

Assessment of the Health Effects of Atmospheric Sulfur Oxides and Particulate Matter: Evidence from Observational Studies

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Steadily rising energy costs have increased the need for reliable information on the health effects of atmospheric sulfur oxides and particulate matter. Because ethical and practical considerations limit studies of this question under controlled conditions, observational studies provide an important part of the relevant information. This paper examines the currently available epidemiologic evidence from population studies of the health effects of these pollutants.

Nonexperimental studies also have important limitations, including the inability to measure accurately the exposure burden of free living individuals, and the potential for serious confounding by other factors affecting health. We begin with a discussion of some of these methodologic issues. The evidence is then reviewed, first in association with fluctuations in 24 hr mean concentration of sulfur oxides and particulate matter, and then in association with differences in mean annual concentration. In the last section, this evidence is summarized and used to approximate the exposure-response relationship linking pollutant concentrations with mortality and morbidity levels.

Introduction

In view of the potential for adverse health effects of air pollution, and the expense of control measures, reliable assessment of the health effects of different air pollutants is an important public health

problem. Lowrance (1) has defined four tasks in this assessment: identifying the health effects; quantifying these effects at various ambient concentrations; estimating how many people are exposed at these levels; and calculating the overall health risk associated with a given degree of air quality. This paper addresses the quantification of the health effects of sulfur oxides and particulate matter, especially at ambient concentrations near the present air quality standards.

The health effects of these air pollutants can be studied to some extent in controlled conditions. Laboratory studies of animals allow careful control of the concentration of individual pollutants and conditions of exposure, as well as detailed study of the effects on study animals. These studies have been useful for identifying possible mechanisms of action and potential health effects. However, it is

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difficult to use animal studies to quantify these effects in human populations, primarily because the basis for extrapolating from animal to man is uncertain. The uncertainty of such extrapolation is increased by significant interspecies variability in the response to pollutants.

Laboratory studies with human subjects avoid extrapolation from animal to man but raise other concerns, such as ethical considerations and practical difficulties in studying long-term exposures. In addition, laboratory studies cannot duplicate the activity patterns and pollutant mixture experienced by free living populations. Within these constraints, studies involving human subjects can be used to establish the response to short-term exposure.

Studies of occupational groups have been suggested as another source of information. Although these studies may provide good estimates of exposure, the mix of pollutants and concentrations is usually different from ambient air. Exposures are for 8 hr or less rather than on a more continuous basis. Temperature and humidity conditions are also likely to differ from those experienced by the general population. Furthermore, the working population differs from the general population in important ways. The very young, elderly and ill persons are not included. There is considerable selection by the employer and self-selection by the worker, so that those with current disease or who are more sensitive or susceptible are not as well represented as in the general population. As a result, one cannot conclude from a negative study in an occupational group that the same exposure is safe for the general population. If an association between an air pollutant and a health effect is found in an occupational setting, there may be a greater association in general populations.

Because of the limitations of each of these types of investigation, epidemiologic studies in general population groups provide much of the relevant information about the health effects of sulfur oxides and particulate matter at levels of exposure near present ambient standards. Here, too, there are limitations with respect to estimating exposure and measuring effects. Other risk factors, such as cigarette smoking and occupational exposures, must be considered, and confounding factors, such as socioeconomic status, race and weather must also be evaluated. In these studies, exposures are not subject to manipulation, though ambient levels can change during the course of a study. This makes it difficult to determine whether mean concentration, peak concentration, variability, or some other aspect of air pollution concentration is the most important determinant of health effects. Observational studies cannot demonstrate cause

and effect, rather we infer causality based on the precepts proposed by the Surgeon General's Advisory Committee on Smoking and Health (2) and by Hill (3): the strength of the association, the consistency of the data, the specificity of the results, the temporality of the observations, the demonstration of a biological gradient and the plausibility and coherence of the results. Ideally, findings will be replicable by specific experimentation, and conclusions will be further strengthened when different approaches or methods yield similar results.

The next section of this paper briefly summarizes the methodological issues which should be considered in evaluating nonexperimental studies of the effects on health of exposure to atmospheric sulfur oxides and particulate matter. We then review the evidence from selected studies of the association between mortality and morbidity levels and 24-hr mean concentration of sulfur oxides and particulate matter the evidence linking mortality and morbidity levels to annual mean concentrations. The evidence is summarized in the final section.

Methodological Issues in Observational Studies

Observational (nonexperimental) studies of the association between health and air pollution are sometimes viewed as natural experiments in which the exposure to pollutants varies over groups or time. However, this view ignores several special characteristics of observational studies of air pollution. One of the most important is inaccurate measurement of the exposure burden of individuals. Pollution data are usually obtained from one or several outdoor monitoring stations, but the exposure burden can vary greatly between individuals living in the same neighborhood because of special features of the outdoor micrometeorology and the indoor environment (4-6). The effects of errors in the independent variable on the estimated associations between air pollution and health effects depends on both the size and expectation of the errors. Many health endpoints, including lung function, hospital admission and frequency of symptoms, also are measured with substantial variability. When an association between air pollution and health is found, collinearity (high correlation) of sulfur oxide and particulate concentrations (7) and the possibility of complex chemical interactions reported from laboratory studies (8, 9) frequently make it difficult to associate the effect with either pollutant alone (10).

Observational studies of respiratory disease or

lung function must consider a host of confounding variables (11), many of which have greater health effects than air pollution. When these variables are ignored or inadequately measured, resulting bias can easily be greater than the association of interest. In addition, many observational studies use linear or other simple models to summarize complex data sets without assessing the adequacy of the model. Unless data displays, simple groupings or other analyses are used to show that these models are properly summarizing the data, one can only have limited confidence in the results.

These factors, taken together, create additional uncertainty in interpreting observational studies in comparison with laboratory experiments. The most difficult problem in interpreting the evidence from a group of observational studies is determining how effectively these potential problems have been addressed in each study.

There is an unavoidable element of subjectivity in the assessment of evidence. In an effort to reduce that subjectivity we have included in the assessment those studies which satisfy five criteria.

(1) They have been reported in the open literature.

(2) Concentrations of both sulfur dioxide and particulate matter were reported.

(3) Major confounding factors were controlled, particularly temperature in studies of acute exposure, and smoking, race and socioeconomic status in studies of chronic exposure.

(4) The findings pertain to concentrations less than $1000 \mu\text{m}/\text{m}^3$ for both sulfur dioxide and particulate matter.

(5) The data collection, analysis and interpretation were free of error or potential bias which could be reasonably expected to substantially affect the results.

Studies failing to meet one or more of these criteria were also included when discussion of their validity and significance was seen as an important part of assessing the evidence from observational studies.

Health Effects of Acute Exposure to Sulfur Oxides and Particulates

The earliest studies of the acute health effects of air pollution focused on dramatic episodes of severe air pollution (12-18). The sudden increases in mortality and morbidity that accompanied these episodes and the frequency and severity of respiratory complaints left little doubt that air pollution was, at least in part, the cause of the adverse health effects. Investigators also recognized that weather,

particularly extreme temperatures, mortality and morbidity rates.

A substantial reduction in ambient sulfur oxide and particulate concentrations, achieved in most English and American cities by the 1970's, produced a gradual decline in severity and eventual disappearance of episodes in which either sulfur dioxide or particulate matter exceeded $1000 \mu\text{g}/\text{m}^3$ (measuring particulate matter either by the British Black Smoke method or as Total Suspended Particulates). Episode studies were gradually supplanted by studies of fluctuations in daily mortality over extended periods, and investigations of potentially more sensitive indices of health effects, including lung function and respiratory disorders. Sensitive population subgroups, such as asthmatics and children, have also been studied. The pollution concentrations in studies of acute exposure have typically been measured by 24-hr mean concentrations, though high level exposures for shorter periods might be important.

Counts of total daily mortality show a seasonal pattern with a peak in winter, and rates on successive days are interdependent. Early studies used the deviation of daily mortality from the 15-day moving average to eliminate seasonal effects. More recently, investigators have used sophisticated time-series-analysis techniques in an effort to eliminate seasonal effects and other long-term trends affecting daily mortality. Elimination of seasonal effects by these methods may be incomplete, and this becomes especially important when investigators attempt to identify pollution effects that are small relative to effects of temperature, season and even day of the week. We will return to this issue in the discussion of individual studies.

Morbidity data are more difficult to gather than daily mortality figures. For that reason, investigations of morbidity effects of acute exposure to sulfur oxides and particulate matter have usually been small, permitting relatively simple analysis. These studies would be unlikely to detect small increases in morbidity at relatively low air pollution concentrations.

Studies reported in this section used three separate measures of particulate pollution. The British studies used the British Black Smoke method and reported particulate levels in $\mu\text{g}/\text{m}^3$ (BS). Some American studies used the filter soiling method and reported particulate concentrations in units of Coefficient of Haze (CoHs). Other American studies measured Total Suspended Particulates (TSP) by the high-volume sampler method. Results are reported for each study in the original units, and the relationship between the different measures is considered when summarizing the evidence.

Mortality Effects of Acute Exposure to Sulfur Oxides and Particulate Matter

In this section, we examine studies of the association between daily mortality rate, as measured by the recorded number of deaths, and 24-hr average concentration of sulfur dioxide and particulate matter. The clearest evidence comes from studies of relatively high pollution concentrations, while studies of lower concentrations have been equivocal, primarily because collinearity of temperature and other weather variables with pollution concentrations have made it difficult to interpret associations between daily mortality and air pollutant concentrations.

Studies of Daily Mortality in London. Two important British studies bearing on mortality effects of acute exposure to SO₂ and particulate matter at concentrations near present 24-hr air quality standards were reported by Martin and Bradley (19) and Martin (20). Martin and Bradley related daily mortality from all causes (and from bronchitis and pneumonia) to the concentrations of SO₂ and black smoke (BS) in London during the winter of 1958-59. The authors found a considerable number of coincident peaks in pollution concentration and daily mortality. The correlation of mortality from all causes with air pollutant concentration, measured on the log scale, was 0.61 for BS and 0.52 for SO₂. The correlation between mortality and mean daily temperature was -0.03 (not significant), while the correlation of mortality with humidity was 0.19 (significant at the 0.05 level). The authors noted that about two-thirds of the air pollution episodes were accompanied by thick fog, and the correlation between mortality and visibility was found to be -0.55. Visibility is influenced both by fog and particulate pollution.

Although the authors emphasized the relation-

ship between differences in pollution concentration and differences in death rate on successive days, their paper provided total deaths, smoke concentration and SO₂ concentration from November 1, 1958 to February 28, 1959. We have re-examined their data after excluding the month of February, as an epidemic of Type A influenza had a significant influence on daily mortality in that month.

For the remaining 92 days, the deviation of each day's total mortality from the 15-day moving average (truncated at each end of the series) was computed. The average deviation is given for intervals of BS concentration in Table 1 and SO₂ concentration in Table 2.

Although Lawther (21) has suggested that the number of deaths increased significantly when BS rose above 750 µg/m³ and SO₂ concentrations exceeded 710 µg/m³, these tables do not suggest those values. If one begins with a threshold hypothesis, that mortality is not affected until air pollution concentrations exceed threshold levels, one might choose threshold values of 500 µg/m³ of BS and 300 µg/m³ of SO₂ from these data. However, the data are also consistent with a monotonic exposure-response hypothesis, that mortality level increases with air pollution concentration over a broad range of values, including those just cited.

A similar analysis was carried out by Martin for the winter of 1959-60 (20). That winter had fewer incidents of high pollution. The significant positive correlation between mortality and pollution was still present, although the author reported that the correlation coefficients were somewhat lower than in the previous year. Tables 3 and 4 show Martin's results combining high pollution days from 1958-59 and 1959-60, excluding days with pollution concentrations lower than the previous day. The mean deviation is positive in every group reported. Bronchitis mortality was also found to be significantly, though less strongly, correlated with pollution level. Pneumonia mortality was not found to be correlated with pollution.

Table 1. Average deviation of daily mortality from 15-day moving average, by concentration of smoke (London, Nov. 1, 1958, to Jan. 31, 1959).^a

Smoke concentration, µg/m ³ (BS)	Number of days	Mean deviation
100-199	6	-20.82
200-299	12	-13.65
300-399	18	-10.80
400-499	19	-7.15
500-599	9	10.89
600-699	6	19.72
700-799	7	4.17
800-1199	10	21.49
1200+	5	38.36

^aData of Martin and Bradley (19).

Table 2. Average deviation of daily mortality from 15-day moving average, by concentration of SO₂ (London, Nov. 1, 1958, to Jan. 31, 1959).^a

Smoke concentration, µg/m ³	Number of days	Mean deviation
100-199	17	-13.01
200-299	29	-12.16
300-399	22	6.87
400-499	11	9.32
500+	13	27.21

^aData of Martin and Bradley (19).

Table 3. Average deviation of daily mortality from 15-day moving average, by concentration of smoke (BS) (London, 1958-60).^a

Smoke concentration, $\mu\text{g}/\text{m}^3$ (BS)	Number of days	Mean deviation
500-599	9	5.2
600-699	6	13.0
700-799	9	9.2
800-1099	8	15.6
1100+	7	40.0

^aData of Martin (20).

These two studies represent an important part of the evidence for mortality effects of short-term elevations in SO_2 and particulate pollution. Although temperature was not an important confounding factor in the two winters studied, fog was an important factor in many air pollution episodes, especially in the winter of 1958-59. Reported analyses have not adequately controlled for the effects of fog on mortality. During this period, daily mean concentrations of SO_2 and BS were highly correlated ($r = 0.89$ for the winter of 1958-59). Consequently, these associations cannot be attributed to either pollutant individually.

Additional evidence for acute effects of short-term elevations in sulfur dioxide and particulate matter concentrations was provided by the analysis of a pollution episode in London in December, 1975 (22, 23). Maximum 24-hr concentrations of $994 \mu\text{g}/\text{m}^3$ (SO_2) and $546 \mu\text{g}/\text{m}^3$ (BS) were reported, and an increase of 100 to 200 deaths above expected totals was observed during the week in which the episode occurred. A doctors' strike in the period immediately prior to this episode had an unknown impact on the mortality data.

Studies of Daily Mortality in New York City. The other principal source of information on variation in daily mortality comes from a series of studies in New York City. This information includes reports

Table 5. Average deviation of daily mortality from normal, by level of smoke shade (CoHs) (New York, 1960-64, October through March).^a

Smoke shade level (CoH)	Number of days	Mean deviation (SE)
<1.0	26	-2.8 (3.5)
1.0-1.9	160	-1.6 (1.4)
2.0-2.9	318	-2.4 (1.0)
3.0-3.9	239	1.5 (1.2)
4.0-4.9	83	2.5 (2.3)
5.0-5.9	19	18.8 (4.3)
6.0+	9	17.2 (7.8)

^aData of Glasser and Greenberg (27).

Table 4. Average deviation of daily mortality from 15-day moving average, by concentration of SO_2 (London, 1958-60).^a

SO_2 concentration, $\mu\text{g}/\text{m}^3$	Number of days	Mean deviation
400-499	9	9.0
500-599	6	11.6
600-799	9	16.0
800-899	6	19.2
900+	5	39.6

^aData of Martin (20).

(24-26) of several air pollution episodes not discussed here, since pollutant concentrations were too high to contribute significantly to our assessment. However, Glasser and Greenburg (27) carried out an analysis of daily mortality in New York City during the five-year period 1960-64, using only data from the months October through March. The 24-hr average pollution concentrations were based on hourly SO_2 and bihourly smoke shade (CoHs) readings from a single monitoring station. Death rates were analyzed both as deviations from a 15-day moving average and as deviations from the five-year average for that day. The two analyses were said to have qualitatively similar results. In cross-tabulation of daily mortality by SO_2 and smoke shade level, SO_2 appeared to be more strongly related to mortality and was used as an index of pollution in some analyses. Multiple regression analysis showed a stronger association of mortality with SO_2 than with either temperature or rainfall.

Tables 5 and 6 summarize the analysis by Glasser and Greenburg. These results have been interpreted as showing a mortality effect for smoke shade above 5 CoHs and SO_2 above $786 \mu\text{g}/\text{m}^3$, though they are again supportive of a monotonic exposure response relationship. Although the observations of daily mortality are correlated, Glasser and Greenburg computed standard errors for the mean deviations by assuming independence. Most

Table 6. Average deviation of daily mortality from normal, by level of SO_2 (New York, 1960-64, October through March).^a

SO_2 concentration, $\mu\text{g}/\text{m}^3$	Number of days	Mean deviation (SE)
<262	112	-3.5 (1.6)
262-524	311	-3.1 (1.0)
525-786	172	1.8 (1.4)
787-1048	66	9.4 (2.0)
>1048	80	11.9 (2.5)

^aData of Glasser and Greenberg (27).

of these standard errors were near 2.0, though the entry 18.8 in Table 5 had a quoted standard error of 4.3. The authors also stratified days by temperature into three groups: those more than five degrees below normal, within five degrees of normal, and more than five degrees above normal. The result of the stratified analysis differed little from the unadjusted analysis. However, this simplified approach to covariance adjustment may not eliminate the confounding effects due to temperature. Multivariate analyses of the New York data described below suggest that more careful control for temperature and other meteorologic factors has a substantial effect on the results.

To analyze possible mortality effects of even lower levels of pollution, the 15-day moving average method is not sufficiently sensitive. Furthermore, some authors have argued that more sophisticated adjustment techniques are necessary to ensure that seasonal and temperature effects are eliminated in the adjusted analysis. To achieve that objective, Schimmel and coworkers (28-30) have reported three analyses of mortality data from New York City in which the adjustment methodology was refined over time. Buechley et al. (31) and Buechley (32) have also analyzed some of the same data.

Schimmel and Murawski (29) emphasized the common seasonal trends in mortality, pollution and temperature in New York City, and the possibility that nonlinear relationships would make linear regression unsatisfactory as an adjustment technique. They eliminated periods associated with heat waves and analyzed the remaining data in three time periods, 1963-66, 1967-69 and 1970-72. While smoke shade level varied little over the three periods, the average SO₂ level declined dramatically, as shown in Table 7.

Schimmel and Murawski estimated the percentage of premature deaths due to air pollution to be 2.78, 2.48 and 3.20, based on regression analysis of the three periods using a model with no lag effects. The percentage attributed to SO₂ was 0.58, 1.22 and 0.62, values not significantly different

from zero. Since the percentage of excess deaths attributed to air pollution differed little in periods with three-fold differences in SO₂ concentration, they concluded that SO₂ concentration is merely an index variable for other unmeasured extraneous variables and not a cause of adverse health effects at these levels.

Schimmel (30) continued his analysis of these data by utilizing time series techniques to eliminate any seasonal or other cyclical effects contributing to associations between pollution and mortality. In this analysis, the regression of mortality on SO₂ was not significant and negative coefficients were obtained in some regressions.

Buechley (31, 32) also sought to identify major nonpollutant variables influencing daily mortality and found that mortality was affected by the annual cycle, summer heat waves, influenza epidemics and a temperature variable. These four variables explained 78% of the variation in daily mortality during the 11-year period 1962-72 in New York City. Although SO₂ concentration and particulate level also entered significantly into the regression equation, Buechley found that the coefficient for SO₂ concentration in regression analysis of daily mortality during the winter of 1971-72 was slightly higher than the corresponding coefficient for the winter of 1967-68, even though the mean SO₂ concentration in the second winter was only 10% of that in the earlier period.

Both Schimmel (30) and Buechley (32) concluded that the associations they found between mortality and air pollution could be explained by joint association with temperature and other weather variables. Their work highlights the limitations of observational studies when the study objective is accurate estimation of small primary relationships when other independent variables are more strongly associated with mortality. These other variables influence the estimate of the primary relationship, and the proper method of adjustment is unknown. Thus, it will be difficult to reliably quantify small mortality effects of fluctuations in ambient pollution concentrations by analyzing observational data.

Table 7. Average pollution levels during three time periods analyzed by Schimmel and Murawski.^a

Time period	SO ₂ level, μg/m ³	CoHs level
1963-66	112	2.07
1967-69	359	2.27
1970-72	155	2.13

^aData of Schimmel and Murawski (29).

Morbidity Effects of Acute Exposure to Sulfur Oxides and Particulate Matter

Levels of air pollution which acutely affect mortality rates should affect other health indices, including incidence and prevalence of respiratory disease as measured by emergency room visits or hospital admissions, prevalence and severity of respiratory symptoms as measured by question-

naire during regular contact with a panel of participants, or changes in various aspects of lung function. Unlike mortality rates, these health data must often be specially obtained by the investigator. This has limited the size of morbidity studies. Many studies have used the diary or panel method, in which a group of participants regularly record or report symptoms. Substantial nonparticipation rates have been a problem in many of these studies, and make it difficult to interpret the symptom reports by those from whom observations are obtained.

Illness data were obtained in many of the early severe pollution episodes (13, 15, 33). This information did little more than confirm the mortality results, though there was some evidence that the increase in illness was not as large in percentage terms as the increase in deaths, and the effects were not so sudden. Martin (20) examined hospital admissions for the winters of 1958-59 and 1959-60 and found, after adjustment for day of the week and correction for 15-day moving average, significant correlations for both cardiovascular and respiratory conditions with BS and sulfur dioxide. The average deviations by pollution concentration, given in Tables 8 and 9, show more irregularity than the mortality data.

Table 8. Average deviation of respiratory and cardiac morbidity from 15-day moving average, by smoke concentration (BS) (London, 1958-60).^a

Smoke concentration, $\mu\text{g}/\text{m}^3$ (BS)	Number of days	Mean deviation
500-599	9	3.2
600-699	6	-0.7
700-799	9	2.4
800-1099	8	4.9
1100 +	7	12.9

^aData of Martin (20).

Table 9. Average deviation of respiratory and cardiac morbidity from 15-day moving average, by SO_2 concentration (London, 1958-60).^a

SO_2 concentration, $\mu\text{g}/\text{m}^3$	Number of days	Mean deviation
400-499	9	2.2
500-599	6	5.1
600-799	9	6.9
800-899	6	12.8
900 +	5	12.8

^aData of Martin (20).

In a second important British study, Lawther et al. (34, 35) collected daily self-reported health status from 194 persons with chronic respiratory disease during the winters of 1959-60 and 1964-65. Health status was reported relative to the previous day, and worsening of health status by self-evaluation was clearly associated with increases in air pollution. The authors reported that this effect could be seen on days when the 24-hr average level of SO_2 exceeded $500 \mu\text{g}/\text{m}^3$ and smoke exceeded $250 \mu\text{g}/\text{m}^3$ (BS). The strength of this response declined as the winter progressed and there was some evidence for an adaptation or desensitization effect or even loss of interest by participants. Lawther et al. commented that these responses could have resulted from brief exposure to maximum concentrations several times the 24-hr average.

Studies of Bronchial Asthma. Some studies of pollution and asthma have reported negative or equivocal results (36, 37). However, Cohen et al. (38) found a weak association between air pollution and the frequency of asthma attacks in a study of patients living near a coal-fueled power plant in West Virginia. Temperature was most strongly correlated with frequency of attacks among 20 patients having at least one attack during the study. In a multiple regression analysis, either SO_2 or TSP concentration was significantly correlated with attack rate after adjustment for temperature ($p < 0.01$). When days were classified as high and low particulate concentration (above or below $150 \mu\text{g}/\text{m}^3$ TSP), or as high and low SO_2 concentration (above or below $200 \mu\text{g}/\text{m}^3$), symptom prevalence was significantly higher on the high pollution days.

These values should not be interpreted as threshold values, since the dividing line seems arbitrary and the table comparing the two groups of days does not seem to be temperature adjusted. The authors provide little information about changes in panel membership over time, and also give insufficient information about their data analysis methods. In particular, they combined data from children and adults participating in the study. The sensitivity of asthmatics to exogenous allergens, respiratory infections, dust, animals, smoking, cold weather and psychological factors also suggests caution in attributing changes in symptom prevalence to changes in air pollution concentration.

Studies of Acute Respiratory Disease. Few studies relating acute exposure to moderate levels of air pollution to increased incidence of acute respiratory disease have been published. Although early studies by Dohan and Taylor (39) and Dohan (40) found an association between the level of suspended sulfates and work absences for respiratory disease among outdoor telephone workers, Ipsen et

al. (41) conducted a near replication of their study and found that apparent associations between absenteeism and air pollution were eliminated by adjustment for temperature, humidity and wind velocity.

Studies of Pulmonary Function. Vander Lende et al. (43) obtained results in a study of respiratory symptoms and lung function in the Netherlands which could represent an acute effect of air pollution. Examination of a large general population group in 1969 and again in 1972 failed to show the expected small decrease in levels of Forced Vital Capacity (FVC) and Forced Expiratory Volume in one second (FEV₁), but rather small significant increases. The authors suggested that this could be attributed to improvement in air quality, from reported maximum 24-hr smoke level of 160 $\mu\text{g}/\text{m}^3$ (BS) and SO₂ concentration of 300 $\mu\text{g}/\text{m}^3$ in 1969 to 40 $\mu\text{g}/\text{m}^3$ (BS) and 100 $\mu\text{g}/\text{m}^3$ (SO₂) in 1972. [This and some other continental European studies used OECD calibration curves to express Black Smoke in $\mu\text{g}/\text{m}^3$. Some reviewers have suggested that the reported values should be increased, perhaps by a factor of 2, to be comparable with the British Black Smoke method (42).]

Expected decreases in pulmonary function were seen in a rural area measured at the same times. The authors explored possible sources of bias in the study but were unable to explain their results on that basis. If real, these changes are most reasonably interpreted as an acute, reversible response to elevated concentrations of air pollution.

Stebbing et al. (44) studied pulmonary function in 272 children during and after an air pollution alert in Pittsburgh in 1975. The 24-hr average SO₂ concentration reached 350 $\mu\text{g}/\text{m}^3$ and the 24-hr TSP level reached 770 $\mu\text{g}/\text{m}^3$. The mean FEV_{0.75} and FVC values, instead of increasing as hypothesized, declined throughout the six-day period. Because the investigators did not have a pre-alert lung function measurement, the values obtained during the alert days could not be compared to "normal" lung function values. Since the children were followed for only the week, the possibility of a later increase in lung function values could not be excluded.

In a later report, Stebbings et al. (45) identified a group of children whose lung functions showed large increases after the alert. Since the proportion of such children was significantly greater in the alert than in a control area, they concluded that the alert had been associated with reduced lung function. Since the analysis was selected in response to the data, was based on unvalidated methodology, and failed to explain the anomalous finding of an excess of children in the alert area whose lung function declined during the study,

these results do not provide sound evidence for health effects of air pollution at the levels reported.

Health Effects of Chronic Exposure to Sulfur Oxides and Particulate Matter

Studies of health effects of chronic exposure to air pollutants are typically cross-sectional, comparing mortality or morbidity rates within or among a number of communities. The possibility that the estimates of air pollution effects will be biased by other community differences related to health is particularly great in these studies. Concentrations of air pollutants are usually higher in urban than in rural areas, and many authors have noted that smoking patterns, family size, age distribution, occupation, domestic crowding, nutrition, physical activity and other characteristics of the population can differ between rural and urban areas. Although some studies have sought to match communities on important characteristics or use multivariate adjustment techniques to control for the effects of these factors, their effectiveness is typically unknown. This is especially true when complex regression models are used for adjustment, for the adjustment is limited by the degree to which the model correctly specifies the relation between these factors and the outcome under study.

Mortality Effects of Chronic Exposure to Sulfur Oxides and Particulate Matter

The study of Buck and Brown (46) was one of the first to show an association between annual average concentration of SO₂ and Black Smoke and mortality rate across communities in Great Britain. However, mortality data were obtained in 1955-59 and pollution was measured in 1962. Pollution levels were falling during this period. Although it has been argued that mortality effects were seen in boroughs where Black Smoke and SO₂ levels exceeded 200 $\mu\text{g}/\text{m}^3$, it is likely that exposures prior to and during 1955-59 were somewhat higher than in 1962. Wicken and Buck (47) also found differences in lung cancer and bronchitis mortality rates between areas of high and low pollution after adjusting for age, smoking habits and social class. However, this study was also limited by unavailability of concurrent air pollution measurements in most of the communities studied.

More recently, several investigators have used multivariate regression techniques to analyze mortality data obtained from vital statistics sources. The following sections discuss these investigations.

Analyses of Total Mortality Rates

As noted above, there are many reasons why mortality rates vary among communities. Therefore, study units should be selected to minimize variation due to factors other than air pollution. On the other hand, study units must be selected to conform with the available data. For mortality studies, Standard Metropolitan Statistical Areas (SMSA's) and cities meet this condition but present several difficulties. Investigators, recognizing that the study units differ with respect to factors other than air pollution, attempt to adjust for these differences by including socioeconomic and demographic variables in their analysis. Nevertheless, it is likely that the effects of variables such as personal habits, occupational exposure, and medical care cannot be fully quantified and eliminated in this way. If any of these factors covaries with air pollution levels, a spuriously large effect will be attributed to air pollution.

The evidence in a multiple regression analysis relating mortality to pollution can be expressed through the coefficients of the pollutants and their standard errors. Comparison of the results of regression analyses from major studies relating mortality rates to pollution levels across communities illustrates the problems that arise in interpreting these studies.

The four regression equations summarized in Table 10 are taken from the work of Lave and Seskin (48). TSP represents the average of 26 biweekly measurements of 24-hr TSP in each SMSA, while SO_4 is the lowest sulfate determination from these 26 observations. Regressions LS1 and LS2 were both obtained from the analysis of 1960 mortality data for 117 SMSA's. The two regression equations differ only in that the second contains one additional adjustment variable, home heating fuel. Adding this variable reduces the coefficients of the air pollutants by a factor of three and they are not significant in LS2. Lave and Seskin argue that this occurs because home heating fuels are a major pollution source, home heating fuels and pollutants are highly correlated. This contrast illustrates one effect of collinearity on the regression coefficients. Regression LS3 results from fitting the model from regression LS1 to 1961 data. Mortality and pollution values were about the same in the two years, and the coefficients are quite similar also. When the same model is fitted to the 1969 data (regression LS4), the estimated effects are larger even though mean TSP level declined from $118 \mu\text{g}/\text{m}^3$ to $96 \mu\text{g}/\text{m}^3$ and the average SO_4 level declined from $4.72 \mu\text{g}/\text{m}^3$ to $3.46 \mu\text{g}/\text{m}^3$. These comparisons show how sensitive these multiple regression analyses are to variable selection, and also raise questions of consistency.

Table 10. Coefficients of TSP and SO_4 in four regressions reported by Lave and Seskin.^a

Regression	Source	Coefficient (SE)		
		TSP	SO_4	Other variables ^b
LS1	Data from 117 U.S. SMSA's in 1960	0.452 (0.169)	6.31 (2.33)	D, A, R, I, P
LS2	Data from 117 U.S. SMSA's in 1960	0.171 (0.158)	1.84 (2.16)	D, A, R, I, P, HHF
LS3	Data from 117 U.S. SMSA's in 1961	0.516 (0.178)	4.56 (2.49)	D, A, R, I, P
LS4	Data from 117 U.S. SMSA's in 1969	0.818 (0.241)	7.74 (3.67)	D, A, R, I, P

^aData of Lave and Seskin (48).

^bSymbols used in this column are defined in Table 12.

Table 11. Coefficients of TSP and SO_4 in regressions analysis by Lipfert and Crocker et al.

Regression	Source	Coefficient		Other variables ^a
		TSP	SO_4	
L1	Data from 60 U.S. SMSA's in 1969 ^b	0.73	5.4	D, A, R, I
L2	Data from 60 U.S. cities in 1969 ^b	0.78	8.2	D, A, R, I
L3	Data from 136 U.S. cities in 1969 ^b	1.00	-2.0	A, R, I, H, B
L4	Data from 181 U.S. cities in 1969 ^b	0.72	-4.3	A, R, I, H, B, C, log D
C1	Data from 60 U.S. cities in 1960 ^c	0.11	-0.31 ^d	MD, MI, E, CH, C, CT, R, MA, DF

^aSymbols used in this column are defined in Table 12.

^bData of Lipfert (49, 50).

^cData of Crocker et al. (51).

^dCoefficient of SO_2 .

Results of four regression analyses reported by Lipfert (49, 50) are shown in Table 11. The first (L1) is based on analysis of 1969 mortality data from 60 U.S. SMSA's, using a model much like regression LS4 in Table 10. Very similar coefficients are obtained. The first two models in Table 11 differ only in that the first uses mortality data from 60 SMSA's while the second uses mortality data from 60 U.S. cities. The coefficient of SO₄ is larger in the second regression using smaller geographic areas. Model L3 differs from L2 in that more cities are included and age of housing and birth rate are added as independent variables, while cigarette consumption is added in L4. Though the coefficient of TSP changes very little, the coefficient of SO₄ is negative in these regressions.

The final regression in Table 11 is taken from an analysis of 60 U.S. cities in 1970 by Crocker et al. (51). In addition to variables used by other investigators, this model includes variables for climate, education, availability of medical care and nutritional habits. Although Crocker uses SO₂ and not SO₄ as a pollution variable, neither pollutant contributes significantly to the regression. Crocker et al. report a correlation between SO₂ and SO₄ of 0.74.

The association between air pollutant concentration and mortality rates in different analyses can be summarized by the elasticity. An elasticity is a dimensionless number that represents the expected percent change in the dependent variable, mortality, associated with a 100% increase from the mean value in each of the pollutant variables in the regression. Elasticity is computed by multiplying each air pollutant regression coefficient by the

average value of that pollutant in the data set, adding these quantities for all pollutants, and dividing by the average mortality over study units. So long as the set of pollution variables chosen contains variables capturing the total association between all air pollutants and mortality, the elasticity will be relatively insensitive to the choice of a subset of these highly collinear pollutant variables. Thus, the elasticities can be viewed, at least approximately, as measuring the total mortality effect of all pollutants included.

Table 13 gives elasticities for the nine regression analyses summarized in Tables 10 and 11. Regressions LS1, LS3, and LS4 were the simplest models used by Lave and Seskin and had the largest elasticity. In regressions using more variables, such as home heating fuel in regression LS2, smaller elasticities were obtained. (When occupation was added to the model for regression LS1, elasticity declined to 0.05). Regressions L1 and L2 included population density, percentage above 65, percentage nonwhite and percentage with income below \$3,000 as independent variables. When birth rate and age of homes were added (L3) or cigarette smoking (L4), elasticity declined to 0.06 and 0.04, respectively. The effect of cigarette smoking should especially be noted. Finally, in the analysis by Crocker et al. (51) using several other added independent variables (C1), the elasticity was nearly zero. These variables included measures of medical care, diet, climate and cigarette consumption and could easily be defended as critically important in any analysis controlling for other factors expected to influence mortality.

Though it has sometimes been argued that smoking is not associated with air pollution concentration, Crocker et al. report a correlation of 0.23 between cigarette consumption and sulfur dioxide in the 60 cities in their study. Certainly the two variables are not causally related, but both may reflect other characteristics of the population.

Schwing and McDonald (52) report on a study of

Table 12. Definitions of other independent variables used in multiple regressions in Tables 10 and 11.

Variable	Definition
D	Population density in person/mile ²
A	Percentage of population 65 or older
R	Percentage of population nonwhite
I	Percentage of population with income below \$3000/year
P	Log arithm of SMSA population
HHF	Percentage of homes using each of several home heating fuels
H	Percentages of housing units built before 1960
B	Births/1000 population/year
MD	No. of physicians per capita
MI	Median income
E	Percentage of persons 25 or older with high school diploma
CH	Percentage of persons living in homes with more than 1.5 persons per room
C	No. of cigarette packs purchased per capita
CT	No. of days with temperature below 0°C
MA	Median age

Table 13. Elasticities for air pollutants in nine regression analyses of mortality.

Regression	Elasticity
LS1	0.09
LS2	0.03
LS3	0.09
LS4	0.12
L1	0.10
L2	0.09
L3	0.06
L4	0.04
C1	0.004

46 SMSA's (1959-61) in which 23 explanatory variables are used, including climate, socioeconomic, occupational and smoking variables and eight air pollutants. This study differs from those summarized in Tables 10 and 11 in that the investigators included all 23 variables in their models. To counter severe collinearity, the authors used two methods of analysis, ridge regression and constrained least squares, rather than ordinary least squares. (The previously reported studies all used ordinary least squares.)

Ridge regression is a numerical method for stabilizing estimates of regression coefficients from a data set that has collinear explanatory variables. While the method does achieve stability, it does so by selecting an arbitrary constant that has the effect of shrinking each estimated coefficient toward zero. Though ridge regression leads to smaller standard errors for the estimated coefficients, these coefficients are no longer interpretable as partial regression coefficients, that is, measures of the effects of changes in a single variable while the other variables are held fixed. As emphasized throughout this presentation, collinear data sets are fundamentally insufficient to allow assignment of mortality effects to individual members of a group of collinear explanatory variables.

Schwing and McDonald also use constrained least squares, constraining the air pollution coefficients to positive values. This may be unreasonable when eight air pollutants are studied simultaneously. Thurston et al. (53) report that respirable sulfate as a fraction of total sulfate is not constant over different levels of air quality. They note that in "dirty" cities the fraction is 0.6 to 0.7 while in "clean" cities the fraction is 0.8 to 0.9. Thus, if the respirable sulfate affects mortality, an indicator of overall air quality such as TSP could take a negative sign, when both TSP and respirable sulfates are included in the model, to account for the difference in the respirable sulfate fraction between cities.

Schwing and McDonald report an elasticity of 0.22 from ridge regression and an elasticity of 0.045 from constrained least squares. These values are still an order of magnitude larger than that reported by Crocker et al. (0.004).

This discussion has been provided to illustrate the limitations of multiple regression analyses of vital statistics data, using explanatory variables defined by data availability rather than intrinsic interest, and complicated by severe collinearity of pollutant and other explanatory variables. The model can only be approximately correct, the surrogate explanatory variables can never lead to an adequate adjusted analysis, and it is impossible to separate associations of mortality rate with pollu-

tant and confounding variables. This group of studies, in our opinion, provides no reliable evidence for assessing the health effects of sulfur dioxide and particulate matter.

Morbidity Effects of Chronic Exposure to Sulfur Oxides and Particulate Matter

This section focuses on those studies that provide the air pollution and health-status data necessary to assess the morbidity effects of chronic exposure to sulfur oxides or particulates. These studies most commonly represent the cumulative exposure to air pollutants as an arithmetic average concentration of sulfur compounds and particulates during an interval including the study period. Since chronic exposure may refer to the lifetime of an individual, this measure of exposure may be misleading when pollution concentrations have changed substantially during the years preceding the study. Morbidity outcomes are generally limited to respiratory symptoms and measured lung function. Respiratory symptoms are most commonly assessed with self- or interviewer-administered questionnaires. The standard questionnaire developed by the British Medical Research Council (54) has been used typically, with modifications or additions. [A standard questionnaire has recently been developed under the joint sponsorship of the American Thoracic Society and the Division of Lung Diseases, National Heart, Lung and Blood Institute, and is recommended for all U.S. population studies (55).] Lung function is generally measured by spirometry from which both forced expiratory volume and flow rates can be determined. Relationships between air pollution and nonrespiratory or systemic morbidity are usually not explored.

Most of the studies reviewed are cross-sectional investigations of morbidity prevalence. Many of the difficulties of inferring a cause-effect relationship between air pollution and health outcome in such studies have been discussed above. Typically, a few cities or areas with different air pollution concentrations are compared. The study populations are either matched on, or analyses standardized for, differences in variables such as age distribution, race, socioeconomic characteristics, occupational categories, and smoking habits. Often only two cities or areas with contrasting air quality are compared. Rarely are more than half a dozen areas compared. The effect of limited observations at differing air pollution levels is partially mitigated by the ability to gather extensive information on outcome variables such as ventilatory function and symptom

prevalence and on potentially confounding factors such as cigarette smoking and occupation. Nevertheless, when only a few observations have been made at different air pollution levels, it is difficult to construct generalizable quantitative dose-response relationships.

The major studies suggesting morbidity effects of exposure to elevated concentrations of particulate matter and/or sulfur oxides have been reported from three countries; Great Britain, Poland and the United States.

British Studies. Lunn et al. (56, 57) studied schoolchildren living in four areas of Sheffield, England with different air pollution concentrations. These concentrations are shown in Table 14 for the two winters studied. Questionnaires were answered by parents and the investigators found substantially higher prevalence of symptoms of respiratory disease in the three more polluted areas than in the less polluted area (Table 15). These children were followed up in 1967-69 when they were nine years old (57). As a result of the institution of smoke control, smoke levels were reduced to about half their former levels. When children from the three dirtier areas were pooled and compared to children from the clean area in the second study, there were no differences in symptom prevalence rates. Pollution concentrations in the later period were 48

$\mu\text{g}/\text{m}^3$ (BS) and $123 \mu\text{g}/\text{m}^3$ (SO_2) in the clean area and averaged about $140 \mu\text{g}/\text{m}^3$ (BS) and $200 \mu\text{g}/\text{m}^3$ (SO_2) in the dirty areas.

Douglas and Waller (58) reported on a study of a sample of children born during one week in March 1946. Air pollution was assessed by creating an index based on coal consumption. The authors created four pollution categories, and found that the prevalence of lower respiratory disease, but not upper respiratory disease increased with increasing pollution when the children were studied at ages 6, 7, 11 and 15.

Comparison of the index to measured BS and SO_2 concentrations in 1962 established a gradient of mean annual pollutant concentrations across the four pollution categories. The lowest pollutant concentrations in 1962 among the categories with increased morbidity were $130 \mu\text{g}/\text{m}^3$ (BS) and $130 \mu\text{g}/\text{m}^3$ (SO_2). Colley et al. (59) followed this cohort at age 20, and Kiernan et al. (60) followed it again at age 25. Neither investigation found an association of respiratory disease symptom with previous air pollution exposure, although at age 20 the prevalence of respiratory symptoms was slightly higher among those who had lived in high pollution areas (11.5%) than among those from low pollution areas (10.2%), and a similar relationship was found at age 25. Respiratory symptom prevalence was associ-

Table 14. Air pollution concentrations in communities studied by Lunn et al.^a

	Concentration (24-hr average), $\mu\text{g}/\text{m}^3$							
	Greenhill		Longley		Park		Attercliffe	
	1964	Winter 1965-66	1964	Winter 1965-66	1964	Winter 1965-66	1964	Winter 1965-66
BS	97	(70-78)	230	177	262	220	301	249
SO_2	123	(109-134)	181	194	219	241	275	301

^aData of Lunn et al. (56).

Table 15. Symptoms by area in the study of Lunn et al.^a

Symptom	Greenhill			Longley			Park			Attercliffe		
	N ^b	P ^c	SE ^d	N	P	SE	N	P	SE	N	P	SE
Nasal discharge	408	6.4	1.2	192	5.2	1.6	130	15.4	3.2	82	14.6	3.9
≥ 3 colds	413	34.4	2.3	194	43.8	3.4	130	48.5	4.4	82	46.3	5.5
Eardrum finding	381	9.4	1.5	178	10.7	2.3	125	14.4	3.1	75	17.2	4.4
Frequent cough	411	22.9	2.1	194	36.1	3.4	130	34.6	4.2	82	50.0	5.5
Cold going to chest	412	34.7	2.4	194	42.8	3.6	130	40.0	4.3	82	53.7	5.5
Lower respiratory infection	413	23.0	4.3	192	36.0	5.8	127	35.0	7.1	82	30.0	9.2

^aData of Lunn et al. (56).

^bThe number of responses obtained.

^cThe percentage of positive responses.

^dThe estimated standard error of the observed percentage.

ated with cigarette smoking at these ages. Because pollution concentrations in 1962 were presumably much lower than those in earlier years, the concentrations cited probably understate the exposure of study participants. We note that exposure during childhood to air pollution concentrations in excess of $130 \mu\text{g}/\text{m}^3$ (BS) and $130 \mu\text{g}/\text{m}^3$ (SO_2) resulted in no significant increase in respiratory illness by adulthood compared to those exposed to lower air pollution concentrations.

Lambert and Reid (61) mailed self-administered questionnaires to 18,379 men and women in Britain to assess the relationship of smoking and air pollution to bronchitis symptoms. The reply rate was 74% from the 35-69 year-old age group studied. From the 9,975 replies analyzed, the authors conclude that the prevalence of respiratory symptoms increased with pollution levels independently of cigarette smoking. Air pollution was found to have a greater effect on the symptoms of smokers than nonsmokers, in terms of the absolute difference in symptom prevalence rates.

The exposure levels in this study are approximate, since only 30% of the population surveyed was covered by actual air pollution measurements. The pollutants measured, BS and SO_2 , were taken from 1965 data of the British National Air Pollution Survey. The balance of the population was assigned to exposure categories based on the Douglas-Waller (58) index which was developed from 1952 domestic coal consumption. A comparison of symptom-prevalence ratios from measurements of BS, SO_2 , and index values shows similar ratios and similar gradients for symptoms with increasing pollution. The lack of complete air pollution data adds uncertainty to the exposure estimates, but in those areas where BS and SO_2 measurements were avail-

able, increased prevalence of symptoms was found in association with BS and SO_2 levels between 100 and $150 \mu\text{g}/\text{m}^3$, as an annual average.

Polish Studies. A study of two areas of contrasting air quality in Cracow, Poland, was conducted by Sawicki. The study began with a cross sectional survey in 1968 and continued with a prospective study until 1973 (62). Annual average particulate values in 1968 were 90 and $170 \mu\text{g}/\text{m}^3$. In 1968, chronic bronchitis prevalence was greater in the more polluted area for men, but not for women. The difference was statistically significant for men who were nonsmokers or present smokers. These data are given in Table 16. Asthmatic disease prevalence was also greater among smokers living in the more polluted area and FEV_1 as a percentage of FVC was lower for most age-sex-smoking-history groups.

Between 1968 and 1973, the annual mean concentration of SO_2 and BS declined slightly for Cracow as a whole but increased slightly at the sites close to the homes of most study participants. In 1973, respiratory disease was again more prevalent among those living in the areas of high pollution for many, but not all of the age, race, and sex groups studied. Mean FEV_1 level was not significantly different in the two areas. The prevalence of obstructive disease was higher in the more polluted area only for present smokers. The authors concluded that smoking and, to a lesser extent, occupational exposure and age had the greatest effect on respiratory illness prevalence, while air pollution at the place of residence was listed as one of several factors having a smaller effect on respiratory illness.

Rudnik et al. (63) reported extensively on the early phase (1970-1976) of a long-term study of the factors which influence development of childhood

Table 16. Prevalence of chronic bronchitis by sex and smoking status in 1968.^a

Smoking status	Low pollution area						High pollution area					
	Men			Women			Men			Women		
	N ^b	P ^c	SE ^d	N	P	SE	N	P	SE	N	P	SE
Total	323	11 ^e	1.7	362	4	1.0	262	19 ^e	2.4	396	5	1.1
Nonsmokers	56	4	2.6	266	2	0.9	58	7	3.4	264	3	1.0
Ex-smokers	46	4	2.9	18	11	7.4	40	5	3.4	34	6	4.1
Present smokers	221	14 ^e	2.3	78	10	3.4	164	27 ^e	3.5	98	10	3.0
Period of smoking												
1-10 years	56	5	2.9	41	7	4.0	42	7	3.9	42	5	3.4
11-20 years	89	9 ^e	3.0	21	14	7.6	38	29 ^e	7.4	18	6	5.6
> 21 years	76	28	5.2	16	13	8.4	84	36	5.2	38	18	6.2

^aData of Sawicki (62).

^bNumber of persons studied.

^cPrevalence of chronic bronchitis.

^dStandard error of the observed rate.

^eRates which are significantly different at the 0.05 level.

chronic nonspecific respiratory disease (CNSRD). The authors discussed an early pilot study that was used to test and develop the design and instruments for the main study. The main study, scheduled for completion in 1982, compares 3805 eight to ten year olds, on respiratory symptoms, illness, and lung function (PEFR), in the Polish communities of Cracow (two areas), Nowy Targ, and Limanowa. The arithmetic mean air pollution values for each of two years in these communities are shown in Table 17. The authors provide detailed information on the distribution and seasonal pattern of the air pollution observations.

Most of the symptoms analyzed and past respiratory illness were less prevalent in the cleaner communities of Nowy Targ and Limanowa than in the two areas in Cracow. There was some indication that symptom rates were lower in the cleanest city of Limanowa than in Nowy Targ. Peak expiratory flow rate (PEFR) was lower in Cracow. In fact, PEFR of children without symptoms in Cracow was lower than in symptom-positive children in the cleaner areas. The authors concluded that living in the more polluted community had a deleterious effect on respiratory symptoms, illness, and lung function. The effect of living in Cracow was greater than the other social, economic and environmental factors investigated by the authors. Unfortunately, PEFR as measured with Wright peak flow meters is subject to considerable variation due to variability between machines. It is not clear from these reports how this phenomenon was controlled.

U.S. Studies. A series of studies conducted in a New Hampshire pulp mill town, beginning in 1961,

represent some of the earliest work on the health effects of chronic exposure to sulfur oxides and particulates in this country. In the initial study, Ferris and his colleagues (64, 65) compared symptom prevalence and lung function in three areas with different pollution levels within Berlin, New Hampshire and found no associations after control for cigarette smoking. In a subsequent study (66), a random survey was carried out in the relatively clean city of Chilliwack, British Columbia. Though the pollution levels were considerably lower than those in Berlin, the prevalence of chronic respiratory disease was not significantly different in the two towns after adjustment for age and smoking habits.

The average values of FEV₁ and peak expiratory flow rate (PEFR) were higher in Chilliwack than in Berlin for 30 of 32 subgroups defined by sex and smoking history after controlling for age and height. The authors suggested that differences in ethnicity, weather, medical facilities and other factors may have confounded the examination of the effect of air pollution.

The Berlin, New Hampshire population was followed up in 1967 and again in 1973 (67-69). During the period between 1961 and 1967, all measured indicators of air pollution fell. In the 1973 follow-up, sulfation rates nearly doubled from the 1967 level (0.469 to 0.901 mg SO₃/100 cm²/day) while TSP values fell from 131 to 80 µg/m³ (Table 18). Concentrations of SO₂ were estimated by assuming that all atmospheric sulfur was in the form of SO₂. For all three periods, concentrations of SO₂ at these sites were below the present annual ambient air standard.

During the 1961 to 1967 period, standardized respiratory symptom rates decreased and there was an indication that lung function also improved. Thus, the higher pollution concentrations seen in 1961 were judged to be associated with increased incidence of respiratory symptoms and impairment of lung function. Between 1967 and 1973, age-sex standardized respiratory symptom rates and age-sex-height standardized pulmonary function levels were unchanged. The authors concluded that either

Table 17. Two-year mean air pollution values.^a

	SO ₂ , µg/m ³		BS, µg/m ³	
	1974	1975	1974	1975
Cracow-1	111.4	108.1	169.7	150.9
Cracow-2	138.2	148.5	204.9	227.4
Nowy Targ	57.1	66.8	82.0	79.8
Limanowa	41.5	64.3	53.4	49.2

^aData of Rudnick et al. (63).

Table 18. Pollution levels, Berlin, New Hampshire, during three study periods.

Year (s)	Total dustfall, g/m ² /30 days	TSP, µg/m ³	Sulfation (lead peroxide), mg SO ₃ /100 cm ² /day	Sulfation converted to SO ₂ , µg/m ^{3a}
1961	18.4	180	0.731	55
1966-67	14.3	~131	0.469	37
1973	—	80	0.901	66

^aAssuming all sulfur in the form of SO₂.

the change in air pollution concentration during the latter period was not associated with a change in respiratory health or that the study was too small to detect an effect. The comparison of health status between 1961 and 1967 suggests morbidity effects at $180 \mu\text{g}/\text{m}^3$ (TSP) and $55 \mu\text{g}/\text{m}^3$ (SO_2). These effects could represent a combination of transient (acute) and irreversible (chronic) effects of air pollution exposure. The TSP value of $180 \mu\text{g}/\text{m}^3$ was based on sampling during the summer months and probably underestimated the annual average concentration. The comparison of 1967 to 1973 is uninformative because of offsetting changes in pollution concentrations, although SO_2 concentrations were below present ambient standards in both periods.

Mostardi and Leonard (70) compared the results of pulmonary function testing in 42 high school students from an urban area with pollution concentrations of $100 \mu\text{g}/\text{m}^3$ (SO_2) and $109 \mu\text{g}/\text{m}^3$ (TSP) and 50 students from a rural area with pollution concentrations of $72 \mu\text{g}/\text{m}^3$ (SO_2) and $83 \mu\text{g}/\text{m}^3$ (TSP) (maximum annual average over five years). This study was flawed by failure to consider smoking effects.

Subsequently, Mostardi and Martell (71) reported on 173 and 161 students respectively from the same urban and rural areas. They tested FVC and $\text{FEV}_{0.75}$ on subjects residing for 4 years or more in the areas. The groups were analyzed separately by sex and nonsmoking males were separately considered. The two groups had similar anthropometric characteristics. Approximately 20% lower values of $\text{FEV}_{0.75}$ and 10% lower values of FVC were reported in the more polluted area for the total group, for males, females, and for non-smoking males. While a higher proportion of smokers was found in the urban area (12% vs. 6% in the rural area) the authors claim this did not influence their results. They did not mention race in this study. In the first report (70) the authors found that the lung function differences persisted after exclusion of the three black students in the urban area.

The observed differences of 20% for $\text{FEV}_{0.75}$ and 10% for FVC in two communities with relatively small differences in ambient concentrations of SO_2 and TSP are striking. Other studies discussed here suggest that air pollution at these levels would not have this large an impact on lung function. This implies that other community differences such as racial composition or socioeconomic status may have contributed to the intercommunity differences. The observed differences cannot be reliably attributed to differences in air pollution concentrations.

The remainder of the evidence for health effects of sulfur oxides and particulate matter comes from the Community Health and Environment Surveil-

lance System (CHESS) program, sponsored by the Environmental Protection Agency during the late 1960's and early 1970's. Much of this work was published in a monograph (72) and subsequently summarized in three brief papers (73-75). These studies have been severely criticized. The most important criticism is that methodology and quality control for aerometric measurements was seriously flawed. In particular, spills of reagent and other errors in handling measuring equipment led to underreporting of SO_2 values by 50 to 100%, while smaller biases were identified in the procedures for particulate measurement, resulting in underreporting by an estimated 10 to 30%. A number of other problems of study design, participant follow-up and data quality control were detected, raising doubts about the accuracy and proper interpretation of reported results. Ultimately, the CHESS studies were the subject of a special Congressional hearing (76) and an investigation by an expert panel convened by a Committee of the U.S. House of Representatives (77). The principal criticism of the CHESS report arising from this review was that the data had been overinterpreted in the CHESS monograph.

As we have indicated, observational studies of the health effects of air pollution are particularly difficult to conduct because individual exposure is poorly measured and populations may not be comparable in ways related to respiratory health. In view of the special problems occurring in the studies published in the CHESS monograph and the failure of subsequent publications to meet these criticisms, we believe that these studies cannot be used to assess the exposure response relationship between sulfur oxide and particulate concentrations and morbidity. This decision substantially reduces the evidence for morbidity effects of chronic exposure to particulates and SO_2 at levels near present air quality standards, in that most of these studies reported health effects in association with pollutant concentrations near these standards. A more extensive discussion of this controversy can be found in the above cited congressional reports and a recent review article (78).

Two studies which were part of the CHESS program were published separately (79, 80). Information in these articles addresses some of the criticisms of the CHESS program. Hammer et al. (79) surveyed children in four metropolitan New York communities chosen for socioeconomic similarity.

Some of the aerometric data used in Hammer's analysis are shown in Table 19. The TSP values for 1968-70 were obtained by extrapolating from the TSP values at the Manhattan station using dustfall values in each borough and the ratio of dustfall to TSP at the Manhattan station. Values of SO_2 in

Table 19. Approximate air pollution concentrations.^a

Pollutant		Air pollution concentration, $\mu\text{g}/\text{m}^3$		
		1968-1970	1971	1972
SO ₂	Riverhead	N/A ^b	23	22
	Queens	175	51	50
	Bronx	250	51	38
TSP	Riverhead	N/A ^b	34	36
	Queens	85	63	89
	Bronx	110	86	60

^aData of Hammer et al. (79).^bNot available.

Queens and Bronx were obtained from stations in the boroughs. Data for Riverhead were provided by Suffolk County (New York). The fourth community, Sheepshead, was geographically contiguous to the area studied in Queens, and was assumed to have similar pollution values. All data for 1971 and 1972 were obtained from the CHES monitoring network. Although Riverhead unquestionably had substantially less air pollution than the other three communities, both historically and during the study, the values cited can be regarded only as approximations to the ambient concentrations in the study communities. Questions on respiratory disease were answered retrospectively by parents. Significant differences were found in rates of lower respiratory disease in the low pollution community compared to the three high pollution communities for all ages from 1 to 12. Sex and education of head of household were considered in the analysis. Although smoking may have been a factor in older children, this study suggests morbidity effects at pollution concentrations of about 175 $\mu\text{g}/\text{m}^3$ (SO₂) and 85 $\mu\text{g}/\text{m}^3$ (TSP), using the average of the annual exposures over the years 1968 to 1970.

Interpretation of this study is complicated by a 10-fold decline in SO₂ and 3-fold decline in TSP over the 12 year period and by the lack of direct local measurement of air pollution concentration. More detailed information might improve exposure estimation for each child by age and period of exposure.

Hammer (80) also conducted a retrospective study, using parent-answered questionnaires covering four years recall of acute lower respiratory disease in 10,000 children aged 1 to 12 years. The two communities chosen for comparison differed in particulate air pollution concentration but had low SO₂ concentrations (Table 20).

The values for 1968-1970 cited in Table 20 were obtained by fitting trend lines to a few data points. As with the New York study, we can be confident that the cleaner community (Charlotte) had lower TSP concentrations, while in this study both com-

munities had very low SO₂ concentrations. However, the TSP concentrations cited are approximate.

Hammer found that lower respiratory disease morbidity was less prevalent for children in the cleaner community (Table 21). A separate analysis of children with bronchial asthma produced more equivocal findings.

Among asthmatics, morbidity rates in the more polluted community were greater for only about half of the comparisons made. In the case of asthmatic blacks, bronchitis rates were greater in the cleaner community. On the whole, this study showed an association between TSP concentration and morbidity level.

Among the remaining studies in the CHES program, the study of chronic respiratory disease prevalence in the Salt Lake Basin (81) is deserving of further attention. Although large and statistically significant differences were found in disease prevalence between communities with high and low levels of SO₂ and sulfates, these pollutants were among those found to be especially inaccurately measured by the CHES aerometric network, and Utah State Aerometric was incomplete for the relevant years. Nevertheless, the health data have not been convincingly criticized, and an air pollution gradient was recognized to exist across the study communities, despite problems of precise measurement. Further work with these data may increase the acceptance of this study.

At the August 1980 meeting of the Clean Air Scientific Advisory Committee, EPA officials reported that unacceptably high data entry error rates had been detected in some CHES data sets, and that data sets for the major CHES studies would be reentered and reanalyzed to establish the validity of earlier results reported from the CHES program. Unfortunately, this report further weakens the credibility of CHES results. Although we cite results from two CHES studies, continued use of these findings is contingent upon successful validation of the data sets by the staff of the EPA.

The studies that have been reviewed in this section provide the observational evidence for mor-

Table 20. Approximate air pollution values for Birmingham and Charlotte, 1968-71 average.^a

Pollutant	City	Air pollution values, $\mu\text{g}/\text{m}^3$	
		1968-70	1971
TSP	Charlotte	<25	<25
	Birmingham	<25	<25
SO ₂	Charlotte	81	74
	Birmingham	141	133

^aData of Hammer (80).

Table 21. Age-adjusted rates (%) of one or more episodes of lower respiratory disease, by race and age interval.^a

Race	Age, yr	Any lower respiratory Disease, %		Bronchitis, %	
		Charlotte	Birmingham	Charlotte	Birmingham
White	1-4	35.0	38.9	23.1	27.7
	5-8	29.9	36.3	20.4	26.2
	9-12	22.0	26.4	14.9	18.6
Black	1-4	27.8	24.0	13.7	10.6
	5-8	16.4	20.6	7.8	7.9
	9-12	12.7	15.9	6.3	6.9

^aData of Hammer (80).

bidity effects of chronic exposure to SO₂ and particulate matter. In the next section, we summarize and interpret all of the evidence for health effects of acute and chronic exposure.

Summary and Conclusions

Individual studies providing evidence on the association between health effects and the ambient concentration of sulfur oxides and particulate matter have been described in preceding pages. This section is devoted to a summary of that evidence in an effort to present a perspective on using the available data to establish concentrations for both acute and chronic exposure associated with increased morbidity or mortality. The analysis in this section has been influenced by the many thoughtful reviews published in recent years (78, 82-89).

For the purposes of this discussion, acute exposure is measured by the 24-hr average concentration of each pollutant. Current National Ambient Air Quality Standards for maximum 24-hr average concentration are 260 µg/m³ for TSP and 365 µg/m³ for SO₂. Exposures over shorter periods may be important, perhaps as measured by the peak hourly concentration in each 24-hr period. Exposures calculated from different short term averaging periods are highly correlated in most situations.

The choice of method for measuring chronic exposure is less straightforward, and can have a significant influence on the determination of concentrations associated with health effects. Most studies reported arithmetic average concentrations of each pollutant over some sampling period including the study period. Although the sampling period did not cover an entire year in every instance, we express the values reported in the various studies as an annual mean concentration. Current National Ambient Air Quality Standards for annual mean concentration are 75 µg/m³ for TSP (computed as the geometric mean of 24-hr samples) and 80 µg/m³ for SO₂ (arithmetic mean). Since arithmetic

means were used almost exclusively for reporting particulate and sulfur oxide concentrations in the studies of chronic exposure, these values have been used in summarizing the evidence. Differences between geometric and arithmetic means are usually unimportant compared to other sources of uncertainty in measuring exposure.

Many of the studies cited failed to obtain concurrent aerometric data. When available, those data were collected at one or a few sites distant from the homes of study participants. The air monitoring techniques were often primitive by current standards, with a resulting potential for substantial bias or variability in measuring concentration. Even when ambient concentrations are optimally measured, the implications for individual exposure are uncertain. Consequently, very great uncertainties about the actual air pollution exposures of study participants in most of the studies discussed weaken analyses of the relationship between exposure and health effect response.

For studies using Black Smoke (BS) to measure particulate concentrations, the conversion to TSP values is highly uncertain and depends upon conditions in the study environment. We convert BS to TSP values using the results of Commins and Waller (89). Since their study was conducted in London between 1955 and 1963, the applicability to other sites or times is unknown. Although we use their conversion to unify the discussion, this introduces additional uncertainty. For the one New York study using Coefficient of Haze (CoHs), we use the conversion developed in New York by Ingram and Golden (90). They equate 5 CoHs to 580 µg/m³ (TSP).

Some studies have reported sulfate concentrations, and there has been considerable interest in the fine particulate fraction (91). However, the correlation between TSP concentrations and its components has been consistently high in observational studies. Thus, these studies provide no basis for separately assessing the health effects of different fractions by size or chemistry of ambient par-

ticulate matter. Further understanding of the proper measure of particulate concentration in terms of health significance will come from advances in understanding of lung physiology and from exposure studies with animals.

Assessing causal relationships from studies of association is a familiar problem for epidemiologists, and the problem is especially difficult in air pollution research. When exposures are near present air quality standards, the health effects of air pollution exposure are likely to be small. Many other individual characteristics influence lung function and the risk of respiratory disease. Some of these, like smoking, occupational differences, and socioeconomic status, are well known but difficult to measure, others like passive smoking have been recognized only recently. The association of lung function and respiratory disease with these characteristics is often much greater than the likely effects of air pollution. The possibility in any observational study that these factors have been inadequately controlled adds additional uncertainty to the interpretation of the nonexperimental studies. Thus, the determination of concentrations associated with adverse effects is tempered by recognition of these potential nonsampling errors.

For all of these reasons, the epidemiologic data base is extremely weak. In particular, it is insufficient to distinguish between a threshold hypothesis, that health effects are seen only above certain concentrations, and a monotonic exposure-response hypothesis, that health effects increase (perhaps very slightly) with air pollution concentration over a very wide range. Although we favor the latter hypothesis as more physiologically plausible, we have chosen to interpret the evidence in terms of concentrations at which health effects have been detected. These values should not be interpreted as threshold values. Finally, SO₂ and particulate concentrations were highly correlated in many of the studies cited. Thus we cite concentrations jointly of SO₂ and TSP at which health effects have been

detected, and then discuss the evidence for health effects of the individual pollutants.

Health Effects of Acute Exposure to SO₂ and Particulate Matter

The studies providing evidence for health effects resulting from acute exposure to SO₂ and particulate matter are summarized in Table 22. The selection criteria excluded studies of SO₂ or TSP exposures above 1000 µg/m³, and the list is strikingly short. The two mortality studies cited (from the same group) found increased mortality associated with TSP concentrations of 500-600 µg/m³ in conjunction with SO₂ concentrations of 300-400 µg/m³. These studies summarize a relatively small body of data from two winters in London. The individual studies do not suggest a threshold phenomenon. Although there is some suggestion of an association at lower concentrations, the evidence is very scanty. For all of the reasons discussed above, this interpretation is subject to considerable uncertainty, and this explains in part the divergent views expressed by different reviewers. Time series analyses of daily mortality records over several years have sometimes suggested small mortality effects of air pollution concentrations at much lower concentrations, particularly in association with particulate concentration in the New York studies, but the results have been highly dependent on model selection and are internally inconsistent.

Only two reports of associations between morbidity and 24 hour average pollutant concentrations are cited in Table 22, and one of these is again the study by Martin. Thus, the acceptable epidemiologic evidence for health effects in association with acute elevations of SO₂ or TSP concentrations below 1000 µg/m³ consists of only two studies. Other reports, including those of Cohen (38), Van der Lende (43), and Glasser and Greenberg (27) are suggestive but subject to numerous ambiguities related to meth-

Table 22. Summary of evidence for health effects of acute exposure to SO₂ and particulate matter.

Type of study	Reference	Effects observed	24-hr average pollutant levels at which effects were detected, µg/m ³	
			TSP	SO ₂
Mortality	Martin and Bradley (19) Martin (20)	Increases in daily total mortality above the 15-day moving average	600	300
		Increases in daily total mortality above the 15-day moving average	600	400
Morbidity	Martin (20) Lawther et al. (34, 35)	Increases in hospital admissions for cardiac or respiratory illness	600	400
		Worsening of health status among 195 bronchitics	350	500

odology and interpretation. Although severe air pollution episodes have frequently been associated with excess mortality and morbidity, there is only a small body of evidence to document such effects at concentrations below 1000 $\mu\text{g}/\text{m}^3$.

Health Effects Associated with Chronic Exposure to SO_2 and Particulate Matter

As noted above, the evidence for mortality effects of chronic exposure to SO_2 or particulate matter is inconclusive. Though several studies have found associations, the methodological uncertainties are so great as to make these studies essentially valueless for quantifying the exposure-response relationship. The morbidity studies that have found differences in levels of health effects in association with differences in pollutant concentrations are summarized in Table 23, and displayed in Figure 1. In these studies, upper and lower respiratory symptoms, chronic bronchitis and reduced pulmonary function were observed in association with TSP concentrations in excess of about 180 $\mu\text{g}/\text{m}^3$. In one study, acute respiratory disease was increased in association with reported TSP concentration of 135 $\mu\text{g}/\text{m}^3$ though these values were estimated from relatively weak aerometric data. As with the studies of acute effects, most of these studies could be interpreted as demonstrating that the prevalence of adverse health effects increases monotonically with exposure over the entire range of exposure studied. These studies provide little evidence to assess the health effects associated with elevated SO_2 concentrations along with moderate particulate concentrations. Although Hammer (79) and the Salt Lake Studies (72) did report such associations, the

problems with methodology and aerometric measurement in those studies limit their value in this assessment. Though exposure to these pollutants at concentrations below those cited may imply some increase in risks, it will be difficult to resolve this question in an observational setting, because health effects of pollutants at these concentrations are likely to be small relative to effects of other factors which vary over communities.

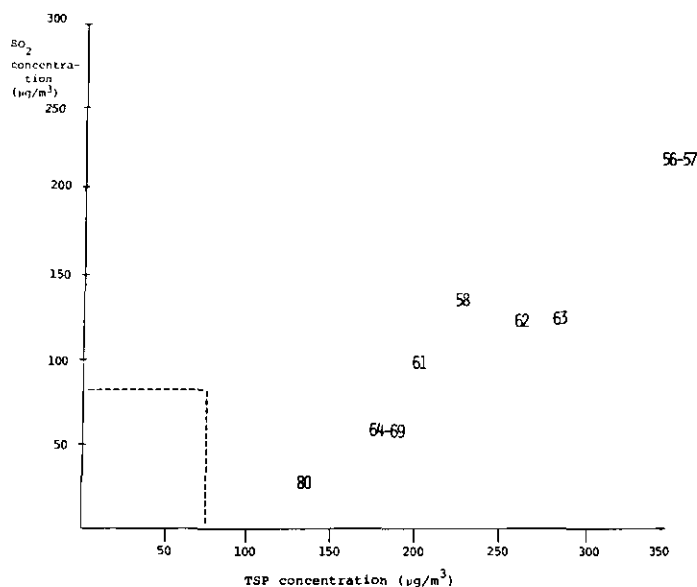


FIGURE 1. Plot of studies in which increased levels of adverse health effects were associated with chronic exposure to higher concentrations of TSP and SO_2 . Studies are plotted at the lowest concentrations at which increases were seen and by the reference numbers in the bibliography. The dashed lines correspond to the current National Ambient Air Quality Standards for annual mean concentration.

Table 23. Summary of evidence for health effects of chronic exposure to SO_2 and particulate matter.

Type of study	Reference	Effects observed	Annual average pollutant levels at which effects noted, $\mu\text{g}/\text{m}^3$	
			TSP	SO_2
Cross-sectional (four areas)	Lunn et al. (56, 57)	Increased frequency of respiratory symptoms; decreased lung function in five-year-olds	360	225
Cross-sectional study across Britain	Lambert and Reid (61)	Increased prevalence of respiratory symptoms	200	100
Cross-sectional (two areas)	Sawicki (62)	More chronic bronchitis, asthmatic disease in smokers; reduced FEV%	270	125
Cross-sectional (four areas)	Rudnik et al. (63)	Increased history and symptoms of respiratory illness	285	125
Longitudinal and cross-sectional	Ferris et al.	Higher rate of respiratory symptoms; and decreased lung function	180	55
Cross-sectional (two areas)	Hammer (80)	Increased frequency of acute lower respiratory disease	135	<25

Summary

The studies summarized in Table 22 indicate that increased mortality and morbidity are associated with exposure to 24-hr average TSP concentrations of 500-600 $\mu\text{g}/\text{m}^3$ and SO_2 concentrations of 300-400 $\mu\text{g}/\text{m}^3$ and a temporary decrease in lung function has been associated with a TSP concentration of 250 $\mu\text{g}/\text{m}^3$ and a SO_2 concentration of 300 $\mu\text{g}/\text{m}^3$. This conclusion is based on only two independent studies. There is little evidence concerning health effects of short term exposure to only one of these pollutants. Various studies not accepted in this assessment have reported health effects at lower pollutant concentrations, but we believe that the evidence from these studies is inconclusive.

The studies summarized in Table 23 indicate that increased morbidity is associated with chronic exposure to TSP concentrations exceeding 180 $\mu\text{g}/\text{m}^3$ (annual average). Though effects were found both with and without parallel increases in SO_2 concentration, there is no basis in these studies for evaluating the effects of elevated SO_2 concentrations without increased particulate pollution. Once again, one cited study (80) and several studies not accepted for this assessment have reported health effects at lower concentrations and with elevated SO_2 concentrations, particularly the studies in the CHES program. In our opinion, the evidence for health effects at these lower concentrations is inconclusive, but should be the subject of continuing investigation. Though we have focused on the evidence from observational studies, the evidence from animal studies and controlled studies of human exposure must also be considered, particularly in relation to the less severe effects of short-term high exposures. These studies will also play an important role in future efforts to link health effects with chemical or size fractions of the SO_2 -TSP pollution complex. Nonexperimental studies provide little information on this issue because of the collinearity of the components of interest. This will be especially important in studying fine particulates.

Although we have given single numbers as concentrations above which various health effects occur, these numbers are based on very sparse data from studies not designed to establish such values. Thus, the numbers are subject to uncertainty which is difficult to quantify.

In view of the limitations of studies based on multivariate analysis of data obtained from sources not oriented to air pollution research, future studies will be most informative if they involve thorough and detailed investigation of well defined populations.

Direct measurement and careful control of poten-

tial confounding factors will be especially important, as will improved measurement of the air pollution exposure of individuals. The need for such research may grow as energy usage patterns shift in response to limited availability of oil and natural gas.

The public health significance of this question is sufficient to justify the commitment of additional resources to improving the data base on health effects of sulfur oxides and particulate matter.

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