BNL--48446

DE93 007281

(DRAFT) COMMUNITY AIR POLLUTION AND MORTALITY: ANALYSIS OF 1980 DATA FROM US METROPOLITAN AREAS

Frederick W. Lipfert
Analytical Sciences Division
Department of Applied Science
Brookhaven National Laboratory
Associated Universities, Inc.

Under Contract No. DE-AC02-76CH00016 with the
U.S. Department of Energy

November 1992

Prepared for the
U.S. Department of Energy
Office of Fossil Energy
Washington, DC 20585

Abstract

1980 data from up to 149 metropolitan areas were used to define cross-sectional associations between community air pollution and "excess" human mortality. The regression model proposed by Ozkaynak and Thurston (1987), which accounted for age, race, education, poverty, and population density, was evaluated and several new models were developed. The new models also accounted for migration, drinking water hardness, and smoking, and included a more detailed description of race. Cause-of-death categories analyzed include all causes, all "non-external" causes, major cardiovascular diseases, and chronic obstructive pulmonary diseases (COPD). Both annual mortality rates and their logarithms were analyzed. Air quality data were obtained from the EPA AIRS database (TSP, $SO_4^=$, Mn, and ozone) and from the inhalable particulate network (PM_{15}, $PM_{2.5}$ and $SO_4^=$, for 63 locations). The data on particulates were averaged across all monitoring stations available for each SMSA and the TSP data were restricted to the year 1980. The associations between mortality and air pollution were found to be dependent on the socioeconomic factors included in the models, the specific locations included in the data set, and the type of statistical model used. Statistically significant associations were found as follows: between TSP and mortality due to non-external causes with log-linear models, but not with a linear model; between estimated 10-year average (1980-90) ozone levels and 1980 non-external and cardiovascular deaths; and between TSP and COPD mortality for both linear and log-linear models. When the sulfate contribution to TSP was subtracted, the relationship with COPD mortality was strengthened. Scatter plots and quintile analyses suggested a TSP threshold for COPD mortality at around 65 ug/m^3 (annual average). $SO_4^=$, Mn, PM_{15}, and $PM_{2.5}$ were not significantly associated with mortality using the new models. The report identifies a number of important uncertainties in the analysis, including possible effects due to the 1980 heat wave.

This research was performed under the auspices of the United States Department of Energy under Contract No. DE-AC02-76CH00016

DISCLAIMER

TABLE OF CONTENTS

List of Figures

Figure 20. Standard errors of regression coefficients in Figure 18 vs. number of remaining observations.

Figure 21. Regression coefficients for log COPD mortality on TSP for successively smaller data sets, after deleting TSP values higher than the values plotted.

Figure 22. Relative risk for major cardiovascular and non-external mortality as a function of ozone quintiles.

Figure 23. Relative risk for COPD and non-external mortality as a function of TSP quintiles.

Figure 24. Relative risk for major cardiovascular and non-external mortality as a function of [TSP] sulfate quintiles.

Appendix B Figures

Figure B-1. Scatter plot of residual log non-external mortality rates vs. the TSP-$SO_4^=$ difference.

Figure B-2. Scatter plot of residual log non-external mortality rates vs. PM_{15}.

Figure B-3. Scatter plot of residual log non-external mortality rates vs. $PM_{2.5}$.

Figure B-4. Scatter plot of residual log non-external mortality rates vs. manganese in TSP.

Figure B-5. Scatter plot of residual log non-external mortality rates vs. [IP] $SO_4^=$.

Figure B-6. Scatter plot of residual log non-external mortality rates vs. lead in inhalable particulate.

Figure B-7. Scatter plot of residual log non-external mortality rates vs. SO_2 computed from the ASTRAP long-range transport model.

Figure B-8. Scatter plot of residual log non-external mortality rates vs. $SO_4^=$ computed from the ASTRAP long-range transport model.

Figure B-9. Scatter plot of residual log non-external mortality rates vs. NO_x computed from the ASTRAP long-range transport model.

Executive Summary

Data from up to 149 metropolitan areas were analyzed in a study of the relationships between community air pollution and "excess" human mortality for the year 1980. Several socioeconomic models, including the model proposed by Ozkaynak and Thurston (1987), were used in cross-sectional multiple regression analyses to account for non-pollution effects such as age, race, education, poverty, migration and smoking. Cause-of-death categories analyzed include all causes, all causes except accidents-suicide-homicide (i.e., "non-external" causes), major cardiovascular diseases, and chronic obstructive pulmonary diseases (COPD). The patterns for the first three groupings were quite similar but differed markedly from the patterns of COPD mortality. Regressions were performed for these cause-of-death groupings as annual mortality rates ("linear" models) and as their logarithms ("log-linear" models).

Two different sources of air quality data were utilized: data from the EPA AIRS database (TSP, $SO_4^=$, Mn, and ozone) and data from the inhalable particulate (PM_{15}) network; the latter data (PM_{15}, $PM_{2.5}$ and $SO_4^=$ from the IP filters) were only available for 63 locations. The data on particulates were averaged across all monitoring stations available for each SMSA and the TSP data were restricted to the year 1980. The associations between mortality and air pollution were found to be dependent on the socioeconomic factors included in the models, the specific locations included in the data set, and the type of statistical model used.

For each mortality variable, a "parsimonious" model was developed that had statistically significant coefficients for the non-pollution variables; most of these coefficients also agreed with exogenous estimates of the "correct" magnitude. Using these models, statistically significant associations were found between TSP and mortality due to non-external causes with the log-linear models evaluated, but not with a linear model. Sulfates, manganese, inhalable particles (PM_{15}), and fine particles ($PM_{2.5}$) were not significantly ($P < 0.05$) associated with mortality with any of parsimonious models.

Statistically significant associations were found between estimated 10-year average (1980-90) ozone levels and 1980 non-external and cardiovascular deaths, using log-linear parsimonious models for 149 SMSAs. Ozone was just significant for major cardiovascular deaths using a linear model. One-hour measured peak ozone data were available for 1980 for 72 SMSAs; neither peak nor long-term average ozone was consistently significantly associated with mortality with this data set. Scatter plots and quintile analyses suggested that the ozone dose-response relationships were dominated by variations among the lower to mid-range ozone locations, rather than those at the upper end of the range. The regression results for ozone must be considered problematic because of the unavailability of appropriate data on ozone concentrations.

Significant associations were found between TSP and COPD mortality for both linear and log-linear models. When the sulfate contribution to TSP was subtracted, the relationship with COPD mortality was strengthened. Scatter plots and quintile analyses suggested that a TSP threshold might be present for COPD mortality, at around 65 ug/m^3 (annual average).

Additional major uncertainties remaining in this analysis include the type of regression model to be used, relationships among those cities which have not been included in the analysis, and the effects of weather, differences in life-style, indoor air quality and the use of air conditioning, and differences in the age distributions among those 65 and over. Expanding the analysis to be more inclusive might result in different conclusions regarding which types of models fit best, the significance of air pollution, and the levels of air quality thresholds present (if any). In addition, examination of additional causes of death might provide insight into the plausibility of causal relationships. Finally, since 1980 was an anomalous year in several ways (drought, heat waves, and a major volcanic eruption), extension of these findings to a more general case must be considered problematic pending resolution of these uncertainties and testing of the models against data from other years.

INTRODUCTION

Control of air pollution in the United States is intended primarily to protect public health. This goal has been supported repeatedly by public surveys and is reflected in the language of the Clean Air Act, which mandates the achievement of health-related ambient air quality standards without regard to costs of the pollution controls required to do so. In the 1970s, the costs of air pollution control in the United States were estimated at $500 million per year (Eisenbud, 1970). The annual cost is now estimated to be about $33 billion; when the 1990 Amendments to the Clean Air Act are fully implemented, this figure may rise to over $60 billion (Portney, 1990; O'Neal, 1991). The total costs of health care, however, reached $620 billion in 1989, or more than 11% of the gross national product (Ginzburg, 1990); it is thus important to estimate the extent to which air pollution may contribute to ill health. This report uses annual mortality rates as a measure of public health and attempts to derive statistical associations between their spatial patterns and the spatial patterns of air pollution. If reliable "dose-response" relationships could thus be defined, they could be useful for estimating the external costs of the various sources (anthropogenic and natural) that produce air pollution.

Objectives of the Analysis

The purpose of this report is explore the sensitivity of statistical mortality/pollution relationships to analysis technique, geographic scale, functional forms, and confounding variables, based on cross-sectional analysis of SMSAs for the year 1980. It is not intended to try to establish "right" and "wrong" results or to attempt to establish causality (which can never be done with statistics alone). The general technique is that of defining regression models which explain the spatial variability of mortality rates by incorporating variables for the known effects of demography and socioeconomics, and testing for effects of environment. The success of such models is judged by the statistical significance of the independent variables, the plausibility of the implied associations, and the robustness to variations in model specification and data input.

Previous Studies of Air Pollution and Mortality

The literature on this topic extends back to the 1950s and earlier, beginning with accounts of the major air pollution disasters (Lipfert, in press). These events remain the best evidence that air pollution can hasten mortality at levels then found in community air. Much of the literature deals with the period before the 1970 Clean Air Act was fully implemented, and thus it is not clear whether these findings apply to the cleaner urban atmospheres currently enjoyed in the United States. Some of the more recent studies dealing with air quality, ca. 1980, are discussed briefly below.

Time-Series Studies. Studies examining short-term (daily or weekly) mortality variations are similar to those analyzing air pollution disasters in that both types of studies deal with the timing of death. Table 1 summarizes time-series studies that have been published in recent years for U.S. cities; note that all of the criteria pollutants except lead have been associated with short-term fluctuations in mortality and that most of the studies include some measure of particulate air pollution. In contrast to cross-sectional studies (discussed below), no time-series study has found a significant association with the sulfate fraction of suspended particulate matter (hereafter referred to as "sulfates" or $SO_4^=$).

Lipfert and Wyzga (1992) examined long-term temporal variability of mortality and air pollution in New York City, Steubenville, Ohio, and Los Angeles, using a variety of methods to attempt to control for exogenous trends. They concluded that the relationships deduced from long-term trend analysis were consistent with those being reported from time-series and cross-sectional studies, but that many important uncertainties remained.

TABLE 1 SUMMARY OF SELECTED TIME-SERIES STUDIES OF DAILY MORTALITY AND AIR POLLUTION

Authors (ref.)	Location	time period	control variables	species	coefficient +/- std err	elasticity	lag
Schwartz (1991)	Detroit (city)	1973-82	weather,time,yr dummies	TSP*	0.546+/-0.145#	0.048	1 day
			weather,time,yr dummies	SO2	0.330+/-0.12	0.010	1 day
Schwartz&Dockery (1992a)	Steubenville,OH (SMSA)	1974-84	weather,time,yr dummies	TSP	0.381+/-0.082	0.043	1 day
			weather,time,yr dummies	SO2	0.40+/-0.16	0.029	1 day
Wyzga (1977)	Philadelphia (city)	1957-66 winters	season, heat waves, flu daily temperature	TSP	0.17+/-0.092	0.028	1 day+
				SO2	0.035+/-0.037	0.009	
				COH	0.35+/-0.12	0.046	
				NO	0.28+/-0.09	0.022	
				NO2	0.20+/-0.16	0.013	
				HC	0.031+/-0.014	0.046	
				CO	0.0024+/-0.0018	0.021	
Schwartz&Dockery (1992b)	Philadelphia (city)	1973-80	weather,time,yr dummies	TSP	0.661+/-0.131	0.051	0-1 day avg
			weather,time,yr dummies	SO2	0.50+/-0.11	0.028	0-1 day avg
Dockery&Schwartz (forthcoming)	St. Louis (SMSA)	9-1-85 to 8-31-86	weather, season dummies, interactions	PM-10	1.50+/-0.69	0.041	1,2 days
				PM-2.5	1.71+/-0.96	0.030	
				SO4	6.08+/-5.77	0.049	
	E. Tennessee (11 counties)	9-1-85 to 8-31-86	weather, season dummies, interactions	PM-10	1.60+/-1.49	0.048	1,2 days
				PM-2.5	2.28+/-1.86	0.048	
				SO4	8.0+/-12	0.070	
Fairley (1990)	San Jose, CA (Santa Clara Co.)	1980-86 (winters)	weather,time,yr dummies	COH	0.48+/-0.17	0.027	1-2 days
Pope et al. (1992)	Provo, UT (Utah Co.)	1985-89	weather,time,yr dummies	PM10	1.47+/-0.31	0.069	5-day avg
Kinney and Ozkaynak (1991)	Los Angeles (county)	1970-79	weather, day-of-week, long-term cycles, years	ozone		0.040 (combined)	1 day
				NO2			none
				smoke			none
Shumway et al.	Los Angeles (county)	1970-79	weather	CO		0.068	weekly
				HC		0.064	data
				smoke		0.052	

*TSP was estimated from daily airport visibility

#coefficients and std errors are given for relative risk per mg/m3

Cross-Sectional Studies for 1980. Cross-sectional studies examine patterns in the places of death. Ozkaynak and Thurston (1987) found associations between mortality and various forms of particulate air pollution in up to 98 U.S. metropolitan areas (SMSAs). They found that the associations were more statistically significant for sulfates and fine particles than for the coarser particles and concluded that this difference was consistent with causal respiratory mechanisms. The authors (O&T) expressed cautions as to the limitations of their data base and the sensitivity of the mortality/pollution relationship to model specification and the selection of locations. Nevertheless, their results have been a candidate for the basis of calculations estimating the external costs of fossil fuel use. However, the O&T study has been criticized (Lipfert and Morris, 1991, 1992) on grounds that the statistical model used was not well established and that the results did not clearly establish that the relationship for sulfates could be distinguished with confidence from the relationships with other pollutants.

Lipfert *et al.* (1988) studied pollution, demographic and mortality data at the city level for over 900 cities for the 1980 time period. Their study included data on several additional socioeconomic variables, drinking water hardness, and cigarette consumption data at the state level. Unfortunately, none of the air pollution variables they used was ideally suited to the task. In an attempt to circumvent problems with some of the ca. 1980 measurements, notably sulfates, they used data from a long-range transport model to estimate city-wide averages for $SO_4^=$, SO_2, and NO_x. While these variables displayed statistically significant relationships with city mortality, subsequent analysis employing more recent air quality measurements, including some from research campaigns, shows that the computed air quality variables may have been influenced by regional bias, which makes these regression results difficult to interpret.

Comparison of Time-Series and Cross-Sectional Study Results. Time-series studies cannot test for the degree of prematurity of death; it is possible that death may have been advanced by only a few weeks or months, because of the general poor state of health of the decedent at the time. Since cross-sectional studies deal with annual rates, they must include the annual (net) sum of short-term variations, by definition. If a cross-sectional study finds a weaker relationship than found by the corresponding time-series study, it may indicate that the short-term responses were premature by less than one year. If it finds a stronger relationship, it may indicate the presence of chronic effects which relate to pollution from earlier years. Of course, in either case, such comparisons between studies may also be affected by flaws in the various studies. Unfortunately, neither of the "1980" cross-sectional studies used pollution data specific to the year 1980, so that it has not been possible to make such comparisons with confidence.

Organization of the Report

Introductory material continues with discussions of epidemiological methods, statistical models, and measures of risk. The variables used in the study are discussed next, with emphasis on the air quality data and the difficulties entailed in deriving representative values for 1980. The regression analysis begins with relatively simple models, including that used by Ozkaynak and Thurston for sulfates and various particulate measures, and then proceeds to more complicated models and additional pollutants. The findings are then summarized in a concluding discussion and recommendations are offered for addressing the remaining uncertainties.

METHODS, VARIABLES, AND DATA

Epidemiological Methods (after Lipfert, in press)

Epidemiology differs from clinical medicine or biomedical research by virtue of its study of populations rather than individual cases or specimens. In many cases, this emphasis stems from a fundamental objective of epidemiology: to improve public health (Kleinbaum *et al.*, 1982.) However, the study of the effects of air pollution usually involves relatively subtle effects (i.e.,

weak associations) that can only be observed in large populations, for which consideration of individual cases is clearly impractical.

For example, the daily mortality rate in a typical U.S. city of one million people is about 20 deaths per day. If this rate were to double for a few days due to an air pollution disaster, only about 0.005% of the population would have been affected. Since we cannot identify those individuals most at risk *a priori*, a very large number of people would have to be monitored in order to determine the individual air pollution exposures of the decedents.

Population Considerations and the Ecological Fallacy. Studies of population health responses to air pollution are thus necessarily observational, i.e., involving naturally occurring rather than manipulated environmental conditions (Kleinbaum *et al.*, 1982). Since the characterization of individual environmental exposures is clearly impractical, such an epidemiological study is likely to be ecological as well as observational, i.e., involving the study of groups rather than of individuals (Piantidosi *et al.*, 1988). According to Kleinbaum *et al.* (1982), the primary feature of an ecologic study is the lack of knowledge of the joint distribution of the study factor (i.e., exposure to air pollution) and the disease within each group. The primary objections to ecologic studies relate to the lack of specificity of the affected individuals and the exposed individuals, because groups are used in the regression analysis. This objection is most valid when the pollutant is very localized (such as emissions from a toxic waste dump) or when the disease is relatively rare (such as leukemia). However, this objection diminishes for regional pollutants, such as fine particles or sulfates, and for mortality from all causes or from very common causes (such as heart disease).

Time-Series Studies. For a time-series analysis, the group is the single city or other geographic entity whose temporal responses are being studied and the "within-group" variation is temporal. Since each day a different subgroup is likely to respond (die, be admitted to hospital, etc.), the ecological hypothesis is that the same set of air monitoring locations faithfully represents the actual exposures of these different subgroups, on all days. The term "ecological fallacy" refers to a situation where this hypothesis is not supported. The likelihood of such support depends strongly on the size of the area being studied and the spatial coverage of the air monitoring network. Time-series studies vary substantially in the numbers of air monitors used to estimate exposure; errors in exposure can affect the magnitudes and statistical significance of the regression coefficients derived.

Cross-Sectional Studies. For cross-sectional analyses, the within-group spatial variance is at issue with respect to the ecological fallacy. We desire that each of the cities or locations we are studying have the same within-city spatial distribution of air quality (assuming that adequate monitoring networks are not always available) and also the same within-city distributions of potential confounding variables such as age, race, poverty neighborhoods, etc. This is not likely to be true in general, but these considerations favor the use of the smallest possible units for geographic analysis. As larger geographic units are used for analysis, for example, Standard Metropolitan Statistical Areas (SMSAs), which are groups of counties surrounding a central city of 50,000 or more, the representativeness of air monitoring is likely to diminish, especially when only one station is used, as many previous studies have done. Also, many of the individuals who succumb in a given year are likely to have been hospitalized during the year or to have been otherwise limited in outdoor activities, such that their primary exposure to air pollution may have been from indoor air pollution sources.

There can be important regional biases in the spatial distributions within SMSAs or counties. The large urban centers of the Northeast and West Coast often contain contiguous SMSAs, and they may be more homogeneous than the isolated SMSAs often found in other parts of the country. These characteristics are not independent of air pollution, which varies both regionally (more sulfur in the East, more ozone in Southern California) and according to the economic activities of the area. Industrial SMSAs may have centrally located poor neighborhoods, while in the South, poverty pockets are often found in the outskirts of cities. Some pollutants are higher

in central cities (CO, particulates) while some may be higher in the suburbs (ozone, aerosol acidity). Use of successively larger geographic units of analysis surrounding an air monitoring station can create a bias since the population characteristics are averaged over the entire area, but the air pollution data used in the analysis usually remain unchanged, as larger areas are considered. Thus, the nature of the central city with respect to its suburbs is an important parameter to consider when selecting the geographic unit of analysis. However, Cohen (1990) argues that there is safety in numbers, i.e., that using large numbers of observations in a geographic study reduces the chance for serious ecological bias.

Interactions Between Air Pollution and the Size of Geographic Unit. The accuracy of estimating exposure to air pollution will also vary with the nature of the pollutant. Some primary pollutants, such as TSP, CO, and SO_2, tend to be distributed very locally, and concentrations may vary substantially within a few city blocks, in addition to varying between indoors and outdoors. Secondary pollutants, such as NO_2, oxidants, and sulfate particles, may exhibit less spatial variability, although ozone can be strongly attenuated locally by the presence of NO_x sources. Most cross-sectional studies have had to work with data from a few air pollution monitors and have made arbitrary assumptions about the size of the area that each monitor is assumed to represent. The lack of true representation of the air pollution exposure of the population constitutes an important source of error in the independent variables for ecological studies.

This source of error is also associated with the choice of the type of political subdivision for the observational unit, since the larger its area, the larger the chances for errors in estimating true population exposures (assuming a fixed number of monitors and that local pollution sources are present). For example, assume that there is a true relationship between particle concentration and mortality (this need not be a causal relationship, since there may be other aspects of the pollution source to consider, such as occupational factors). Often there have been available two measures of particle concentration: total suspended particulate matter (TSP), which tends to be somewhat local because the measurement may include particles up to 50 um in diameter; and the sulfate portion of the particulate catch, which is usually distributed regionally since the particles are much smaller and tend to travel further. Recently, particulate monitoring in the United States has separated fine and coarse particles, initially by collecting particles with a median diameter of 15 um (PM_{15}) and currently with a median diameter of 10 um (PM_{10}). When relatively small areas (such as cities or portions of cities) are used as the observational units, TSP exposures may be reasonably well-represented. On the other hand, if larger units are used with the same monitoring network, such as entire counties or metropolitan conurbations, any "true" TSP effect on mortality is likely to be masked by the exposure error, since many of the people "assigned" to the TSP monitor live so far away that they are not actually exposed to the pollution measured there. Now, if at the same time there is a regional trend towards higher mortality in the region of high sulfates (or any other regionally-distributed pollutant), the regional pollutant will become the significant variable. This result may appear to be a health-based causal finding, since small particles can penetrate deeper into the lung, but, in this case, the result appeared as a statistical artifact because a regionally-distributed pollutant was matched with a regionally-distributed mortality trend. An analysis based on large geographic units is unlikely to capture local pollution effects, only regional ones, but a city-based analysis should be able to detect either type. This distinction is similar to separating the high-frequency (short-term) effects from the seasonal effects in a time-series analysis. Richardson *et al.* (1987) recommends checking the stability of results from ecological analyses in relation to geographic scale.

However, mortality rates may be statistically unstable if the population base is too small. One solution to this problem is to use small geographic areas (i.e., central cities) with data pooled over several years, which will improve the stability of estimates of both mortality and air pollution exposure. If the analysis is intended for comparison with time-series findings, it is important to maintain the matching between pollution and mortality data by year.

Confounding. The term confounding refers to the incorrect assignment of an effect to an agent when in fact a third variable (the confounder) is responsible. Such a situation requires that the confounder have an effect on the outcome variable and be correlated with the first agent. In other words, a confounder must have the property of different distributions for exposed and nonexposed subjects (Miettinen and Cook, 1981). A hypothetical example might be a situation in which smokers are more likely to be exposed to air pollution because they work outdoors. According to Stellman (1987), confounding is the "cause of great angst among epidemiologists." In ecological case-control studies of environmental factors, in which a single exposed city is compared to an unexposed city, the opportunity for confounding is very large since there are many other ways in which two such population groups may differ. As the number of locations or time periods increases and multiple regression methods come into play, the opportunities for serious confounding are diminished.

Population migration patterns can cause errors in estimated pollution exposures, as well as confounding of regression results. Confounding results from either selective migration of sick people or of the more economically advantaged. For example, Bultena (1969) reports that retirees moving from the Midwest to Florida and Arizona tended to be better educated and had higher status occupations than the average; in such cases, the population left behind may be in worse health, on average, than the populations of the destination cities (for reasons that have nothing to do with air pollution). Although there may be anecdotal reports of people with respiratory ailments moving to the Southwest to seek improvements, we are aware of no analyses of the actual extent of such migration. In either case, current (local) air quality may not represent the true long-term exposures of current residents; thus it may be unreasonable to try to interpret the findings of cross-sectional regressions based on same-year air quality as representing long-term effects. Polissar (1980) gives some examples where migration biases the estimation of cancer risk based on geographic comparisons. However, Cohen (1992) recently estimated, based on a telephone survey, that as a national average, people spend over 70% of their lives within 25 miles of the location of death. These percentages are higher in the Northeast)up to 90%) and lower in Florida, California, and Arizona (ca. 50% in these high migration states).

Other problems can arise when unadjusted total mortality data are used (all causes, ages, races; both sexes). Often, for smaller geographic subdivisions, only this type of data is available. Age adjustment is the most important correction to make, since the probability of dying in a given year increases exponentially with age above about age 35. If mortality rates are available for detailed age groups, they can be combined into one age-adjusted total rate by reference to the age distribution of a standard population. If, on the other hand, only total deaths are available but details are available on the population's age distribution, then the expected total number of deaths may be computed on the same basis. In many cross-sectional studies, neither procedure was followed, but surrogate age adjustments were attempted by using a population age descriptor as an independent variable in the multiple regression or "model." "Percentage of population aged 65 and over" is a common choice, for example. If all populations have similar age distributions, such a choice may be acceptable, but simple algebra shows that the regression coefficient for "Percentage of population aged 65 and over" should be numerically equal to the mortality rate for this age group minus the rate for the under-65 group (Lipfert *et al.*, 1988). Many studies do not meet this simple test, which suggests that the "Percentage of population aged 65 and over" variable may have captured some other effects. Similar considerations apply to other explanatory variables employing percentages of the population, such as "percent nonwhite" or "percent poverty". Such checks are tantamount to comparing the ecological regression results with studies on individuals.

Statistical Models

Some studies of air pollution health effects have been content to identify the existence of associations, primarily by means of calculating correlation coefficients. In general, bivariate correlations are not only inadequate to define the relationships which are ultimately of interest, they can be misleading because of confounding variables (Lipfert and Hammerstrom, in press).

Furthermore, at this stage in our knowledge of air pollution health effects, in many cases the existence of associations is no longer an important issue. This report is thus largely concerned with establishing consistency or coherence and in estimating the relative magnitudes of the important relationships.

When temporal variability is at issue, both confounding variables (such as weather patterns) and intervening variables (such as seasonal or day-of-week effects) must be taken into account in order to derive the true associations with air pollution. Meteorological factors can confound because they can affect both health status and air quality. For example, breathing cold air can precipitate respiratory distress and viral infections are more common in winter; lower outside temperatures call for increased space heating and pollutant emissions. Cold weather may also cause some people (especially those in poor health) to remain indoors, where some fraction of them may be exposed to indoor air pollution sources or to contagious disease. Similar confounding can occur in the summer with heat wave distress and increased ozone Seasonal and day-of-week effects can exert independent influences on health (viral outbreaks) and on the reporting of health-based events (availability of clinics and physicians). When air pollution patterns correspond to these exogenous temporal patterns, spurious correlations result.

For spatial or cross-sectional analysis, there are more opportunities for confounding, since the same sources that create more air pollution in a given location can have many other effects on the population. Industrial neighborhoods are generally less desirable for residential purposes; hence their populations may be less economically advantaged or educated. Many other life-style differences accompany such socioeconomic gradients, including smoking, alcohol consumption, diet, access to medical care, etc. On the other hand, industrial workers per se are often healthier than the general population, because of self-selection. It should thus be evident that analysis of air pollution health effects by means of spatial gradients must include many factors in addition to the obvious demographic adjustments for age, sex, and race.

There can also be interactions between temporal and spatial factors. Those cities with older, poorer, and more highly-stressed populations (including a higher percentage of smokers) would be expected to exhibit stronger temporal effects of air pollution. Similarly, when comparing across cities for a specific year, short-term phenomena such as flu epidemics or heat waves, which do not occur everywhere in a given year, could confound the spatial air pollution relationships. For example, Mt. St. Helens erupted in May, 1980, and the resulting ash may have been responsible for some of the high TSP levels recorded in the West for that year.

The ways in which a researcher chooses to deal with the need for multivariate analysis constitutes his/her statistical model. The literature varies greatly with regard to these methods and models, and some data sets have been subjected to several different types of analysis. One of the first decisions to be made is whether to pre-adjust for a potentially confounding variable (this may be thought of as two-stage analysis) or to perform a multivariate analysis which allows the confounding variable to interact with the air pollution variables. This dichotomy occurs most often with time-series analyses and the need to account for simultaneous weather effects. If the data are pre-adjusted without recourse to exogenous data to define the adjustments, there is a risk that some portion of the pollution effect may have been assigned to the weather effect. We may have more confidence in such procedures if the weather "adjustments" are consistent with known physiological responses.

For cross-sectional data, we must distinguish between the process of trying to define a model and that of estimating its coefficients. These two processes have often been combined unwittingly, and it should be obvious that two independent data sets are required to do justice to both tasks. This is one of the motivations for quantitative comparisons of independent data analyses. Since we have no basis for a "true" model of the spatial variability of health indices (especially for mortality) and the data available for analysis are always limited, we must resort to empirical "specifications" of the important terms. It follows that there can be any number of such models, and the prudent researcher will investigate whether his/her findings of effects due

to air pollution are robust to plausible variations in these models. Further, he/she may wish to test the distributions of residuals to determine whether similar models result in statistically significant differences in their assignments of pollutant effects (Lipfert *et al.*, 1988).

Researchers also differ in the types of multivariate analyses conducted. Two-way contingency tables were used to display the interactions of variables in some of the earlier studies (Winkelstein *et al.*, 1967), but multiple regressions seem to be the current method of choice. Some researchers use stepwise variable selection methods; some of these are sensitive to the order of variable entry. Others have pre-defined their models and used "forced" variable entry. In cross-sectional studies, models with up to ten variables are not uncommon and collinearity can be very important as the last few variables enter. Suffice it to say that the burden of proof remains with the researcher to show that his findings *vis-a-vis* air pollution and health are robust to changes in model specifications and data set.

Regional vs. Local Relationships

Time-series studies often go to great lengths to separate long-term (such as seasonal) variability from short-term variability, reasoning that most seasonal trends are caused by factors other than air pollution, and that sharp (daily) mortality increases and decreases in phase with air pollution perturbations are more likely to be causally related. Similar problems exist with respect to the spatial patterns of interest to the cross-sectional analyst; regional trends are analogous to seasonal patterns and local variability to daily perturbations.

Figures 1 and 2 show regional patterns in heart and respiratory disease mortality, for example. Heart disease is highest in the East and Midwest, and COPD is highest in the West. We also know from air monitoring data that sulfur oxides tend to be higher in the East and suspended particulate matter in the West (much of it from fugitive dust). These regional trends will prevail in a cross-sectional regression unless compensating factors interfere on the local level, such as smoking, education, income, migration, for example. For this reason, models which have not accounted for all of the local factors will tend to associate all-cause and heart disease deaths with $SO_4^=$ and COPD with particulates. The challenge to the analyst is to know when his model is "complete" and not "over-specified." The approach taken in this report is to try all reasonably conceivable variables (for which data are available) and then to trim down to that set of variables that are significant or nearly so. These trimmed-down models have been called "parsimonious" (Mendelsohn and Orcutt, 1979). This analysis is concerned with spatial variations; a similar approach was used by Schwartz and his colleagues to account for seasonal trends and weather variables in time-series analyses.

Measures of Risk

Risk can be quantified as the probability of an event occurring within a given time. If ten members of a group of one thousand die within a year, the observed annual mortality rate is 10 per thousand population, which is a statement that each person in that group had a 1% chance of dying in that year. Of course, we also know that the individual risk increases exponentially with age, above about age 35. The annual risk to those aged 65 and over is about 6%, for example (Lipfert, 1978). In this report, we are primarily interested in how exposure to air pollution might also increase the risk within such a group.

For contributory factors like air pollution, we are interested in the incremental or "excess" risk associated with given levels of ambient air concentrations. The fundamentals of excess risk must be developed from various statistical measures of association, such as correlation or regression coefficients. The classical linear regression equation is given by

$$y = a_0 + \sum_i b_i x_i + u \qquad (1)$$

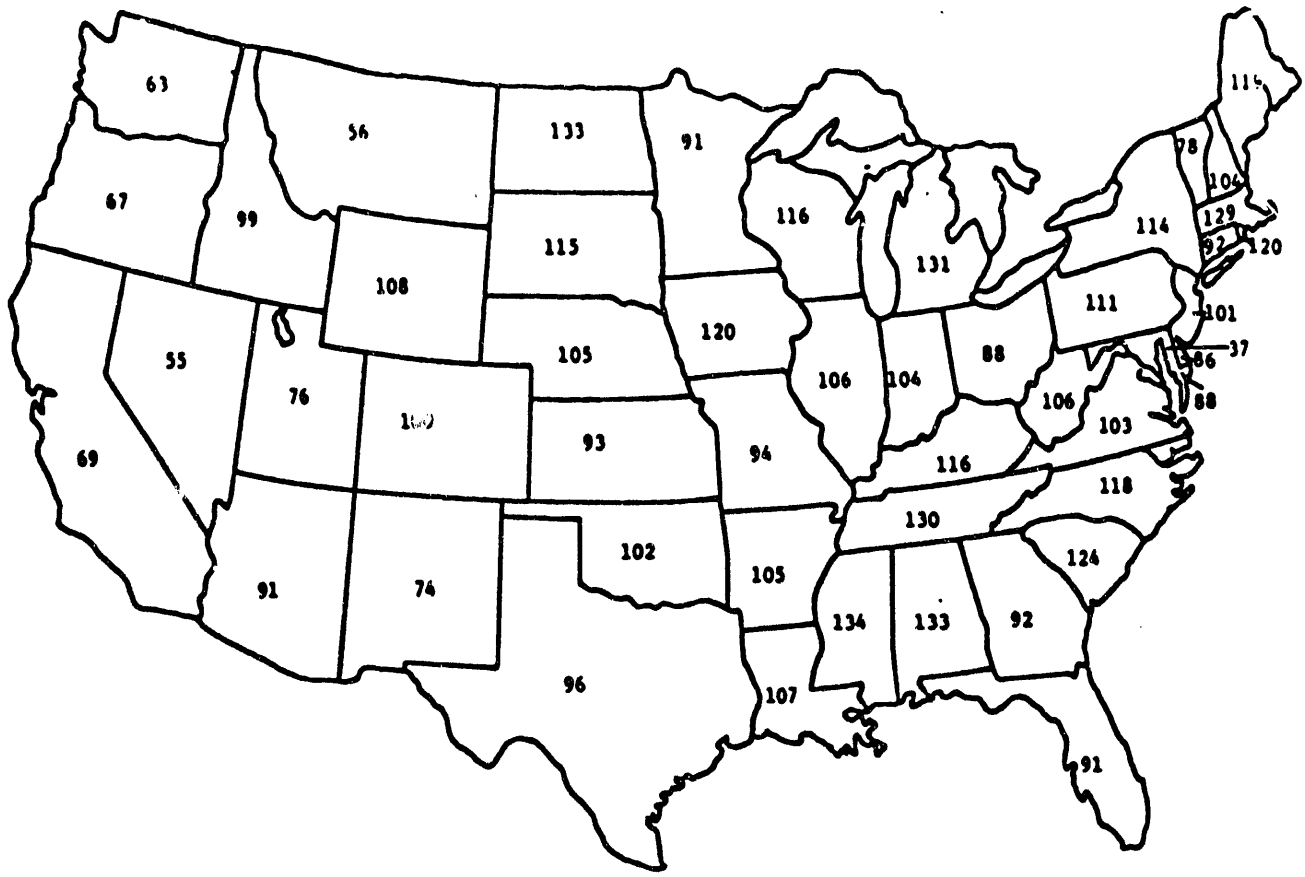

Figure 1a. Observed/expected white male deaths due to acute myocardial infarction, 1979-85. Data source: National Longitudinal Mortality Study.

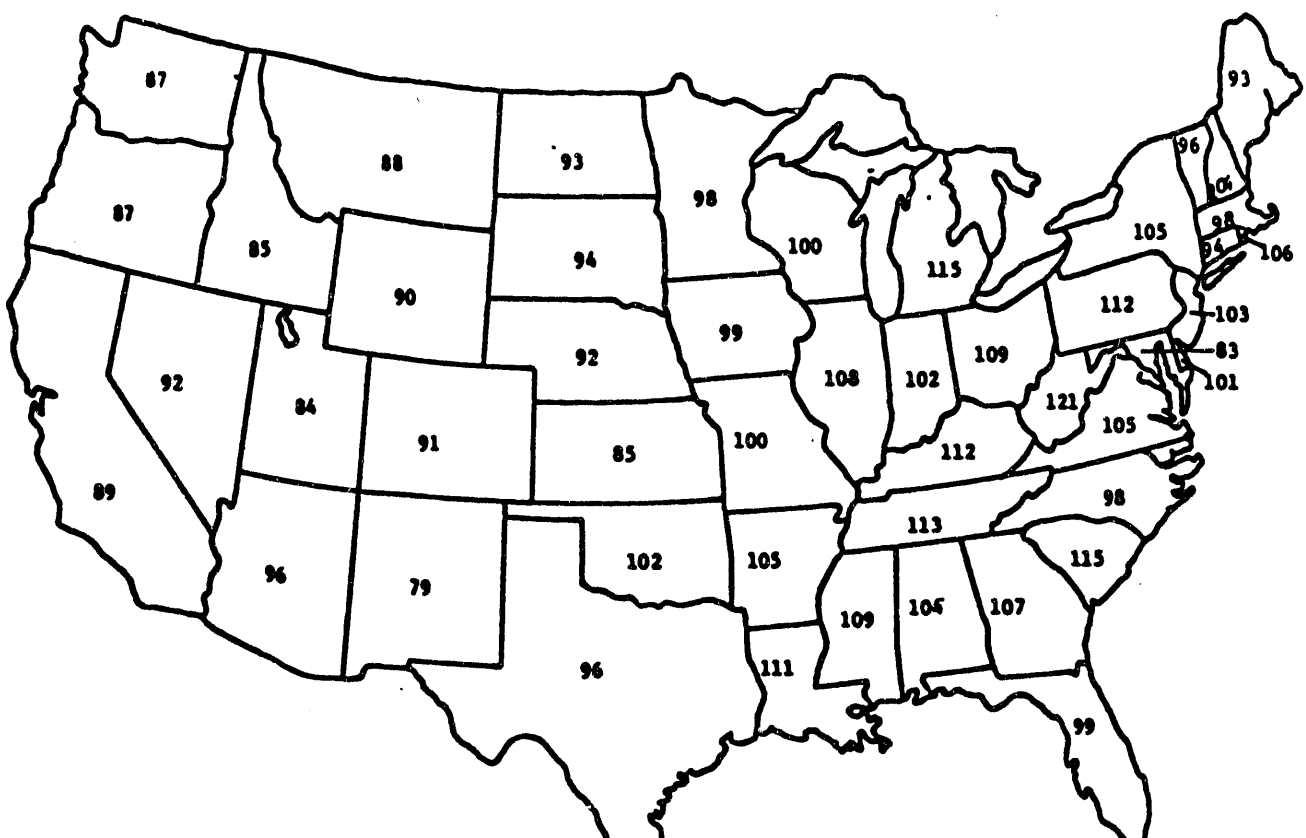

Figure 1b. Observed/expected deaths for all cardiovascular causes, white males and females, 1979-85. Data source: National Longitudinal Mortality Study.

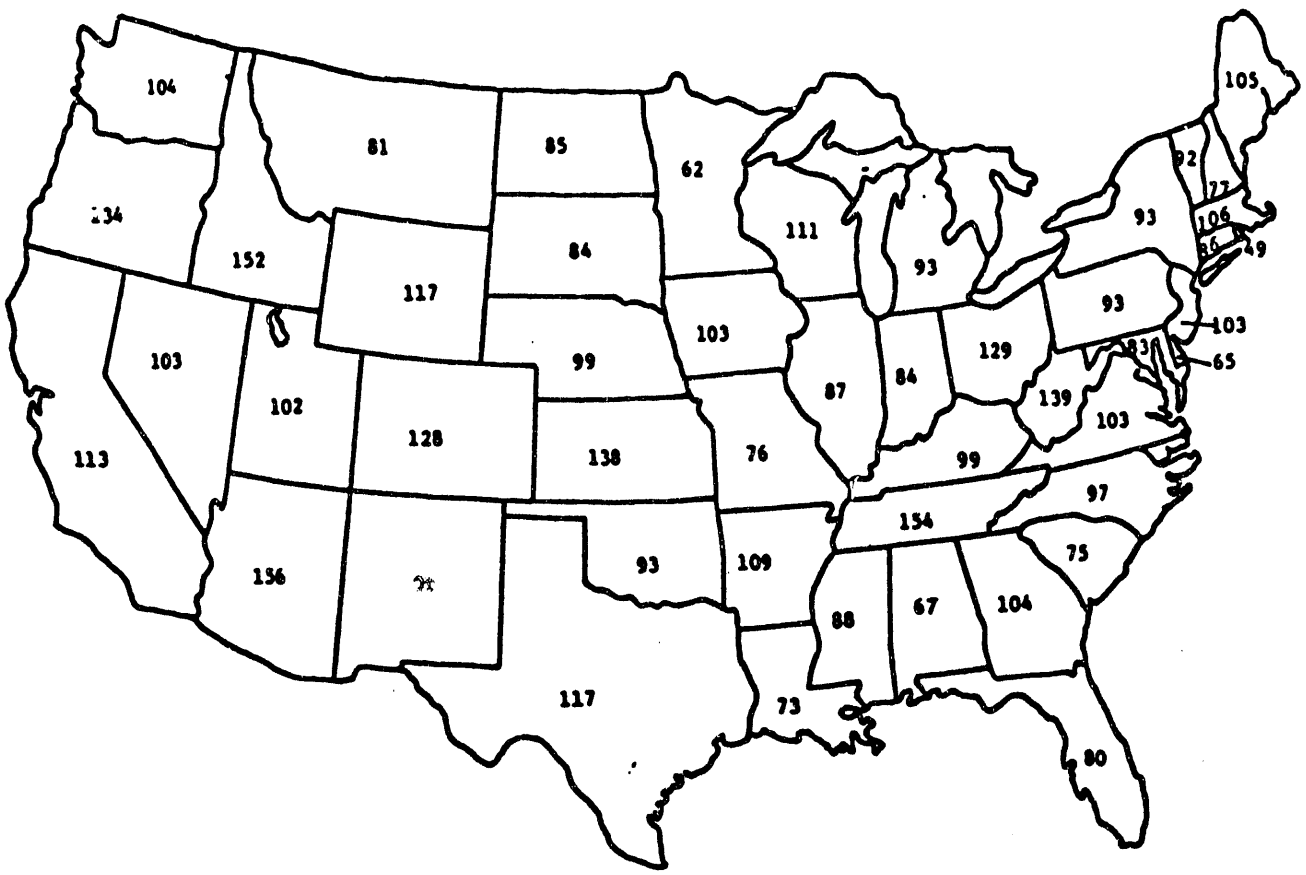

Figure 2. Observed/expected white female from all respiratory diseases, 1979-85. Data source: National Longitudinal Mortality Study.

where the b_i are the regression coefficients for the independent variables x_i and u is the residual error. For a linear dose-response model such as Eq. 1, which is the simplest form, the excess risk ($b_i x_i$ (where i refers to air pollution variables) may be expressed per unit of air concentration regardless of concentration level. For example, some time series analyses have derived daily risk factors for smoke exposure (b_{smoke}) of about 4% excess deaths per 100 ug/m^3 of smoke (Table 1). Thus, if the normal risk of dying is 6% per year (0.0164% per day), in a population of 125,000 persons aged 65 and over, the expected death rate of this group is about 20 per day. On a day with a smoke concentration of 125 ug/m^3, this risk would be increased by 5%, so that one "excess" death would be expected on that day. This analysis methodology presumes that the agents and exposures of concern have been identified (in this case, smoke).

Since the regression coefficients in Eq. 1 must be expressed in units consistent with the dependent and independent variables, it is often difficult to assess their practical importance based on numerical values. A useful concept is that of the elasticity (at the mean), a term taken from economics defining a nondimensional regression coefficient as

$$e_i = b_i \bar{x}_i / \bar{y} \qquad (2)$$

Elasticities are often expressed in percent and offer another measure of attributable risk, based on the mean values of the x_i. Elasticities for nonlinear models are discussed below. The elasticity concept based on mean values breaks down when independent variables are subjected to certain transformations which alter their mean values. For example, adding (or subtracting) a constant changes the means but not the standard deviations. The regression coefficients will not change correspondingly (as they would due to a change in scale factors), so that the elasticities are also changed as a result of the transformation. One must thus be careful in the application of the elasticity concept.

The absolute excess risk in the above example is seen to be 1:125,000, but this figure depends on the baseline level since the fundamental dose-response relationship was expressed as a percentage increase. Obviously the absolute risk from air pollution is much less for a group of healthy teen-agers than for a group of senior citizens.

Comparison of Models

According to the exacerbation model of air pollution effects on health, air pollution seldom, if ever, is the only factor contributing to the prevalence of a health effect. In the multiple regression model given above

$$y = a_0 + \sum_i b_i x_i + u \qquad (1)$$

air pollution variables will account for only some of the x_i.

If we desire to evaluate Eq. 1 for alternative pollutant species which are highly correlated, such as smoke versus SO_2, the only practical method is to evaluate the model for each species separately, which may give rise to models which may differ very little from one another. There is always a temptation to declare the model with the highest adjusted correlation coefficient (R) value or the highest t statistic for the pollution variable as "best," however close its competitors might be. This practice ignores the fact that a given data set represents only one realization from the universe of possible data sets, and that its regression statistics thus all carry confidence limits. When alternative models are independent, the conventional confidence limits for R may be used as as a guide towards defining statistically significant differences between models. However, in the cases of interest here, models generally only differ in the pollution variables chosen and thus are not independent, and special techniques are required in order to test the differences for statistical significance (Lipfert *et al.*, 1988).

Dose-Response Functions

When quantitative estimates of the effect of an independent variable are required, the regression equation or some portion thereof becomes in effect a dose-response function (drf). The mathematical form of such a function can be very important, especially when extrapolating beyond the range of the original data (which is always dangerous).

For a simple linear regression model, there are two parameters, the slope and the intercept. If the x-intercept is positive (negative y-intercept), the function is said to have a threshold, which, in the case of ambient air pollution, is a basis for air quality standards. Such a function has a constant slope, but the elasticity is usually defined at the mean. Obviously, the function

$$e = \frac{dy}{dx}\frac{x}{y}$$

takes on different values along the curve of $y = mx + b$ if b is not zero. Thus two different drfs having the same slope may have very different elasticities if the ranges of the x values are greatly different.

Some investigators have found that logarithmic transforms provide a better fit to their data. For the model

$$\ln(y) = m \ln(x) \tag{3}$$

the elasticity is simply $e = m = \frac{dy}{dx}\frac{x}{y} = \frac{d[\ln(y)]}{d[\ln(x)]}$

and is constant along the entire length of the drf. Obviously, the slope of Eq. 3 increases near the origin (in cartesian coordinates). A model which fits this definition provides the same percentage response regardless of the absolute value of x and implies increased toxicity per unit of dose at low doses, which seems physiologically implausible. However, when dealing with heterogeneous populations, applications of the concepts of toxicology derived from relatively uniform populations may not be immediately obvious.

The final model paradigm considered here is the log-linear model

$$\log y = a_0 + \sum_i b_i x_i + u, \text{ or } y = \exp(a_0 + \sum_i b_i x_i + u) \tag{4}$$

in which only the dependent variable has been transformed to logarithms. The elasticity of this model is given by

$$e_i = B_i \bar{x_i} \tag{5}$$

when natural logarithms are used, and $B_i\bar{x_i}/\ln_a(e)$ when base a is used; the logarithmic models employed in this report use base 10 logarithms. The log-linear model postulates an exponentially increasing effect per unit of increased dose, which is consistent with an increasingly sensitive fraction of the total population, as concentration levels increase.

For data sets of limited range in x and small values of e, these three types of models may be essentially equivalent. For data sets with substantial variability, plots of the regression residuals may be required to establish the best form of model.

The Air Quality Data Base

As discussed above, cross-sectional studies have usually been intended to study long-term differences among locations. For this reason, it has not generally been regarded as particularly im-

portant to use environmental data taken exclusively during the nominal year of study (1980, in this case), although clearly this would be desirable from the standpoint of uniformity and in order to deal with specific attributes of that year, including the heat wave that occurred in the central and eastern portions of the nation (Bair, 1992). Missing or incomplete air quality data are a common problem with observational epidemiological studies; for example, Mendelsohn and Orcutt (1979) used 1974 air quality data in their study of 1970 mortality patterns, arguing that the geographic patterns were stable in time and that the later measurements were more complete. Others have averaged over several years in order to obtain more reliable long-term averages (Lipfert, 1978; Lipfert *et al.*, 1988).

Sulfate Aerosol Data. 1980 was an especially problematic year for particulate pollution measurements. Size-classified measurements were being explored but the PM_{10} network had not yet been established; PM_{15} data were being acquired on a research basis (Watson *et al.*, 1981). The glass fiber filters used in the routinely operated high volume samplers for total suspended particulates (TSP) and their chemical constituents ($SO_4^=$, NO_3^-, etc.) were found to be unusually alkaline for the years 1979-81 (U.S. EPA, 1984). One of the well-known characteristics of such filters is their tendency to convert SO_2 (gas) in the ambient air being sampled to $SO_4^=$ particles on the filter (Stevens, 1981); this problem was thought to be especially acute during 1979-81. The outcome would be values reported for TSP and $SO_4^=$ that would be biased high in locations with appreciable ambient SO_2 levels.

For the present study, all the sites assigned to a given SMSA, as defined by the 1980 Census, were combined to provide SMSA-wide estimates. These data were retrieved from the EPA AIRS data base (Link, 1991); AIRS is the successor to SAROAD. Annual median $SO_4^=$ values, which tend to run 10-20% lower than annual mean values, were used because of the typically skewed frequency distributions and the relatively sparse frequency of measurement found in most locations. Data were assembled separately by year for the purpose of comparison. The following summary statistics were derived:

Year	No. of SMSAs	Mean $SO_4^=$ (ug/m^3)
1978	111	8.95
1979	97	9.20
1980	95	9.80
1981	100	9.86
1982	38	9.17

However, the differences by year were more pronounced when compared for the 33 SMSAs that had adequate data in each year, especially when the reduction in nationwide SO_2 emissions is taken into account. Figure 3 plots the ratio of average median $SO_4^=$ concentration divided by annual SO_2 emissions in million tons (U.S. EPA, 1986). 1980 and 1981 stand out as higher than the other three years, by about 10%. Since the suspect high-volume sampler filters were also used in 1979, it is difficult to assign all the blame to the filters. An alternative explanation is the low rainfall that occurred in the summers of 1980 and 1981, since precipitation tends to remove both SO_2 and $SO_4^=$ from the atmosphere. If meteorological factors are the main reason for the high sulfates recorded in 1980 and 1981, then the data should be regarded as valid for those particular years (but not necessarily representative of the long term).

Since one interpretation of a long-term cross-sectional study is that of the sum of short-term effects (Evans *et al.*, 1984a), differences among years were explored further by regressing 1980 (crude) mortality against each of the five years, in turn. The slopes and correlations were higher for the years 1979, 1980, and 1981, with the highest values occurring in 1981. The difference in slope between 1982 and 1981 was not quite statistically significant. Thus no special relationship was apparent for the 1980 measurements, leading to the hypothesis that artifacts formed on the filters used in 1979-81 resulted in the improved correlation, rather than coincidence in time.

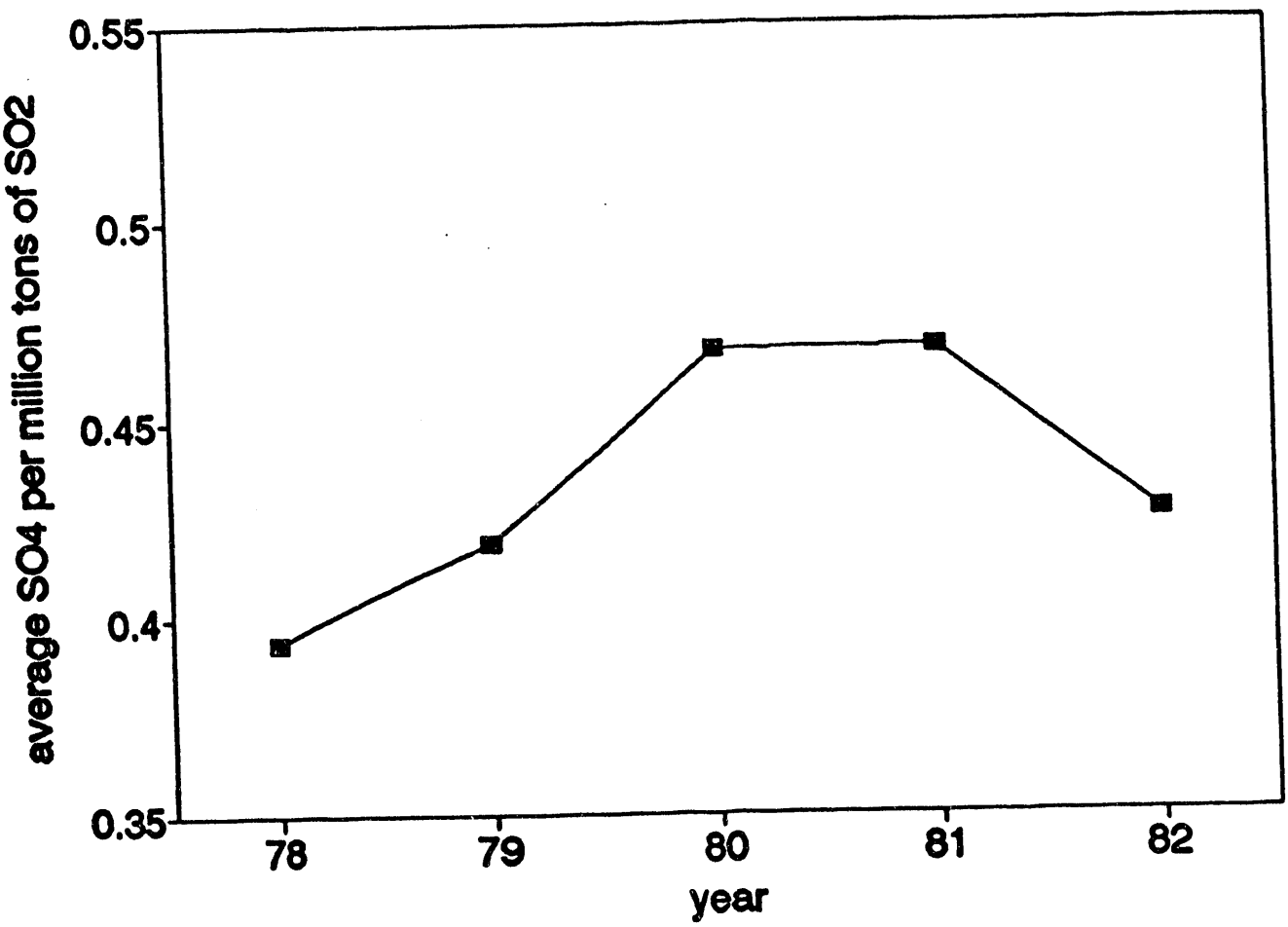

Figure 3. National average ambient $SO_4^=$ per million tons of SO_2 emitted (33 SMSAs with AIRS data in all years). Data source: U.S. Environmental Protection Agency.

The sulfate data used for multiple regressions in the present study (149 locations) were then obtained by averaging all the observations available for the period 1978-82. Missing locations (Chicago, Savannah, Eugene, OR, Chico, CA, Richmond, VA, Green Bay, WI, Jackson, MI, Atlantic City, NJ, Augusta, GA, Macon, GA, Beloit, WI, Rockford, IL, Wheeling, WV) were estimated either from nearby locations or from alternate time periods. Figure 4 plots the final data set against the 1980 measurements. There is appreciable scatter but appears to be little bias.

Other sources of sulfate air quality data include measurements from the PM_{15} (also referred to as "IP", for inhalable particulate), and estimates made with computer models. The IP data were obtained with unreactive (Teflon) filters and are thought to be more reliable than data obtained with high volume samplers using glass fiber filters; the correlation between the two measures was 0.63 (Lipfert *et al.*, 1988). The two $SO_4^=$ measures were related by

$$\text{AIRS [TSP] } SO_4^= = 3.5 + (1.18 +/- 0.23) * \text{[IP] } SO_4^= \text{ (two-sigma CLs).} \quad (6)$$

Thus, the slope was not significantly different from unity, which implies that a single unit of sulfate had the same meaning in both measurement systems.* However, the AIRS data were 3.5 ug/m^3 higher than the IP data, on average, presumably because of the filter artifacts. Equation (6) implies that both measures should derive the same regression coefficient, and that the 3.5 ug/m^3 intercept should not play a role in the effects attributed to AIRS sulfate. Thus, the intercept should be subtracted from the AIRS mean value when estimating elasticities and previous estimates of air pollution effects based on $SO_4^=$ obtained from hi-vol filters should be reduced accordingly. The overall levels of the [IP] $SO_4^=$ values were in better agreement with $SO_4^=$ values obtained from various air quality research efforts carried out during this period than the SAROAD values. In most cases, there was only one IP monitor per city.

Given the apparent superiority of the [IP] $SO_4^=$ measurements, the regression given by Eq. 6 could also be used to estimate the variance due to measurement error associated with the [TSP] $SO_4^=$ data. The standard error of estimate from Eq. 6 provides such an estimate (2.28 ug/m^3). According to Snedecor and Cochran (1967, p. 165), a regression coefficient based on an independent variable measured with error variance s_e^2 will be biased low by an amount given by $1+ s_e^2/s_x^2$. Although the formula given by Snedecor and Cochran is not strictly applicable to multiple regressions, it suggests that sulfate regression coefficients based on the [TSP] $SO_4^=$ measurements are likely to be biased low by as much as a factor of 1.4.

In their study of 1980 mortality and air pollution in U.S. cities, Lipfert *et al.* (1988) extensively used modeled ambient air quality values derived from a long-range transport computer model (Shannon, 1981). Modeled SO_2, $SO_4^=$, and NO_x were all found to be important predictors of excess mortality in that study of about 900 locations. However, as mentioned above, subsequent evaluations of these modeled air quality estimates cast some doubt on their validity. Scatter plots against the IP data and against data from the SURE (Mueller and Hidy, 1983) show good agreement within some regions but differences between regions. The correlation between computed $SO_4^=$ and [IP] $SO_4^=$ was 0.70. Since the long-range transport model is essentially a transfer function between source emissions and ambient air, averaged over grid cells of about 120 km on each side, a correlation between health and computed air quality may also represent a correlation with industrial activity and the various accompanying socioeconomic factors. The computed $SO_4^=$ values are based only on combustion and smelter emissions, and thus do not include sulfates from natural sources or particles such as $CASO_4$. The grid-averaged values are incapable of reflecting local phenomena that might affect SO_2 oxidation rates or local primary emissions of $SO_4^=$.

---

* A similar relationship was found by comparing $SO_4^=$ data from TSP filters with $SO_4^=$ data obtained from PM_{10} filters in New York State, on a temporal basis.

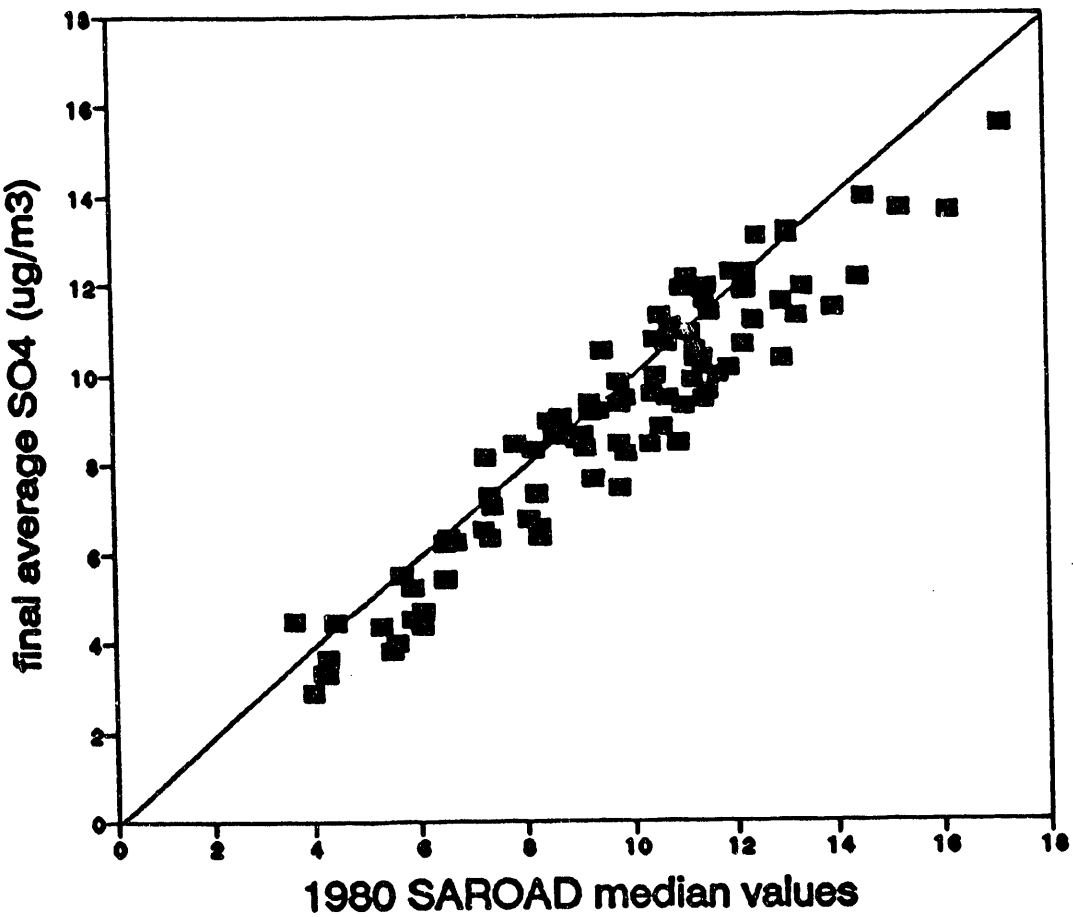

Figure 4. Comparison of $SO_4^=$ data used in the regression analysis with the available $SO_4^=$ data for 1980. Data source: U.S. Environmental Protection Agency.

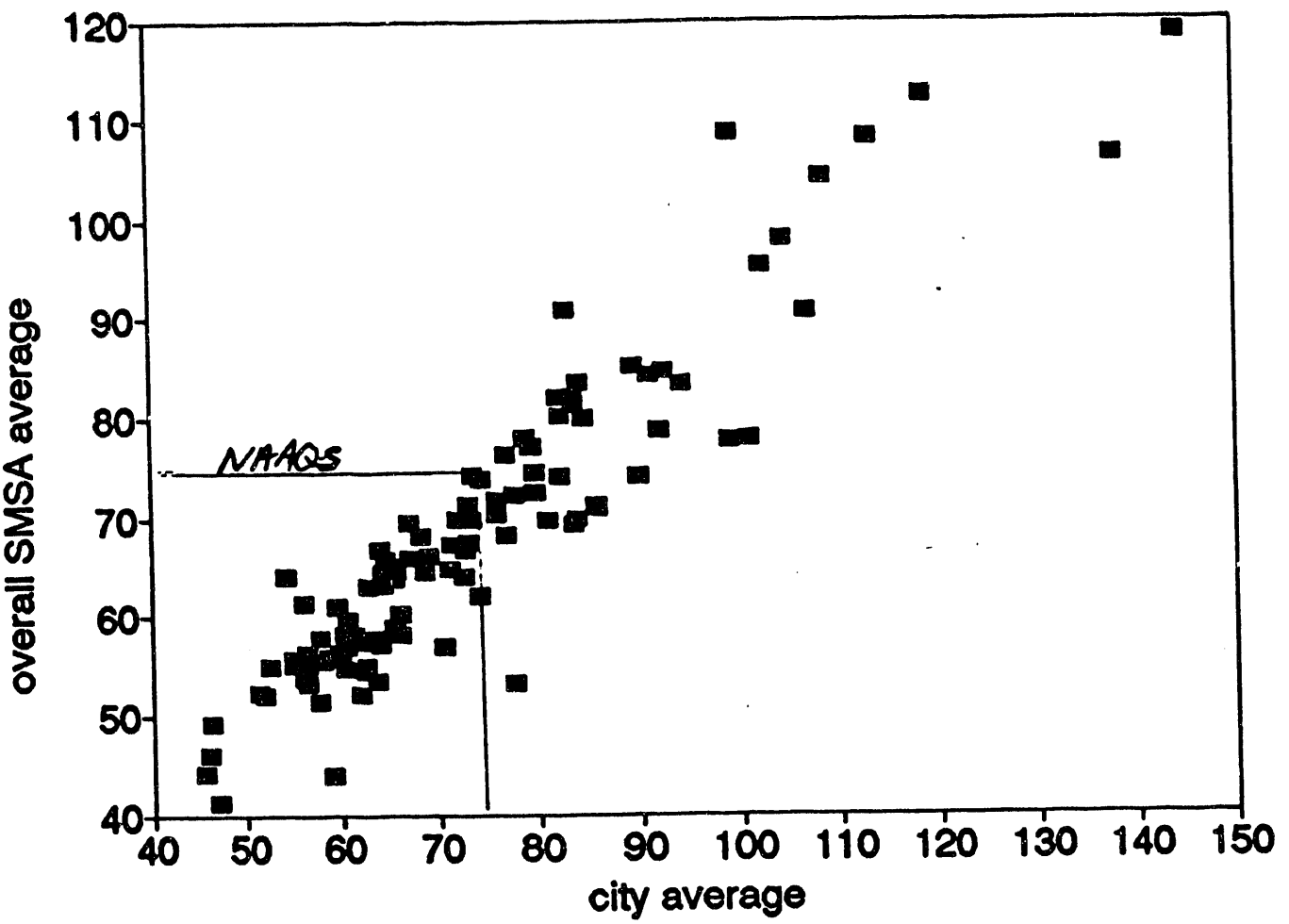

Figure 5. SMSA vs. central city average TSP for 1980 (112 SMSAs). Data source: U.S. Environmental Protection Agency.

Total Suspended Particulate Data. Lipfert *et al.* (1988) made only a few cursory regressions employing TSP. That data base consisted of 1978 and/or 1982 values for each city, with no attempt to derive city-wide averages. A similar approach was used by Ozkaynak and Thurston (1987), in that a single monitoring site was used to represent each SMSA.

In an effort to improve the estimation of actual exposures to particulates within each SMSA, data from the EPA AIRS database were used to construct spatial averages for 1980. All TSP monitors with at least 11 observations for 1980 were used; the annual means were averaged (without weighting) to provide an SMSA-wide estimate. There were a few cases of source-oriented networks in the data base (Granite City, IL [St. Louis SMSA] and networks surrounding some of the TVA power plants). These subsets were averaged separately and then entered into the dataset for the SMSA in question as a single observation, in order to preclude undue weighting because of the large number of monitors representing a limited geographic area. Separate files were constructed for the main central cities of each SMSA and the surrounding area; the overall means were 72.5 ug/m^3 and 64.4 ug/m^3 for 112 SMSAs. City and SMSA averages are compared in Figure 5. The standard deviation of the 112 SMSA averages was 14.9 ug/m^3; this compares with the average within-SMSA standard deviation of 13.9 ug/m^3, which suggests that there is typically almost as much variation within SMSAs as between SMSAs.

The overall mean for 149 SMSAs was 68.4 ug/m^3. A total of 1581 monitoring stations was used in this effort. The maximum annual mean value for an individual monitor was 280 ug/m^3 (East Chicago, IN, near a car wash); the minimum value was 22 ug/m^3 (near Portland, OR). The maximum SMSA average was in Spokane, WA (142 ug/m^3); the minimum was in Atlantic City, NJ (41 ug/m^3).

Year-by-year TSP comparisons were made on the basis of the maximum annual means recorded in each SMSA for the years 1978-82. The averages for 112 SMSAs decreased from 90 ug/m^3 in 1978 to 69 ug/m^3 in 1982. However, when compared to the national estimates of particulate emissions (U.S. EPA, 1986), it appears that the ambient data for 1980 and 1981 were about 5% higher than expected. As was the case with sulfates, this could have resulted from either sulfate artifacts on the filters or from the low rainfall that occurred in those years (U.S. EPA, 1986).

Comparison with the Air Quality Data of Ozkaynak and Thurston (O&T). Ozkaynak and Thurston (1987) did not tabulate the air quality values they used for individual SMSAs in their paper, but their plots of mortality rates vs. TSP and $SO_4^=$ (their Figures 1 and 2) provide this information, albeit indirectly. Data were obtained from these plots and compared to the independent estimates used in this re-analysis (Figures 6 and 7). The major outliers (deviations from the diagonal 1:1 line) were examined on a case-by-case basis.

For $SO_4^=$, major differences between O&T and the five-year average SAROAD data were found for Gary, IN, Wilmington, DE, Houston, Baltimore, Richmond, VA, and Toledo. Most of these could be explained by O&T's use of incomplete seasonal data; sulfate has a strong seasonal cycle and if either winter or summer data are missing, a biased estimate of the annual mean will result. The high value that O&T used for Houston was not found among the 29 measuring stations listed in the AIRS data base for Harris County, TX, and thus could not be explained.

For TSP, major differences between O&T's data and the SMSA-wide averages were found for Cleveland, Denver, Portland, OR (O&T values were high) and for Houston (O&T value was low). The value they used for Houston was the lowest of the 44 stations that reported data in that SMSA for 1980. The plots indicate that large differences can result from selecting individual monitoring stations to represent an entire SMSA, as opposed to averaging them all.

In assembling their air quality data base for U.S. cities, Lipfert *et al.* (1988) limited the high volume sampler-based $SO_4^=$ data (which they labeled "SAROAD,") to the years 1978 and 1982. By individual city, these data retrievals ranged from single monitors with as few as five obser-

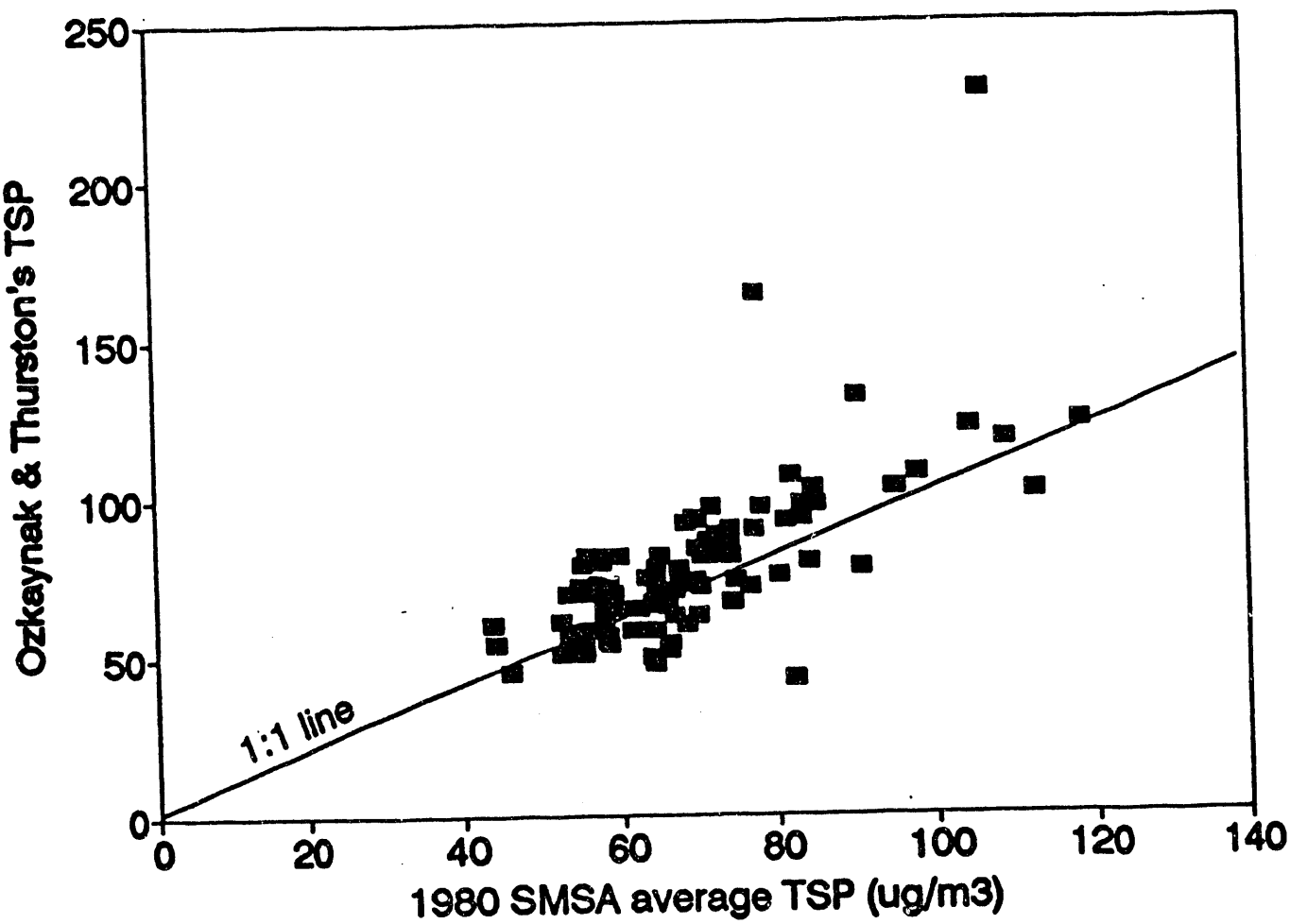

Figure 6. Comparison of TSP data used by Ozkaynak and Thurston (1987) with 1980 SMSA averages (98 SMSAs).

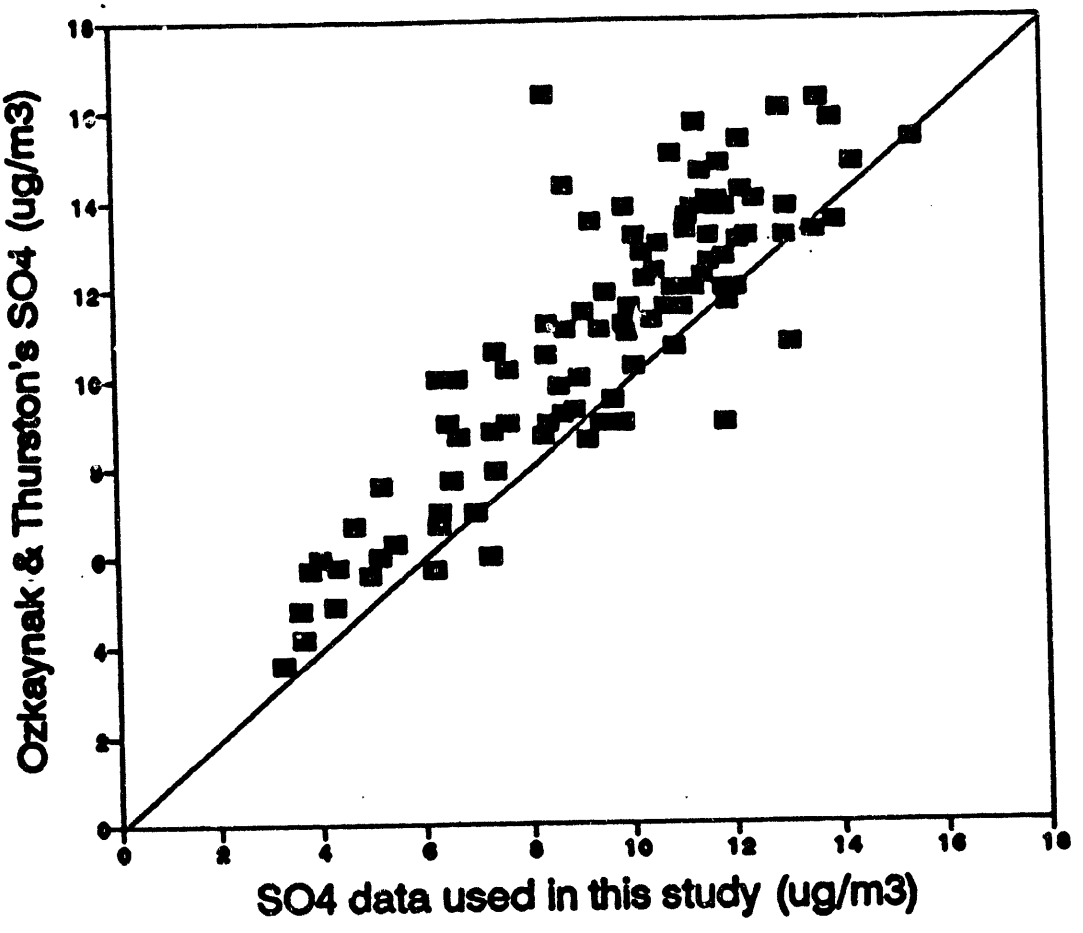

Figure 7. Comparison of $SO_4^=$ data used by Ozkaynak and Thurston (1987) with the $SO_4^=$ data used in the present study (98 SMSAs).

vations to Houston, TX, where 30 monitors recorded over 5000 observations during this period. The mean values for 1978 and/or 1982 for each sampler were then averaged by site, and the median of these means was used to obtain an estimate of the city-wide average.

Other Pollutants

Ozone (ppm): two separate sources of ozone data were utilized in this analysis. Peak 1-hr values were available for 1980 for 72 SMSAs (U.S. EPA, 1984), which were generally the largest SMSAs in the nation. These data represented the highest readings for each SMSA, and are not necessarily representative of average exposure across the entire SMSA. Seasonal average 8-hr maximum values were available for the entire data set, as obtained for a smooth isopleth map based on interpolated measurements taken from 1980-1990 (Figure 8a), ca. 1978 (McCurdy, 1992). These data represent the average from April to October of the highest 8-hr period of the day, regardless of the time at which it occurred. However, the probability of outdoor exposure varies with time of day, so that it is not clear that this is an appropriate metric for human health effects. In addition, 1980 was known to be a high ozone year and the relationship between annual exposure and these April-October averages will probably vary with latitude. The results from the long-term average ozone variable should thus be used with caution.

Most of the analysis was conducted for the seasonal average data set, because of its completeness and the likelihood of better representing spatial averages across each SMSA. However, it is also possible that use of the same definition of "season" in all locations, regardless of latitude or climate, has created a bias with respect to the true annual average ozone level. On the other hand, since most of the short-term peaks are likely to have occurred during these months, this metric could represent an operational average of peaks. Figure 8b plots peak values as obtained from individual monitoring stations vs. seasonal average ozone levels for the larger SMSAs; a reasonably-consistent relationship is seen. Note also the large number of locations in violation of the NAAQS.

Manganese (ug/m^3): based on analysis of high-volume sampler filters. Data were estimated from previous years for several SMSAs.

Particle data from the dichotomous sampler (IP or PM_{15}) network (1979-83): Total mass and fine particle mass, total sulfate, fine lead (Pb) (ug/m^3); samples taken every 3 or every 6 days. IP data for SMSAs with more than one IP monitoring site were averaged over all the sites in that SMSA. The size-fractionated particulate (IP) data, described by Watson *et al.* (1981), were based on Teflon filters and show systematically lower sulfate values; these values are generally regarded as the "true" sulfate measures. The differences between the two sulfate measures are not consistent and presumably depend on a number of site-specific environmental factors. These measurements were replaced by PM_{10}, which began with a few sites in 1983, too late to be used with the 1980 census and mortality data.

Other Variables Used in the Study

Mortality Data (dependent variables). Mortality counts were taken from *Vital Statistics, 1980, Part B* (Table 8-6), for which the SMSA boundaries were based on the 1981 definitions, which is consistent with the State and Metropolitan Area Data Book, from which population data were taken. (In New England, death counts are given only for New England County Metropolitan Areas (NECMAs), which are comprised of whole counties. We therefore based our demographic data for New England on NECMAs. New England SMSAs are comprised of cities and towns, which are sometimes only parts of counties.)

Four different groupings of causes of death were analyzed. Rates were computed by dividing the numbers of deaths in each group for the calendar year 1980 (all ages, races, both sexes) by the population estimated by the U.S. Census as of April 1, 1980. Thus, small errors would be

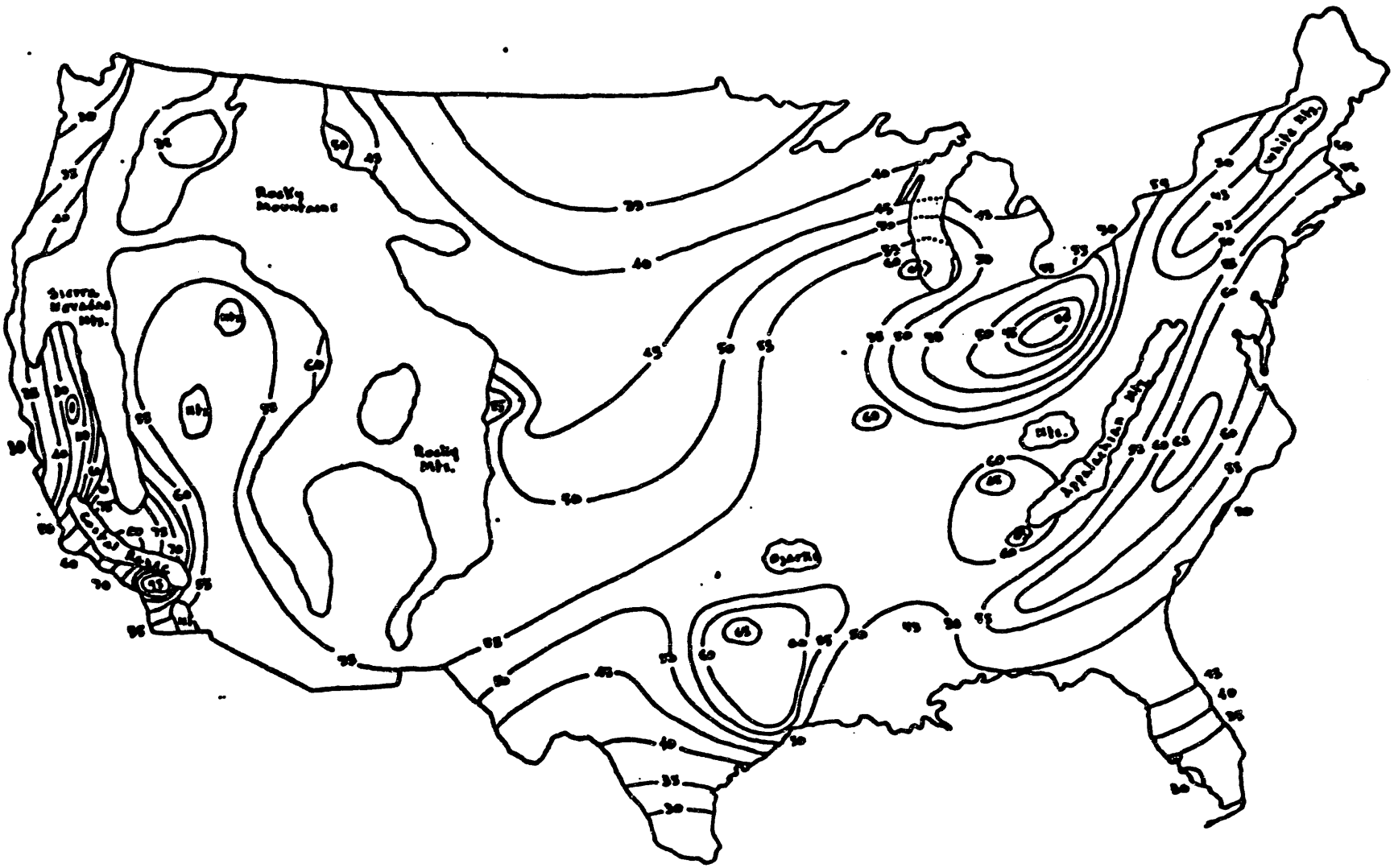

Figure 8a. Smoothed average ozone data for 1980-90, based on maximum daily 8-hr averages, averaged from April to October (values in ppb). Source: T. McCurdy, U.S. Environmental Protection Agency.

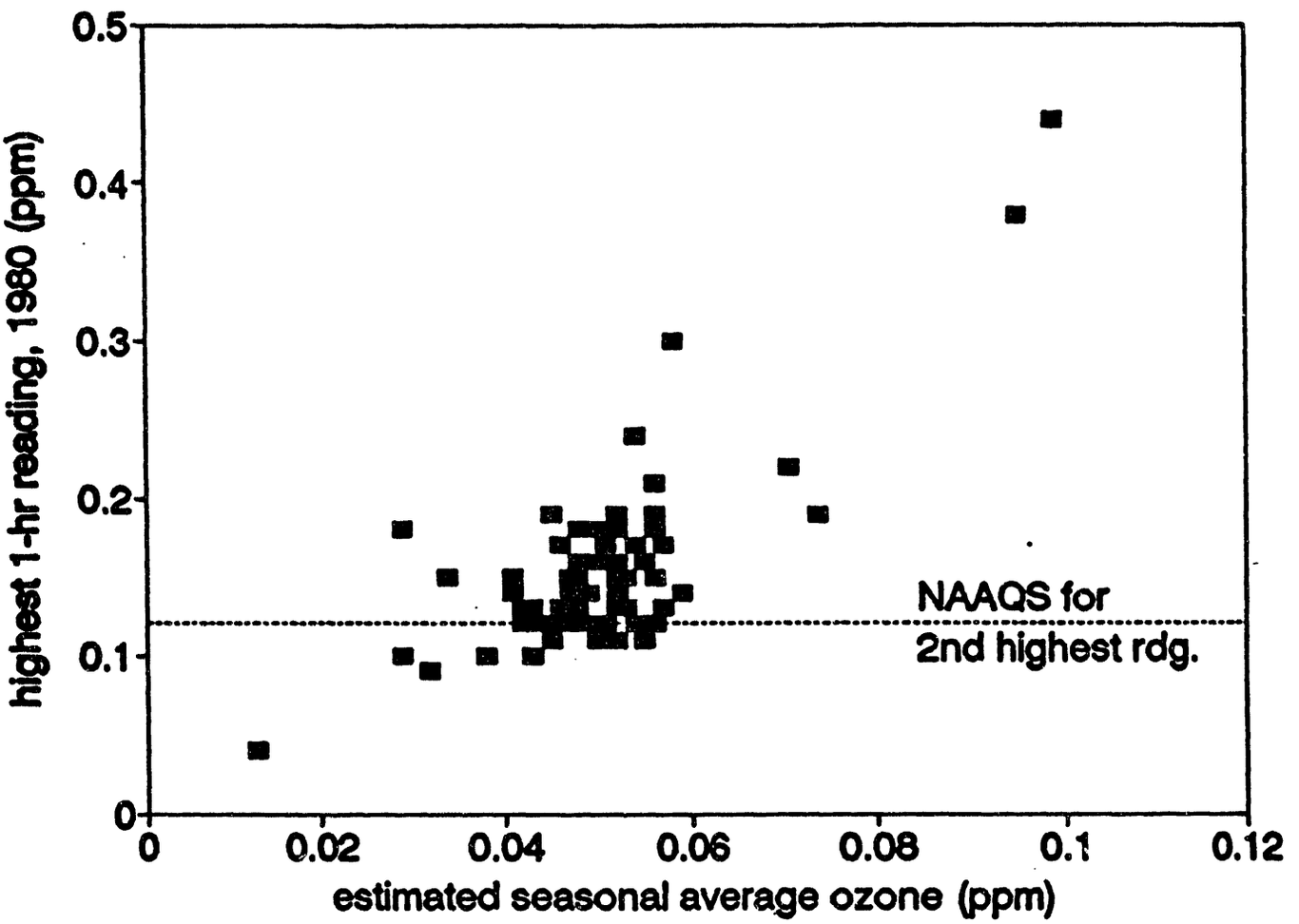

Figure 8b. Comparison of 1-hr peak and seasonal average of maximum daily 8-hr average ozone (72 SMSAs over 500,000 population).

entailed by any population changes which took place during the year; an independent variable for percentage population change was included in the regressions, in part for this reason. Deaths were assigned to locations on the basis of usual residence rather than on the basis of the location at which the death actually occurred. In this report, the term "mortality" should be interpreted as the crude (unadjusted) figure, unless otherwise specified.

The causes of death analyzed and their mean values and standard deviations (deaths per thousand population) are listed below, based on 149 SMSAs. ICD9 codes refer to the Ninth Revisions of the International Classification of Diseases. These selections were made to eliminate causes of death which are unlikely to have resulted from air pollution (external causes) and to specifically examine those major causes which have previously been linked with air pollution (heart and lung disease). No distinctions were made by age, race, or sex.

Non-external Causes: all causes less accidents, homicides, and suicides (ICD9 1-800). Mean = 7.82, standard deviation = 1.48.

Major Cardiovascular Diseases: includes acute heart attacks, chronic heart disease, hypertension, and stroke (ICD9 390-448). Mean = 4.19, standard deviation = 0.95.

Chronic Obstructive Pulmonary Disease (COPD): Includes bronchitis, emphysema, and chronic airways obstruction, but not acute respiratory disease, pneumonia, influenza, or occupational pneumoconiosis (ICD9 490-496). Mean = 0.251, standard deviation = 0.075.

All Causes: included primarily to facilitate comparison with other studies which did not remove external causes of death. Mean = 8.50, standard deviation = 1.48.

In terms of the coefficients of variation, COPD was the most variable grouping and all-cause mortality was the least variable.

Demographic/Socioeconomic Variables. Population descriptive data were obtained for 149 US SMSAs from the 1982 State and Metropolitan Area Data Book (SMADB), as follows. A brief rationale for each variable is also given. Variable names, as used below, are given in bold in parentheses.

1. Percent of population 65 years of age or more (65+). Above about age 35, mortality rates are exponentially related to age, but this variable is the only useful age statistic available from SMADB. "Median age" was used by Ozkaynak and Thurston but tends to be collinear with "percent > 65." Median age statistics add little new information where it is most needed: the age distribution within the 65-and-older group.

2. Racial and ethnic distribution: percent black (**BLACK**), percent other nonwhite (**OTHERNW**: Asian, American Indian, etc.), and percent Hispanic (**HISP**). Each of these groups tends to have mortality rates different from whites and thus cities with higher than average percentages of these groups would be expected to have correspondingly different mortality rates for the total population. Race was self-defined in the 1980 census, which leads to a certain amount of confusion, mainly in heavily Hispanic cities in the Southwest. We consider three groupings: whites, blacks, and others; they sum to 100%. "Hispanics" are a separate grouping not defined by race. In most cities, the fraction of "other" is small, but in El Paso, TX, it is about 38%, apparently because many Latinos do not consider themselves white. However, the classification of deaths by race uses a different criterion, since the 1980 deaths for El Paso were listed as 97% white. This means that death rates cannot be computed accurately by race for these locations. Ozkaynak and Thurston used the combined nonwhite population percentage (NW).

3. Percent of individuals below poverty level (**POOR**). We feel this is a better income variable than, say, median income, since if there is an effect of income on mortality, it

would be expected to be most obvious at the low end of the scale.

4. percent with four or more years of college (COLLEGE). Education may be a better socioeconomic variable than income since some persons may have low income because they have poor health, not vice versa. Educational attainment, as a socioeconomic indicator, will not be changed by subsequent illness.

5. Percent population change since 1970 (CHNG70). This variables is intended to characterize population stability and migration, which can be important for several reasons. First, cities with high rates of inmigration may attract healthy people looking for better economic opportunities. A contrary effect would result if ill health were a factor in the decision to migrate to a more favorable climate (or to return home where family support may be available). Finally, long term exposure to air pollution would be affected by migration.

6. Average annual heating degree days (HDD). This is essentially a climate variable reflecting long-term rather than current weather conditions.

7. Population density (logarithm, LPD). Before the conquest of infectious diseases, population density was an important determinant of mortality (Farr, 1885; Lipfert, in press). When applied to county units or larger, this statistic is now of limited use due to the heterogeneity of land use typically found in larger areas, and tends not to capture the average density at which people actually live. However, it is capable of distinguishing the 100% urban SMSAs (such as Jersey City) from most of the others, which are usually mixed urban/suburban.

Drinking Water Quality Data. Previous studies(Lacey, 1981; Lipfert, 1984) have implicated soft water as a contributing factor in heart disease, primarily for males. Data on drinking water hardness in ppm (HARDNESS) were obtained from a data base compiled by the National Institutes of Health (Feinleib *et al.*, 1979). These data were for the ca. 1970 time period and earlier, but it was felt that drinking water supply data would be reasonably stable over time. The NIH data base was for cities rather than SMSAs; the value for the main city of each SMSA was selected; no attempt was made to average over all the component cities of an SMSA. Data were available for 144 SMSAs out of the above set of 149; the other five values were obtained by telephone from the respective water supply authorities.

Data on Smoking Habits. Cigarette consumption data have been estimated from state sales tax data for three time periods: 1955, 1969, and 1980 (Lipfert, 1978; Lipfert *et al.*, 1988) The estimates are based on regression analysis on state level sales data (annual packs per capita for the population aged 18 and over), using various economic and demographic variables as predictors. The presence of lower sales taxes in adjoining states was found to be an important factor in explaining cigarette sales differences. These regression results were then used to predict cigarette consumption in each state. It was not possible to derive cigarette consumption data at finer geographic resolution, and thus we are forced to assume uniform consumption throughout the state with discontinuities at the borders. These errors are likely to lead to an underprediction of the effect of smoking on mortality, particularly for interstate SMSAs.

Earlier analyses of smoking patterns typically found large urban-rural differences, and it has long been assumed that city people smoke more. In the study of 1980 smoking data, SMSA tobacco sales data from the 1977 Census of Retail Trade were compared to state-wide sales data from the same source, and a consistent relationship was found, amounting to an annual urban-statewide difference of about 5 packs per year per person (out of 185). This small (but still statistically significant) difference suggests that regional smoking patterns are now probably more important than urban-rural differences within regions, which supports the use of state level data in the analysis of mortality effects.

Finally, a comparison was made of our estimates of cigarette consumption with independent state level survey data on the percentage of people who smoke (smoking prevalence). The correlation coefficient relating these two measures was only about 0.5 (explaining 25% of the variance) for the 29 states which had conducted surveys. Possible explanations for this rather poor result include variations in amount consumed per smoker and under-reporting by those responding to the survey. We prefer to use consumption data rather than prevalence since heavy smokers have a much higher relative mortality risk than light smokers, and since consumption may reflect the possible effects of passive (involuntary) smoking. Cigarette consumption rates are analogous to air pollution emission rates, with respect to passive smoking effects.

For an analysis of chronic health effects, it is not clear whether current cigarette smoking rates or some time integral is the appropriate metric (the same question exists for air quality as well). For this reason, we considered two possible smoking variables: the 1980 data, as described above, and 1969 data. Because of collinearity between the two (r=0.48), regression models are limited to one or the other (or alternatively, the average (SMOKING78), which was used in the regression runs reported below).

Locations Studied

This study employs Standard Metropolitan Statistical Areas (SMSAs) as the geographic unit of analysis. The U.S. Bureau of the Census (1983) defines an SMSA as a group of counties (except in New England; see below) having a total population of at least 100,000 with an urbanized area population of at least 50,000. Two counties in Montana, with populations of 77,000 (Missoula) and 34,000 (Silver Bow County, which includes the city of Butte), which do not qualify as SMSAs, were also added to the data set in order to take advantage of their air quality data. Consolidated Metropolitan Areas, which combine several SMSAs, such as Los Angeles, New York, or Chicago, were not used in this analysis.

The 112 SMSAs first studied by Lave and Seskin (1970) and later by Evans *et al.* (1984b) and others comprised the primary list of locations. These were originally selected on the basis of the availability of air monitoring data, ca. 1960, but the actual geographic definitions in terms of the counties included have changed somewhat over the years, as defined in each decennial Census. In general, SMSAs are comprised of whole counties but include independent cities in Virginia and portions of counties in New England (CT, MA, ME, NH, RI, VT). For comparability of mortality and socioeconomic data, New England County Metropolitan Areas (comprising whole counties) were used in these six states.

Ozkaynak and Thurston (1987) selected a subset of 98 SMSAs from this list, based on availability of ca. 1980 air quality data and conformance with their mortality model. Comparisons are presented below using this model and data set. They also defined a subset of 38 SMSAs which had air quality data obtained from the Inhalable Particulate (IP) Network, which featured size-classified particle concentration data. In this report, we use the entire IP data set, comprising 63 locations including the two Montana counties.

Further subsets of SMSAs were defined on the basis of the availability of air quality data, as discussed below. Mean values of all variables are given in Appendix A.

REGRESSION ANALYSIS RESULTS

Multiple regression analyses were used to deduce associations between SMSA mortality rates and various air pollutants. These were performed using the algorithms of Quattro ®-Pro, a spreadsheet analysis program (Borland International, 1989). All regressions were run with models specified *a priori*; stepwise regression was not used. The intent was to develop mortality models which contain only those socioeconomic terms which are statistically significant (or nearly so) and to evaluate these models using various air pollutants. The two-sided 0.05 level was selected as indicating statistical "significance."

Regression Results for $SO_4^=$ and TSP

The Ozkaynak and Thurston Model (O&T). Ozkaynak and Thurston (1987) published the first analysis of mortality gradients for the year 1980; their work has been widely cited and recommended for use in cost-benefit analyses. They found sulfate to be the most important air pollutant and assigned from 4-9% of U.S. total mortality to this cause. The range of regression coefficients for $SO_4^=$ was from 0.046 to 0.075 deaths per thousand population per ug/m^3, with two-sigma confidence limits of about =/- 0.03 deaths per thousand population per ug/m^3 ($p < 0.001$). In this sense, they confirmed the findings of previous analyses dealing with air quality from the 1960s and 1970s (Lave and Seskin, 1978; Chappie and Lave, 1982; Mendelsohn and Orcutt, 1979). However, each of these previous studies has been found to contain serious flaws (Lipfert, in press) and in particular, reanalysis of the Lave and Seskin work has produced much lower (and even negative) estimates for the effects of sulfate on mortality (Evans *et al.*, 1984; Lipfert, 1980, 1984). For this reason, careful attention was given to the Ozkaynak/Thurston (O&T) study.

O&T postulated that (crude) mortality rates in U.S. SMSAs could be defined using six socioeconomic variables: median age (MEDIAN), percentage 65 and over (65+), percentage nonwhite (NW), percentage classified as below the poverty line (POOR), the log of population density (LPD), and the percentage with four or more years of college (COLLEGE). However, they presented no regression results for these variables and the variable they labeled as "COLLEGE" appeared to be something else, since its mean value did not correspond to either the 1970 or 1980 Census data for "percent with four or more years of college." Further, we could not be certain as to the exact air quality data they used, since no details were given on the inhalable particle data and the only available information on $SO_4^=$ and TSP had to be read from the published graphs. However, as discussed above, we did find a few important differences in the $SO_4^=$ and TSP data. These uncertainties, which undoubtedly resulted from the constrictions of journal publication space, make detailed comparisons with the present work difficult.

Table 2 presents recalculation of regressions based on this model and set of locations, using the input data developed for this study and all-cause mortality. The coefficients for $SO_4^=$ and TSP check the O&T results quite well, which indicate that they portray mainly regional rather than local effects. Note that O&T reported R^2 values from 0.89 to 0.92; we derived slightly higher values, suggesting that the actual "COLLEGE" and air quality variables constituted improvements in fit. These differences not withstanding, Table 2 shows that we successfully replicated the basic O&T findings, using their model and independently derived input data.

When sulfate was entered as the sole pollutant (Regression 2.1), three of the six socioeconomic variables failed to reach significance (MEDIAN, POOR, LPD). When TSP was substituted for $SO_4^=$ (regression 2.3), MEDIAN became significant and LPD nearly so, but TSP was highly insignificant. These results indicate an interaction between the $SO_4^=$ and socioeconomic variables.

Table 2 also shows results for 149 SMSAs using this model. The $SO_4^=$ coefficient increased by about 20% relative to the 98-SMSA case and the TSP coefficient remained insignificant, but NW

TABLE 2

MULTIPLE REGRESSION RESULTS FOR THE O&T MODEL
(Mortality from all causes)

Regression No.	2.1	2.2	2.3	2.4
Variable	All Cause	All Cause	All Cause	All Cause
% > = 65	0.554 (0)	0.480 (0)	0.533 (0)	0.433 (0)
median age	0.0716 (0.10)	0.131 (0.014)	0.0977 (0.04)	0.169 (0.002)
% nonwhite	0.0248 (0.0002)	0.0072 (0.28)	0.0244 (0.0009)	0.0067 (0.35)
% college	-0.049 (0)	-0.049 (0.0002)	-0.068 (0)	-0.081 (0)
% poor	0.0148 (0.50)	0.0365 (0.10)	0.0198 (0.41)	0.0371 (0.11)
log population density	0.0383 (0.74)	-0.105 (0.44)	0.179 (0.14)	0.106 (0.43)
$SO_4^=$ (ug/m^3)	0.064 (0)	0.079 (0)	X	X
particulates (TSP-ug/m^3)	X	X	0.0002 (0.94)	-0.003 (0.26)
# observations	98	149	98	149
R^2	0.933	0.870	0.919	0.856
std error of estimate	0.352	0.550	0.387	0.579

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

became insignificant and the 65+ coefficient decreased by 13-19%. There were important differences in the coefficients for COLLEGE and 65+ according to which pollutant was included.

Regressions were also computed for the other three cause-of-death groupings using this model, for both the 98 and 149 SMSA data sets (Tables 3, 4, and 5). For non-external causes, sulfate was significant in both cases, but TSP nearly reached negative significance* for 149 SMSAs. Wide fluctuations were seen in the socioeconomic coefficients. For cardiovascular causes, the results were similar except that TSP was highly negatively* significant (p=0.004) for 149 SMSAs and NW, MEDIAN, and POOR were never significant. For COPD, TSP was significant (+) in both cases, and $SO_4^=$ was negatively* significant for 149 SMSAs. There were wide variations in the socioeconomic coefficients among the four regressions. The negative pollution coefficients derived by the O&T model are counterintuitive and are indicative of incomplete or improper model specification. Although the pollutant regression coefficients checked well with the values reported by Ozkaynak and Thurston (for the 98 SMSA case), taken as a whole, these results suggest that the O&T mortality model is not completely specified and that the selection of locations for analysis may also be important.

The "Complete" Socioeconomic Model. Since three of the six socioeconomic variables postulated by O&T failed to reach significance, the next step in this process was to examine associations between the three specific cause-of-death variables and a larger suite of (non-pollution) independent variables. (All-cause mortality was eliminated from the analysis at this point, since external causes of death tend to be higher in the West and thus could confound results for any air pollutants which also varied systematically from East to West, such as sulfates, for example.) The independent variables were selected from those that are known *a priori* or suspected to influence spatial variations in mortality rates and included: 65+, POOR, COLLEGE, LPD, percentage black (BLACK), percentage of Hispanic origin (HISP), percentage of nonwhites other than blacks (OTHERNW), estimated cigarette consumption (SMOKING78), drinking water hardness (HARDNESS), annual heating degree days (HDD), and percentage population change between 1970 and 1980 (CHNG70). These variables had previously been investigated with respect to city mortality rates (Lipfert et al., 1988). This analysis was limited to the 149 SMSA data set; TSP and $SO_4^=$ were each entered separately.

Table 6 presents these results. For non-external mortality and cardiovascular causes, neither pollutant reached significance although for non-external deaths, $SO_4^=$ was close and the coefficient for TSP was similar to values which have been reported for time-series analyses (Schwartz and Dockery, 1992a,b). TSP was highly significant for COPD deaths, with about the same regression coefficient as found with the O&T model. Among the other independent variables, SMOKING78 was significant for non-external deaths and nearly significant for COPD and major cardiovascular deaths. OTHERNW, HISP, HDD, and HARDNESS were never significant, COLLEGE and CHG70 were significant for cardiovascular and non-external deaths, and POOR and LPD were only significant for COPD. BLACK was significant (positive) for non-external and cardiovascular deaths, but significant (negative) for COPD. In general, we found that the socioeconomic coefficients were not sensitive to which pollutant was entered, indicating that the interactions seen with the O&T model had been eliminated.

These results suggest that this model may be "overspecified." For example, the Hispanic population tends to be higher in the Southwestern portion of the country where heating degree days are low; thus, only one of these variables should be entered. Since Hispanics have been shown to have lower rates of heart disease (Rosenwaike, 1987), presumably because of differences in diet, and since there is no currently operational hypothesis for an effect of space

---

* negative coefficients, which imply that pollution prolongs life, if taken naively at face value, indicate that mortality rates for that disease tend to be lower in those parts of the country where the pollutant in question tends to be higher; these are usually regional trends and may be indicative of incomplete model specification.

TABLE 3

MULTIPLE REGRESSION RESULTS FOR THE O&T MODEL
(Mortality from Non-External Causes)

Regression No.	3.1	3.2	3.3	3.4
Variable	Non Ext	Non Ext	Non Ext	Non Ext
% > = 65	0.564 (0)	0.503 (0)	0.534 (0)	0.445 (0)
median age	0.0479 (0.26)	0.0868 (0.08)	0.079 (0.10)	0.133 (0.01)
% nonwhite	0.0153 (0.017)	0.0010 (0.87)	0.0151 (0.04)	0.0002 (0.96)
% college	-0.0418 (0)	-0.0425 (0.001)	-0.0663 (0)	-0.0804 (0)
% poor	0.0133 (0.53)	0.0268 (0.21)	0.0165 (0.50)	0.0274 (0.23)
log population density	0.224 (0.04)	0.0895 (0.49)	0.391 (0.0013)	0.328 (0.010)
$SO_4^=$ (ug/m^3)	0.077 (0)	0.0933 (0)	X	X
particulates (TSP-ug/m^3)	X	X	-0.002 (0.43)	-0.005 (0.58)
# observations	98	149	98	149
R^2	0.939	0.884	0.920	0.865
std error of estimate	0.341	0.521	0.390	0.561

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 4

MULTIPLE REGRESSION RESULTS FOR THE O&T MODEL
(Major Cardiovascular Deaths)

Regression No.	4.1	4.2	4.3	4.4
Variable	MCV	MCV	MCV	MCV
% > = 65	0.361 (0)	0.330 (0)	0.340 (0)	0.289 (0)
median age	-0.011 (0.72)	0.0074 (0.83)	0.0098 (0.78)	0.0386 (0.29)
% nonwhite	0.0057 (0.22)	-0.0022 (0.64)	0.0057 (0.29)	-0.0028 (0.56)
% college	-0.0397 (0)	-0.0396 (0)	-0.0564 (0)	-0.065 (0)
% poor	-0.014 (0.36)	-0.0084 (0.58)	-0.0122 (0.48)	-0.0082 (0.60)
log population density	0.219 (0.007)	0.130 (0.15)	0.330 (0.0001)	0.267 (0.002)
$SO_4^=$ (ug/m^3)	0.0514 (0)	0.0599 (0)	X	X
particulates (TSP-ug/m^3)	X	X	-0.002 (0.36)	-0.005 (0.004)
# observations	98	149	98	149
R^2	0.922	0.862	0.902	0.849
std error of estimate	0.249	0.363	0.279	0.380

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 5

MULTIPLE REGRESSION RESULTS FOR THE O&T MODEL (COPD Deaths)

Regression No.	5.1	5.2	5.3	5.4
Variable	COPD	COPD	COPD	COPD
% > = 65	-0.0028 (0.61)	0.0133 (0.010)	-0.0006 (0.90)	0.0170 (0.0007)
median age	0.0147 (0.006)	0.0069 (0.21)	0.0136 (0.009)	0.0044 (0.42)
% nonwhite	-0.0029 (0.0004)	-0.0012 (0.075)	-0.003 (0.0002)	-0.0012 (0.09)
% college	-0.0001 (0.91)	~0 (0.96)	0.0012 (0.29)	0.0020 (0.08)
% poor	0.0075 (0.004)	0.004 (0.08)	0.008 (0.002)	0.0041 (0.07)
log population density	-0.022 (0.12)	-0.044 (0.002)	-0.027 (0.04)	-0.05 (0)
$SO_4^=$ (ug/m^3)	-0.003 (0.14)	-0.004 (0.03)	X	X
particulates (TSP-ug/m^3)	X	X	0.0008 (0.015)	0.0008 (0.003)
# observations	98	149	98	149
R^2	0.384	0.460	0.407	0.476
std error of estimate	0.043	0.056	0.042	0.056

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 6

MULTIPLE REGRESSION RESULTS FOR THE "COMPLETE" MODEL
(149 SMSAs)

Regression No.	6.1	6.2	6.3	6.4	6.5	6.6
Variable	Non Ext	Non Ext	MCV	MCV	COPD	COPD
% > = 65	0.557 (0)	0.552 (0)	0.327 (0)	0.322 (0)	0.0185 (0)	0.020 (0)
% Hispanic	-0.0043 (0.51)	-0.0090 (0.17)	-0.0027 (0.54)	-0.0032 (0.49)	-0.0009 (0.028)	-0.0014 (0.08)
% black	0.022 (0.004)	0.022 (0.004)	0.011 (0.038)	0.011 (0.038)	-0.0021 (0.033)	-0.0021 (0.03)
% other non w	-0.002 (0.77)	-0.004 (0.65)	-0.002 (0.69)	-0.0030 (0.58)	0.0001 (0.90)	0.0003 (0.77)
% college	-0.037 (0.007)	-0.042 (0)	-0.037 (0.0002)	-0.042 (0)	0.0003 (0.81)	0.0017 (0.19)
% pop. change, 1980-1970	-0.017 (0.008)	-0.020 (0)	-0.012 (0.0002)	-0.013 (0)	0.0002 (0.71)	0.0004 (0.52)
drinking water hardness	-0.00064 (0.12)	-0.00065 (0.12)	-0.0004 (0.19)	-0.00038 (0.19)	3.6×10^{-5} (0.50)	3.6×10^{-5} (0.49)
% poor	0.0195 (0.36)	0.0246 (0.26)	-0.0019 (0.89)	-0.0028 (0.85)	0.0058 (0.03)	0.0069 (0.01)
cigarette sales (1970-80 av'g)	0.0040 (0.029)	0.0048 (0.009)	0.0019 (0.13)	0.0022 (0.084)	0.00041 (0.08)	0.00042 (0.06)
heating degree days	4×10^{-5} (0.26)	3×10^{-5} (0.40)	4×10^{-5} (0.065)	4×10^{-5} (0.11)	-2×10^{-6} (0.67)	-1×10^{-6} (0.79)
log population density	-0.038 (0.75)	0.044 (0.71)	0.006 (0.93)	0.0356 (0.66)	-0.036 (0.02)	-0.035 (0.01)
particulates ($TSP-ug/m^3$)	X	0.0030 (0.24)	X	-0.0009 (0.61)	X	0.00084 (0.006)
$SO_4^=$ (ug/m^3)	0.031 (0.08)	X	0.0175 (0.16)	X	-0.0025 (0.29)	X
# observations	149	149	149	149	149	149
R^2	0.920	0.920	0.907	0.906	0.488	0.510
std error of estimate	0.438	0.440	0.303	0.305	0.056	0.050

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 7

MULTIPLE REGRESSION RESULTS FOR THE PARSIMONIOUS MODELS
(Non-External Mortality)

Regression No.	7.1	7.2	7.3	7.4	7.5	7.6
Variable	Non Ext	Non Ext	Non Ext	Non Ext	Non Ext	Non Ext
% > = 65	0.550 (0)	0.550 (0)	0.553 (0)	0.553 (0)	0.550 (0)	0.548 (0)
% Hispanic	-0.0028 (0.59)	X	-0.0059 (0.16)	-0.0084 (0.056)	-0.0055 (0.30)	X
% black	0.0201 (0)	0.020 (0)	0.0212 (0)	0.0242 (0)	0.0232 (0)	0.0228 (0)
% other non w	-0.0077 (0.29)	-0.0099 (0.09)	X	X	-0.0070 (0.33)	-0.0112 (0.06)
% college	-0.041 (0)	-0.040 (0)	-0.042 (0)	-0.045 (0)	-0.044 (0)	-0.044 (0)
% pop. change, 1960-1970	-0.0195 (0)	-0.0196 (0)	-0.0197 (0	-0.022 (0)	0.0222 (0)	0.0226 (0)
drinking water hardness	-0.00068 (0.09)	-0.00069 (0.09)	-0.00067 (0.10)	-0.00071 (0.08)	-0.00071 (0.08)	-0.00073 (0.07)
cigarette sales (1970-80 av'g)	0.0035 (0.04)	0.0034 (0.046)	0.0039 (0.018)	0.0046 (0.004)	0.0042 (0.011)	0.0041 (0.014)
particulates (TSP-ug/m^3)	X	X	X	0.0026 (0.28)	0.0025 (0.30)	0.0018 (0.44)
$SO_4^=$ (ug/m^3)	0.025 (0.14)	0.026 (0.11)	0.024 (0.15)	X	X	X
# observations	149	149	149	149	149	149
R^2	0.919	0.919	0.918	0.918	0.918	0.918
std error of estimate	0.437	0.436	0.437	0.439	0.439	0.439

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 8

PARSIMONIOUS MODEL RESULTS
(MCV and COPD Mortality)

Regression No.	8.1	8.2	8.3	8.4
Variable	MCV	MCV	COPD	COPD
% > = 65	0.320 (0)	0.317 (0)	0.0177 (0)	0.0179 (0)
% Hispanic	-0.0072 (0.014)	-0.0074 (0.016)	-0.0008 (0.27)	-0.0011 (0.01)
% black	0.0056 (0.069)	0.0064 (0.033)	-0.002 (0.01)	-0.002 (0.01)
% college	-0.037 (0)	-0.041 (0)	X	X
% population change 1980-1970	-0.0155 (0)	-0.017 (0)	X	X
drinking water hardness	-0.00037 (.20)	-0.0004 (0.19)	X	X
% poor	X	X	0.0061 (0.017)	0.0065 (0.011)
cigarette sales (1970-80 avg)	0.0026 (0.026)	0.0029 (0.011)	0.00043 (0.04)	0.00045 (0.03)
log population density	X	X	-0.0405 (0.001)	-0.036 (0.004)
TSP (ug/m^3)	X	-0.0007 (0.66)	0.00075 (0.013)	X
$SO_4^=$ (ug/m^3)	0.0132 (0.26)	X	X	X
TSP - $SO_4^=$ (ug/m^3)	X	X	X	0.00092 (0.003)
# observations	149	149	149	149
R^2	0.903	0.902	0.492	0.501
std error of estimate	0.305	0.306	0.055	0.054

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

heating, *per se*, on health**, HISP was selected for retention. A few additional regressions were performed with OTHERNW substituted for HISP. Similarly, because of ambiguities in racial definitions in the 1980 Census, Hispanics are sometimes indicated as "other" nonwhites; therefore, OTHERNW was dropped. The variables for education and poverty were shown to be somewhat collinear; COLLEGE was retained since it was usually more significant and an argument could be made that education is a more robust measure of socioeconomic status since a person's classification would not be affected by subsequent ill health (which may not be the case with poverty status).

Results for "Parsimonious" Models. Based on selective elimination of variables from the "complete" model, as described above, 65+, BLACK, HISP, COLLEGE, CHG70, and SMOKING78 were highly significant predictors of non-external mortality in 149 SMSAs; HARDNESS was nearly significant (Table 7). All of these variables entered with the "correct" sign. $SO_4^=$ was nearly significant, with a coefficient similar to that found with the "complete" model but less than half of that found with the O&T model. TSP was not significant, but its coefficients were similar in magnitude to those reported for time-series analyses (Schwartz and Dockery, 1991a,b).

For cardiovascular causes (Table 8), all of the same non-pollution variables were highly significant as for non-external mortality; smoking was slightly less significant for cardiovascular causes. Neither TSP nor $SO_4^=$ was significant with this model; TSP tended to be negative. For COPD, the TSP coefficient was about the same as with previous models and was relatively insensitive to the inclusion of socioeconomic variables. However, the SMOKING78 coefficient lost significance when compared to the "complete" model (Table 6).

Results Using Log-linear Regression Models. Many of the more recent time-series analyses of the relationships between air pollution and mortality used a Poisson regression model, in which the logarithm of mortality is regressed against a suite of (untransformed) variables. The formal rationale given for this choice is based on analyses where mortality is a relatively rare event (Steubenville, Ohio, for example, with an average of 3 deaths per day [Schwartz and Dockery, 1991a]), but it has also been extended to large cities like Philadelphia (average of 48 deaths/day (Schwartz and Dockery, 1991b]), where this refinement may not strictly be needed. The log-linear model essentially postulates an exponentially-increasing mortality response to linearly increasing air pollution levels. Lipfert (in press) has found that a log-linear model fits mortality-air pollution relationships from eight major episodes in London from 1948-62, including the major 1952 disaster during which over 4000 excess deaths were recorded.

The current cross-sectional analysis is based on mortality rates, which are the ratios of deaths to population and may tend to vary excessively among the smaller geographic entities, just because of randomness. Indeed, the highest (non-external) mortality rate was found for Silver Bow County (Butte), MT, which had a 1980 population of about 34,000. Furthermore, the number of annual COPD deaths per SMSA was as low as 18, which suggests that a Poisson (log-linear) model might be appropriate. Extending the analysis to include log-linear models also provides a comparison with previous time-series analyses and checks on model robustness. In general, we found that use of log-linear models yielded slightly higher correlation coefficients than the corresponding linear models.

Use of the log-linear model for non-external mortality (Table 9) showed only minimal changes in significance for the non-pollution variables (HARDNESS lost significance but SMOKING78

**Neither the effects of climate or weather were considered in this analysis, owing in part to lack of data on suitable measures describing known physiological effects. These effects may include heat stress (notably, high temperature deviations from normal weather patterns), indoor air pollution resulting from unvented or leaky heaters, and the indirect effects of crowding and exposure to contagion indoors during inclement weather.

TABLE 9

MULTIPLE REGRESSION RESULTS FOR LOG-LINEAR MODELS
(Non-External Deaths)

Regression No.	9.1	9.2	9.3	9.4	9.5	9.6
Variable	Non Ext	Non Ext	Non Ext	Non Ext	Non Ext	Non Ext
% > = 65	0.0298 (0)	0.0293 (0)	0.0300 (0)	0.0295 (0)	0.0296 (0)	0.0294 (0)
% Hispanic	-0.00057 (0.013)	X	0.0007 (0.0015)	X	-0.00034 (0.22)	-0.0010 (0.007)
% black	0.0015 (0)	0.0013 (0)	0.0016 (0)	0.0015 (0)	0.0015 (0)	0.0013 (0)
% other non w	X	-0.00115 (0.0003)	X	-0.0012 (0)	-0.0010 (0.009)	-0.00015 (0.59)
% college	-0.0027 (0)	-0.0025 (0)	-0.0026 (0)	-0.0024 (0)	-0.0024 (0)	-0.0025 (0)
% pop. change, 1960-1970	-0.0014 (0)	-0.0013 (0)	-0.0010 (0)	-0.0015 (0)	-0.0014 (0)	-0.0013 (0)
drinking water hardness	$-3x10^{-5}$ 0.18	$-3x10^{-5}$ (0.15)	$-3x10^{-5}$ (0.14)	$-3x10^{-5}$ (0.12)	$-3x10^{-5}$ (0.13)	$-3x10^{-5}$ (0.16)
cigarette sales (1970-80 av'g)	0.00035 (0.0002)	0.00028 (0.002)	0.00037 (0)	0.00030 (0.0006)	0.00032 (0.0004)	0.00029 (0.0019)
particulates ($TSP-ug/m^3$)	X	X	0.00028 (0.031)	0.00020 (0.070)	0.00026 (0.037)	X
$SO_4^=$ (ug/m^3)	0.0006 (0.55)	0.0007 (0.43)	X	X	X	0.00063 (0.49)
# observations	149	149	149	149	149	149
R^2	0.923	0.926	0.925	0.928	0.928	0.926
std error of estimate	0.0239	0.0233	0.0235	0.0230	0.0230	0.0233

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

gained), but made drastic changes for the pollution variables. $SO_4^=$ became highly nonsignificant and TSP became significant in two of the three cases. Table 10 shows that cardiovascular causes were associated with the same (non-pollution) variables; neither TSP nor $SO_4^=$ was significant; the TSP coefficients tended to be essentially zero. Drinking water hardness, which had been associated with reduced heart disease in some previous studies (Lacey, 1981), was highly non-significant with this model. TSP was a more significant contributor to COPD deaths in the log-linear model than in the linear model. In general, the elasticities for the log-linear models were higher, in addition to usually being more statistically significant. For example, for nonexternal mortality, the TSP elasticity increased from 0.023 to 0.043; for COPD, it increased from 0.22 to 0.25.

Regression Runs Employing Other Pollutants

Ozone. As discussed above, two separate sources of ozone data were utilized in this analysis. Peak 1-hr values were available for 1980 for 72 SMSAs (U.S. EPA, 1984), which were generally the largest SMSAs in the nation. These data represented the highest readings for each SMSA, and are not necessarily representative of average exposure across the entire SMSA. Seasonal average values were available for the entire data set, as obtained for a smooth isopleth map (Figure 8a), averaged over 1980-90 (McCurdy, 1992). Most of the analysis was conducted for the seasonal average data set, because of its completeness and the likelihood of better representing spatial averages across each SMSA. The correlation between the two ozone measures was 0.75.

Table 11 presents regression results for non-external mortality and estimated seasonal average ozone, using both linear and log-linear models. Ozone was only significant in the log-linear models (149 SMSAs), regardless of whether other pollutants were included. However, including ozone caused TSP to lose significance in both types of models. When both $SO_4^=$ and ozone were included in a linear model, neither was significant. Ozone was associated with deaths from cardiovascular causes but was not associated with COPD deaths (results not shown). Changing from linear to log-linear models caused the ozone elasticity for nonexternal mortality to increase from 0.026 to 0.057; for major cardiovascular causes, it increased from 0.033 (not significant) to 0.092 (significant).

The regression results for peak ozone were largely non-significant, for both linear and log-linear models, and for both non-external and major cardiovascular deaths. The results for log major cardiovascular deaths reached a p-value of 0.068, with an elasticity of about 0.035 (Regression 11.4). The results for this subset of 72 SMSAs using average ozone were slightly better, reaching p=0.047 and an elasticity of about 0.07 (Regression 11.6). However, this particular result was achieved with a non-optimum model, and it can be seen that in general the results for ozone set were somewhat sensitive to which socioeconomic variables were included in the model. Apparently, reducing the data set from 149 to 72 SMSAs had a major effect on the robustness of the ozone relationships. This precludes any firm conclusions as to what the findings might have been for peak ozone with the full complement of 149 locations.

Non-Sulfate TSP. TSP includes both sulfates and other types of particles, as collected (or formed) on glass-fiber filters used in high-volume samplers. Subtracting the sulfate portion is one way of accounting for some of the artifacts that may have been formed and of examining the largely insoluble portion of the catch. A composition midway between ammonium sulfate and ammonium bisulfate was assumed in making these computations; the new variable was labeled "NET TSP." Subtracting $SO_4^=$ from TSP made little difference in the results; significance declined slightly. When included with ozone in the same regression, there was little difference between the two TSP measures, indicating that the non-$SO_4^=$ portion may have been the most "active" portion. This was also true for COPD deaths, except that statistical significance improved when $SO_4^=$ was subtracted. As mentioned above, the negative dependence of COPD mortality on $SO_4^=$ is viewed as a non-causal regional artifact, and removal of this portion of TSP is tantamount to improving the precision of measurement.

TABLE 10

REGRESSION RESULTS FOR LOG-LINEAR MODELS
(Cardiovascular and COPD mortality)

Regression No.	10.1	10.2	10.3	10.4
Variable	MCV	MCV	COPD	COPD
% > = 65	0.0324 (0)	0.0323 (0)	0.0282 (0)	0.0286 (0)
% Hispanic	-0.0012 (0)	-0.0013 (0)	-0.0016 (0.14)	-0.0020 (0.06)
% black	0.0011 (0.0001)	0.0011 (0.0003)	-0.0033 (0.005)	-0.0031 (0.006)
% college	-0.0042 (0)	-0.0040 (0)	X	X
% population change 1980-1970	-0.0020 (0)	-0.0020 (0)	X	X
drinking water hardness	X	$-2x10^{-5}$ (0.80)	X	X
% poor	X	X	0.0089 (0.019)	0.0094 (0.012)
cigarette sales (1970-80 av'g)	0.00044 (0.0001)	0.00045 (0)	0.00086 (0.006)	0.00090 (0.003)
log population density	X	X	-0.051 (0.005)	-0.043 (0.02)
participants TSP (ug/m^3)	X	$9x10^{-5}$ (0.57)	0.00156 (0)	X
$SO_4^=$ (ug/m^3)	$1.6x10^{-5}$ (0.97)	X	X	X
TSP - $SO_4^=$ (ug/m^3)	X	X	X	0.00176 (0)
# observations	149	149	149	149
R^2	0.902	0.916	0.534	0.542
std error of estimate	0.0306	0.0298	0.081	0.080

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 11

REGRESSION RESULTS FOR OZONE
(Log-linear Model)

Regression No.	11.1	11.2	11.3	11.4	11.5	11.6	11.7	11.8
Variable	Non Ext	Non Ext	Non Ext	MCV	MCV	MCV	MCV	MCV
% > = 65	0.0265 (0)	0.0268 (0)	0.0294 (0)	0.0276 (0)	0.028 (0)	0.029 (0)	0.0281 (0)	0.0319 (0)
% Hispanic	X	X	-0.00035 (0.21)	X	-0.0004 (0.40)	-0.0003 (0.44)	X	-0.0008 (0.012)
% black	0.0012 (0.0006)	0.0012 (0.0006)	0.0013 (0)	0.0005 (0.21)	0.0009 (0.05)	0.00087 (0.05)	0.0005 (0.20)	0.00079 (0.002)
% other non w	-0.0014 (0)	-0.0013 (0)	-0.0009 (0.02)	-0.0019 (0)	X	X	-0.0018 (0)	-0.0014 (0.002)
% college	-0.008 (0.0001)	-0.0026 (0.0003)	-0.0025 (0)	-0.0045 (0)	-0.0052 (0)	-0.0048 (0)	-0.0043 (0)	-0.0037 (0)
% pop. change, 1980-1970	-0.004 (0)	-0.0015 (0)	-0.0014 (0)	-0.0019 (0)	-0.0020 (0)	-0.0021 (0)	-0.0020 (0)	-0.0020 (0)
drinking water hardness	-1.5×10^{-5} (0.72)	-1.8×10^{-5} (0.67)	-3×10^{-5} (0.12)	-3×10^{-5} (0.52)	-5×10^{-5} (0.37)	-5×10^{-5} (0.33)	-3×10^{-5} (0.47)	X
cigarette sales (1970-80 av'g)	0.0001 (0.42)	0.0001 (0.44)	0.00029 (0.0009)	0.0002 (0.24)	0.00042 (0.017)	0.00038 (0.27)	0.0002 (0.25)	0.00034 (0.0015)
peak ozone (ppm)	0.057 (0.21)	X	X	0.095 (0.07)	0.091 (0.16)	X	X	X
Avg ozone (ppm)	X	0.288 (0.22)	0.509 (0.014)	X	X	0.611 (0.047)	0.426 (0.11)	0.815 (0.0011)
# observations	72	72	149	72	72	72	72	149
R sq.	0.936	0.936	0.929	0.939	0.918	0.921	0.938	0.928
std error of estimate	0.022	0.022	0.023	0.025	0.029	0.029	0.025	0.028

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

Inhalable Particles (IP). Data were available on sulfates and on two size classifications of suspended particle concentrations, $PM_{2.5}$ and PM_{15}, for 63 locations. Initial regression runs showed Butte, MT, to be an outlier; it had the highest crude mortality rate in the data set, although it was not an outlier in the context of all 149 locations. Most of the regressions for IP pollutants were thus conducted with only 62 observations (excluding Butte), in an attempt to derive reasonably robust results.

Using the O&T model (Table 12), $SO_4^=$ was significant for n=62, but not when Butte was included (Regressions 12.1 and 12.2). The coefficients tended to be slightly higher than found for $SO_4^=$ measured on high-volume sampler filters. Fine particles ($PM_{2.5}$) were also significant, for both all-cause and external mortality, with a substantially lower coefficient. PM_{15} (inhalable particles) were not significant. These results also pertained to major cardiovascular diseases; for COPD, only PM_{15} was significant (Regression 12.13). We also note that the coefficient for "65+" appeared to be sensitive to the inclusion of the sulfate variable, which suggests interaction between socioeconomic and pollution variables with this model and data set.

With a log-linear version of the O&T model (Table 13), no pollutant was significant for all-cause mortality when Butte was included (Regressions 13.1 and 13.2), but sulfate was significant in both cases for non-external mortality (elasticity about 0.05). (We expect *a priori* that a log-linear model might be more tolerant of outliers than a linear model.) Fine particles had about the same elasticity as $SO_4^=$ but this pollutant did not achieve statistical significance for any of the cause of death groupings with Butte included. The coefficient and significance for COPD and PM_{15} were also reduced with Butte included (Regression 13.8).

The results for an expanded model specification and IP pollutants are given in Table 14, for linear models. No pollutant achieved statistical significance, but $PM_{2.5}$ was close for non-external deaths (Regression 14.1, elasticity = 0.043). The elasticities for sulfate and PM_{15} were 0.02 and 0.027, respectively. Note that the results were considerably less significant for MCV, whereas an improvement was expected due to consideration of a specific cause-of-death category.

It is also interesting to compare findings for the two sulfate measures and for fine particles. The hypothesis advanced by Ozkaynak and Thurston (1987) is that the $SO_4^=$ ion is the "active" ingredient in the particle mix. As discussed above, we expect that SAROAD sulfate consists of a mixture of airborne sulfate and $SO_4^=$ particles formed on the filters, hence the substantially higher mean values with respect to [IP] $SO_4^=$ (obtained from unreactive Teflon filters). If this were the case, we would expect to find the same regression coefficient in all three cases, according to O&T's hypothesis that only $SO_4^=$ affects mortality. However, we find that, while both sulfate variables yield approximately the same coefficient (but not the same elasticities, since the mean values differ), the coefficient for all fine particles (which includes $SO_4^=$), is substantially lower, with about the same or higher elasticity. This implies that there is nothing special about the sulfate portion of fine particles and that all three variables should be considered as indicators of fine particles.

Similar considerations apply to the comparisons of COPD regression coefficients for TSP, PM_{15}, and $PM_{2.5}$. For the purpose of exploring COPD relationships further, a new fine-particle variable was defined ("non-S $PM_{2.5}$") by subtracting the sulfate portion in the same manner as NET TSP (described above). This implicitly assumes that all of the sulfate is in the fine particle mode, which is usually the case. If only a specific fraction of particles were biologically active, say the small particles, we would expect to see the same regression coefficient for all three measures. The results are as follows:

TABLE 12

MULTIPLE REGRESSION RESULTS FOR THE O&T MODEL WITH IP DATA

Regression No.	12.1	12.2	12.3	12.4	12.5	12.6	12.7
Variable	All Causes	All Causes	All Causes	All Causes	Non Ext	Non Ext	Non Ext
% > = 65	0.388 (0)	0.328 (0)	0.313 (0)	0.287 (0)	0.348 (0)	0.329 (0)	0.298 (0)
% median age	0.228 (0.02)	0.241 (0.0007)	0.265 (.0002)	0.288 (0)	0.204 (0)	0.233 (0.0011)	0.260 (0.0004)
% nonwhite	0.0162 (0.26)	0.0124 (0.22)	0.0156 (0.12)	0.0210 (0.04)	0.0018 (0.85)	0.0057 (0.58)	0.0117 (0.27)
% college	-0.0927 (0.0005)	-0.0877 (0)	-0.094 (0)	-0.118 (0)	-0.079 (0)	-0.087 (0)	-0.114 (0)
% poor	-0.016 (0.71)	-0.0008 (0.96)	-0.0053 (0.86)	-0.0184 (0.57)	-0.0016 (0.94)	-0.0040 (0.89)	-0.018 (0.58)
log population density	-0.034 (0.86)	0.116 (0.43)	0.170 (0.24)	0.197 (0.19)	0.384 (0.018)	0.413 (0.005)	0.443 (0.004)
IP-SO_4 (ug/m^3)	0.0568 (0.23)	0.0819 (0.013)	X	X	0.0973 (0.003)	X	X
PM-2.5 (ug/m^3)	X	X	0.0252 (0.043)	X	X	0.0293 (0.02)	X
PM-15 (ug/m^3)	X	X	X	-0.0029 (0.60)	X	X	-0.0026 (0.65)
# observations	63	62	62	62	62	62	62
R sq.	0.870	0.923	0.920	0.915	0.925	0.921	0.914
std error of estimate	0.642	0.455	0.463	0.479	0.454	0.467	0.489

TABLE 12 (cont'd)

MULTIPLE REGRESSION RESULTS
FOR THE O&T MODEL WITH IP DATA

Regression No.	12.8	12.9	12.10	12.11	12.12	12.13
Variable	MCV	MCV	MCV	COPD	COPD	COPD
% > = 65	0.194 (0)	0.186 (0)	0.168 (0.0002)	0.0160 (0.014)	0.0182 (0.005)	0.0184 (0.003)
% median age	0.108 (0.028)	0.122 (0.012)	0.137 (0.0055)	0.0072 (0.32)	0.0045 (0.54)	0.0050 (0.47)
% nonwhite	-0.0064 (0.36)	-0.0046 (0.52)	-0.0003 (0.95)	-0.0016 (0.11)	-0.0020 (0.047)	-0.0025 (0.01)
% college	-0.066 (0)	-0.069 (0)	-0.088 (0)	0.0012 (0.52)	0.0026 (0.17)	0.0042 (0.011)
% poor	-0.017 (0.43)	-0.019 (0.36)	-0.029 (0.17)	0.0060 (0.049)	0.0067 (0.029)	0.0079 (0.008)
log population density	0.364 (0.0004)	0.40 (0)	0.41 (0)	-0.040 (0.006)	-0.045 (0.002)	-0.043 (0.002)
IP-SO_4 (ug/m^3)	0.0530 (0.02)	X	X	-0.0051 (0.13)	X	X
PM-2.5 (ug/m^3)	X	0.0177 (0.04)	X	X	-0.0004 (0.76)	X
PM-15 (ug/m^3)	X	X	-0.0032 (0.40)	X	X	0.0011 (0.045)
# observations	62	62	62	62	62	62
R sq.	0.901	0.907	0.901	0.648	0.633	0.658
std error of estimate	0.329	0.319	0.329	0.046	0.047	0.045

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 13

MULTIPLE REGRESSION RESULTS FOR THE O&T MODEL
(log-linear) WITH IP DATA

Regression No.	13.1	13.2	13.3	13.4	13.5	13.6	13.7	13.8
Variable	All Causes	All Causes	Non Ext	Non Ext	Non Ext	MCV	MCV	COPD
% > = 65	0.0196 (0)	0.0185 (0)	0.0229 (0)	0.0208 (0)	0.0216 (0)	0.0266 (0)	0.0255 (0)	0.0249 (0)
% median age	0.0115 (0.027)	0.0129 (0.012)	0.0098 (0.079)	0.0102 (0.042)	0.0117 (0.036)	0.0072 (0.30)	0.0089 (0.20)	0.0153 (0.19)
% nonwhite	0.0013 (0.08)	0.0015 (0.04)	0.0008 (0.30)	0.0007 (0.34)	0.0011 (0.036)	0.0003 (0.75)	0.0005 (0.58)	-0.0041 (0.016)
% college	-0.0052 (0.0002)	-0.0058 (0)	-0.0052 (0.0005)	-0.0050 (0.0002)	-0.0059 (0)	-0.0079 (0)	-0.0084 (0)	0.0046 (0.10)
% poor	-0.0002 (0.32)	-0.0026 (0.25)	-0.0024 (0.32)	-0.0018 (0.39)	-0.0028 (0.24)	-0.0056 (0.055)	-.0060 (0.04)	0.0107 (0.03)
log population density	-0.0046 (0.67)	-0.0017 (0.87)	0.0087 (0.45)	0.014 (0.18)	0.0126 (0.27)	0.028 (0.046)	0.032 (.022)	-0.084 (0.0005)
IP-SO_4 (ug/m^3)	0.0036 (0.14)	X	0.0050 (0.05)	0.0059 (0.011)	X	0.0053 (0.10)	X	X
PM-2.5 (ug/m^3)	X	0.00071 (0.43)	X	X	0.0011 (0.24)	X	0.0015 (0.23)	X
PM-15 (ug/m^3)	X	X	X	X	X	X	X	0.00137 (0.12)
# observations	63	63	63	62	63	63	63	63
R sq.	0.864	0.860	0.870	0.886	0.864	0.857	0.853	0.662
std error of estimate	0.0334	0.0340	0.036	0.032	0.036	0.045	0.045	0.078

Values in this table are regression coefficients
( ) indicates probability that the true value is zero
X indicates the variable was not included

TABLE 14
REGRESSION RESULTS FOR THE COMPLETE MODEL WITH IP DATA
(n = 62, Butte deleted)

Regression No.	14.1	14.2	14.3	14.4	14.5	14.6	14.7	14.8
Variable	Non Ext	Non Ext	Non Ext	MCV	MCV	MCV	COPD	COPD
% > = 65	0.504 (0)	0.497 (0)	0.496 (0)	0.273 (0)	0.268 (0)	0.268 (0)	0.0228 (0)	0.0221 (0)
% Hispanic	-0.012 (0.37)	-0.013 (0.32)	-0.0142 (0.29)	-0.0125 (0.17)	-0.0013 (0.14)	-0.0014 (0.14)	X	X
% black	0.0186 (0.08)	0.0165 (0.15)	0.0192 (0.075)	0.0006 (0.92)	0.0048 (0.94)	0.0014 (0.85)	-0.0018 (0.013)	-0.0026 (0.001)
% other non w	0.014 (0.59)	0.014 (0.60)	0.011 (0.67)	0.0077 (0.67)	0.0077 (0.67)	0.0071 (0.70)	X	X
% college	-0.056 (0.0008)	-0.060 (0.0004)	-0.060 (0.0003)	-0.051 (0)	-0.055 (0)	-0.055 (0)	0.0011 (0.49)	0.0021 (0.20)
% pop. change, 1980-1970	-0.020 (0)	-0.020 (0)	-0.022 (0)	-0.014 (0)	-0.014 (0)	-0.015 (0)	0.0007 (0.15)	0.0004 (0.40)
drinking water hardness	-0.0011 (0.14)	-0.0010 (0.20)	-0.0011 (0.14)	-0.00035 (0.49)	-0.0003 (0.55)	-0.0003 (0.50)	X	X
% poor	0.0079 (.78)	0.0092 (0.76)	0.012 (0.69)	~0 (0.98)	~0 (0.98)	0.0005 (0.96)	X	0.0051 (0.03)
cigarette sales (1970-80 avg)	0.0036 (0.14)	0.0038 (0.13)	0.0043 (0.079)	0.0029 (0.086)	0.0031 (0.07)	0.0033 (0.051)	~0 (0.82)	0.0012 (0.67)
heating degree days	$3.7x10^{-5}$ (0.45)	$2.6x10^{-5}$ (0.60)	$3x10^{-5}$ (0.56)	$2x10^{-5}$ (0.72)	$1x10^{-5}$ (0.74)	$1x10^{-5}$ (0.72)	X	X
log population density	0.15 (0.27)	0.15 (0.28)	0.17 (0.21)	0.22 (0.020)	0.22 (0.02)	0.23 (0.015)	-0.029 (0.058)	-0.032 (0.04)
PM-2.5 (ug/m^3)	0.0188 (0.078)	X	X	0.010 (0.18)	X	X	X	X
IP-SO_4 (ug/m^3)	X	0.0356 (0.26)	X	X	0.0112 (0.61)	X	X	X
PM-15 (ug/m^3)	X	X	0.0056 (0.23)	X	X	0.00148 (0.65)	0.00056 (0.28)	X
Non-S PM-2.5 (ug/m^3)	X	X	X	X	X	X	X	0.0008 (0.54)
# observations	62	62	62	62	62	62	62	62
R^2	0.953	0.952	0.952	0.944	0.942	0.942	0.661	0.683
std error of estimate	0.378	0.384	0.384	0.260	0.264	0.264	0.045	0.044

TABLE 15

REGRESSION RESULTS FOR COMBINATIONS OF POLLUTANTS INCLUDING MANGANESE

Regression No.	15.1	15.2	15.3	15.4	15.5	15.6	15.7
Variable	Non Ext	Non Ext	Non Ext	Non Ext	MCV	MCV	MCV
% > = 65	0.522 (0)	0.532 (0)	0.535 (0)	0.537 (0)	0.301 (0)	0.303 (0)	0.301 (0)
% Hispanic	-0.0051 (0.41)	X	X	X	X	X	X
% black	0.018 (0.016)	0.0238 (0)	0.0220 (0)	0.0225 (0)	0.0062 (0.028)	0.0050 (0.09)	0.0045 (0.14)
% other non w	-0.0082 (0.29)	X	X	X	X	X	X
% college	-0.037 (0.0003)	-0.038 (0)	-0.033 (0.0012)	-0.033 (0.0017)	-0.036 (0)	-0.033 (0)	- 0.034 (0)
% pop. change, 1980-1970	-0.0218 (0)	-0.024 (0)	-0.0223 (0)	-0.0227 (0)	-0.0189 (0)	-0.0178 (0)	-0.0172 (0)
drinking water hardness	-0.00093 (0.022)	-0.0010 (0.013)	-0.0010 (0.016)	-0.0010 (0.017)	-0.0006 (0.035)	-0.0005 (0.059)	-0.0005 (0.058)
% poor	0.020 (0.34)	X	X	X	X	X	X
cigarette sales (1970-80 av'g)	0.0042 (0.013)	0.0045 (0.004)	0.0041 (0.009)	0.0042 (0.0095)	0.0030 (0.005)	0.0027 (0.011)	0.0026 (0.014)
heating degree days	$4x10^{-6}$ (0.90)	X	X	X	X	X	X
log population density	0.0156 (0.88)	-0.079 (0.44)	-0.111 (0.29)	-0.111 (0.29)	-0.044 (0.56)	-0.062 (0.38)	-0.063 (0.38)
particulate (ug/m^3)	X	X	X	0.0014 (0.56)	X	X	-0.0018 (0.26)
SO_4 (ug/m^3)	X	X	0.022 (0.18)	0.022 (0.19)	X	0.0149 (0.19)	0.0149 (0.19)
manganese (ug/m^3)	2.36 (0.10)	2.53 (0.07)	2.06 (0.16)	1.76 (0.26)	1.49 (0.12)	1.17 (0.24)	1.56 (0.14)
# observations	138	138	138	138	138	138	138
R^2	0.925	0.922	0.923	0.924	0.911	0.913	0.913
std error of estimate	0.409	0.408	0.407	0.408	0.277	0.276	0.276

Regression No.	Model	Variable	Coefficient	Significance
5.4	O&T	TSP	0.0008	0.003
6.6	Complete	TSP	0.00084	0.0006
8.4	Parsimonious	TSP	0.00074	0.007
12.13	O&T	PM_{15}	0.0011	0.045
14.7	Parsimonious	PM_{15}	0.00056	0.28
12.12	O&T	$PM_{2.5}$	-0.0004	0.76
14.8	Parsimonious	Non-S $PM_{2.5}$	0.00084	0.54

We find that TSP and PM_{15} have the same coefficients, within statistical tolerances, but that $PM_{2.5}$ is different. However, removing the sulfate portion of $PM_{2.5}$ (as described above) brings the non-sulfate $PM_{2.5}$ coefficient effectively into this common range of coefficient values (0.0006-0.0011). This implies that all of these particle measures exhibit the same effect on mortality per unit of mass, and since the only particles common to all of them are the non-sulfate fine particles, we are led to the conclusion that this may be the "biologically-active" fraction.

This comparison would be more compelling if the particle variables other than TSP were also statistically significant. The poor performance of these other variables may relate in part to the smaller numbers of observations available for analysis or the fact that not all of the observations were taken in 1980. However, if we accept the hypothesis that only the small non-sulfate particles are biologically active, then the elasticity should be computed by multiplying the coefficient by the mean value of the non-S $PM_{2.5}$ variable (12.6 ug/m^3), which would constitute a major reduction in the estimated effect upon mortality. This would also apply to time series studies. For example, Dockery *et al.* [in press] derived similar coefficients for PM_{10} and $PM_{2.5}$ in St. Louis; however, only the PM_{10} value was statistically significant (Table 1). Neither $SO_4^=$ nor H^+ came even close to statistical significance in that time-series study.

It thus appears from the above considerations that the magnitude of the indicated effects on mortality cannot be estimated with confidence for a pollutant with many constituents (such as TSP or total oxidants) until the biologically active components of the pollutant have been identified. The regression coefficient may still be a valid measure of relative changes, but it will not be possible to apply this slope to contributions from specific pollution source categories without knowledge of the "active ingredients" of the TSP mix.

Manganese. In previous studies, iron (Fe) and manganese (Mn) have been found to be significant predictors of spatial variations in mortality (Lipfert, 1978; Lipfert, 1984; Lipfert *et al.*, 1988). However, these species are also markers for ferrous metal manufacturing activities, which may have other associations with health, either directly because of occupational hazards or indirectly because of life-style differences. For example, Brackbill *et al.*, (1988) found that the metal industries were among the highest in terms of percentages of smokers. Lipfert (1984) found that Mn was only significant for males (65+), which suggests long-term occupational effects rather than community air pollution.

Table 15 presents regressions for Mn, as the sole "pollutant" and in combination with $SO_4^=$ and TSP, for the maximum possible data set of 138 locations. Mn was never statistically significant, although it was close for non-external deaths, and its regression coefficient was about 1/4 of that found for 1980 mortality in U.S. cities (Lipfert *et al.*, 1988). This suggests that the effects of Mn, whatever they may be, are experienced more in central cities than in the entire SMSAs (which are often largely suburbs), since the measurements for metals are usually made in central locations. Comparing Tables 15 and 7 shows only minor interactions between other pollutants and Mn, when entered in combination.

Dose-Response Functions

Two types of models have been used in this regression analysis: linear models, which assume a straight-line relationship between mortality and all other variables (including air pollution), and log-linear models, which assume that mortality rates rise exponentially in response to (all of) the independent variables. In either case is a threshold are considered for ambient air quality; the models assume that the type of relationship is independent of the absolute level of air pollution.

This is in contrast to the current philosophy of air pollution control, which assumes that safe concentration levels exist for most community air pollutants, below which health effects are essentially zero. These "no-effect" thresholds and an appropriate margin of safety are then used to establish National Ambient Air Quality Standards (NAAQS), which are to be met throughout the country by controlling the responsible air pollutant emissions. It is thus important to try to reconcile the results of this study with this prevailing concept of NAAQS and the corresponding no-effect thresholds. An important consideration in this regard is the extent to which a few SMSAs with poor air quality, in violation of the NAAQS, may influence the outcomes of these regression models. Three different types of analysis were performed towards this end; these analyses were limited to the parsimonious log-linear models.

Scatter Plots. The first technique involved scatter plots in which an "adjusted" or residual value of mortality was computed, accounting for all variables in the regression equation other than air pollution. These values were then plotted against each of the pollutants in turn, in order to display which, if any, locations might be influential with regard to the regression slopes. Figures 9 to 11 present such plots for the log of non-external mortality. Against SAROAD sulfate, Figure 9, no relationship is seen, in keeping with the non-significant regression slope. The lowest "adjusted" mortality cities (Honolulu and Tampa), have measured sulfate values in the mid-range, and the scatter of the remaining cities is spread more-or-less uniformly across the entire range of $SO_4^=$ values. Figure 9 is in sharp contrast with Figure 1 of Ozkaynak and Thurston, in which crude mortality was plotted against sulfate and a strong relationship was apparent. The implication of this comparison is that the apparent association between mortality and sulfate displayed by Ozkaynak and Thurston appears to have been a relationship between sulfate and all the other socioeconomic variables that also affect longevity.

Figure 10 plots the residual mortality data against SMSA-averaged TSP. A weak relationship is seen, in part because the lowest mortality SMSAs also have low TSP; however, there are also low-TSP locations with high mortality residuals, but there are no high-TSP locations with low mortality residuals. In that sense, the high TSP locations might be influential.

Average ozone levels are used in Figure 11; ozone has the strongest pollution-mortality association of the three pollutants considered in this regression. The Honolulu and Southern California points would appear to be influential and since all of these locations have racial/ethnic populations that differ from most of the rest of the country, correct handling of these variables would seem to be important.

Additional scatter plots for non-external mortality and the various other pollutants which were available in the data base are presented in Appendix B.

Logarithmic residuals for cardiovascular mortality are plotted against average ozone in Figure 12 and peak ozone in Figure 13. In Figure 12, the two highest ozone cities are Los Angeles and San Bernadino; the two largest positive residuals (cardiovascular mortality higher than predicted) are Columbia, SC, and Atlantic City, NJ, neither of which has any known attributes that might explain their relatively high MCV mortality. Note that a log residual of 0.1 corresponds to about 25% excess mortality. The dose-response relationship shown in Figure 13 for peak ozone consists of a cloud of data around the ozone NAAQS (0.12 ppm) and a few higher and lower points that form the basis for the nearly significant ($p = 0.07$) association. The four highest residuals in the data cloud are Orlando, FL, Austin, TX, Jersey City, NJ, and New York City.

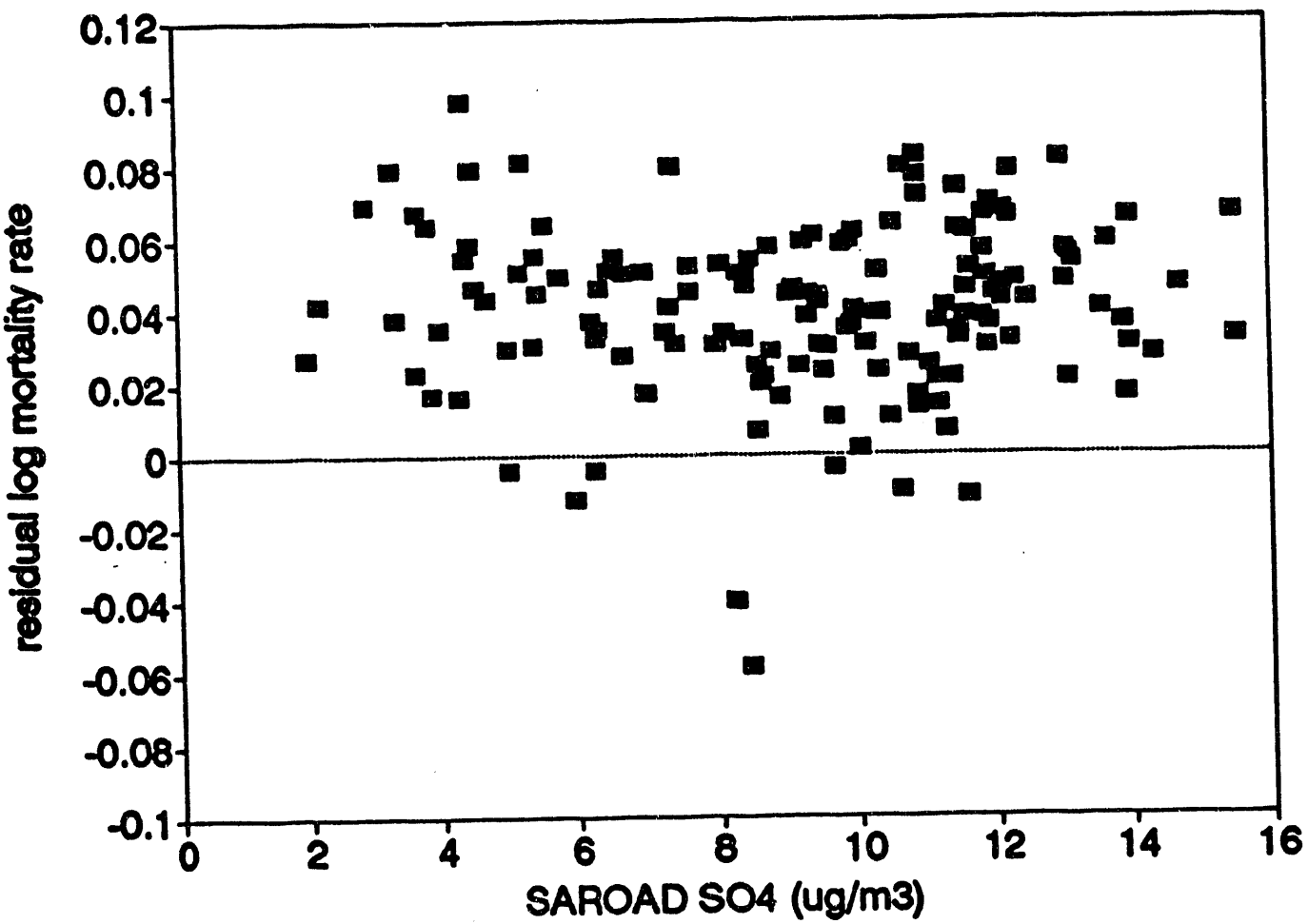

Figure 9. Scatter plot of residual log non-external mortality rates vs. [TSP] $SO_4^=$.

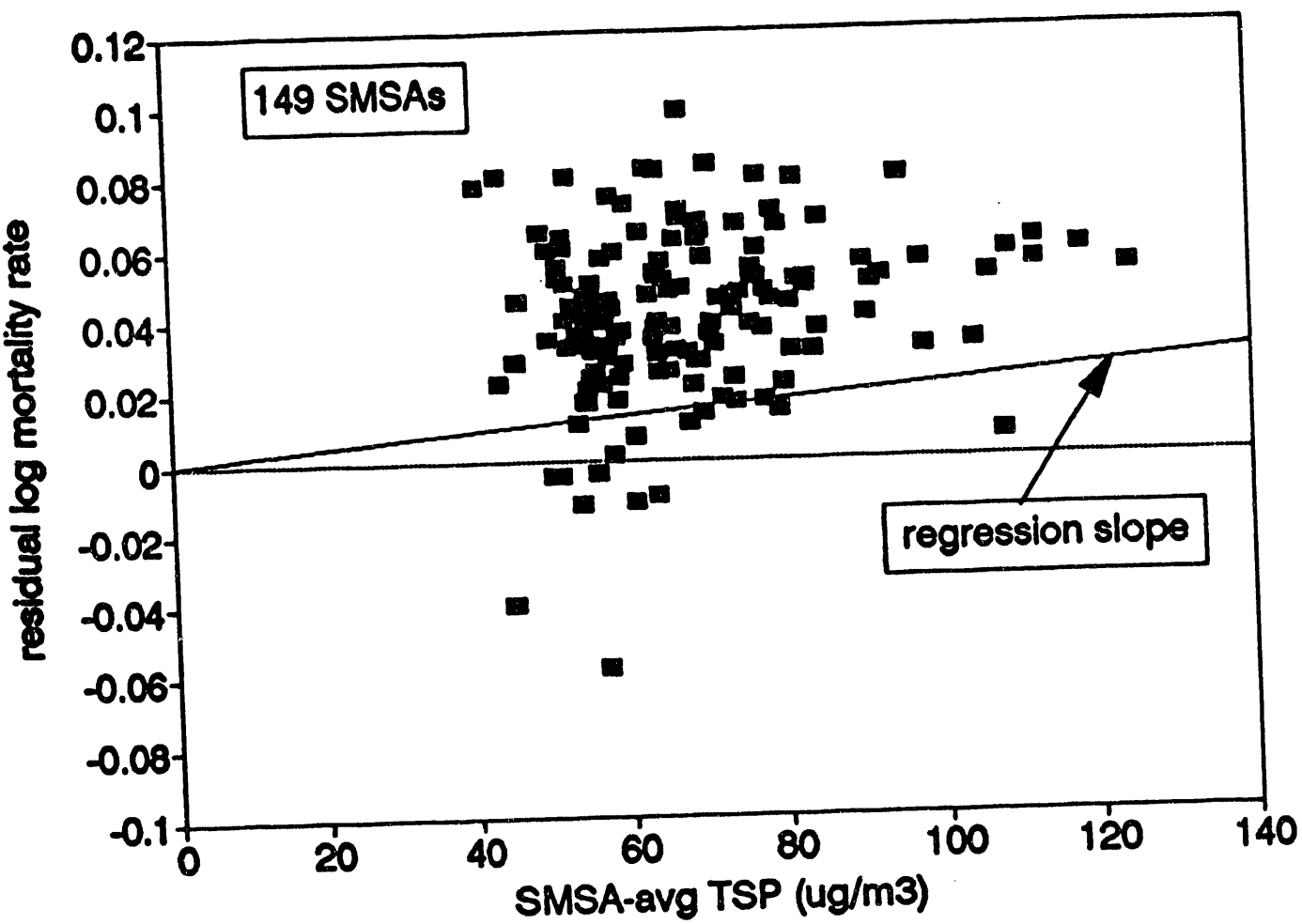

Figure 10. Scatter plot of residual log non-external mortality rates vs. TSP.

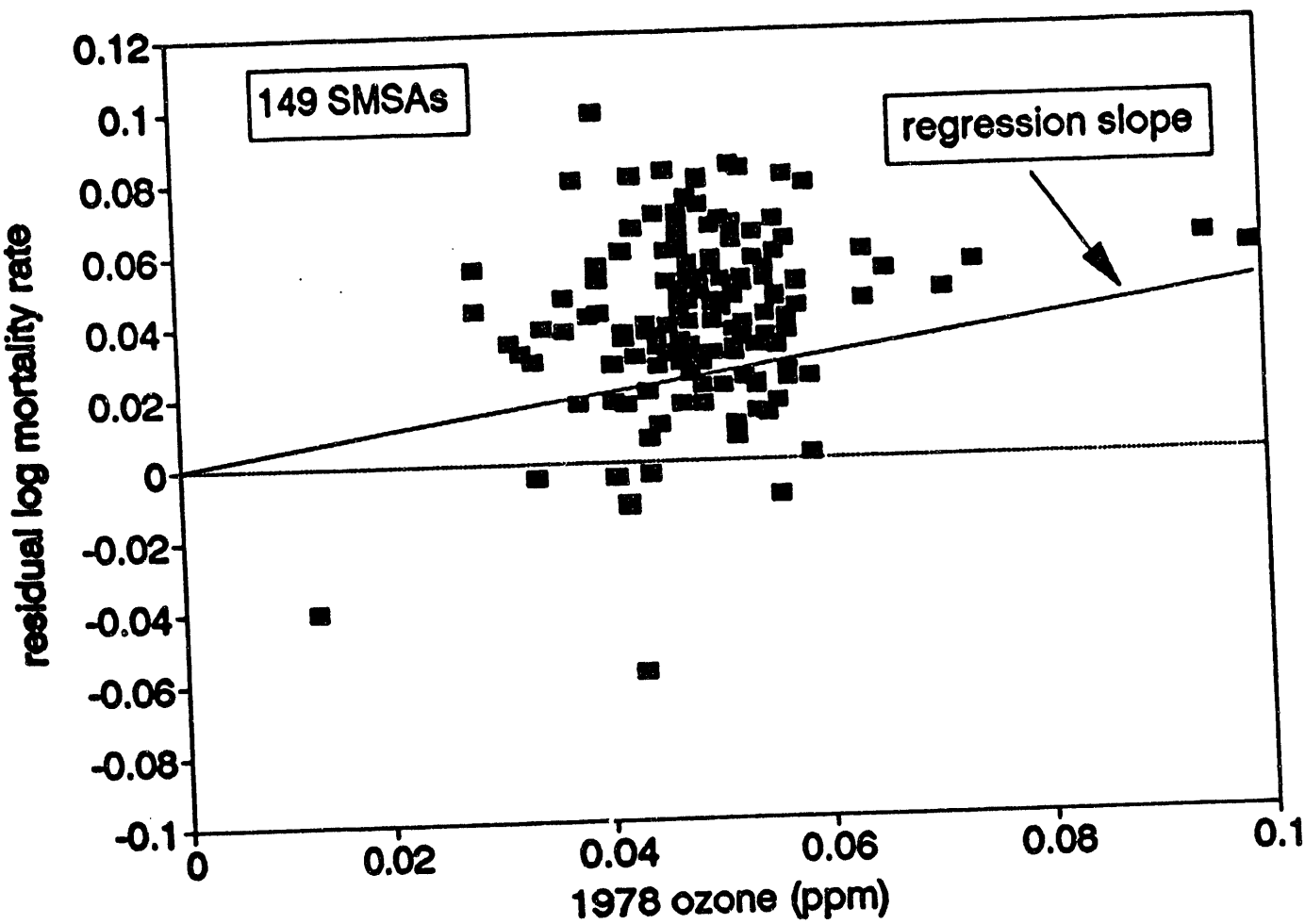

Figure 11. Scatter plot of residual log non-external mortality rates vs. average ozone.

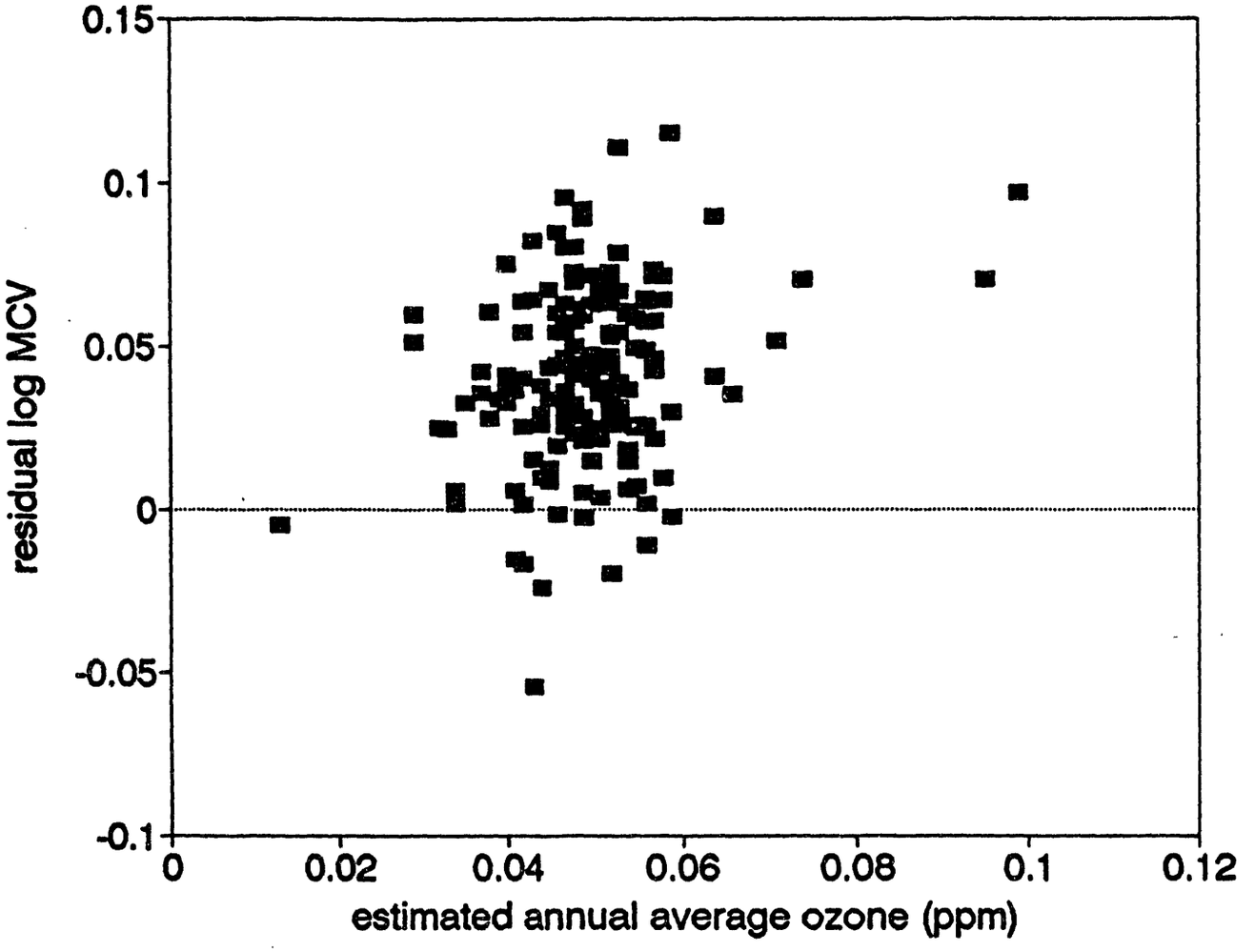

Figure 12. Scatter plot of residual log major cardiovascular mortality rates vs. average ozone.

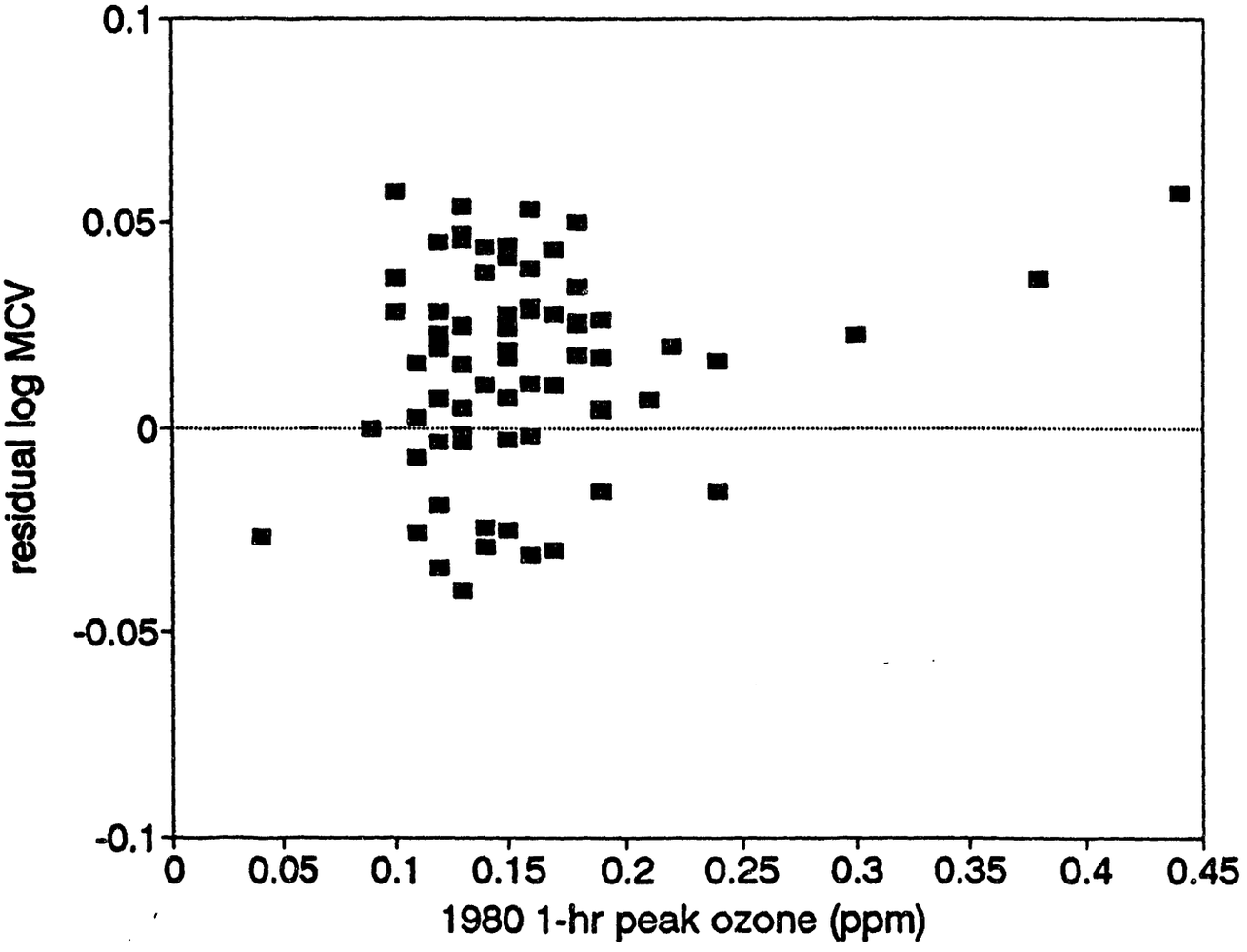

Figure 13. Scatter plot of residual log major cardiovascular mortality rates vs. peak ozone (72 SMSAs).

It seems clear that many more observations with both higher and lower peak ozone values would be required to clarify this relationship.

COPD mortality is considered in Figure 14; three high residuals (Butte, MT, Tucson, AZ, and Albuquerque, NM) are seen to be influential, although the bulk of the data support a positive relationship. Explanations for the three high residuals include the mining industry in Butte and the likelihood of retirees in the Southwest with existing lung disease; deleting these three observations increased the TSP coefficient slightly. The highest TSP point is Spokane, WA, which may have been influenced by the eruption of Mt. St. Helens; this datum is not remarkable, given the general trend and level of scatter.

Successive Truncation. The next technique involved dropping groups of the highest pollution locations from the analysis, thus reducing both the range of the independent variable and the number of observations. These results are presented in Figures 15 to 20, for non-external mortality and one pollutant at a time.

For TSP and non-external mortality (Figure 15), the regression coefficient remains essentially constant for data sets with maximum TSP values from about 80 to 140 ug/m^3. The frequency distribution of TSP in this data set is given in Figure 16; 109 of the 149 SMSAs have average TSP levels within the former NAAQS for TSP (75 ug/m^3). As seen in Figure 17, the standard errors of the regression coefficient increase monotonically as the number of observations decreases; this square-root relationship is as expected from statistical theory. Thus, one may conclude that the mortality-TSP relationship is not dominated by a few high TSP cities, and that a coefficient of about 0.0003 is the best unbiased estimate for data sets having maximum TSP locations from about 80 ug/m^3 upward (SMSA averages). Below this value, this type of analysis is indeterminate.

Similar data are presented for (average) ozone in Figure 18. The regression coefficient is essentially constant for all but the smallest data set considered (n = 40). However, the frequency distribution for average ozone is substantially skewed (Figure 19); only seven SMSAs exceed 0.06 ppm. Figure 8b showed that most of the SMSAs were in violation of the 1-hr standard in 1980. The standard error of the ozone-mortality coefficient decreased monotonically with the number of observations, as with TSP, but adding the last few high-ozone observations resulted in a disproportionate decrease in the standard error (Figure 20). The regression coefficients themselves were not affected, however (Figure 18).

COPD mortality is addressed in Figure 21; as the high TSP locations are removed from the data set, the regression coefficient increases in value (but not statistically significantly so, because of the widening confidence limits) down to about 65 ug/m^3, at which point it becomes negative and the confidence limits expand greatly. This TSP level probably corresponds to the removal (by truncation) of the lowest of the three high residual points seen on Figure 14.

Quintile Analysis. The final technique employed a dummy variable technique similar to that used by Schwartz and Dockery (1992a,b). New regressions were run in which the continuous pollutant variable was replaced by n-1 dummy variables, where n=5 for the case in which the entire data set is subdivided into quintiles based on ranked TSP values. The regression coefficient for each dummy variable represents the best unbiased estimate of the logarithm of mortality for that quintile relative to the lowest TSP quintile (controlling for all other variables). When these values are plotted against the corresponding TSP values for each quintile, a rudimentary dose-response function results. One expects some loss of statistical significance with such an analysis, since the effect of the continuous variable is now being indicated by four different variables. The advantages of this approach are that linearity is not assumed *a priori*, and that the entire data set is considered at once.

Figure 22 presents results for ozone and non-external and cardiovascular mortality. Slight variations in the non-pollution variables were exercised to determine sensitivity of the new

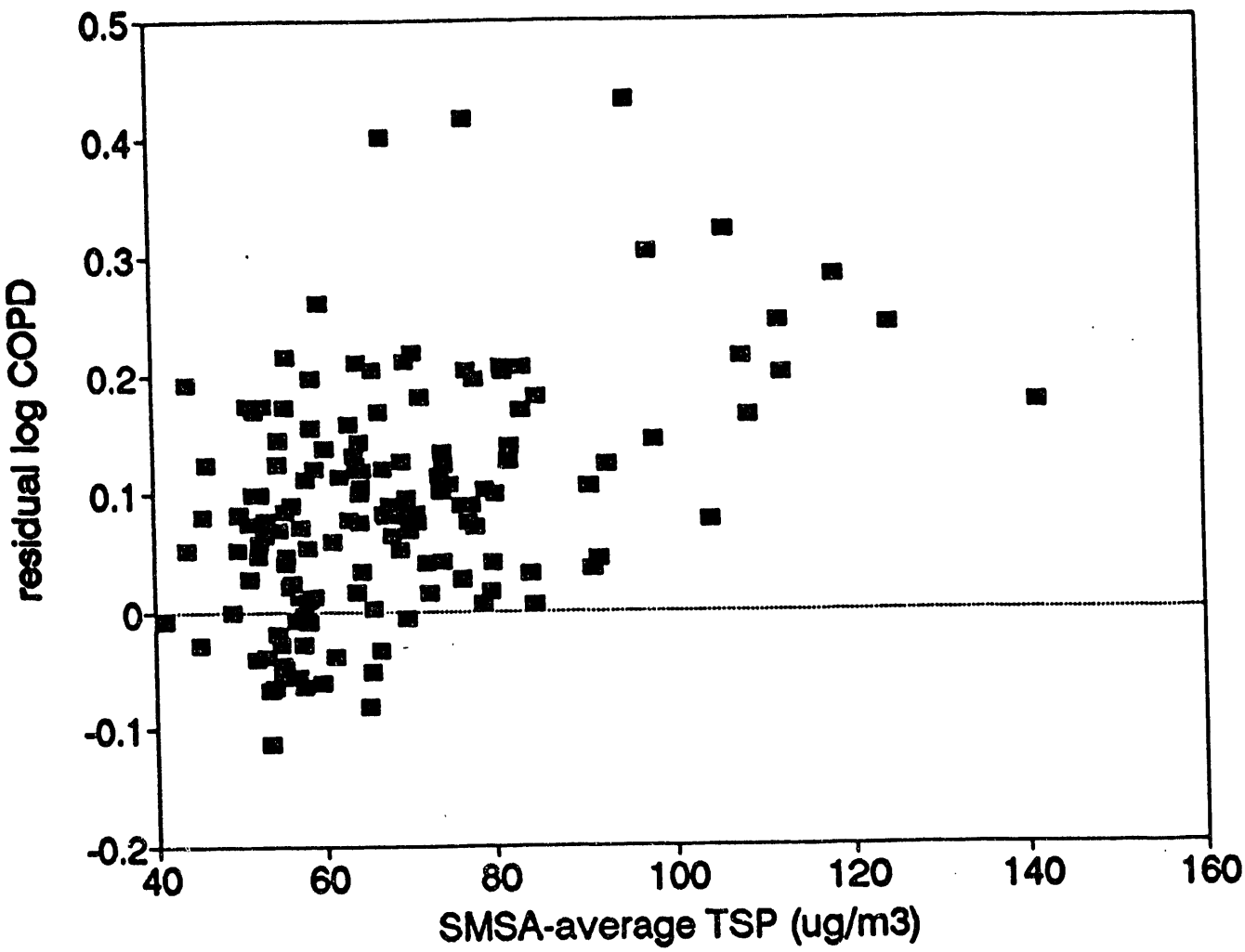

Figure 14. Scatter plot of residual log COPD cardiovascular mortality rates vs. TSP.

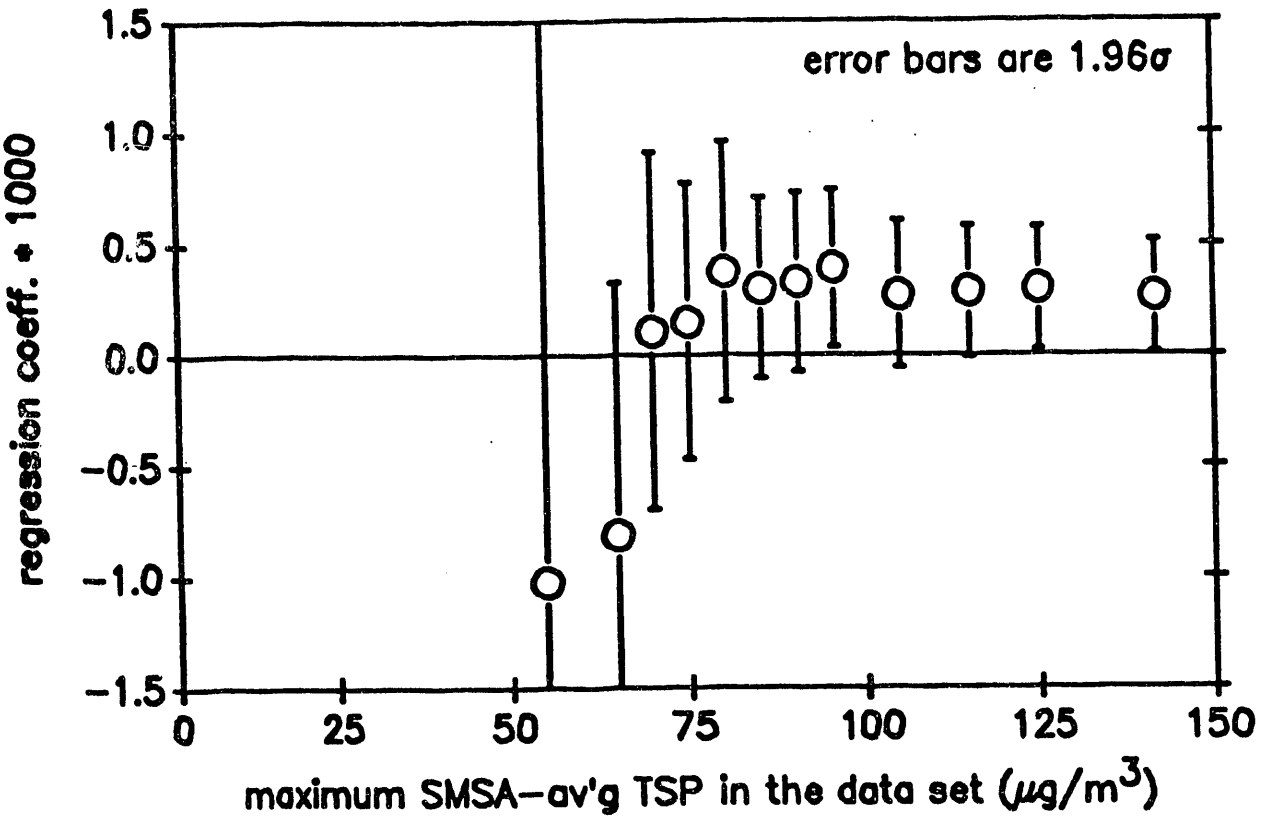

Figure 15. Regression coefficients for log non-external mortality on TSP for successively smaller data sets, after deleting TSP values higher than the values plotted.

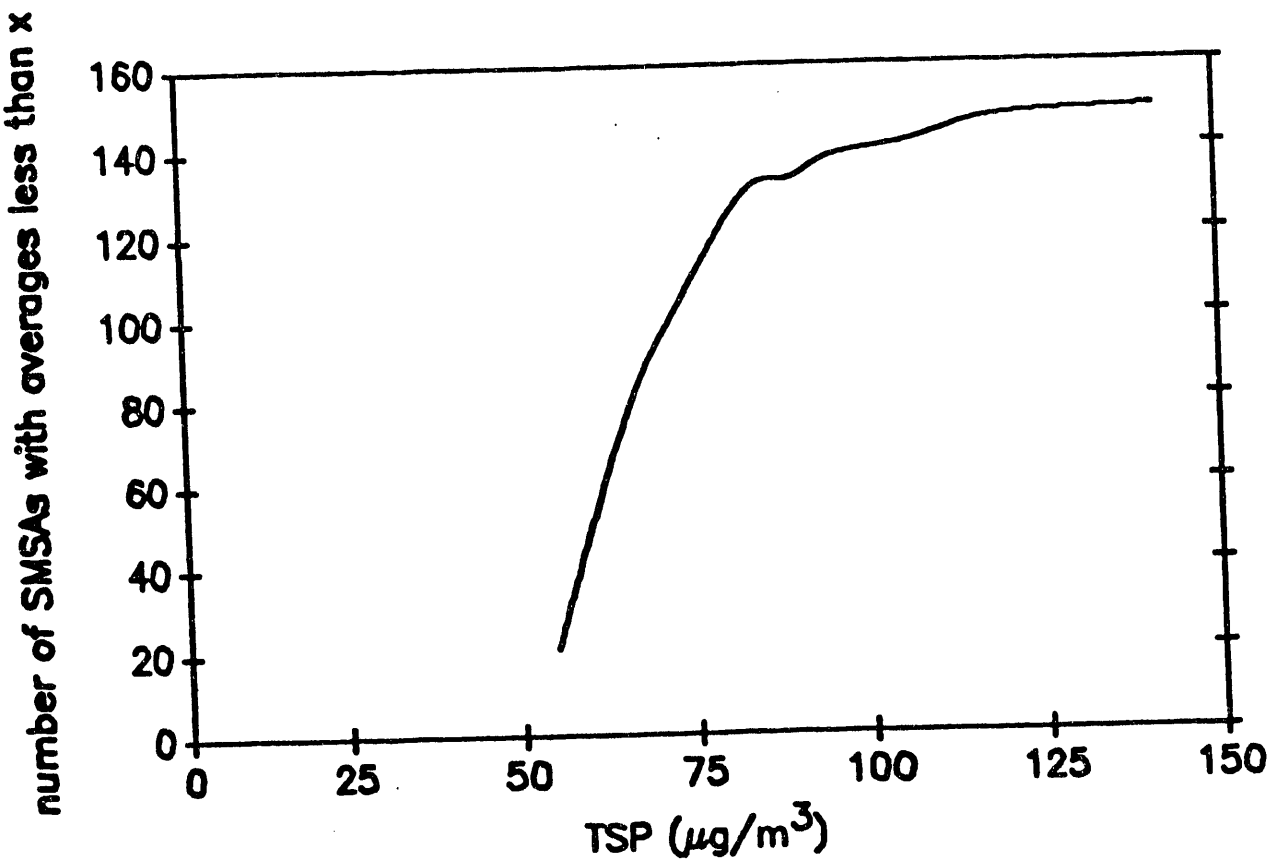

Figure 16. Frequency distribution of 1980 average TSP for 149 SMSAs.

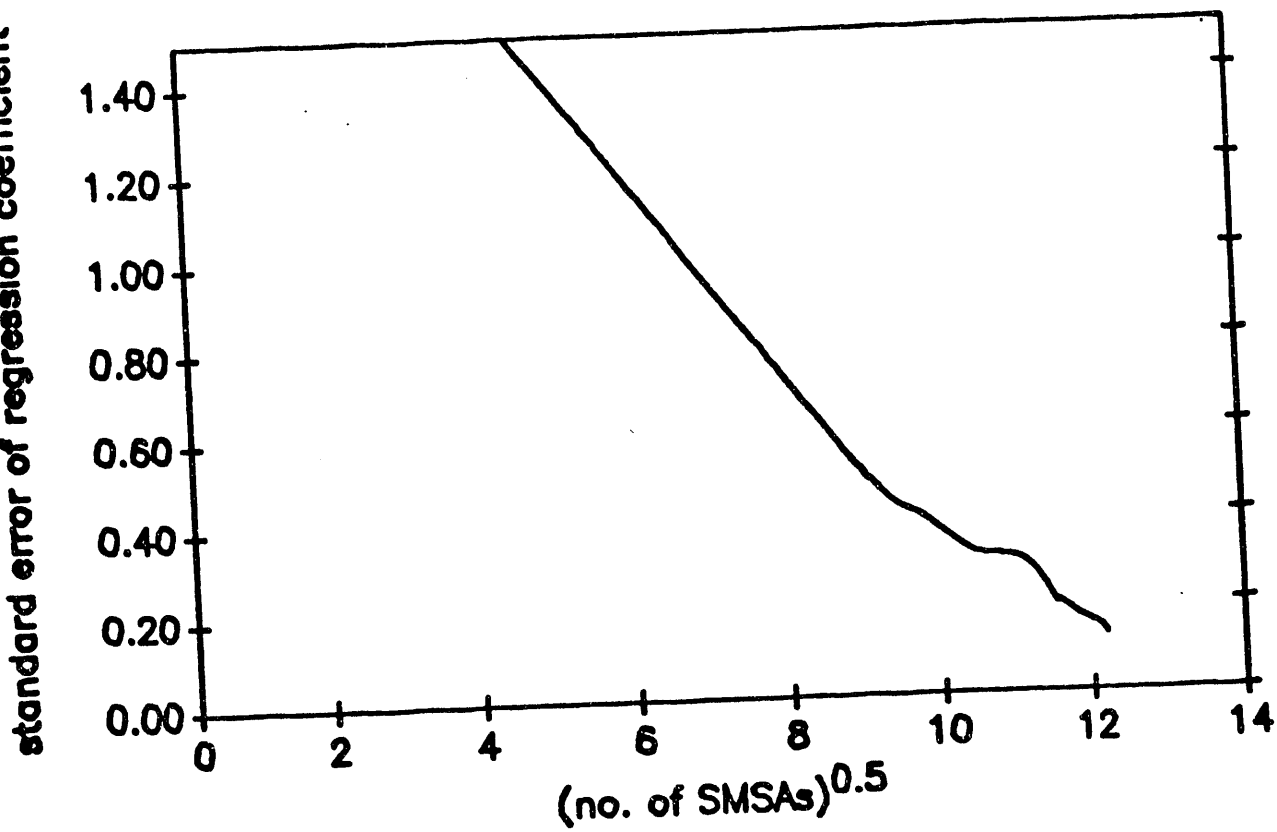

Figure 17. Standard errors of regression coefficients in Figure 15 vs. number of remaining observations.

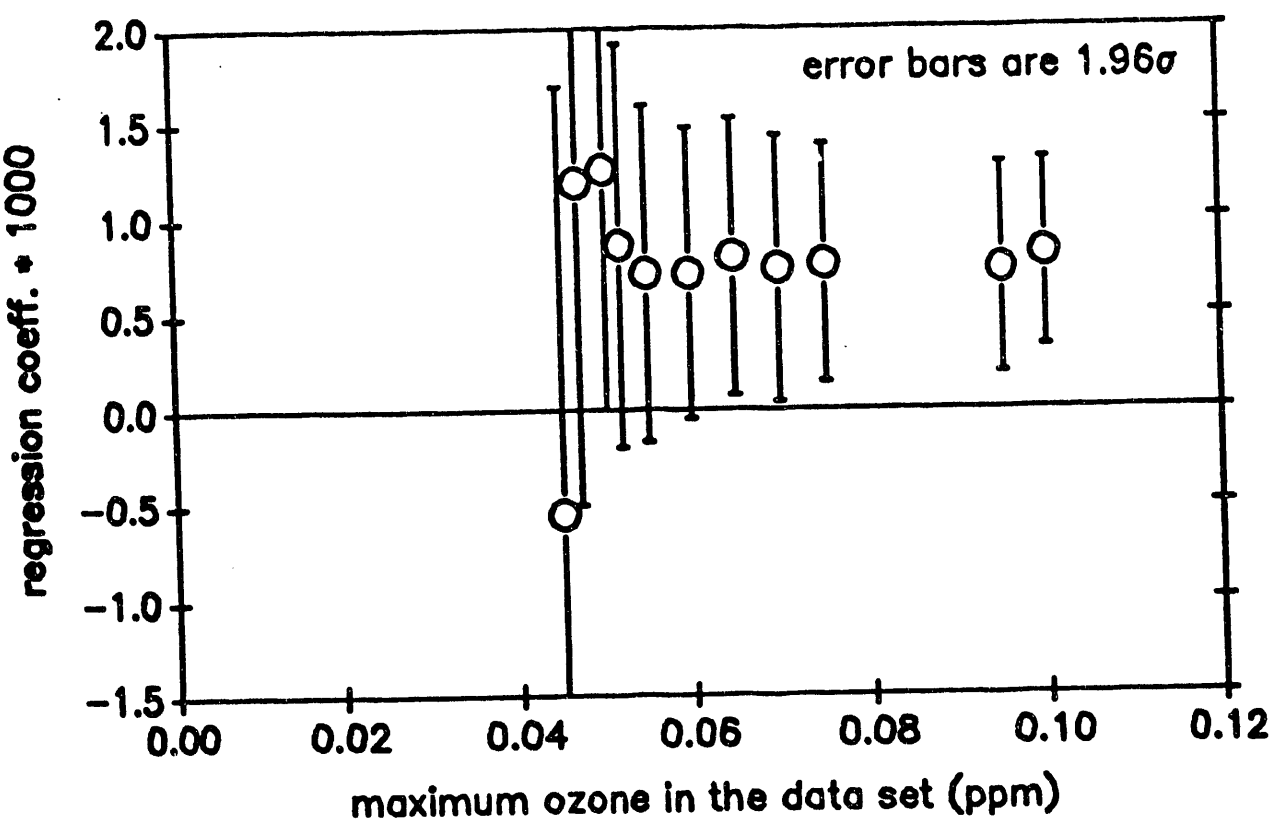

Figure 18. Regression coefficients for log non-external mortality on ozone for successively smaller data sets, after deleting ozone values higher than the values plotted.

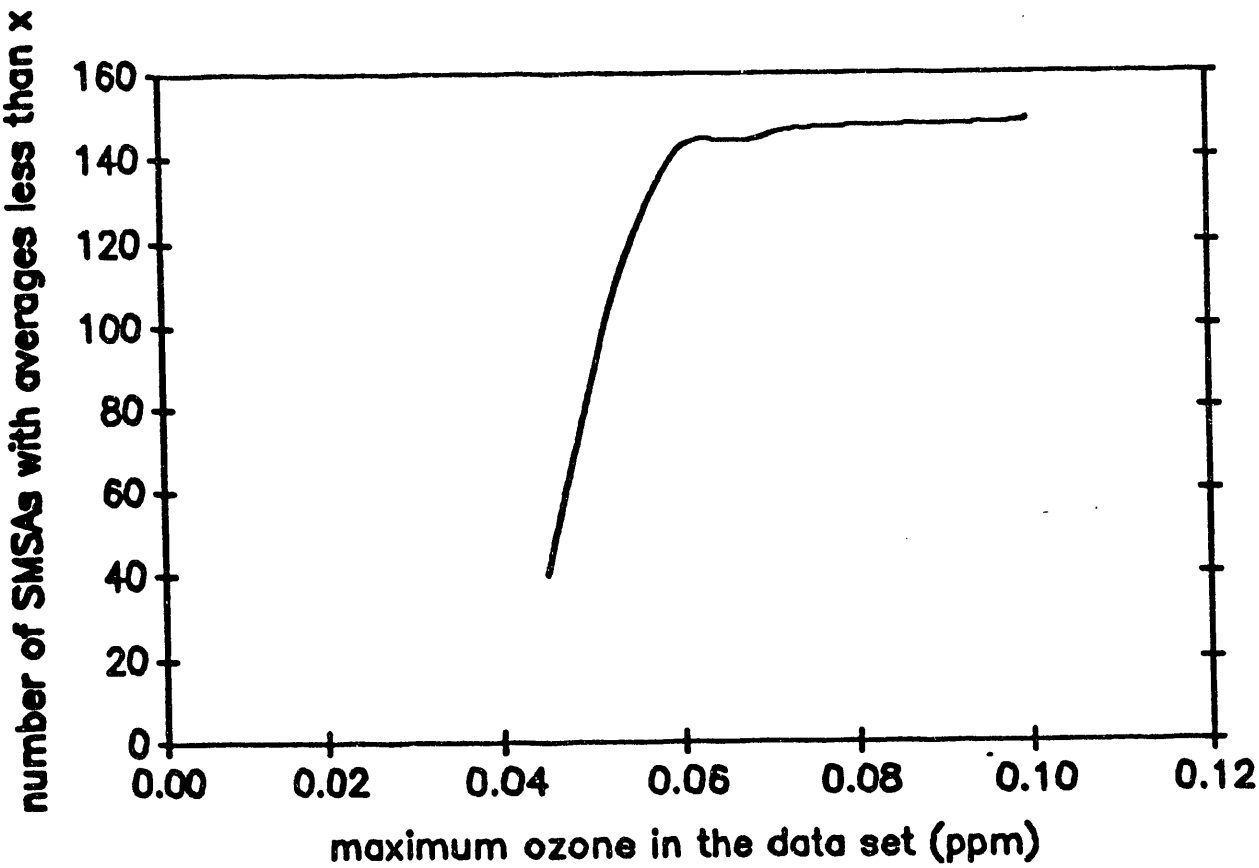

Figure 19. Frequency distribution of 1980-90 average ozone for 149 SMSAs.

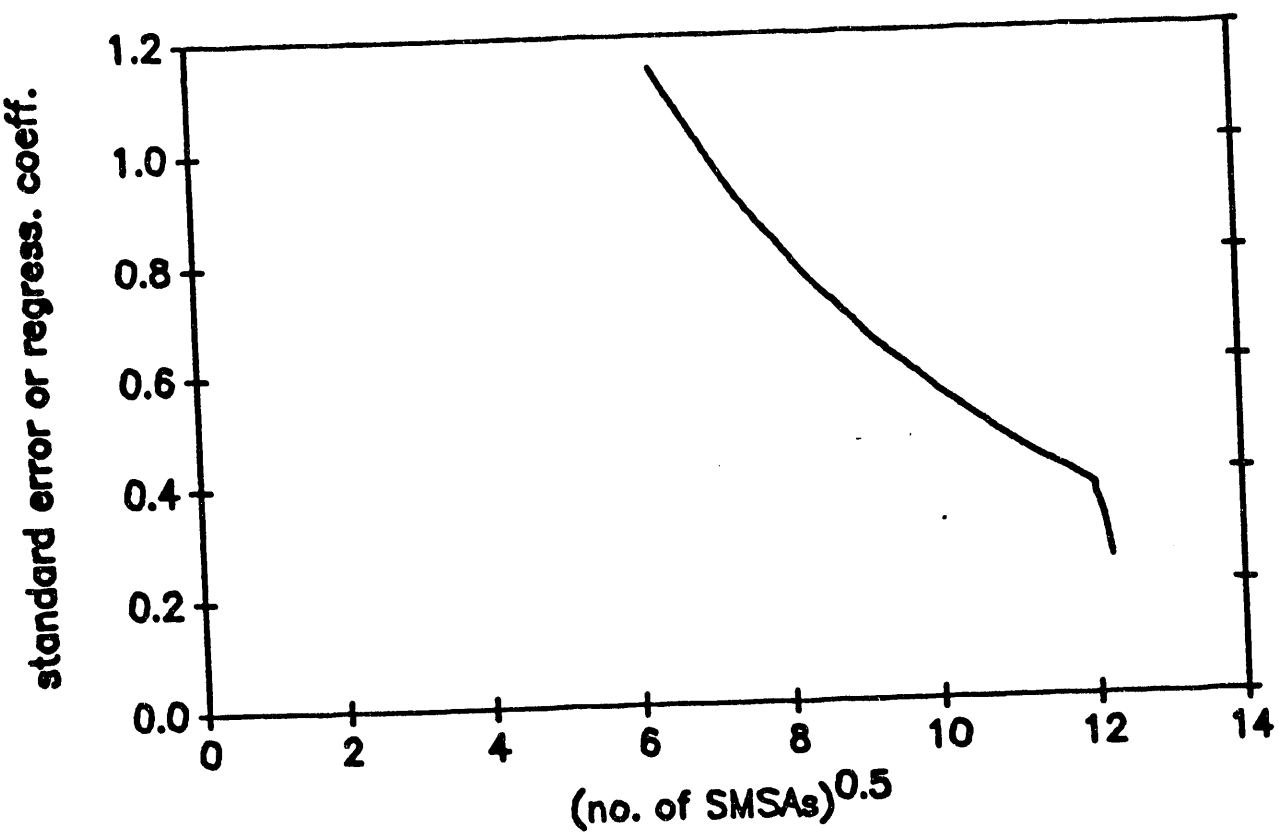

Figure 20. Standard errors of regression coefficients in Figure 18 vs. number of remaining observations.

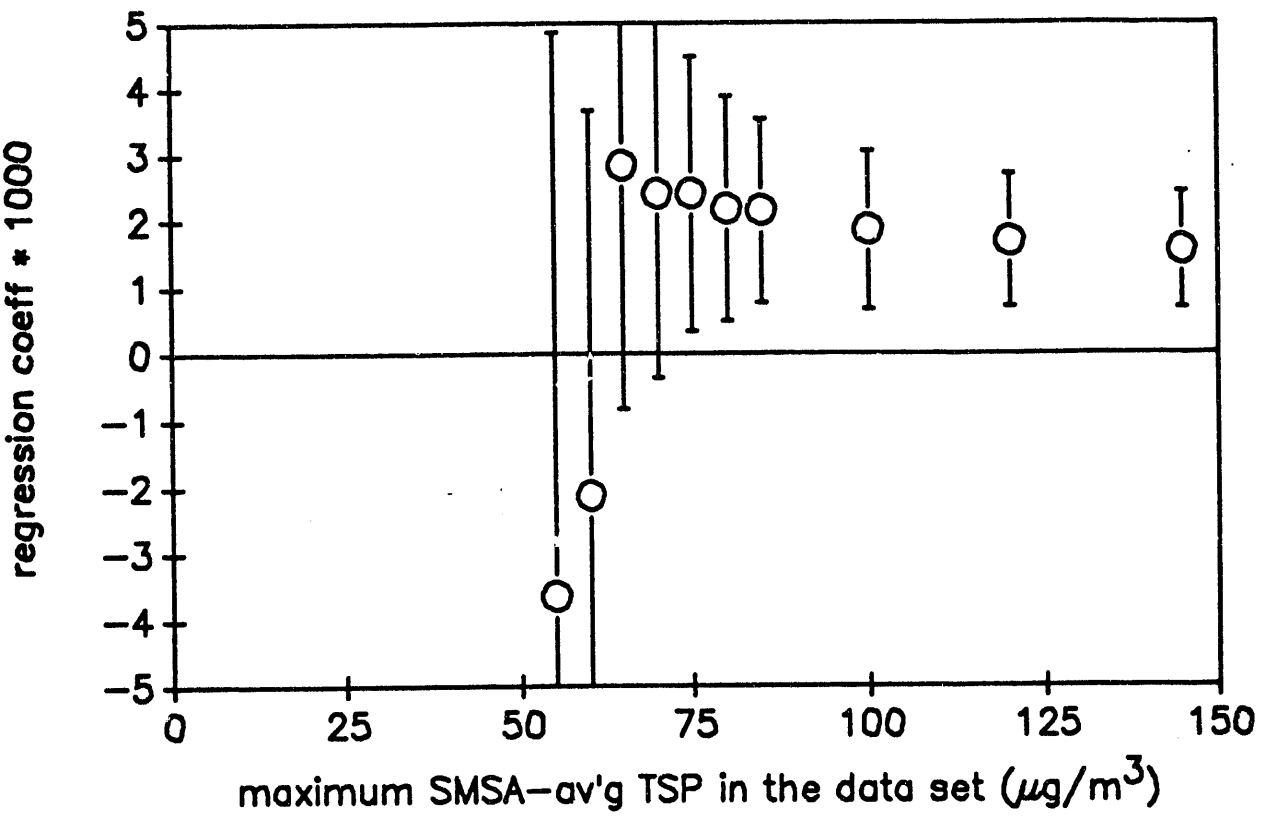

Figure 21. Regression coefficients for log COPD mortality on TSP for successively smaller data sets, after deleting TSP values higher than the values plotted.

dummy variables to model specification, which is seen to be minimal. In both cases, most of the "signal" appears to be in the lowest three quintiles, rather than in the highest ozone locations. Thus, although the analysis confirms that the high ozone locations are not unduly influential, the resulting "dose-response" functions are not intuitive and suggest that the model may be misspecified, especially for non-external deaths.

TSP is considered in Figure 23, for both COPD deaths and non-external deaths. Again, the strongest rise in mortality is in the mid-range of TSP values, although the COPD relationship is reasonably linear. The coefficients for the highest three TSP quintiles were all statistically significant; the low coefficient and p-value (~0.70) for the second lowest quintile suggests that a threshold may be present.

Figure 24 presents results for sulfate, which are presented to check for data anomalies that might have influenced the results. The dose-response functions are U-shaped, and even if only the right-hand half were considered, the excess risk is small. Note that the maximum excess risk for non-external deaths exceeds that for cardiovascular causes. Normally, one would expect that a potentially causal relationship would strengthen when one considers a specific cause of death (as in the case with TSP and COPD, for example).

It is of course possible that combinations of pollutants, at different levels, may be involved, especially for non-external deaths, which represents the sum of all diseases. However, such an analysis does not seem practical with only 149 observations.

CONCLUDING DISCUSSION

This analysis has developed regression models which appear to offer substantial improvements over previous studies of SMSAs (including that of Ozkaynak and Thurston [1987]), in that 92% or more of the mortality rate variance has been "explained" and that most of the (non-pollution) terms in the regressions were highly statistically significant. Improvements in fit were made when external causes were removed and when specific cause-of-death groupings were analyzed (although the regressions for COPD mortality probably suffered from the small numbers of deaths occurring in a given year in each location). Use of log-linear models, in which the logarithms (base 10) of mortality rates were regressed against linear combinations of independent variables, also provided improved fits to the data.

Summary of Regression Results

Tables 2 to 15 presented selected regression results in their entirety, including regression coefficients for all the independent variables. This degree of detail is useful in comparing model specifications and in judging the validity of the overall approach. In contrast, Tables 16 and 17 are intended to facilitate comparisons among diseases and pollutants. Regression coefficients, their standard errors, and significance levels are presented in Table 16; Table 17 presents comparable information based on elasticities. Statistically significant results ($p >= 0.05$) are shown in bold italic type; those values which failed to reach significance must be regarded as less robust than the others and may be unreliable estimates of the true underlying relationships. Furthermore, one must keep in mind that statistical significance alone is not sufficient evidence that the "true underlying relationship" has indeed been identified; such a causal conclusion requires plausible physiological mechanisms as well. Evidence of this truism is seen in the statistically significant negative entries in Tables 16 and 17 (implying that air pollution prolongs life, or, more likely, that the regression model is incompletely specified).

Regression Coefficients. One use for the regression coefficients is in comparing the contributions of a given pollutant to the variations in mortality rates for different diseases, based on the same or similar models. While rigorous comparisons can only be made among those coefficients that are statistically significant, each of the coefficients in Table 16 represents the best linear

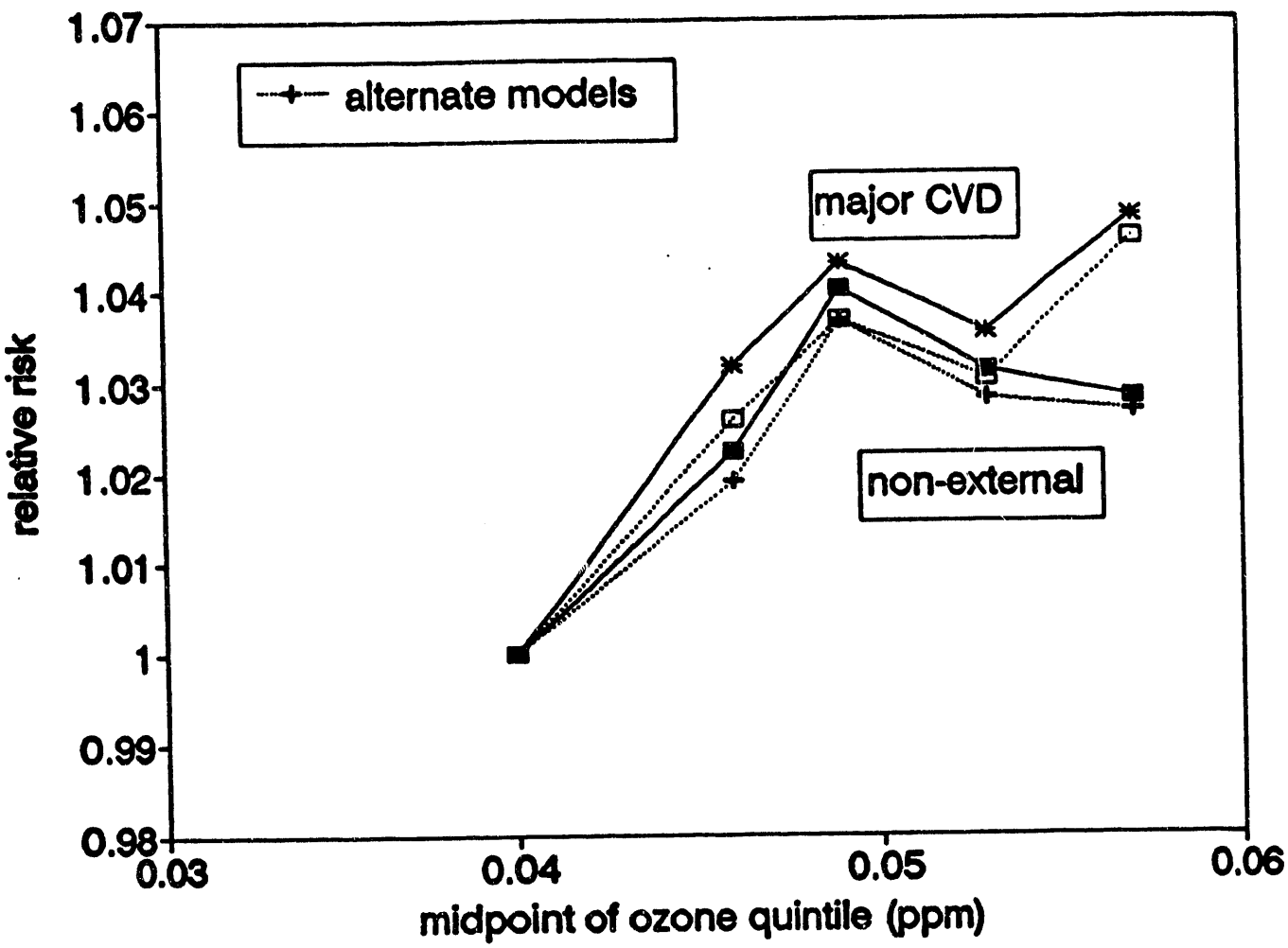

Figure 22. Relative risk for major cardiovascular and non-external mortality as a function of ozone quintiles.

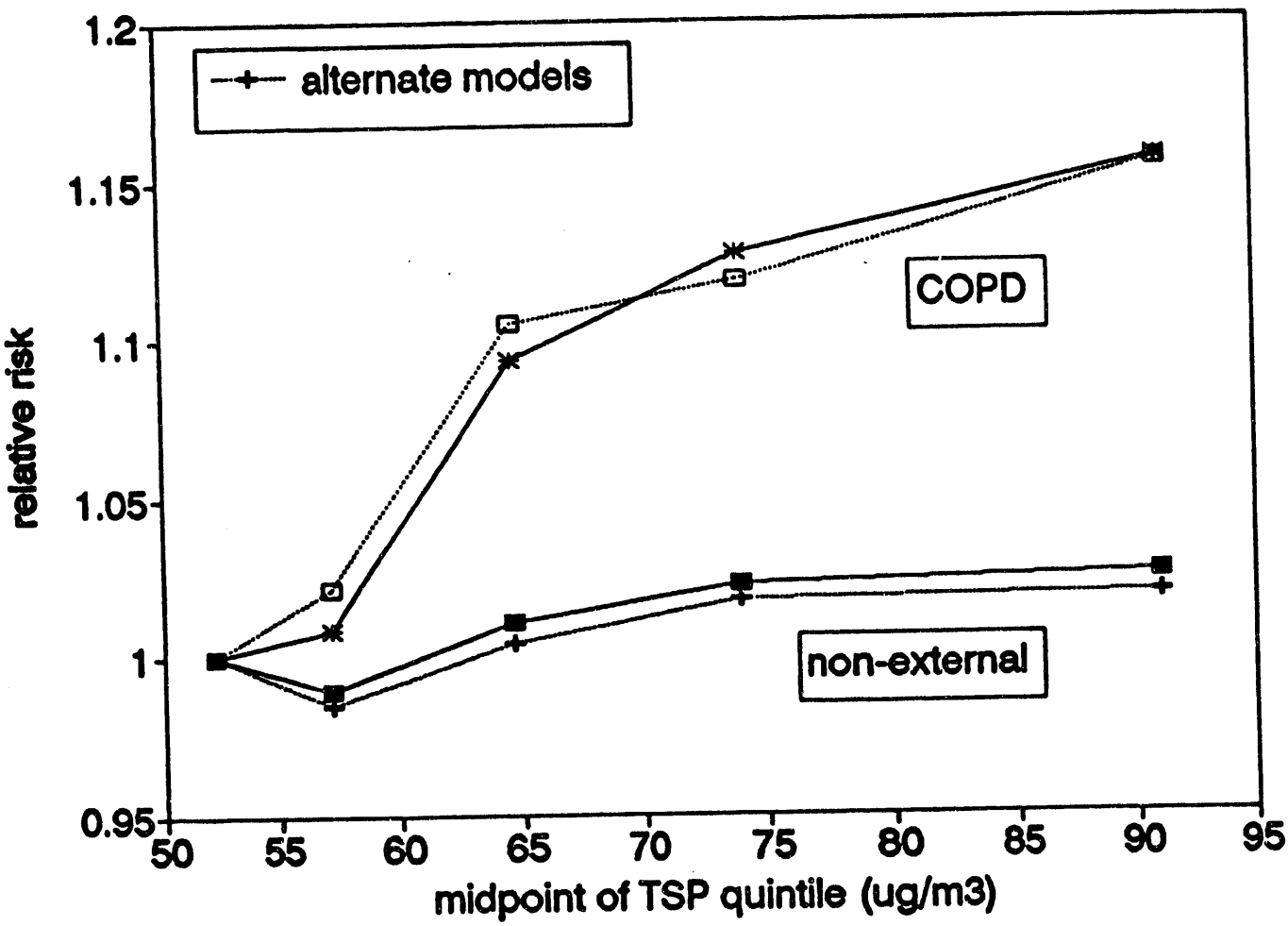

Figure 23. Relative risk for COPD and non-external mortality as a function of TSP quintiles.

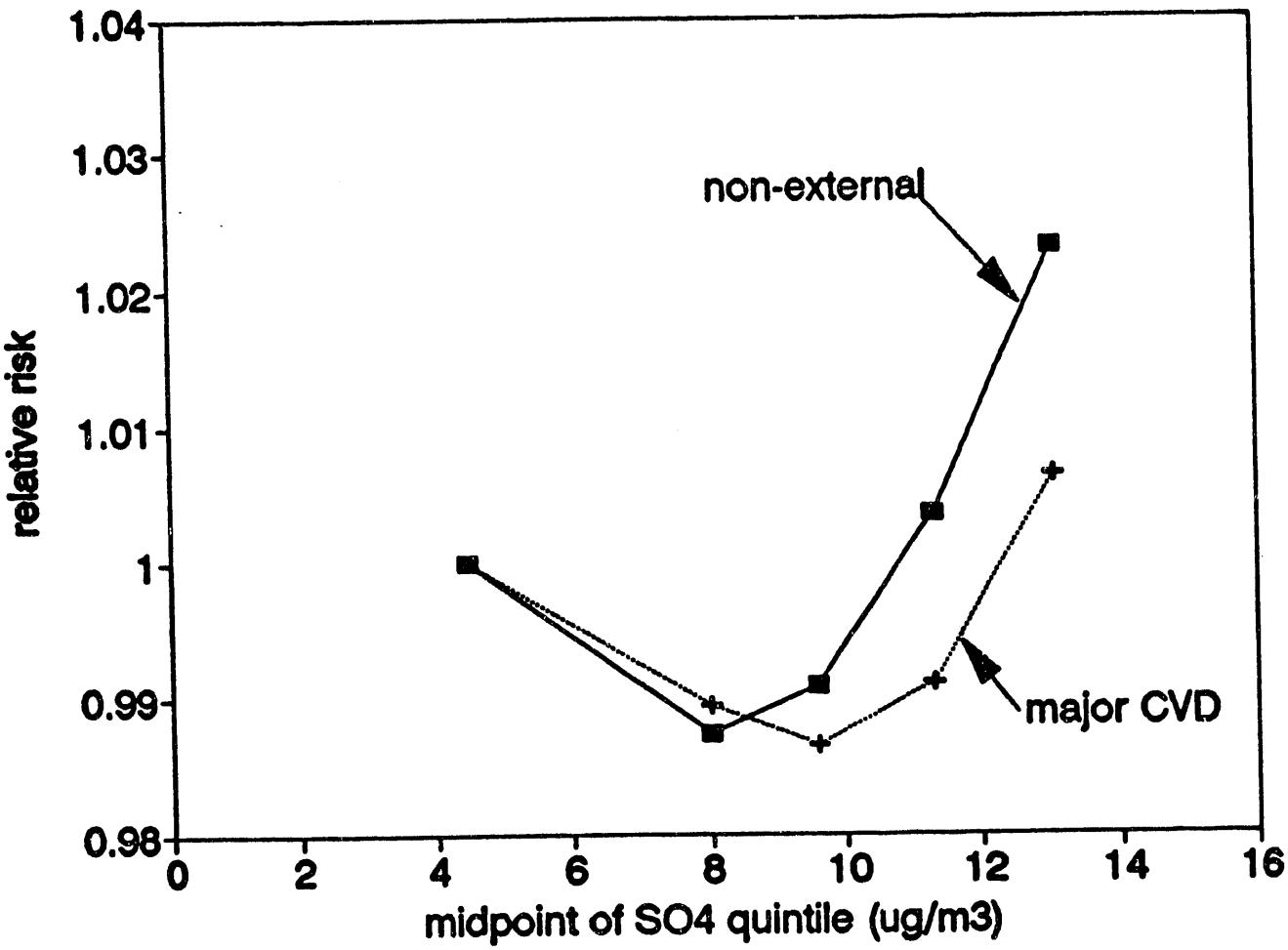

Figure 24. Relative risk for major cardiovascular and non-external mortality as a function of [TSP] sulfate quintiles.

unbiased estimate for the data and models indicated. The numerical value of a regression coefficient also depends directly on the mean values of dependent and independent variables; the coefficients of the linear models have units of death rates per thousand people per unit of pollution (the units of pollution include both ppm [ozone] and ug/m^3 [all other species]). For the log-linear models, the regression coefficients represent incremental effects on mortality ratios.

For the O&T model, Table 16 shows both positive and negative significant regression coefficients, which confirms the reservations expressed above about the adequacy of the O&T specification in controlling for non-pollution effects on mortality. Comparisons among pollutants and diseases with the O&T model may thus be problematic.

The complete and parsimonious linear models show significant associations only for ozone/cardiovascular causes and TSP/COPD. The log-linear models confirmed these findings and also found significance with non-external causes for each of these pollutants. Since the mortality grouping for non-external causes includes both major cardiovascular (MCV) and COPD in addition to many other causes of death, it is of some interest to compare the pollution effects on each of these cause-of-death groupings. This may be done by directly comparing the regression coefficients of the linear models, or by comparing the products of the log-linear regression coefficients and the mean mortality values (given in Appendix A).

These comparisons (which are all based on the 10-year average ozone variable) suggest that the association between ozone and MCV can account for all of the indicated association between ozone and non-external deaths. Note that the estimates of the contributions of COPD to the ozone/non-external death relationship are essentially nil. Further insights into the plausibility of these ozone-mortality relationships require several avenues of investigation. First, long-term average ozone data for the year 1980 should be used in lieu of the smoothed 10-year average data from Figure 8; data on peak ozone values should be extended to all 149 locations. Then, if the relationships with mortality persist, the components of MCV (heart attack, stroke, etc.) should be examined individually with regard to physiological plausibility.

In contrast to the ozone findings, the association between TSP and COPD appears to account for only a fraction (about 20%) of the association between TSP and nonexternal deaths. It thus follows that some other disease components of non-external deaths (excluding MCV, for which the best estimate of the TSP contributions are nil) might be associated with TSP. If other associations between TSP and specific diseases could be identified, the information might be useful in assessing whether any of the relationships shown in Table 16 might be causal or whether some portions appear to be artifactual. Note also that artifactual relationships could also be present in the extant indicated associations between mortality and air pollution (see "Uncertainties," below).

With respect to the regressions for sulfate (both [TSP] $SO_4^=$ and [IP] $SO_4^=$), we note that the results for [IP] $SO_4^=$ are consistently less significant than those for [TSP] $SO_4^=$, even though the coefficients are quite similar (this was also the case when TSP $SO_4^=$ was limited to the 62 cities having IP data). As discussed above, we expect that [IP] $SO_4^=$ is the more reliable measurement, by virtue of the types of filters used, and that the [TSP] $SO_4^=$ regression results may be biased low by as much as 30% due to the measurement errors; the superiority in fit shown by [TSP] $SO_4^=$ in Table 16 was thus unexpected and suggests that the filter artifacts characteristic of the TSP sampling technology may somehow be contributing to the apparent relationships with mortality (which seems counterintuitive since filter artifacts are not inhaled!). We also note that none of the sulfate results, using either measure, reached statistical significance with the complete or parsimonious models.

Elasticities. Since elasticities are dimensionless (Table 17), they may be readily compared among pollutants, models, and diseases. For non-external mortality, there is a remarkable degree of uniformity among the various pollutants, for the complete and parsimonious models (linear and log-linear). Elasticities range from 0.009 to 0.051; standard errors, from 0.006 to 0.024 (eliminating manganese from this comparison would narrow the range considerably). For TSP,

Table 16 REGRESSION COEFFICIENTS

All Non-External Causes

		TSP (n=149)		SO4 (n=149)		av'g ozone (n=149)		PM-15 (n=62)		PM-2.5 (n=62)		IP SO4 (n=62)		manganese (n=136)	
		Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear
Ozkaynak & Thurston model	1	-0.005	-0.00029	0.093	0.0086	4.8	0.50	-0.0029	-0.0003	0.029	0.0018	0.097	0.0089		
	2	0.0028	0.00017	0.018	0.0011	4.9	0.29	0.0056	0.0004	0.013	0.0009	0.033	0.0023		
	3	(0.058)	(0.10)	(0)	(0)	(0.38)	(0.10)	(0.65)	(0.45)	(0.02)	(0.07)	(0.003)	(0.01)		
complete model	1	0.003		0.031				0.0056		0.0188		0.0356		2.36	
	2	0.0025		0.0178				0.0046		0.0107		0.0312		1.43	
	3	(0.24)		(0.08)				(0.23)		(0.08)		(0.26)		(0.10)	
parsimonious model	1	0.0018	0.00028	0.026	0.0007	4.70	0.45	0.0028	0.00026	0.0188	0.00070	0.040	0.00038	2.45	0.111
	2	0.0023	0.00013	0.016	0.00066	3.88	0.21	0.0044	0.00026	0.0104	0.00062	0.030	0.00180	1.41	0.062
	3	(0.44)	(0.031)	(0.11)	(0.43)	(0.23)	(0.031)	(0.53)	(0.32)	(0.07)	(0.26)	(0.18)	(0.83)	(0.07)	(0.18)

Major Cardiovascular Causes

		TSP (n=149)		SO4 (n=149)		av'g ozone (n=149)		PM-15 (n=62)		PM-2.5 (n=62)		IP SO4 (n=62)		manganese (n=136)	
		Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear
Ozkaynak & Thurston model	1	-0.005	-0.00059	0.060	0.0058	4.0	0.72	-0.0032		0.018	0.0015	0.053	0.0053		
	2	0.0019	0.00021	0.013	0.0014	3.4	0.37	0.0038		0.0066	0.0012	0.023	0.0032		
	3	(0.004)	(0.005)	(0)	(0)	(0.30)	(0.045)	(0.40)		(0.04)	(0.23)	(0.02)	(0.10)		
complete model	1	-0.0009		0.0175				0.00148		0.01		0.0112			
	2	0.00171		0.0123				0.0032		0.0074		0.0214			
	3	(0.61)		(0.16)				(0.65)		(0.18)		(0.61)			
parsimonious model	1	-0.00074	9E-05	0.0132	1.6E-05	5.42	0.62	0.0015	0.0001	0.011	0.00062	0.019	-0.0010	1.40	0.11
	2	0.00166	0.00016	0.0115	0.0011	2.73	0.25	0.0032	0.0003	0.007	0.00075	0.022	0.0021	0.94	0.10
	3	(0.66)	(0.57)	(0.26)	(0.97)	(0.05)	(0.001)	(0.65)	(0.76)	(0.14)	(0.41)	(0.38)	(0.66)	(0.12)	(0.26)

Chronic Obstructive Pulmonary Disease

		TSP (n=149)		SO4 (n=149)		av'g ozone (n=149)		PM-15 (n=62)		PM-2.5 (n=62)		IP SO4 (n=62)		manganese (n=136)	
		Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear
Ozkaynak & Thurston model	1	0.00084	0.0018	-0.004	-0.006	0.11	0.72	0.00105	0.0019	-0.0004		-0.0051			
	2	0.00028	0.0004	0.002	0.003	0.50	0.75	0.00052	0.00063	0.0013		0.0033			
	3	(0.003)	(0)	(0.03)	(0.04)	(0.85)	(0.40)	(0.045)	(0.023)	(0.76)		(0.13)			
complete model	1	0.00084		-0.0025				0.0006		0.00028		-0.00023			
	2	0.00031		0.0023				0.00053		0.0012		0.0036			
	3	(0.006)		(0.29)				(0.26)		(0.82)		(0.94)			
parsimonious model	1	0.00075	0.00166	-0.0030	-0.0036	0.15	0.67	0.00042	0.0010	-0.00075	-0.0014	-0.0023	-0.0046	0.19	0.28
	2	0.00039	0.00044	0.0019	0.0029	0.51	0.76	0.00050	0.0006	0.0011	0.0018	0.0038	0.0060	0.19	0.28
	3	(0.012)	(0)	(0.11)	(0.22)	(0.80)	(0.25)	(0.28)	(0.24)	(0.50)	(0.50)	(0.54)	(0.45)	(0.32)	(0.32)

notes: 1 regression coefficient (death rate per unit of pollution)

2 standard error of coefficient (death rate per unit of pollution)

3 (significance level)

Table 17 ELASTICITIES

All Non-External Causes

		TSP (n=149)		SO4 (n=149)		av'g ozone (n=149)		PM-15 (n=62)		PM-2.5 (n=62)		IP SO4 (n=62)		manganese (n=136)	
		Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear
Ozkaynak & Thurston model	1	-0.044	-0.046	0.110	0.120	0.030	0.057	-0.013	-0.027	0.065	0.073	0.053	0.058		
	2	0.024	0.027	0.021	0.024	0.031	0.033	0.028	0.035	0.029	0.038	0.018	0.023		
	3	(0.055)	(0.10)	(0)	(0)	(0.38)	(0.10)	(0.65)	(0.45)	(0.02)	(0.07)	(0.003)	(0.01)		
complete model	1	0.026		0.037				0.026		0.042		0.019		0.011	
	2	0.022		0.021				0.023		0.024		0.017		0.007	
	3	(0.24)		(0.06)				(0.23)		(0.08)		(0.26)		(0.10)	
parsimonious model	1	0.016	0.044	0.031	0.015	0.030	0.051	0.014	0.023	0.042	0.026	0.022	0.004	0.011	0.009
	2	0.020	0.020	0.019	0.019	0.024	0.024	0.022	0.023	0.023	0.025	0.016	0.018	0.006	0.007
	3	(0.44)	(0.031)	(0.11)	(0.43)	(0.23)	(0.031)	(0.53)	(0.32)	(0.07)	(0.26)	(0.18)	(0.83)	(0.07)	(0.18)

Major Cardiovascular Causes

		TSP (n=149)		SO4 (n=149)		av'g ozone (n=149)		PM-15 (n=62)		PM-2.5 (n=62)		IP SO4 (n=62)		manganese (n=136)	
		Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear
Ozkaynak & Thurston model	1	-0.002	-0.003	0.133	0.145	0.047	0.052	-0.029		0.076	0.061	0.054	0.052		
	2	0.031	0.033	0.028	0.030	0.040	0.042	0.035		0.036	0.049	0.023	0.031		
	3	(0.004)	(0.005)	(0)	(0)	(0.30)	(0.045)	(0.40)		(0.04)	(0.23)	(0.02)	(0.10)		
complete model	1	-0.015		0.039				0.014		0.042		0.011			
	2	0.026		0.027				0.029		0.031		0.022			
	3	(0.61)		(0.16)				(0.65)		(0.18)		(0.61)			
parsimonious model	1	-0.012	0.014	0.029	0.000	0.064	0.053	0.014	0.009	0.046	0.025	0.019	-0.010	0.012	0.009
	2	0.027	0.025	0.025	0.024	0.032	0.028	0.029	0.027	0.029	0.030	0.022	0.021	0.006	0.006
	3	(0.66)	(0.57)	(0.26)	(0.97)	(0.05)	(0.001)	(0.65)	(0.76)	(0.14)	(0.41)	(0.36)	(0.66)	(0.12)	(0.2...

Chronic Obstructive Pulmonary Disease

		TSP (n=149)		SO4 (n=149)		av'g ozone (n=149)		PM-15 (n=62)		PM-2.5 (n=62)		IP SO4 (n=62)		manganese (n=136)	
		Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear	Linear	Log-linear
Ozkaynak & Thurston model	1	0.229	0.252	-0.148	-0.128	0.022	0.062	0.161	0.168	-0.026		-0.067			
	2	0.076	0.083	0.074	0.064	0.066	0.065	0.060	0.073	0.091		0.056			
	3	(0.003)	(0)	(0.03)	(0.04)	(0.85)	(0.40)	(0.045)	(0.023)	(0.76)		(0.13)			
complete model	1	0.229		-0.093				0.092		0.020		-0.004			
	2	0.084		0.065				0.061		0.064		0.061			
	3	(0.006)		(0.29)				(0.26)		(0.82)		(0.94)			
parsimonious model	1	0.204	0.252	-0.111	-0.077	0.030	0.099	0.064	0.069	-0.053	-0.057	-0.039	-0.045	0.027	0.023
	2	0.062	0.069	0.070	0.062	0.100	0.066	0.077	0.071	0.077	0.073	0.065	0.059	0.027	0.023
	3	(0.012)	(0)	(0.11)	(0.22)	(0.80)	(0.25)	(0.2 ,	(0.24)	(0.50)	(0.50)	(0.54)	(0.45)	(0.32)	(0.32)

1 elasticity at the mean (dimensionless)

2 standard error of elasticity

3 (significance level)

ozone, and PM_{15}, elasticities are higher for the log-linear models than the linear models; the opposite holds for sulfate, $PM_{2.5}$, and manganese. These tendencies probably reflect differences in the relative contributions of high and low mortality locations. The uniformity among elasticities for different pollutants does not hold for the specific disease groups; ozone and $PM_{2.5}$ show the largest elasticities for major cardiovascular diseases while TSP and (to a lesser extent) PM_{15} show the largest elasticities for COPD. The standard errors of the elasticities are larger for the specific diseases than for non-external mortality but differ much less among pollutants.

An interesting comparison may be made among the five models shown for sulfate, for non-external and major cardiovascular deaths. As one moves down the sulfate columns in Table 17, from the O&T model to the parsimonious model, the elasticity drops markedly, but its standard error decreases also. Thus the loss in significance for $SO_4^=$ that resulted from using more complete model specifications stems from the reduced values of the coefficients (which are the best unbiased estimates in all cases), not from increases in the standard errors. Since one of the hallmarks of multicollinearity is an increase in the standard errors (variance inflation), these results suggest that the drop in sulfate elasticity shown by the new models is due to better fits and not due to collinearity, *per se*.

We note also that the five different model results shown for COPD and TSP are all essentially the same, showing a remarkable degree of uniformity independent of model specification. This is also true, to a slightly lesser extent, for major cardiovascular deaths with respect to ozone or $PM_{2.5}$.

Finally, given the large number of regressions shown in Tables 16 and 17, one wonders whether the relatively few significant results that were found could have occurred due to chance. For each model, there are three mortality variables and seven pollutants, giving a maximum of 21 results. We would expect to find one of these to be significant at the 5% level, just due to chance. Since there are two significant findings for the linear (parsimonious) model and four for the log-linear model, two of which exceed the 0.001 level, we conclude that most of the significant findings are not likely to be due to chance alone. This conclusion would be reinforced if manganese were not considered or if only one sulfate variable were included in the comparison.

Discussion of Specific Pollutant-Disease Associations

These elasticities also compare reasonably well with the time series results given in Table 1. Kinney and Ozkaynak (1991) found ozone to be a slightly better predictor of daily cardiovascular mortality than for non-external causes in Los Angeles (1970-79); they used a linear model and their elasticities are only slightly lower than the corresponding values given in Table 16. We have no basis for comparing the ozone results for log-linear models, except that Schwartz (1992) did not find ozone to be a significant predictor of daily mortality in Detroit. Ozkaynak and Kinney did not find ozone or particles to be significant predictors of respiratory deaths in Los Angeles, but Schwartz and Dockery (1991) derived a log-linear elasticity for TSP and COPD in Philadelphia of about 0.14, which compares reasonably well with Table 14. No statistically significant time-series associations have been shown for sulfate, although weak relationships have been derived for SO_2 (Table 1).

The Ozone-MCV Association. The lack of consistent (i.e., monotonic) dose-response relationships for ozone should be discussed and several possible explanations come to mind, other than statistical variability or the effects of using inappropriate (long-term average) ozone data. First, some people adapt to ozone and, since ozone levels have been improving in Southern California, it is possible that the population is now less sensitive there. However, it is also possible that the mid-range levels of (average) ozone, which occur in most medium to large U.S. cities, are simply a surrogate for the mix of ozone precursors, including NO_x. For example, Kleinman (1992) reports a strong correlation between values of ozone over background (about 29 ppb) and

the difference between NO_y and NO_x. Compounds included in this increment include PAN, HNO_3, and HONO. Finally, because of the severe heat wave that occurred in the Central and Eastern U.S. in 1980, it is possible that ozone effects have been confounded with heat wave effects (see below).

Regional Dependence of the TSP-COPD Relationship. Although the association between COPD mortality and TSP appears to be quite robust to changes in the model and data set, it is possible that the relationship is confounded by regional characteristics. For example, some western cities have been noted (anecdotally) as retirement destinations for people already suffering from lung disease, which may have originated in other parts of the country. Some portion of the higher TSP levels found in the west is regional in nature, having to do with lower frequencies of precipitation and increased levels of windblown dust. Thus, the association between COPD and TSP could be circumstantial, at least in part. We note that the migration variable (CHNG70) tends to be positive for COPD mortality, and one wonders whether the regressions are picking up the individual characteristics of cities (east and west) or simply the characteristics of the western region as a whole. An example of such regional dependence was seen in the relationship between $SO_4^=$ and all-cause mortality (as shown by Ozkaynak and Thurston, 1987), in which the association is heavily dependent upon cities in Ohio and Appalachia.

Three additional regressions were run to explore regional confounding with respect to COPD and TSP. First, the 149 SMSAs were coded as to location east or west of the Mississippi River (St. Louis and Minneapolis were considered "east," as was Honolulu; these assignments were not critical to the outcome of the analysis). Separate regressions were run for each subset for the logarithm of COPD mortality rate using the same model as for the entire data set. TSP was not significant for either subset, although the regression coefficients were positive with about the same values. For the "east" subset (n=105), the TSP coefficient was 0.00094 (p=0.15); all other terms in the model remained significant except population density. For the "west" subset (n=44), the TSP coefficient was 0.00064 (p=0.3), and the variables for poverty, population density, and Hispanic ethnicity lost significance. Smoking remained significant in both subsets with about the same coefficient.

Next, a dummy variable was added to the model designating east-west location and a regression was run for the combined data set. This variable was highly significant, reflecting the higher COPD mortality rates in the West, but the TSP coefficient was only slightly reduced in magnitude (0.0012) relative to Table 16 and remained significant (p=0.006). The conclusion follows that the COPD-TSP relationship does not appear to be confounded by regional differences.

Additional locations would be required to study the details of the relationship in the West. In general, COPD mortality rates are higher in the West, hence the negative association with sulfate. TSP levels also tend to be high in some Western locations, presumably because of fugitive dust but also because of forest slash burning and residential wood smoke. Volcanic ash is another possibility, of course (Mt. St. Helens erupted May 18, 1980 and Spokane had the highest TSP levels in the data set). It is also noteworthy that COPD deaths have been rising nationwide (presumably because of the delayed effects of smoking), while TSP levels have generally been falling (presumably because of emissions controls). Cross-sectional analyses are incapable of distinguishing whether an association represents a bona-fide cause and effect relationship, or a circumstantial one: the selective migration of people with (pre-existing) respiratory problems to locations which happen to be high in dust loading (see Figure 14 and the ensuing discussion). While such a scenario would rule out a chronic relationship between TSP and COPD, it could still be consistent with deaths from acute (daily) effects. This hypothesis could be evaluated directly by performing a time-series analysis in a location with high fugitive dust levels, including the year 1980.

Previous Findings by Cause of Death

Support for these cross-sectional results is also found in the literature on various mortality studies which also considered separate cause of death groupings. In some cases, because of differences in study design, one can only note whether the relative effects are similar, i.e., ranking of regression coefficients or elasticities or concordance in associations of diseases and pollutants.

Cross-sectional Studies. Most of the extant cross-sectional studies suffered from incomplete or flawed model specifications, and sometimes from problems with air quality data. Lipfert's (1978) study of 1970 city mortality, which also considered county and state mortality, had some of these problems also, but selected results by cause of death are presented here for reference. Lipfert did not consider cardiovascular causes per se, but did present results for deaths not classified as respiratory, cancer, or external, most of which were cardiovascular. On average, over 70% of deaths were in this category, and the regression coefficients were very similar to those for all non-external causes (elasticities were higher). Typical elasticities (for TSP) were 0.054 for all non-external causes and 0.065 for the unspecified (cardiovascular) category. (Lipfert did not include data for ozone in his 1978 analysis, but he found significant relationships between ozone and all-cause mortality in his 1984 study of 1970 SMSA mortality.) The respiratory disease grouping used in the 1978 city study included asthma deaths and accounted for a total of only about 1.7% of all deaths. The respiratory disease regressions were most successful at the state level, for which the TSP elasticity was about 0.21.

Time-Series Studies. Only a few of the many time series studies which have appeared over the years have considered separate causes of death. Schimmel and Greenburg's (1972) study of 1963-68 mortality in New York City was one of the most thorough. They looked at nine cause-of-death categories against SO_2 and smoke (regressed jointly), for lags up to seven days, controlling for temperature. Results were presented for the entire city and for a smaller section located around the air monitoring site. The elasticities were slightly higher for the smaller section, as might be expected, but mainly for SO_2; the smokeshade coefficients scaled approximately with the population. In their joint regressions on SO_2 and smokeshade, smokeshade accounted for 2/3 of the excess deaths for total, respiratory and cardiovascular cause of death groupings (for the smaller district); the split for the entire city was weighted more towards smokeshade because of the depression of the SO_2 coefficients when city-wide mortality was regressed against local SO_2. Schimmel and Greenburg used linear models and presented regression results for same-day mortality and for deaths accumulated for seven days after the air pollution measurement. The latter elasticities were about 0.025 for all causes, 0.031 for cardiovascular causes, and 0.097 for respiratory diseases. These values are lower across-the-board than the present cross-sectional results, but agree qualitatively.

Kinney and Ozkaynak (1991) did not find a stronger relationship for respiratory disease deaths in their study of Los Angeles, which used linear models and lags up to one day. However, they did not examine TSP or any other particle measures, for respiratory disease mortality. They found relationships with ozone and NO_2 (regressed jointly) for total mortality and cardiovascular mortality, with combined elasticities of about 0.04 and 0.05, respectively.

Time-series analyses of Philadelphia (Schwartz and Dockery, 1992a), Utah County (Pope et al., 1992) and Santa Clara County, CA (Fairley, 1990) were all limited to some measure of particulates in their investigations of specific causes of death. The elasticities found are given below:

	Elasticity		
Cause of death	Philadelphia	Utah County	Santa Clara County
all (non-external)	0.051	0.072	0.030
cardiovascular	0.071	0.084	0.030
respiratory	0.14	0.17	0.13
cancer	0.028	--	0.029

These figures indicate reasonable quantitative agreement with the present cross-sectional findings; however, the disagreement with regard to associations between particulate matter and cardiovascular mortality is noteworthy and may indicate fundamental differences in the relationships. For example, it is possible that the time-series relationship for cardiovascular deaths reflects prematurity of death less than one year, so that it is not reflected in the annual rates. Similarly, it is possible that the ozone-MCV association reflects chronic effects, at least in part, so that it is not picked up by a daily mortality analysis. Of course, all of this speculation assumes that both types of analyses are not confounded by statistical or data artifacts of various kinds.

Summary of Non-Pollution Mortality Relationships

We chose to base our conclusions on the "parsimonious" models because they fit the data better and had highly statistically significant coefficients for most of the terms. It is thus also important to examine these results in detail, since it has been shown that the extent to which "excess" mortality is assigned to sulfate is strongly dependent on the way in which socioeconomic and lifestyle variables are handled. The issue of regional vs. local effects was discussed above. Table 18 compares elasticities for these variables. We see that using elasticities as a measure, many of the non-pollution effects account for smaller fractions of mortality than we are currently estimating for air pollution. Note also that the values for smoking may be underestimates, especially since official estimates tend to blame smoking for almost all of COPD deaths. This may be an inappropriate comparison, however, since age is the overwhelming factor in Table 18 and the effects of smoking *per se* are usually stated after age adjustments have been made. Also, the smoking data used in the present analysis are "ecological" in that they are based on entire states and are not specific to decedents for particular causes of death. The ensuing errors will tend to depress the smoking regression coefficients.

We find that the factors associated with higher all-cause (non-external) mortality rates in a given area are age, percentage of blacks, poverty and smoking. Beneficial factors include the presence of Hispanics, of other non-whites, college education, drinking water hardness, and in-migration. For cardiovascular diseases, the age, education, smoking, and in-migration effects are increased; this sheds some doubt on the validity of the "soft-water" hypothesis, since it was originally directed towards heart disease (Pocock, 1980). All the remaining trends conform more-or-less to the "conventional wisdom." Note that poverty and education are strongly collinear in this data set and that independent estimates of their separate effects may be unreliable. For COPD, the findings are somewhat problematic, since population density is a strong negative predictor and we might have otherwise associated respiratory problems with crowded central cites. This may indicate rural sources of respiratory problems, such as farmer's lung, or perhaps that wind-blown dust is more common in low-density areas in the West. The positive coefficient for in-migration may indicate that some portion of elevated COPD mortality is due to selective migration of persons suffering from the disease.

Table 19 presents a listing of previous (some independent) estimates of regression coefficients for some of the variables used in this study. Agreement appears satisfactory, with the possible exception of % > 65 and smoking. The uncertainties suggested by these discrepancies are discussed below.

Table 18 - Elasticities for Non-Pollutant Variables

	Non-external Causes		Major Cardiovascular		COPD	
variable	linear	log-linear	linear	log-linear	linear	log-linear
% 65+	0.74	0.73	0.81	0.79	0.75	0.69
% black	0.022	0.033	0.015	0.038	-0.09	-0.08
% other non-white	-0.004	-0.01	-	-	-	-
% Hispanic	-0.004	-0.005	-0.009	-0.015	-	-
% with 4yr college	-0.089	-0.095	-0.15	-0.16	-	-
log pop. density	-	-	-	-	-0.40	-0.29
cigarette sales	0.11	0.14	0.12	0.19	0.32	0.37
drnkg water hardness	-0.01	-0.007	-0.01	-0.005	-	-
% pop. change,1970-80	-0.033	-0.038	-0.049	-0.059	-	-
% in poverty	-	-	-	-	0.27	0.23

Table 19. Independent Estimates of Regression Coefficients

Variable	Est. Coeff. (Exogenous Data)	Basis	Results from this Study (SMSAs) non-external causes	Results for 1980 Cities (Lipfert et al.,1988) all causes
% > 65	0.465	Difference in total US mortality rates for %>65 - %<65	0.55	0.54
% Black	0.0276	Difference in age-adjusted total US rates, white-black	0.022	0.008-0.027
% Other NW	-0.02	Difference in 1980 age-adjusted total US rates, white-"all other"	-0.01	
	-0.0042*	based on 1960 data		
% Hispanic	-0.017	Difference in age-adjusted total US rates, Mexican, Puerto Rican or Cuban born, all whites + all blacks adjusted for poverty	-0.006	-0.04--0.05
Smoking	0.012	Relative risk, by amount smoked (Surg. Gen. Rpts)	0.004	0.008-0.018
Water Hardness	-0.0015	(Great Britain)	-0.0007	-0.007--0.06
	-0.0072	(Italy)		
	-0.004	(Great Britain)		
% Poverty	0.11-0.17	1970, cities	0.049	0.04-0.06
	0.02-0.06	1970, SMSAs		
	0.034	1970 expected value		
% College Graduates	-0.03 to -0.09	1970, cities	-0.04	0 - -0.08
	-0.018	1960, individuals*		

*from Kitagawa and Hauser (1973)

Comparison with Previous Findings for Cities and SMSAs

Since one of the important issues in the design of cross-sectional studies is the selection of geographic units for study, it is important to compare the present results with those of a similar previous study based on 1980 data for cities (Lipfert *et al.*, 1988). That study found slightly different combinations of demographic and socioeconomic variables to be optimal, but did not employ log-linear models and did not use city-wide averages for TSP. If the model truly represents what it purports, we should find the same regression coefficients for both cities and SMSAs. If the variables are merely serving as surrogates, we might expect to find the same elasticities. Table 19 indicates good agreement between regression coefficients in most cases.

Since there are no two cross-sectional studies in the literature which employed common analysis methods and models, it is not possible to make definitive comparisons between 1970 and 1980,

i.e., to examine whether benefits in reduced mortality have accrued as a result of the Clean Air Act. Such a comprehensive analysis should be given a high priority.

Uncertainties Remaining in the Analysis and Recommendations for Their Resolution

The regression results presented above comprise a reasonably coherent picture, after sources of confounding and error are taken into account. However, many important uncertainties remain and it is fair to assume that, if they were all accounted for, this picture would be likely to change in ways that cannot now be predicted.

Age Distributions. In spite of the appearance of consistency in these results, many important uncertainties remain. The lack of agreement with of the coefficient for 65+ implies that use of this simple metric may not be handling spatial variations in age distributions properly. To the extent that systematic regional differences in the distributions exist within the 65 and over age group, confounding could result. Note that use of "median age" by Ozkaynak did not seem to help, presumably because the problem lies with the elderly, not with people around the median age (30s). Either age-specific deaths should be analyzed (which are often problematic because of the smaller counts involved), or the age distribution in each city should be used to compute an "expected" death rate for each location.

Weather/Climate Effects. Recent analyses (Kalkstein *et al.*, 1991) have identified heat wave mortality as more important than summer air pollution in some U.S. cities. 1980 was a severe drought and heat wave year (Bair, 1992), but not all locations were affected equally. Since ozone also responds to sunlight, and TSP tends to be higher in the absence of precipitation, weather variables should be added to the analysis. Evans *et al.* (1984b) and Mendelsohn and Orcutt (1979) found that weather/climate variables could make significant contributions to cross-sectional mortality regressions. In may be important to include departures from normal conditions and durations of hot spells in such formulations.

Indoor Air Pollution. While Lipfert and Wyzga (1992) found that indoor and outdoor air quality for respirable particulates tended to be highly correlated in time when averaged over a community, this will not be the general case for spatial comparisons. Some communities have more air conditioning, which protects against heat and outdoor air pollution, and some locations use more unvented indoor heaters and wood stoves, which are important sources of indoor air pollution. Variables describing the prevalence of heating and air conditioning equipment should be added to the analysis.

Smoking and Life-Style. The lack of agreement for the smoking variable in this study was also disappointing and deserves further study. The raw data should be examined for outliers (New Hampshire is a candidate, because of the high levels of out-of-state sales). Data on smoking prevalence from surveys should also be evaluated, along with other data on personal risk factors such as exercise, obesity, alcohol use, etc. The "pace of life" has been shown to vary substantially across the nation and may be a contributor to differences in heart disease.

Chronic vs. Acute Effects. As discussed earlier, cross-sectional regressions may reflect either phenomena that occurred during the year of study or the sequelae of trends that built up over a long time. It is important to try to reconcile this uncertainty, which might be approached by examining mortality for 1979 and 1981 (with regard to 1980 air pollution, heat waves, flu epidemics, etc.). TSP data could also be compiled specifically for these years. There are also uncertainties as to the correct pollution dose metric, with regard to both chronic and acute responses. Cross-sectional analyses tend to use long-term averages; time-series studies use daily averages or peaks. The duration of peak periods is often neglected by both types of studies.

Other Causes of Death. Etiological insights might be gained by examining both causal and non-causal hypotheses (controls). Additional causes of interest include various cancers, influenza, and pneumonia; control causes might include diabetes or urinary disorders, for example.

The component causes of death comprising "major cardiovascular" (heart attack, stroke, chronic ischemic heart disease, etc.) should be investigated individually in order to further explore the findings with respect to ozone.

Concluding Assessment

This study broke new ground in its treatment of the air quality data for SMSAs and in its exploration of log-linear regression models. Both of these developments turned out to be very important and suggest that all previous (national-level) cross-sectional studies of mortality should be re-examined in these contexts.

Although the previous finding of Lipfert *et al.*, (1988) was confirmed, that mortality from all (non-external) causes may be associated with any of several pollutants with an elasticity around 0.05 (and that it is difficult to separate the effects of different pollutants), two specific pollutant-disease associations were also identified: TSP-COPD and ozone-cardiovascular. The latter association was judged to be problematic because of flaws in the ozone data used and the appearance of the apparent dose-response relationship, but the ozone findings appear worthy of further investigation, these defects notwithstanding. The TSP-COPD association survived all attempts to identify confounding or artifacts, but should be confirmed with data for additional locations and time periods.

Finally, the study confirmed previous findings (Evans *et al.*, 1984; Lipfert, 1978; Lipfert, 1984; Lipfert *et al.*, 1988) that the association between sulfate and all-cause or cardiovascular mortality is extremely dependent upon the extent to which non-pollution effects on mortality have been controlled for. This characteristic stems from the regional nature of $SO_4^=$ in the Northeastern United States. Important variables include smoking, a detailed racial breakdown, and population migration. It was shown that the results of Ozkaynak and Thurston (1987) are not robust, in part because of lack of consideration of these variables and in part because of their failure to average air quality data across each SMSA.

Acknowledgments

This work was supported by the U.S. Department of Energy, Office of Fossil Energy. Thomas J. Grahame was the project officer and his contributions, criticisms, and support are gratefully acknowledged.

REFERENCES

F.E. Bair, editor, The Weather Almanac, Gale Research, Inc., Detroit. 1992.

Borland International, Inc., QUATTRO ® Pro User's Guide, Scotts Valley, CA. 1989

R. Brackbill, T. Frazier, and S. Shilling (1988), Smoking Characteristics of US Workers, 1978-80, Am. J. Ind. Med. 13:5-42.

G.L. Bultena (1969), Health Patterns of Aged Migrant Retirees, J.Amer. Ger. Soc. 17:1127-1131.

M. Chappie and L.B. Lave (1982), The Health Effects of Air Pollution: A Reanalysis, J.Urban Econ. 12:346.

B.L. Cohen (1990), Ecological versus Case-Control Studies for Testing a Linear-No Threshold Dose-Response Relationship, Int.J.Epidemiology 19:680-684.

B.L. Cohen (1992), Percentage of Lifetime Spent in Area of Residence at Time of Death, Envir. Res. 57:208-211.

N. Eisenbud, (1970), Environmental Protection in the City of New York, Science 170:706-712.

J.S. Evans, P.L. Kinney, J.L. Koehler, and D.W. Cooper (1984a), Comparison of Cross-Sectional and Time-Series Mortality Regressions, J.APCA 34:551.

J.S. Evans, T. Tosteson, and P.L. Kinney (1984b), Cross-sectional mortality studies and air pollution risk assessment. Environ. Int. 10:55-83.

D. Fairley, The Relationship of Daily Mortality to Suspended Particulates in Santa Clara County, 1980-1986. Env.Health Persp. 89:159-168 (1990).

W. Farr, (1885), Vital Statistics: a memorial volume of selections from the reports and writings of William Farr. N. Humphreys, ed. Sanitary Institute of Great Britain, London. 563 pp. p. 415.

M. Feinleib, R. Fabsitz, and A.R. Sharrett (1979), Mortality from Cardiovascular and Non-Cardiovascular Disease for U.S. Cities. U.S. Department of Health, Education, and Welfare (PHS), Nat. Inst of Health Publ. No. (NIH) 79-1453, 1979

E. Ginzburg, (1990), p. 257 in The Medical Triangle, Physicians, Politicians, and the Public, Harvard University Press, Cambridge, MA. 314 pp.

E.J. Kitagawa and P.M. Hauser, Differential Mortality in the United States: A Study in Socioeconomic Epidemiology, Harvard University Press, Cambridge, MA (1973).

L.S. Kalkstein (1991), A New Approach to Evaluate the Impact of Climate upon Human Mortality, Envir.Health Perspect 96:145-150.

P.L. Kinney and H. Ozkaynak, Associations of Daily Mortality and Air Pollution in Los Angeles County, Env.Res. 54:99-120 (1991).

D.G. Kleinbaum, L.L. Kupper, and H. Morgenstern, H. Epidemiologic Research, Principles and Quantitative Methods, Wadsworth, Belmont, CA, 1982.

L.R. Kleinman (Brookhaven Nat'l Lab.), personal communication, November 1992.

R.F. Lacey (1981), Changes in Water Hardness and cardiovascular Death-Rates, Tech. Rep. TR 171, Water Research Center, Medmenham, England, Nov. 1981.

L.B. Lave and E.P. Seskin (1978), Air Pollution and Human Health, Johns Hopkins University Press for Resources for the Future.

T. Link, personal communication, 1991.

F.W. Lipfert, Air Pollution and Community Health, Van Nostrand Reinhold, New York (in press).

F.W. Lipfert, "A Review of the Relationships Between Hospital Admissions and Air Pollution," Paper IU-21B.09, 9th World Clean Air Congress, Montreal, Canada, 1992.

F.W. Lipfert, The Association of Human Mortality with Air Pollution: Statistical Analyses by Region, by Age, and by Cause of Death, Ph.D. Dissertation, Union Graduate School, Cincinnati, Ohio, 1978. Available from University Microfilms, 1978.

F.W. Lipfert, Air Pollution and Mortality: Specification Searches Using SMSA-based Data:, J.Env.Econ.&Mgmt. 11:208-243 (1984).

F.W. Lipfert and S.C. Morris, Air Pollution and Mortality, Science 255:606 (1991) and Science 256:722 (1992) (letters).

F.W. Lipfert, R.G.Malone, M.L. Daum, N.R. Mendell, and C-C. Yang, A Statistical Study of the Macroepidemiology of Air Pollution and Total Mortality, BNL Report 52122, to U.S. Dept. of Energy, Brookhaven National Laboratory, 1988.

F.W. Lipfert and R.E. Wyzga, Observational Studies of Air Pollution Health Effects: Are the Temporal Patterns Consistent? Paper IU-21A.09, presented at the 9th World Clean Air Conference, Montreal, Canada, September 1992.

F.W. Lipfert and T. Hammerstrom, Temporal patterns in air pollution and hospital admissions, Environmental Research (in press).

R. Mendelsohn and G. Orcutt (1979), An Empirical Analysis of Air Pollution Dose-Response Curves, J.Envir.Econ.& Mgmt. 6:85-106.

Miettinen, O.S., and Cook, E.F. (1981), Confounding: Essence and Detection, Am.J.Epidemiology 114:593-603.

P.K. Mueller and G.M. Hidy (1983), The Sulfate Regional Experiment: Report of Findings, Vols. 1-3, EPRI EA-1901, Electric Power Research Institute, Palo Alto, CA.

H. Ozkaynak and G.D. Thurston, Associations Between 1980 U.S. Mortality Rates and Alternative Measures of Airborne Particle Concentration, Risk Analysis 7:449-62 (1987).

W. O'Neal (1991), U.S. Environmental Protection Agency, Washington, DC. personal communication to F.W. Lipfert, Jan. 9, 1991.

Piantidosi, S., Byar, D.P., and Green, S.B. (1988), The Ecological Fallacy, Am.J.Epidemiology 127:893

Polissar, L. (1980), The Effect of Migration on Comparison of Disease Rates in Geographic Studies in The United States, Am.J.Epidemiology 111:175-182.

C.A. Pope, III, J. Schwartz, and M.R. Ransome, "Daily mortality and PM_{10} pollution in Utah Valley," Arch. Env. Health (1992).

Portney, P.R. (1990), Economics and the Clean Air Act, J.Econ.Perspectives 4:173.

Richardson, S., L.Stucker, and D. Hemon (1987), Comparison of Relative Risks Obtained in Ecological and Individual Studies: Some Methodological Considerations, Int.J.Epidemiology 16:111-120.

J. Schwartz, Particulate Air Pollution and Daily Mortality in Detroit, Env.Res. 56:204-213 (1991).

J. Schwartz and D.W. Dockery, Increased Mortality in Philadelphia Associated with Daily Air Pollution Concentrations, Am.Rev.Resp.Dis. 145:600-604 (1992a).

J. Schwartz and D.W. Dockery, Particulate Air Pollution and Daily Mortality in Steubenville, Ohio, Am.J.Epidemiology 135:12-25 (1992b).

J.D. Shannon. A Model of Regional Long-term Average Sulfur Atmospheric Pollution, Surface Removal, and Wet Horizontal Flux, Atm.Env. 15:689-701 (1981).

G.W. Snedecor and W.G. Cochran, Statistical Methods, 6th ed., The Iowa State University Press, Ames, Iowa. pp 164-166 (1967).

S.D. Stellman, Confounding, Prev. Med. 16:165-82 (1987).

R.D.S. Stevens, The Sampling and Analysis of Airborne Sulphates and Nitrates: A Review Of Published Work and Synthesis of Available Information, prepared for Environment Canada, EPS 5-AP-82-14 (1981)

U.S. Department of HEW (1982), Vital Statistics of the United States, 1980. Part B, Mortality. U.S. Gov't Printing Office, Washington, DC.

U.S. EPA (1984), National Air Quality and Emissions Trends Report, 1982. Report EPA-450/4-84-002, March 1984. U.S. Environmental Protection Agency, Research Triangle Park, NC.

U.S. EPA (1986), National Air Quality and Emissions Trends Report, 1984. Report EPA-450/4-86-001, April 1986. U.S. Environmental Protection Agency, Research Triangle Park, NC.

J.G. Watson, J.G. Chow, and J.J. Shah, Analysis of Inhalable and Fine Particulate Matter Measurements, EPA-450/4-81-035, December 1981, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711.

W. Winkelstein, Jr., S. Kantor, E.W. Davis, C.S. Maneri, and W.E. Mosher, The Relationship of Air Pollution and Economic Status to Total Mortality and Selected Respiratory System Mortality in Men I. Suspended Particulates, Arch.Env.Health 14:162 (1967); II. Sulfur Oxides, Arch.Env. Health 16:401 (1968).

R.E. Wyzga and F.W. Lipfert, Inferred Particulate Exposure For a Group of Susceptibles: A Pilot Study, AWMA Paper 92-65.01, presented at the Annual Meeting of the Air and Waste Management Association, Kansas City, MO, June 1992.

APPENDIX A

STATISTICS OF VARIABLES USED

variable name	# obs	mean (149)	mean (98)	std dev. (149)	max (149)	min (149)
TSP (ug/m3)	149	68.38	67.72	16.94	141.57	41.25
SO4 (ug/m3)	149	9.29	9.60	3.10	17.00	2.00
TSP-SO4 net	149	56.43	55.37	17.74	135.72	27.23
computed SO2 (ug/m3)	147	16.91	17.59	10.93	46.38	0.56
computed SO4 (ug/m3)	147	6.66	7.04	3.90	13.86	0.44
computed NOx (ug/m3)	147	15.08	16.14	8.57	46.98	1.44
1978 av'g ozone (ppm)	149	0.0494	0.0495	0.0095	0.0990	0.0130
1980 peak ozone (ppm)	72	0.156	-	0.0575	0.44	0.04
manganese (ug/m3)	138	0.0357	0.0365	0.0265	0.1930	0.0086
PM-2.5 (ug/m3)	63	17.62	-	5.96	37.14	7.21
PM-15 (ug/m3)	63	38.48	-	12.22	68.64	21.91
IP-SO4 (ug/m3)	63	4.27	-	2.46	12.32	1.03
IP-Pb (ug/m3)	63	0.203	-	0.12	0.62	0
population count	149	928330	1091937	1289727	9120346	38092
population density	149	596	673	1174	12108	29
log pop. density	149	2.52	2.59	0.43	4.08	1.47
% white	149	84.57	83.60	10.79	98.80	33.10
% black	149	11.14	12.77	9.66	39.90	0.10
% other nonwhite	149	4.29	3.63	6.84	64.70	0.30
% nonwhite	149	15.43	16.40	10.79	66.90	1.20
median age	149	29.77	29.82	1.94	38.40	25.00
% 65 and over	149	10.60	10.47	2.17	21.40	6.20
% pop. change,1970-80	149	12.83	11.62	14.96	69.45	-9.30
smoking (1980)	149	186.84	186.97	24.16	324.55	125.21
smoking (1970)	149	191.30	191.03	27.09	303.00	115.00
smoking,avg 1970,1980	149	189.07	189.00	22.70	299.28	121.75
% 4 yr college (1970)	98	11.27	11.27	3.42	23.40	5.10
% 4 yr college (1980)	149	16.58	16.85	4.43	32.80	8.00
% below poverty	149	11.14	11.24	3.01	21.70	6.80
% Hispanic	149	5.30	4.55	9.11	61.90	0.30
Drnkg water hardness	149	107.05	97.46	94.23	484.00	0.00
heating degree days	149	4733	4592	2083	9901	0
deaths (all causes)	149	7963	9330	11924	95550	487
deaths less external	149	7334	8589	11065	89675	425
deaths (cardiov.)	149	3912	4573	6056	50279	217
deaths (COPD)	149	218	250	277	1771	18
mort rate(all causes)	149	8.502	8.531	1.486	13.704	4.907
mort rate (nonext)	149	7.826	7.850	1.485	12.899	4.377
mort rate(cardiov.)	149	4.193	4.201	0.950	7.686	2.027
mort rate (COPD)	149	0.251	0.241	0.075	0.683	0.122
log mort rate (all)	149	0.923	0.925	0.076	1.137	0.691
log mort rate(nonext)	149	0.886	0.888	0.083	1.111	0.641
log mort rate (CV)	149	0.611	0.613	0.100	0.886	0.307
log mort rate (COPD)	149	-0.616	-0.629	0.116	-0.166	-0.914

Appendix B Additional Scatter Plots for Non-External Mortality

Figures B-1 to B-9 present scatter plots of these residuals against the additional pollutant variables which were not specifically considered in these regressions. NET TSP appears similar to TSP (Figure B-1). PM-15 (Figure B-2) has one high-value influential observation (San Bernadino, CA); the fine particle plot shows three such points (Figure B-3). Manganese in TSP shows a positive relationship (Figure B-4) in that all of the Mn values above 0.05 have have positive residuals, but there is no apparent effect of dose. Mn may thus be acting as an indicator variable for ferrous metal manufacturing operations. rather than as a pollutant, *per se*. Both $SO_4^=$ (Figure B-5) and Pb (Figure B-6) from the inhalable particle samplers show scattered relationships with little trend.

Figures B-7 to B-9 present plots of these residuals against three variables derived from a long-range transport model for air pollution (Shannon, 1981). Only the values intended to represent NOx (Figure B-9) suggest any kind of trend.

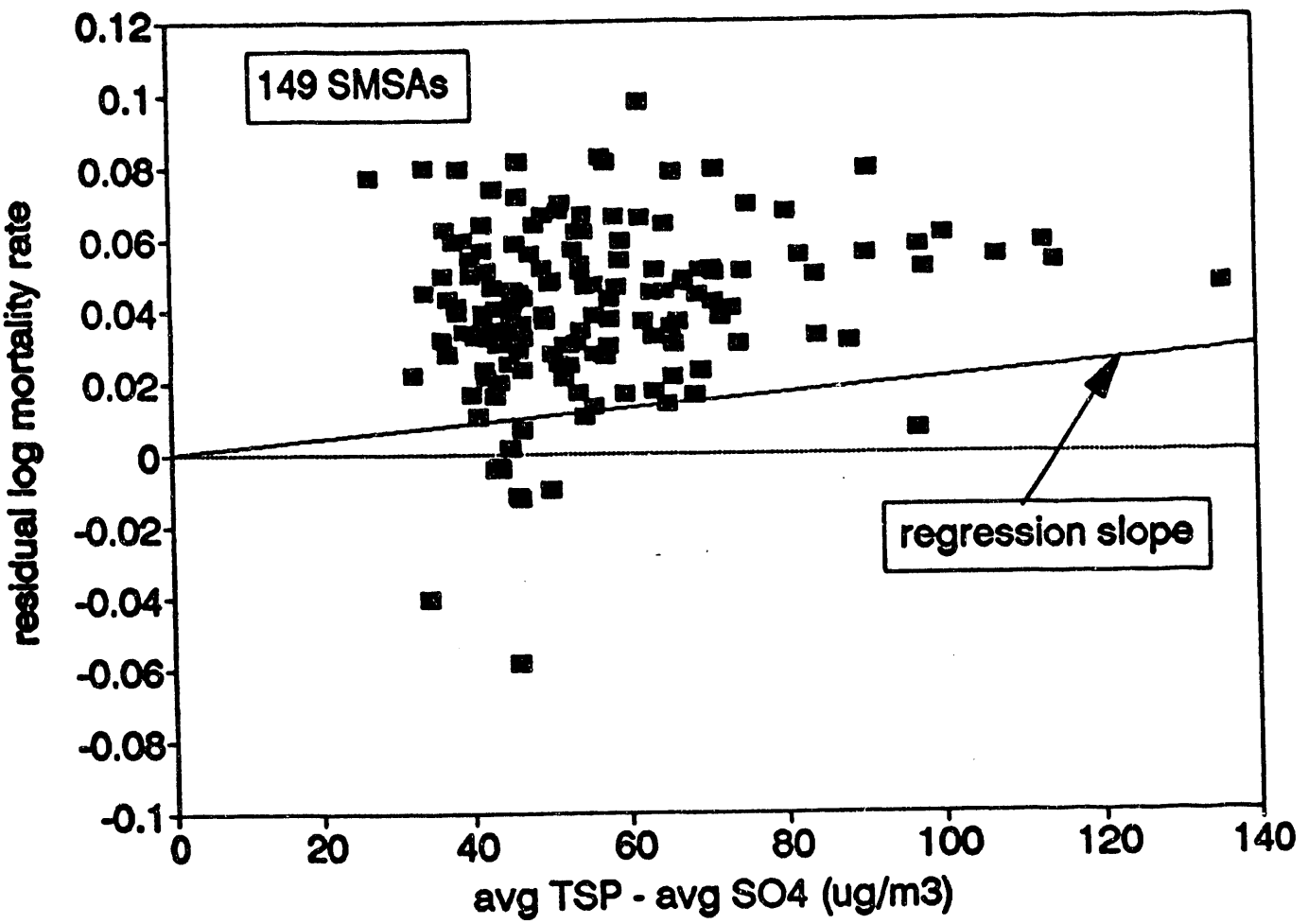

Figure B-1. Scatter plot of residual log non-external mortality rates vs. the TSP-$SO_4^=$ difference.

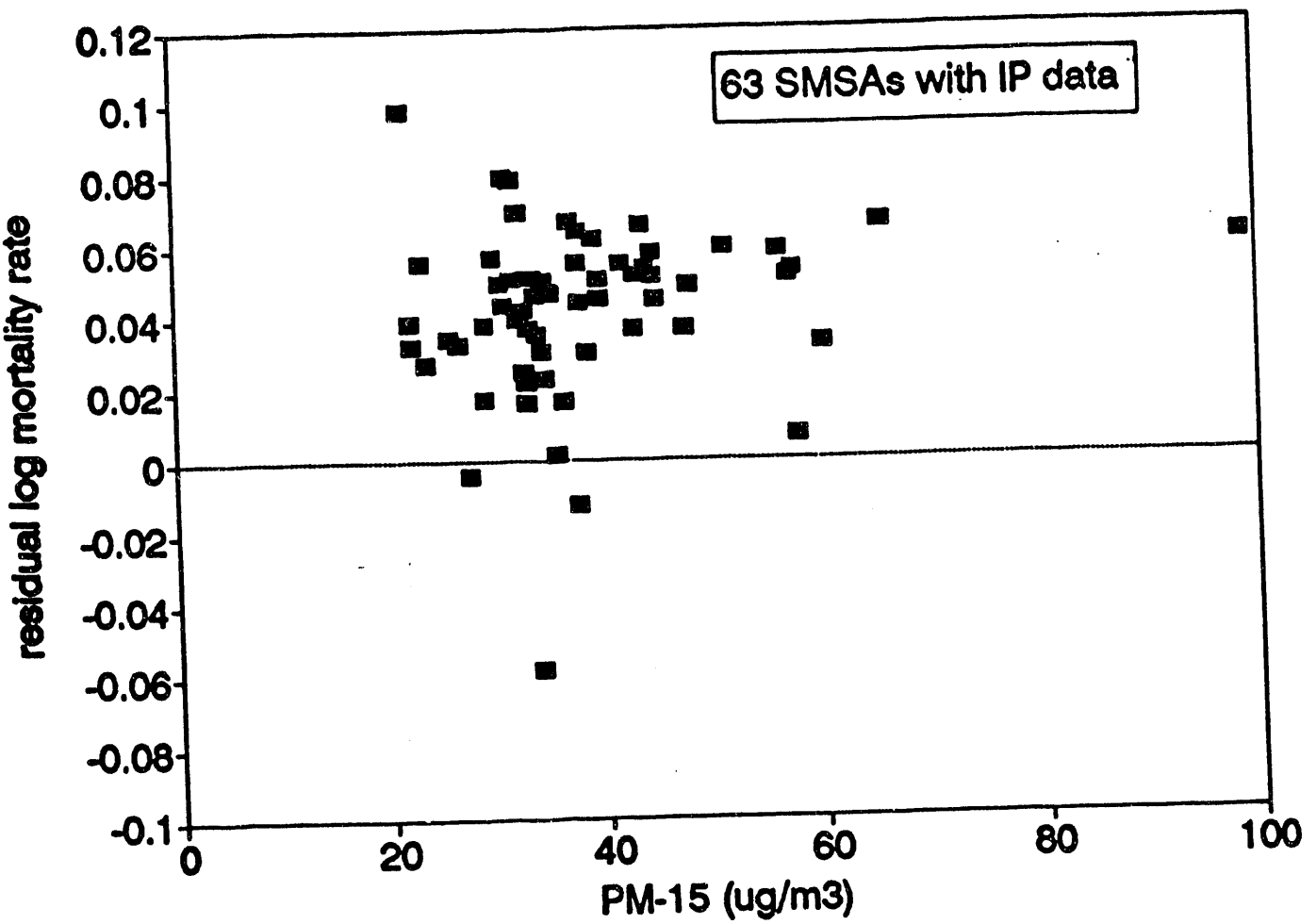

Figure B-2. Scatter plot of residual log non-external mortality rates vs. PM_{15}.

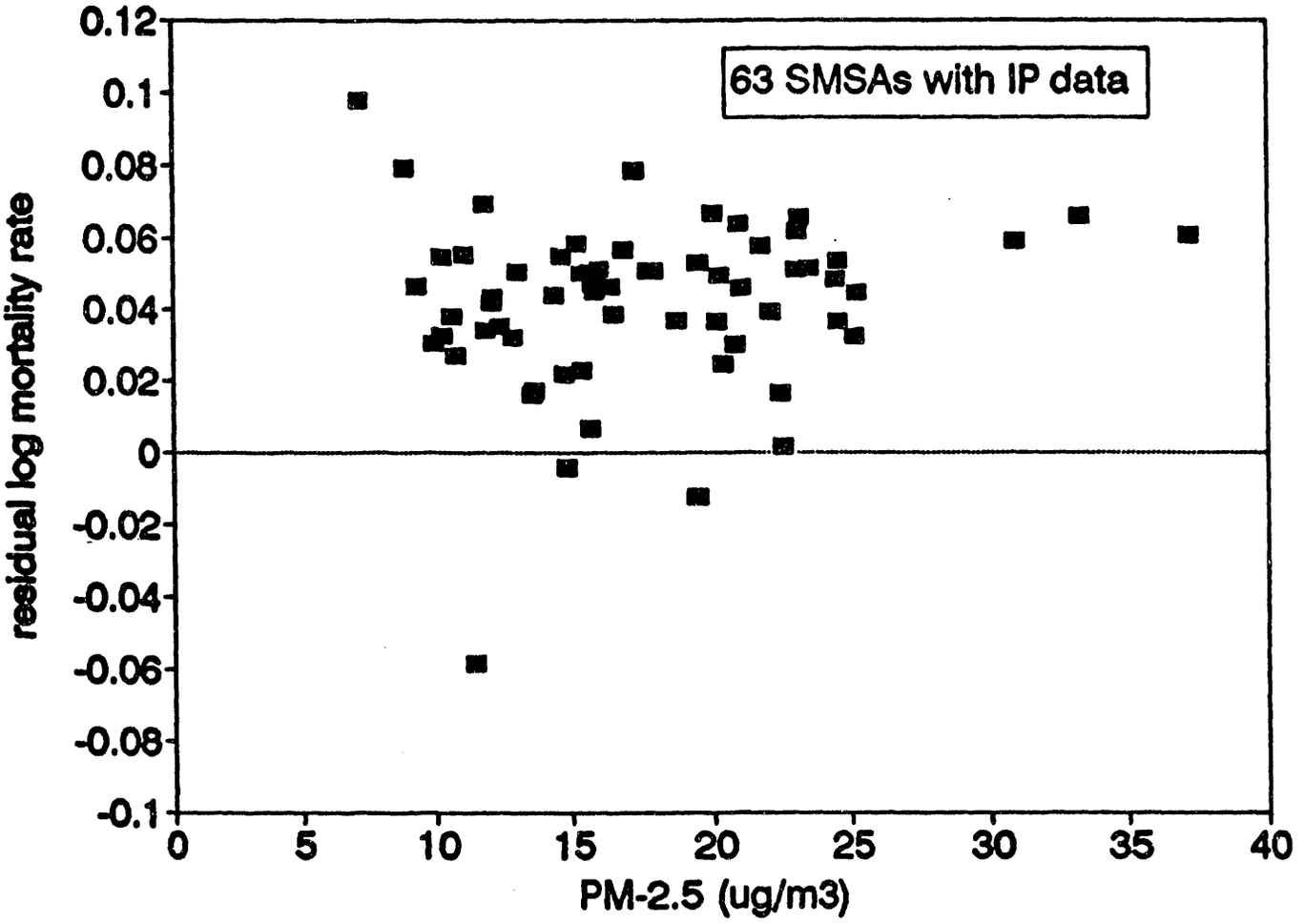

Figure B-3. Scatter plot of residual log non-external mortality rates vs. $PM_{2.5}$.

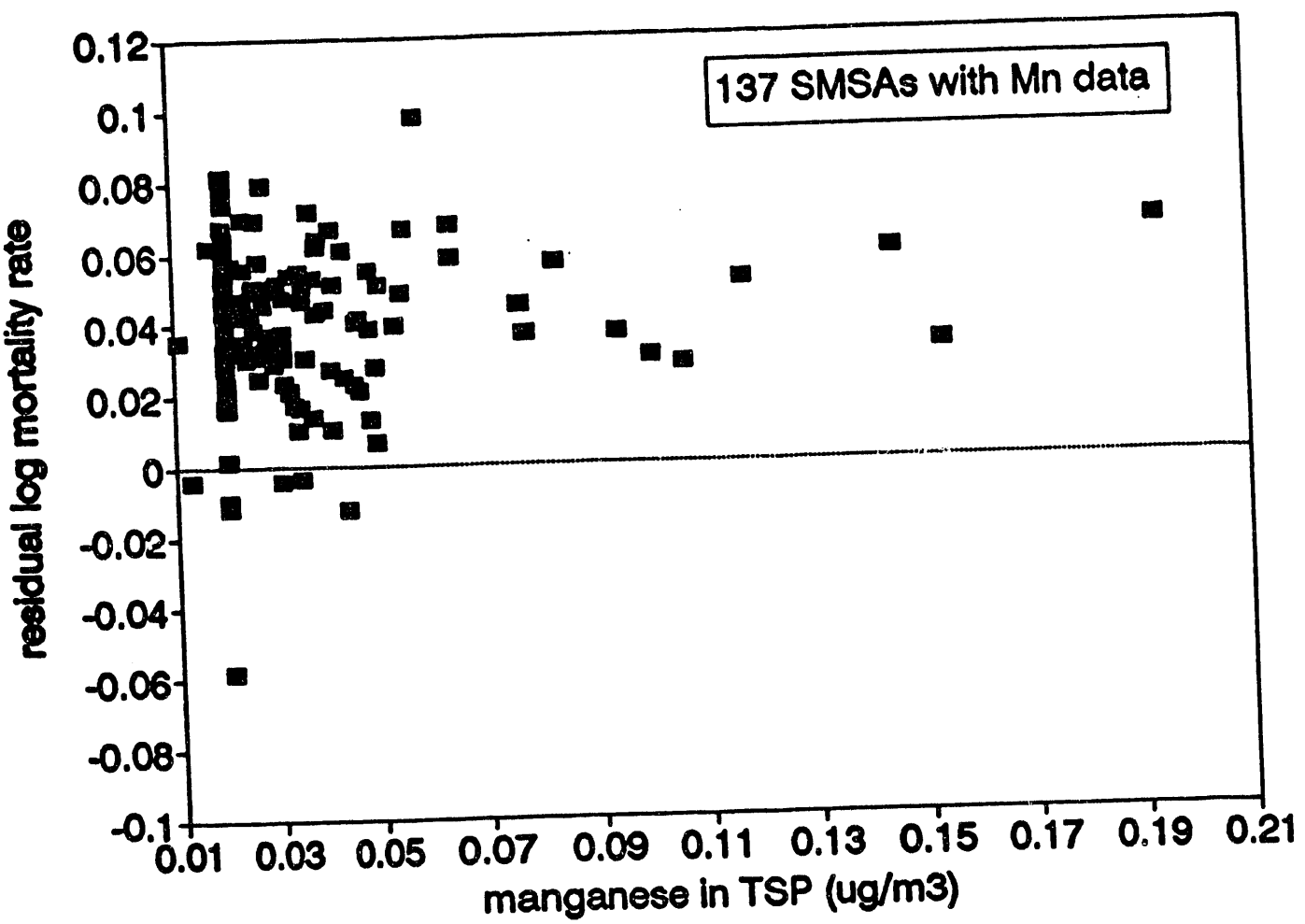

Figure B-4. Scatter plot of residual log non-external mortality rates vs. manganese in TSP.

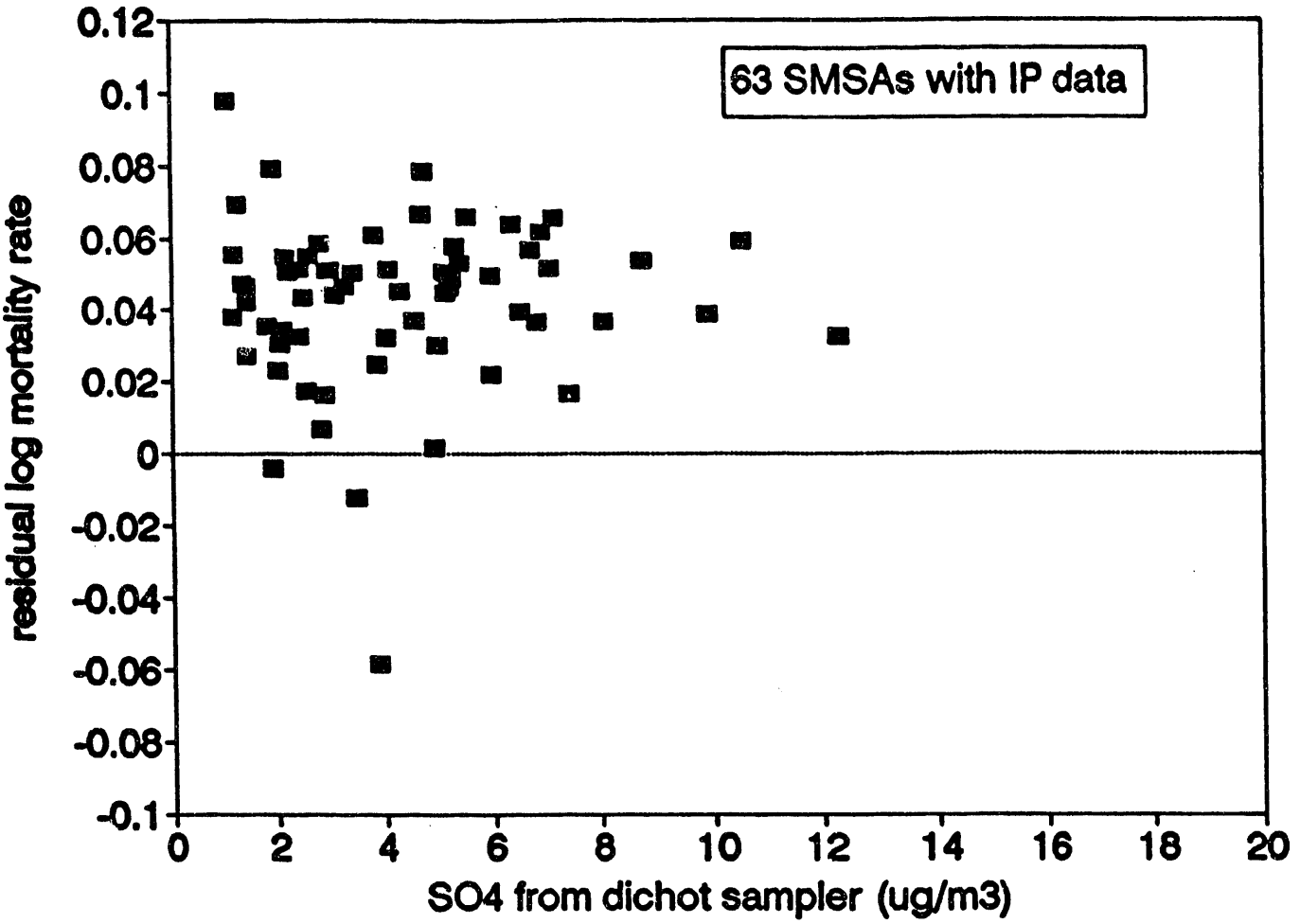

Figure B-5. Scatter plot of residual log non-external mortality rates vs. [IP] $SO_4^=$.

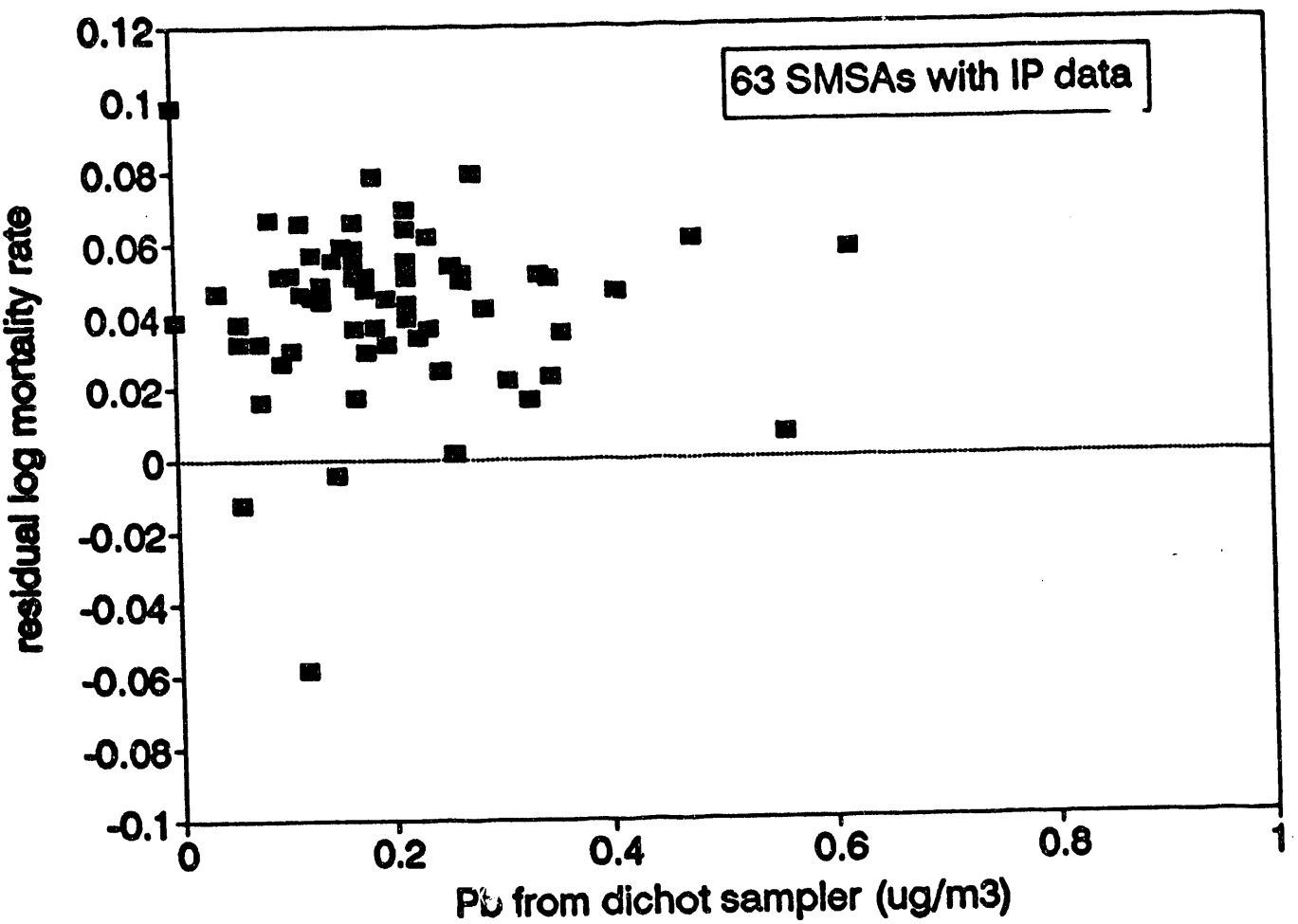

Figure B-6. Scatter plot of residual log non-external mortality rates vs. lead in inhalable particulate.

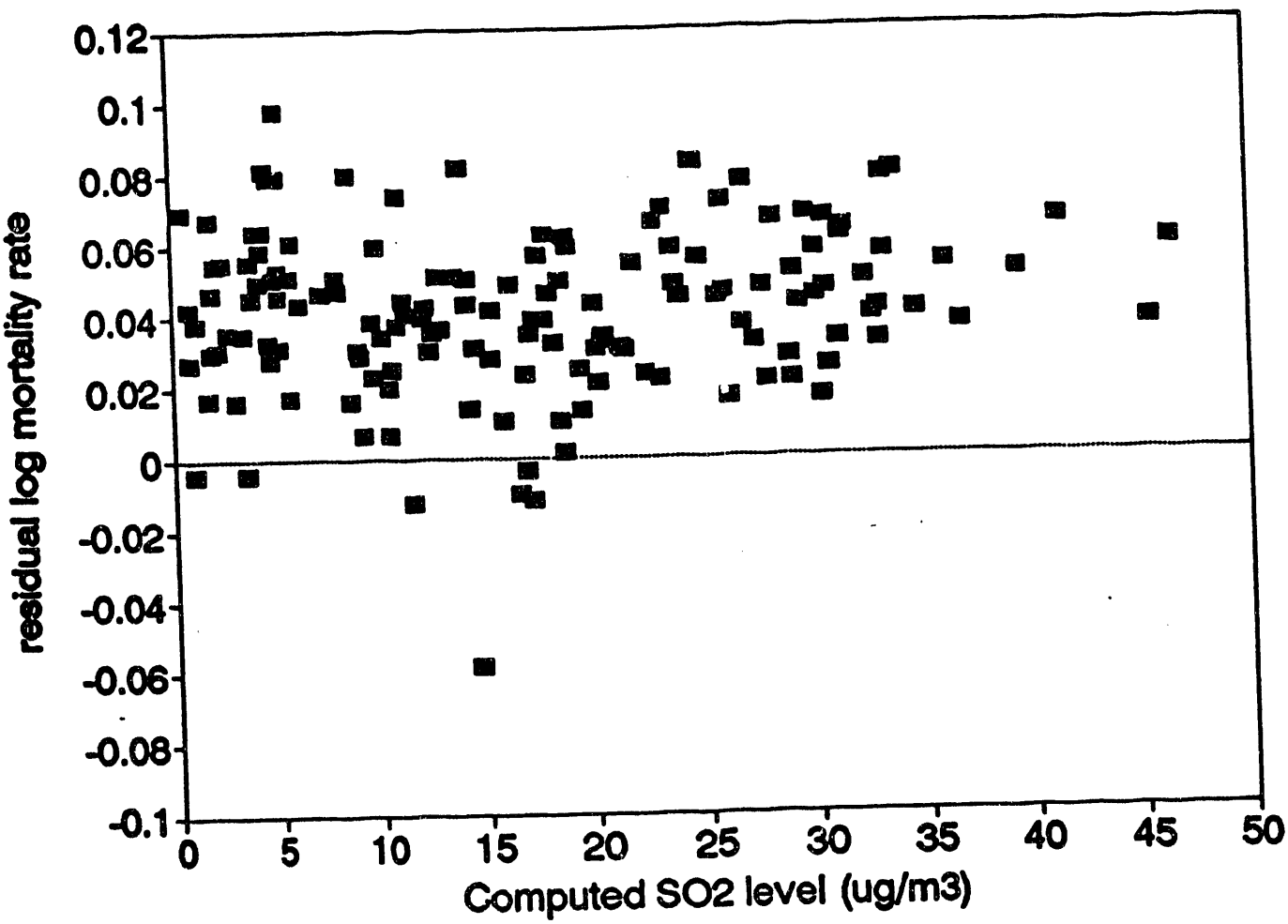

Figure B-7. Scatter plot of residual log non-external mortality rates vs. SO_2 computed from the ASTRAP long-range transport model.

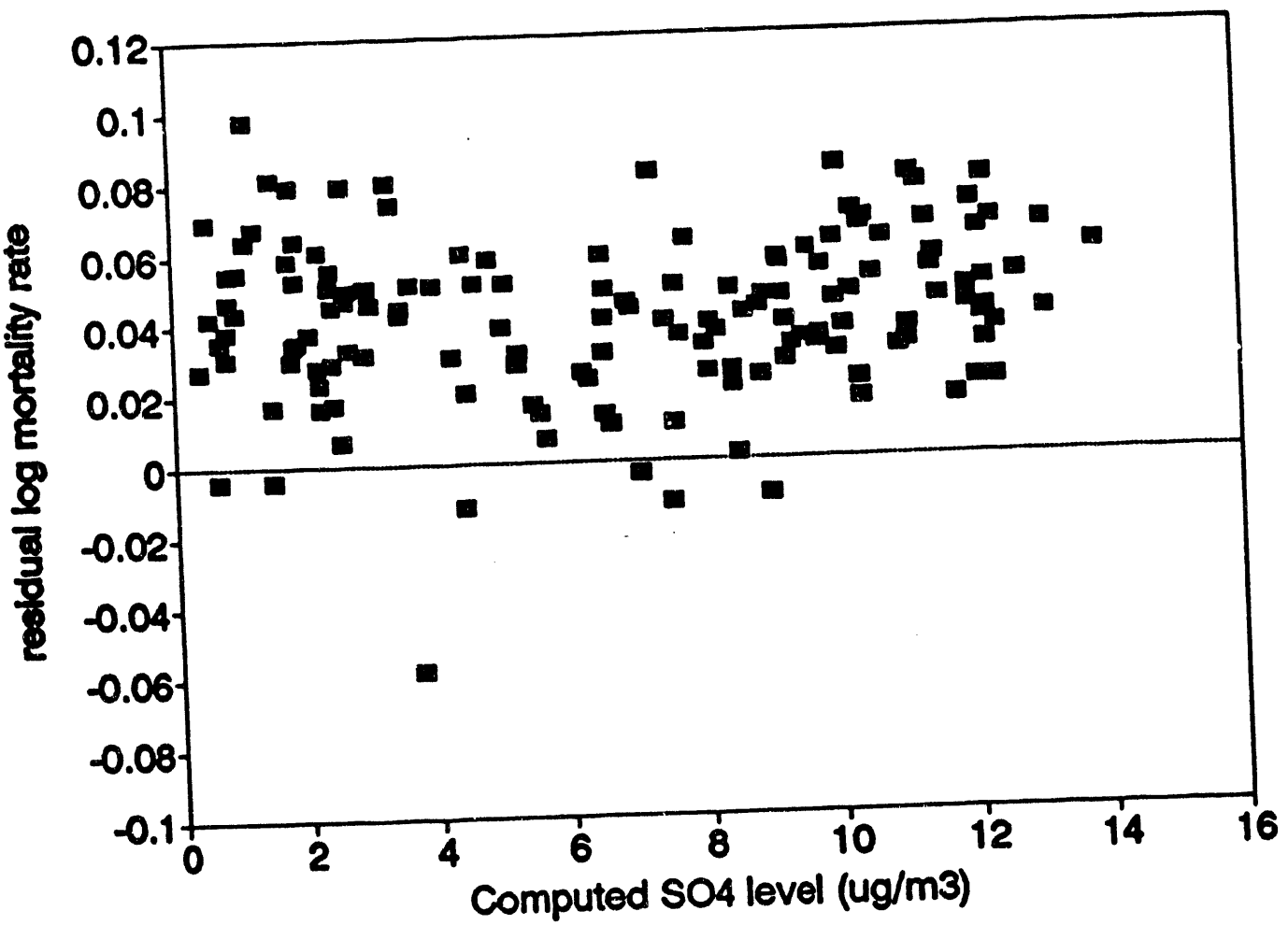

Figure B-8. Scatter plot of residual log non-external mortality rates vs. $SO_4^=$ computed from the ASTRAP long-range transport model.

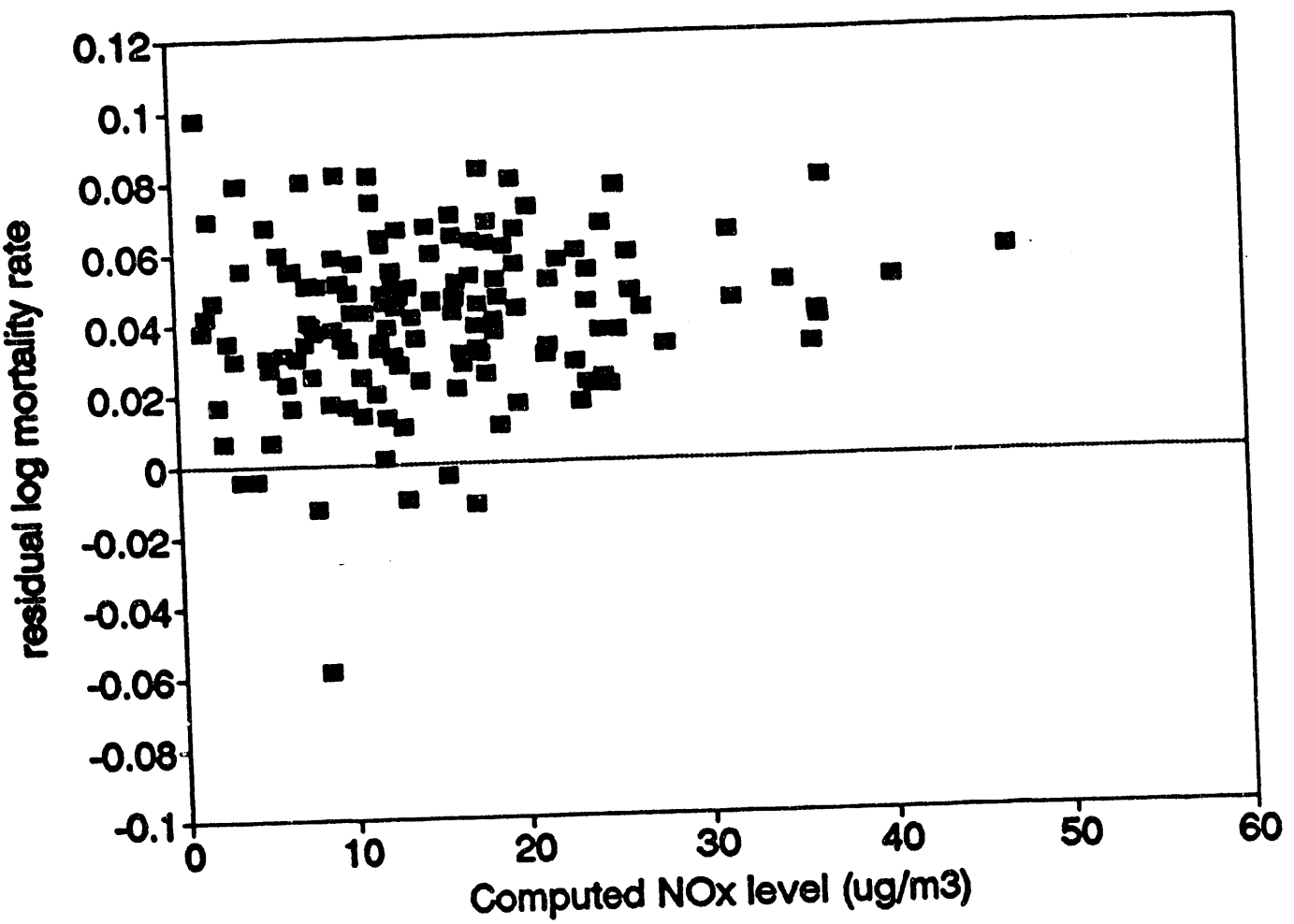

Figure B-9. Scatter plot of residual log non-external mortality rates vs. NO_X computed from the ASTRAP long-range transport model.

END

DATE FILMED

5/3/93