence of respiratory disease lasting more than seven days in women (mean of three years) versus concentration of suspended particulate sulfates in the city air at test sites.
From: Dohan, F.C. and Taylor, E.W. Am. J. Med. Sc., 337-339 (1960).

Lippmann (1989) proposed that SO4= is the best surrogate for H+ exposure, the latter being the most likely causal factor for the observed associations between PM and chronic mortality. The hypothesis, illustrated in Figure 13, was based on the Ozkaynak and Thurston (1987) annual mortality analysis. Their actual data, for SO4= and mortality, are shown in Figure 14. There has been a reluctance on the part of many to accept the SO4=-mortality association as likely to be causal on the basis of ecological analyses such as those of Ozkaynak and Thurston (1987), or the earlier analyses of Lave and Seskin (1977). Many skeptics felt that the results could have been due to confounding by differences among the communities in smoking, occupations, ethnicity, etc. However, later prospective cohort studies, to be discussed in the next section, have reported similar associations. Other examples of associations between human health effects and ambient SO4= concentrations are illustrated in Figures 15-17.

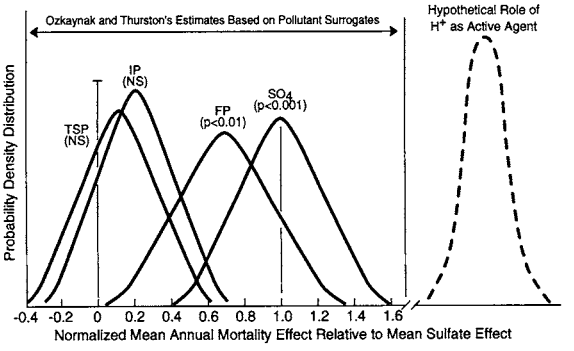


Figure 13. Hypothetical role of H+ in relation to analysis of annual mortality associations in 98 U.S. SMAS by Ozkaynak and Thurston, Risk Anal. 7:449-461 (1987).

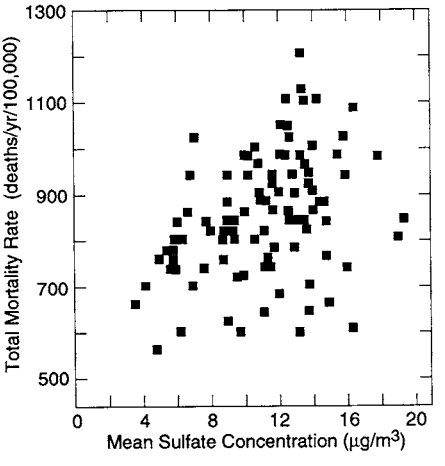


Figure 14. Plot of total mortality rate vs. annual mean SO4= concentration in 98 U.S. SMSA's in 1980. From: Ozkaynak and Thurston, Risk Anal. 7:449-461 (1987).

An important recent study that addressed morbidity in a large number of individuals also adjusted for individual risk factors. Ostro (1990) examined lost-time due to respiratory causes vs. ambient particulate matter. It was based on interview data on a random sample of U.S. households in 25 communities in the national Health Interview Survey (HIS) of 1979-1981. The lost-time was most closely related to SO4=. As shown in Figure 16, the

associations, in terms of exposure-response slopes and scatter, were similar in nature to those seen for mortality in Figures 14 and 15.

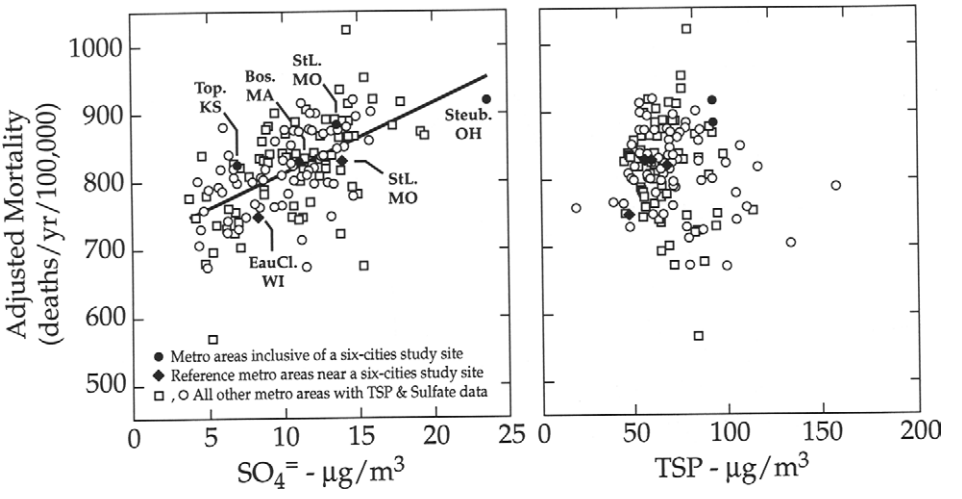


Figure 15. Age-sex-race adjusted mortality rates from Pope et al. (1995), including six communities studied by Dockery et al. (1993). The results are consistent, yet could lead to different interpretations concerning the utility of TSP as a useful measure of risk. Adapted from Figure V-6 of PM Staff Paper (EPA, 1996).

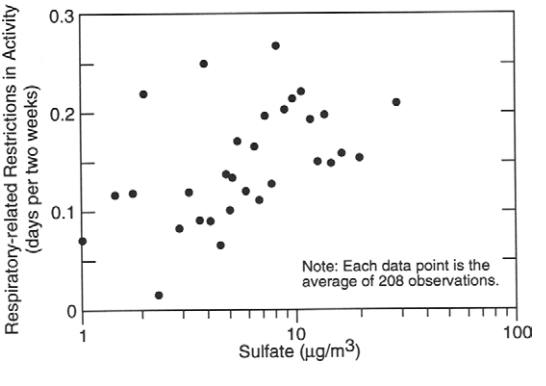


Figure 16. Association between respiratory morbidity and sulfates, controlling for covariates. From: Ostro, B.D., Risk Anal. 10:421-427 (1990).

In terms of hospital admissions, SO4= was significantly associated with hospital admissions in all of the studies for which is was available. The results of one such study, by Burnett et al. (1994), are illustrated in Figure 17.

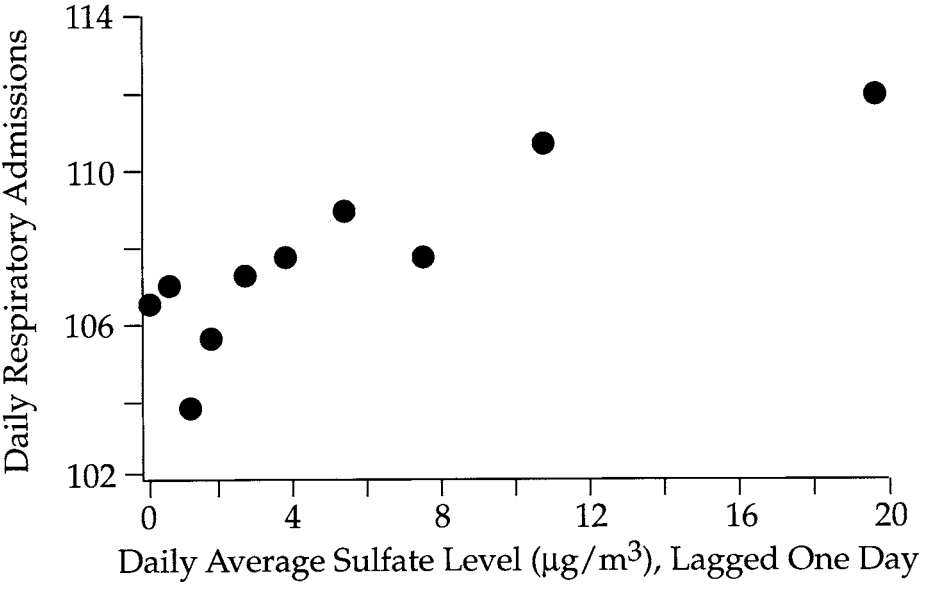


Figure 17. Hospital admissions in Southern Ontario in relation to daily average SO4= concentration in ambient air.

4. RECENT STUDIES BASED ON THORACIC (PM10) AND FINE PARTICLE (PM2.5) MASS CONCENTRATIONS

In the past seven years there has been a great increase in the number of time-series studies of the associations between daily ambient air pollutant concentrations and daily rates of mortality and hospital admissions for respiratory diseases. Also, there is now important information from two prospective cohort studies of annual mortality rates. In terms of morbidity, there has been a rapid growth of the literature showing associations between airborne particle concentrations and exacerbation of asthma, increased symptom rates, decreased respiratory function and restricted activities.

Much of the recent literature was summarized by Pope et al. (1995a). They converted

historically measured values for CoH and TSP to estimated levels of PM10, and remarked that very similar coefficients of response were determined in all locations. Table 5 shows Thurston's (1995) independent analysis of acute mortality studies in nine communities with measured PM10 concentrations, including four of the ten studies cited by Pope et al. (1995a). As indicated in this table, the coefficients of response tend to be higher when the PM10 is expressed as a multiple-day average concentration, and lower when other air pollutants are included in multiple-regression analyses. In any case, the results in each city (except for the very small city of Kingston, TN) indicate a statistically significant association.

It is also clear from recent research that the associations between PM10 and daily mortality are not seriously confounded by weather variables or the presence of other criteria pollutants. Figure 18 shows that the calculated relative risks for PM10 are relatively insensitive to the concentrations of SO2, NO2, CO, and O3. The results are also coherent as described by Bates (1992). Figure 19 shows that the relative risks (RR's) for respiratory mortality are greater than for total mortality, and the RR's for the less serious symptoms are higher than those for mortality and hospital admissions.

Table 5

Comparison of Time-Series Study Estimates Total Mortality Relative Risk (RR) for a 100 μg/m3 PM10 Increase

Study Area (Reference)	Measured PM10 Concentrations Mean (μg/m3)	Maximum (μg/m3)	RR for 100 μg/m3	95% CI for 100 μg/m3
1. Utah Valley, UT (Pope et al., 1992)	47	297	1.16*††	(1.10-1.22)
2. St. Louis, MO (Dockery et al., 1992)	28	97	1.16*†	(1.01-1.33)
3. Kingston, TN (Dockery et al., 1992)	30	67	1.17*†	(0.88-1.57)
4. Birmingham, AL (Schwartz, 1993)	48	163	1.11*††	(1.02-1.20)
5. Athens, Greece (Touloumi et al, 1994)	78	306	1.07*†	(1.05-1.09)
			1.03**†	(1.00-1.06)
6. Toronto, Can. (Özkaynak et al., 1994)	40	96	1.07*†	(1.05-1.09)
			1.05**†	(1.03-1.07)
7. Los Angeles, CA (Kinney et al., 1995)	58	177	1.05*†	(1.00-1.11)
			1.04**†	(0.98-1.09)
8. Chicago, IL (Ito et al., 1995)	38	128	1.05**†	(1.01-1.10)
9. Santiago, Chile (Ostro et al., 1995)	115	367	1.08*†	(1.06-1.12)
			1.15*††	(1.08-1.22)

* Single pollutant model (i.e. PM10).
** Multiple pollutant model (i.e. PM10 and other pollutants simultaneously).
† One-day mean PM10 concentration employed.
†† Multiple-day mean PM10 concentration employed.

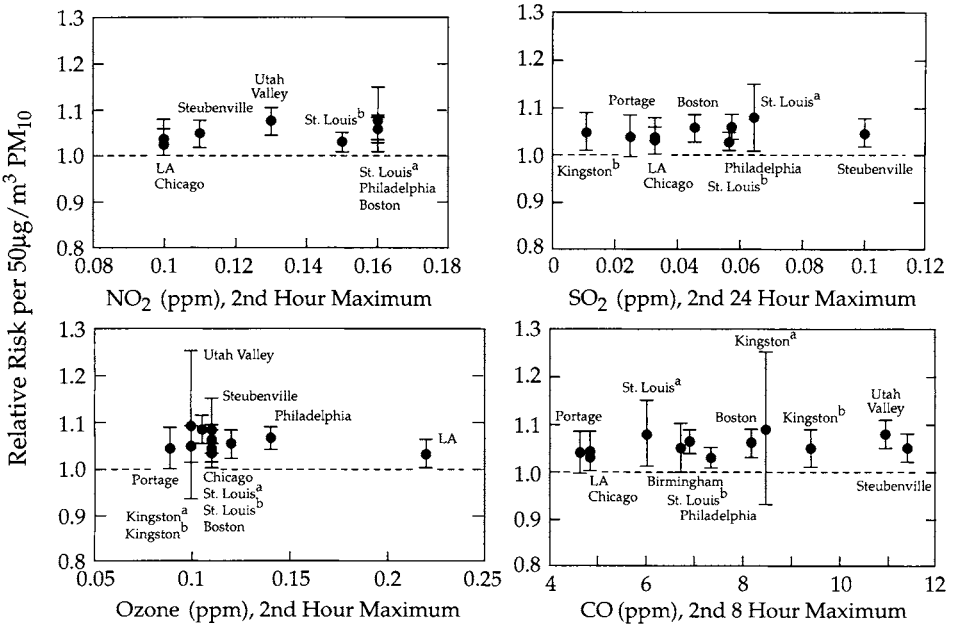
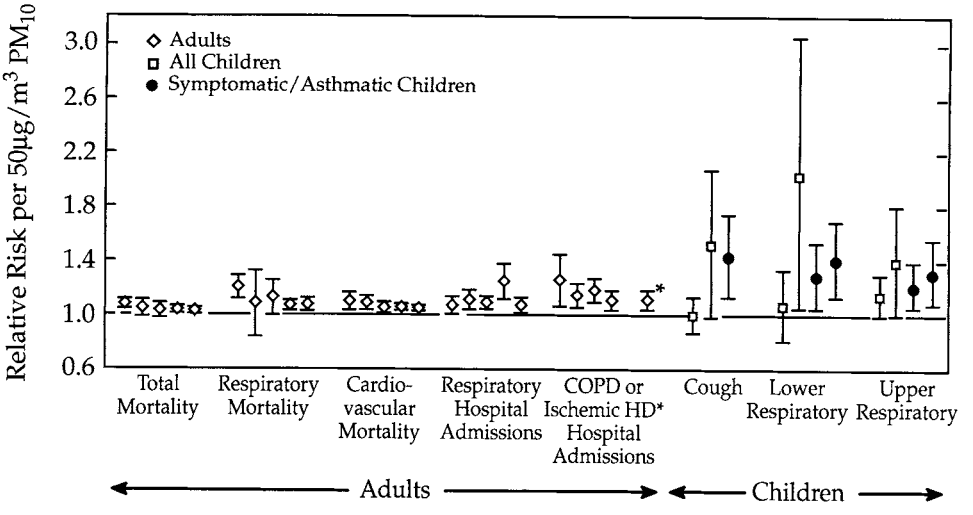


Figure 18. Relationship between RR associated with PM10 and peak daily levels of other criteria pollutants. Adapted from Figure V-3a of PM Staff Paper (EPA, 1996).



Total, Respiratory, Cardiovascular Mortality
1. Pope et al. (1992) 2. Schwartz (1993) 3. Styer et al. (1995) 4. Ostro et al. (1995a)
5. Ito and Thurston (1996)

Respiratory Hostipal Admissions
1. Schwartz (1995) New Haven, CT 2. Schwartz (1995) Tacoma,WA 3. Schwartz (1996) Spokane, WA
4. Ito and Thurston (1994) Toronto, Canada

COPD or Ischemic HD* Hostipal Admissions
1. Schwartz (1994f) Minneapolis, MN 2. Schwartz (1994c) Birmingham, AL
3. Schwartz (1996) Spokane, WA 4. Schwartz (1994d), Detroit, MI
*5. Schwartz & Morris (1995), Detroit, MI, Ischemic HD

Cough, Lower Respiratory, Upper Respiratory
1. Hoek and Brunekreef (1993) 2. Styer et al. (1994) 3. Pope & Dockery (1992), symptomatic children

Figure 19. Relationships between relative risks per 50 μg/m3 PM10 and health effects. Adapted from Figure V-2 in PM Staff Paper (EPA, 1996).

While there is mounting evidence that excess daily mortality is associated with short-term peaks in PM10 pollution, the public health implications of this evidence are not yet clear. Key questions remain, including:

- which specific components of the fine particle fraction (PM2.5) and coarse particle fraction of PM10 are most influential in producing the responses?
- do the effects of the PM10 depend on co-exposure to irritant vapors, such as ozone, sulfur dioxide, or nitrogen oxides?
- what influences do multiple day pollution episode exposures have on daily

responses and response lags?

- does long-term chronic exposure predispose sensitive individuals being 'harvested' on peak pollution days?
- how much of the excess daily mortality is associated with life-shortening measured in days or weeks vs. months, years, or decades?

The first four questions above are complex, and difficult to answer at this time on the basis of current knowledge. The Discussion section will examine them in greater detail.

The last question above is a critical one in terms of the public health impact of excess daily mortality. If, in fact, the bulk of the excess daily mortality were due to 'harvesting' of terminally ill people who would have died within a few days, then the public health impact would be much less than if it led to prompt mortality among acutely ill persons who, if they did not die then, would have recovered and lived productive lives for years or decades longer. An indirect answer to this question is provided by the results of two recent prospective cohort studies of annual mortality rates in relation to long-term pollutant exposures.

Dockery et al. (1993) reported on a 14-to-16 year mortality follow-up of 8,111 adults in six U.S. cities in relation to average ambient air concentrations of TSP PM2.5, fine particle SO4=, O3, SO2 and NO2. Concentration data for most of these pollutant variables were available for 14-16 years. The mortality rates were adjusted for cigarette smoking, education, body mass index and other influential factors not associated with pollution. The two pollutant variables that best correlated with total mortality (which was mostly attributable to cardiopulmonary mortality) were PM2.5 and SO4=. The overall mortality rate ratios were expressed in terms of the range of air pollutant concentrations in the six cities. The rate-ratios for both PM2.5 and SO4= were 1.26 (1.08-1.47) overall, and 1.37 (1.11-1.68) for cardiopulmonary. The mean life-shortening was in the range of 2-3 years.

Pope et al. (1995b) linked SO4= data from 151 U.S. metropolitan areas in 1980 with individual risk factor on 552,138 adults who resided in these areas when enrolled in a prospective study in 1982, as well as PM2.5 data for 295,223 adults in 50 communities. Deaths were ascertained through December, 1989. The relationships of air pollution to all-cause, lung cancer, and cardiopulmonary mortality was examined using multivariate

analysis which controlled for smoking, education, and other risk factors. Particulate air pollution was associated with cardiopulmonary and lung cancer mortality, but not with mortality due to other causes. Adjusted relative risk ratios (and 95% confidence intervals) of all-cause mortality for the most polluted areas compared with the least polluted equaled 1.15 (1.09 to 1.22) and 1.17 (1.09 to 1.26) when using SO4= and PM2.5 respectively. The mean life-shortening in this study was between 1.5 and 2 years. Figure 15 shows the range of values for the adjusted mortality rates in the various communities versus annual average SO4= and TSP concentrations. The results appear, both by inspection and analysis, to be quite similar to those found in the previous studies of Ozkaynak and Thurston (1987) (See Figure 14) and Lave and Seskin (1970). Thus, the results of these earlier studies provide some confirmatory support for the findings of Pope et al. (1995b), while the Pope et al. (1995b) results indicate that the concerns about the credibility of the earlier results, due to their inability to control for potentially confounding factors such as smoking and socioeconomic variables, can be eased.

The Dockery et al. (1993) study had the added strength of data on multiple PM metrics. As shown in Figure 20, the association becomes stronger as the PM metric shifts from TSP to PM10. Within the thoracic fraction (PM10) the association is much stronger to the fine particle component (PM2.5) than for the coarse component. Within the PM2.5 fraction, both the SO4= and non-SO4= fractions correlate very strongly with annual mortality, suggesting a non-specific response to fine particles.

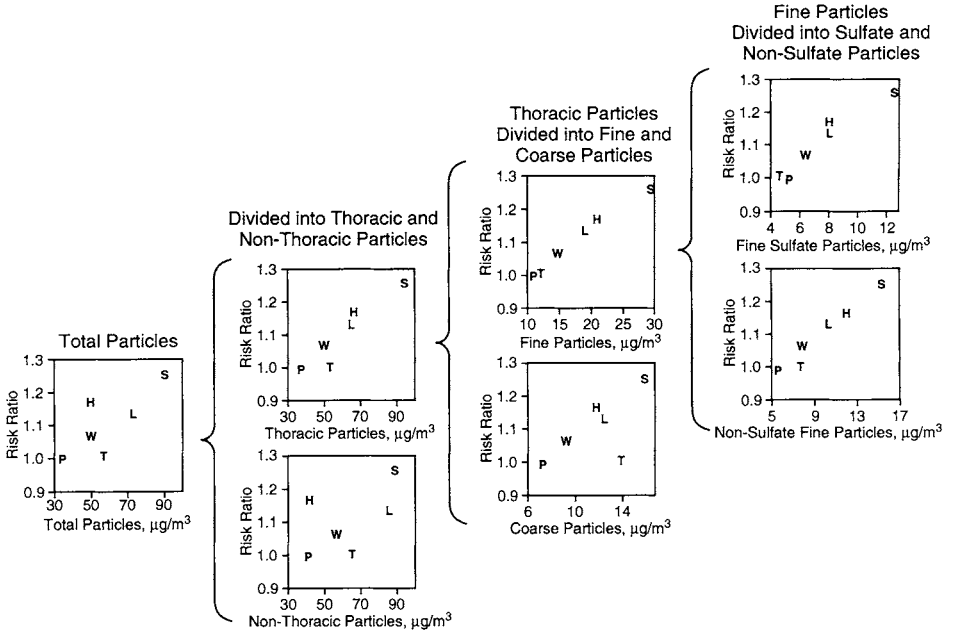


Figure 20. Adjusted relative risks for annual mortality are plotted against each of seven long term average particle indices in the Six City Study, from largest size range (total suspended particulate matter (lower left), through sulfate and nonsulfate fine particle concentrations (upper right). Note that a relatively strong linear relationship is seen for fine particles, and for its sulfate and non-sulfate components. Topeka, which has a substantial coarse particle component of thoracic particle mass, stands apart from the linear relationship between relative risk and thoracic particle concentration. Adapted from Figure V-5 of PM Staff Paper (EPA, 1996).

The importance of the fine particles as a risk factor for subnormal vital capacity in children is illustrated in Figure 21, which shows data collected in the Harvard-Health Canada cross-sectional study of 22 U.S. and Canadian communities (Raizenne et al., 1996). There was a significant association between the percentage of children with FVC < 85% of predicted and fine particle mass concentration, but no apparent association with the coarse component of PM10. Actually, the strongest association observed in this comparison was for the H+ component of the fine particles. Most of the recent epidemiological studies have not had the advantage of available PM2.5, SO4= or H+ data, and have had to rely on PM10 data. A summary of such PM10 epidemiology, in

terms of relative risks and 95% confidence intervals, is shown in Figure 19. There is coherence in the data, as defined by Bates (1992), in terms of the relative risk ratings, with mortality risks increasing from total to cardiovascular to respiratory, and with cough and respiratory conditions being more frequent than mortality.

In the absence of any generally accepted mechanistic basis to account for the epidemiological associations between ambient fine particles on the one hand, and mortality, morbidity and functional effects on the other, the causal role of PM remains questionable. However, essentially all attempts to discredit the associations on the basis of the effects being due to other environmental variables that may co-vary with PM have been unsuccessful. As shown in Figure 18, the relative risk for daily mortality in relation to PM10 is remarkably consistent across communities that vary considerably in their peak concentrations of other criteria air pollutants. The possible confounding influence of adjustments to models to account for weather variables has also been found to be minimal (Samet et al., 1997, Pope and Kalkstein, 1996).

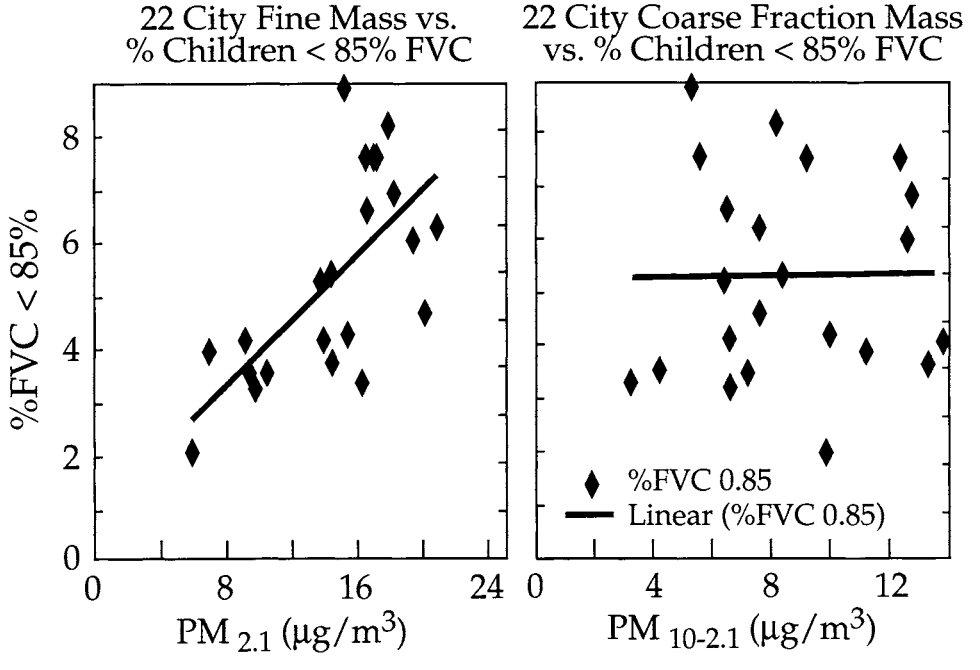


Figure 21. Plot appearing in PM Staff Paper (EPA, 1996). Based on data reported by Raizenne et al. (1996).

The findings of Dockery et al. (1993) and Pope et al. (1995b), in carefully controlled prospective cohort studies, indicating that mean lifespan shortening is of the order of two years implies that many individuals in the population have lives shortened by many years, and that there is excess mortality associated with fine particle exposure greater than that implied by the cumulative results of the time-series studies of daily mortality.

5. DISCUSSION AND CURRENT KNOWLEDGE ON THE HEALTH EFFECTS OF PM

The results of studies in recent years, summarized above, have made it possible to frame the remaining issues in a more coherent and focussed manner.

One key issue is the role of SO4=, and why it consistently correlates with mortality and morbidity as well as, or better than, other metrics of PM pollution. It is extremely unlikely that SO4=, per se, is a causal factor. If it is not, then it must be acting as a surrogate index for one or more other components in the PM mixture.

One possibility is that the effects are really due to the PM2.5 mass, irrespective of particle composition, and that SO4= is a more stable measurement of airborne PM2.5 than is the reported PM2.5 itself. The ambient PM2.5 includes nitrates (primarily ammonium nitrate) and organics formed by photochemical reactions in the atmosphere. There can be considerable volatilization of these species on sampling filters, resulting in negative mass artifacts whose magnitude varies with source strengths and ambient temperature.

Another possibility is that SO4= is serving as a surrogate for H+, a more likely active agent on the basis of the results of controlled exposure studies in humans and animals. The support for this hypothesis is summarized in Table 6. The utility of SO4= as a surrogate for H+, especially for time-series studies in a given region without complex topography, is illustrated in Figure 22, which demonstrates that both H+ and SO4= concentrations are almost the same at two sites sixty miles apart, and that the concentration of both ions tend to rise and fall together.

Table 6

Components of Ambient Air Particulate Matter (PM) that may Account for Some or all of the Effects Associated with PM Exposures

Component	Evidence for Role in Effects	Doubts
Strong Acid (H+)	▸ Statistical associations with health effects in most recent studies for which ambient H+ concentrations were measured	▸ Similar PM-associated effects observed in locations with low ambient H+ levels
	▸ Coherent responses for some health endpoints in human and animal inhalation and in vitro studies at environmentally relevant doses	▸ Very limited data base on ambient concentrations
Ultrafine Particles ($D \leq 0.2$ μm)	▸ Much greater potency per unit mass in animal inhalation studies (H+, Teflon, and TiO2 aerosols) than for same materials in larger diameter fine particle aerosols	▸ Only one positive study on response in humans
	▸ Concept of 'irritation signalling' in terms of number of particles per unit airway surface	▸ Absence of relevant data base on ambient concentrations
Soluble Transition Metals	▸ Recent animal study evidence of capability to induce lung inflammation	▸ Absence of relevant data on responses in humans ▸ Absence of relevant data on ambient concentrations
Peroxides	▸ Close association in ambient air with SO4=	▸ Absence of relevant data on responses in humans or animals
	▸ Strong oxidizing properties	▸ Very limited data base on ambient concentrations

A third possibility is that the causal factor is the number concentration of irritating particles, which would be dominated by the particles in the ultrafine mode (diameters below 50 nm) (Oberdörster et al., 1995). Epidemiologic support for this hypothesis has been provided by Peters et al. (1997), who reported closer associations between peak expiratory flow rates and symptoms in adult asthmatics with particle number concentration than with fine particle mass concentration in Erfurt, Germany.

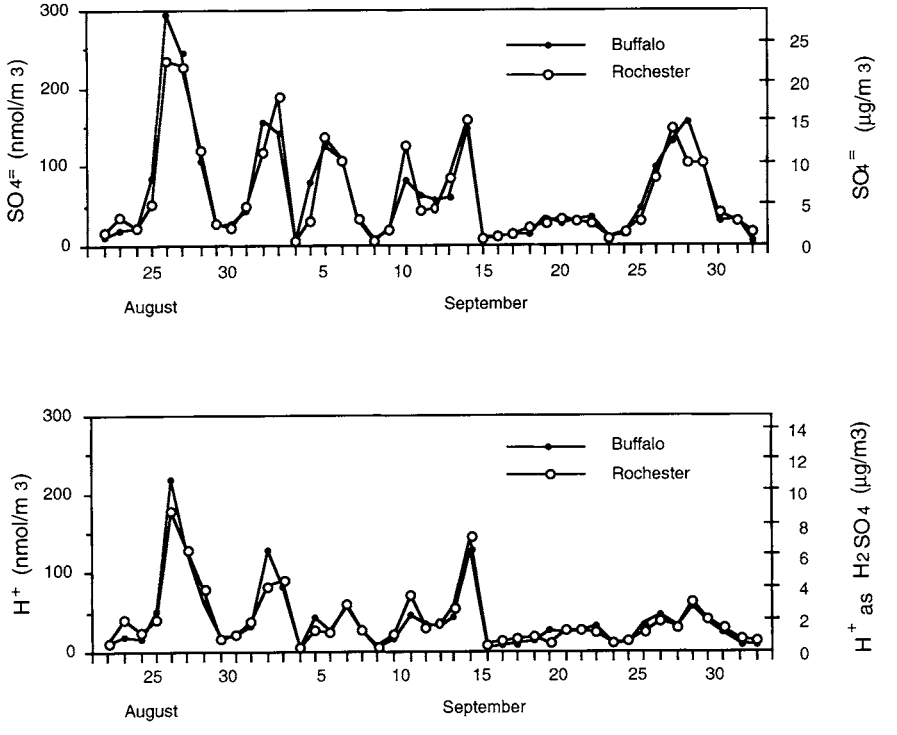


Figure 22. Intercomparison of Rochester, NY and Buffalo, NY sulfate and daily acid aerosol concentrations (August 22 - October 2, 1990).

A fourth possibility is that soluble transition metals in the ambient PM generate sufficient amounts of reactive oxygen species in the respiratory tract airways to cause inflammatory responses and chronic lung damage (Pritchard et al., 1996).

A fifth possibility has been proposed by Friedlander and Yeh (1996), i.e., that reactive chemical species, such as peroxides, are responsible for the health effects associated with fine particles, and that SO4=, being a product of chemical reactions involving hydrogen peroxide, is serving as a surrogate measure of the airborne peroxides.

It is also possible that effects are related to a hybrid of H+ and ultrafines, i.e., acid-coated ultrafine particles. As shown in Figure 23, sulfuric acid coatings on ultrafine zinc oxide particles produce about the same responses as pure sulfuric acid for a given number of equivalent sized particles, yet the coated particles only had one-tenth of the

acid content per unit volume of air. Thus, the response may be related to the number of acidic particles that deposit on the lung surfaces rather than the amount of acid deposited. In other words, the total concentration of H+ may be a better surrogate of the active agent than SO4= or PM2.5, but it still is a crude index for the number concentration of irritant particles. Amdur and Chen (1989) suggested that number concentration was important for sulfuric acid aerosol, and Hattis et al. (1987, 1990) gave the concept a name, i.e., 'irritation signalling'. Research of Chen et al. (1995) indicate that acid-coated particles much smaller than those discussed by Hattis et al. (1987, 1990) were capable of producing lung responses.

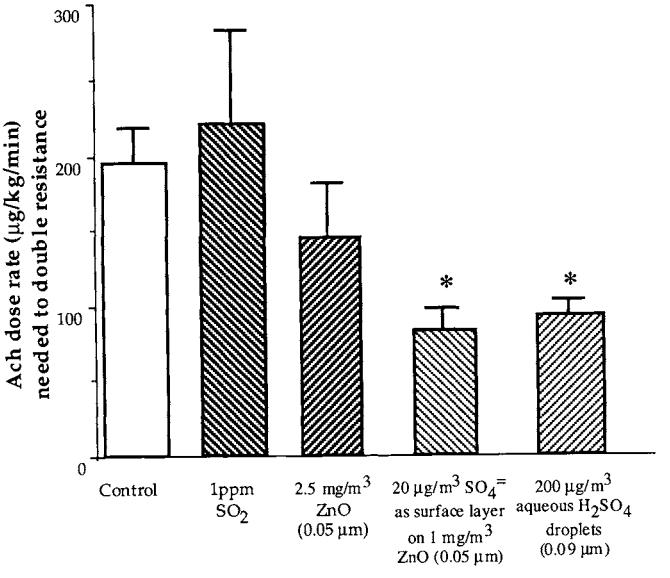


Figure 23. Dose of intravenously infused acetylcholine required to double airway resistance in guinea pigs from baseline levels 2 hours after a 1 hour inhalation exposure. Values are mean ± S.E. The asterisks indicate reductions significant at $p < 0.05$. For the aerosols, the median particle diameters are indicated in parentheses.

If the number concentration of acid-coated particles is the most relevant index of the active agent in ambient PM, then new sampling techniques will be needed to characterize ambient air concentrations and personal exposures.

Other components of the ambient ultrafine aerosol have not been well characterized either, and they may also be important health stressors. One class is the volatile trace metals (such as As, Cd, Cu, Pb, Zn) which condense as ultrafine particles in the effluent airstream of fossil fuel combusters (Amdur et al., 1986) and are inefficiently captured by air cleaners for fly ash collection. Another class is the ultrafine organics from atmospheric photochemical reaction sequences.

Any remaining inconsistency between the epidemiological findings and the results of the controlled exposure studies may be explicable on the basis that the relatively rare individuals who respond in the epidemiological populations are an especially responsive subset of the overall population, and the low probability that such sensitive individuals would be included in the controlled exposure studies in the laboratory. An alternative hypothesis is that the controlled exposure atmospheres have not contained the highly toxic components or ultrafine particle sizes that may be present in ambient atmospheres.

In summary, excess daily mortality and morbidity have been related to ambient pollution at current levels in many communities in the U.S. and around the world using available pollutant concentration data. However, it is not at all clear whether any of the pollutant indices used are causally related to the health effects or, if none of them are, which is the best index or surrogate measure of the causal factor(s). This gap can best be addressed by analyses of pollutant associations with mortality and morbidity in locations where a number of different pollutant metrics are available simultaneously, using analytic methods not dependent on arbitrary model assumptions.

6. POLICY IMPLICATIONS

While more research is needed on causal factors for the excess mortality and morbidity associated with PM in ambient air, and on the characterization of susceptibility factors, responsible public health authorities cannot wait for the completion and peer review of this research. It is already clear that the evidence for adverse health effects attributable to PM challenges the conventional paradigm used for setting ambient air standards and guidelines, i.e., that a threshold for adversity can be identified, and a margin of safety

can be applied. Excess mortality is clearly an adverse effect, and the epidemiological evidence is consistent with a linear non-threshold response for the population as a whole. A revision of the Air Quality Guidelines of the World Health Organization-Europe (WHO-EURO) is currently nearing completion. The Working Group of WHO-EURO on PM, at meetings in October 1994 and October 1996 in Bilthoven, The Netherlands, determined that it could not recommend a PM Guideline. Instead, it prepared a tabular presentation of the estimated changes in daily average PM concentrations needed to produce specific percentage changes in: 1) daily mortality; 2) hospital admissions for respiratory conditions; 3) bronchodilator use among asthmatics; 4) symptom exacerbation among asthmatics; and 5) peak expiratory flow. The concentrations needed to produce these changes were expressed in PM10 for all five response categories. For mortality and hospital admissions, they were also expressed in terms of PM2.5 and SO4=. Using this guidance, each national or local authority setting air quality standards can decide how much adversity is acceptable for its population. Making such a choice is indeed a challenge.

In the U.S., the EPA Administrator proposed revised PM NAAQS on November 26, 1996 in recognition of the inadequate public health protection provided by enforcement of the 1987 NAAQS for PM10. For PM10, the 50 μg/m3 annual average would be retained without change, and the 24-hr PM10 of 150 μg/m3 would be relaxed by applying it only to the 98th% value (8th highest in each year) rather than to the 4th highest over 3 yrs. These PM10 standards would be supplemented by the creation of new PM2.5 standards. The annual average PM2.5 would be 15 μg/m3, and the 24 hour PM2.5 of 50 μg/m3 would apply to the 98th% value. It is only by implementing the new PM2.5 NAAQS that the degree of public health protection for ambient air PM would be substantially advanced, and then only in the eastern U.S. and in some large cities in the west where fine particles are major %'s of PM10. In these locations the greatest reductions in adverse health effects are feasible and most cost-effective.

In my view, the proposed PM NAAQS are not too strict. In terms of its introduction of a more relevant index of exposure and a modest degree of greater public health protection, it represents a prudent judgment call by the Administrator. These NAAQS may not be strict enough to fully protect public health, but there remain significant knowledge gaps

on both exposures and the nature and extent of the effects that make the need for more restrictive NAAQS difficult to justify at this time. It is essential that adequate research resources be committed to filling these gaps before the next round of NAAQS revisions early in the next decade. The costs of the research, while substantial (on the order of $50x106 per year), are quite small in comparison to the health benefits resulting from exposure reductions resulting from the controls.

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