Appendix C

Key Particulate Matter (PM) Epidemiologic Findings Related to PM NAAQS Decisions

C.1 Overview of Key Findings Supporting 1997 PM NAAQS Decisions

C.2 Prospective Cohort Studies of Long-Term Ambient PM Exposure Effects

C.1. Overview of Key Findings Supporting 1997 PM NAAQS Decisions

In promulgating the 1997 PM NAAQS (Federal Register, 1997), EPA relied mainly on the relative risk (RR) levels for increased risks of mortality or morbidity associated with acute (short-term) and chronic long-term measures of PM exposure reported in U.S. and Canadian PM epidemiology studies, which provide the most directly pertinent quantitative risk estimates as inputs to U.S. PM NAAQS decisions. These included (a) relative risk (RR) estimates for mortality or morbidity associated with 50 $\mu g/m^3$ increases in 24-h PM_{10} concentrations (Table C-1) or with variable increases in fine particle indicators, e.g., 25 $\mu g/m^3$ increment in 24-h $PM_{2.5}$ concentrations (Table C-2); and (b) analogous relative risk estimates for health effects related to specified increments in long-term (e.g., annual mean or median) levels of fine particle indicators (Table C-3). The study results summarized in these tables reproduced from Chapter 13 of the PM CD (U.S. EPA, 1996a)[1] were found to provide sufficient evidence for concluding that significant associations of increased mortality and morbidity risks were likely attributable to fine particles, as indexed by various fine particle indicators, e.g., $PM_{2.5}$, sulfates (SO_4), etc.; but possible toxic effects of the coarse fraction of PM_{10} (i.e., $PM_{10-2.5}$) could not be ruled out. Some inhalable coarse fraction particles subsumed under PM_{10} do reach the lower respiratory tract, and some health effects of concern are suggested by some epidemiology results.

Both the PM CD (U.S. EPA, 1996a) and Staff Paper (U.S. EPA, 1996b) noted the very limited extent of available toxicologic findings by which (a) to identify key PM constituents of urban ambient air mixes that may be causally related to mortality/morbidity effects observed in the community epidemiologic studies; or (b) to delineate plausible biological mechanisms by which such effects could be induced at the relatively low ambient PM concentrations evaluated in the epidemiologic studies. As discussed in the PM CD, several types of mechanisms have been shown to underlie toxic effects observed with acute or chronic exposures to various PM species or mixtures (e.g., acute lung inflammation; impaired respiratory function; impaired pulmonary defense mechanisms, etc.), but generally at much higher PM levels than now typically encountered in U.S. ambient air. As also discussed in the 1996 PM CD, several fine particle constituents were hypothesized as being likely important contributors to ambient PM effects, e.g., acid aerosols (indexed by sulfates; H+ ions, etc.); transition metals (e.g., Fe, Mn, etc.); and ultrafine particles. Nevertheless, despite the lack of more definitive characterization of pertinent underlying biological mechanisms, several aspects of the epidemiologic evidence (e.g., the consistency and coherence of the epidemiologic findings), as discussed in the PM CD, support the conclusion that exposure to ambient PM, acting alone or in combination with other air pollutants,

[1]Full reference citations for each study identified in Tables C-1, C-2, and C-3 can be obtained in the bibliographic listing for Chapter 13 in U.S. EPA (1996a).

is probably a key causal agent contributing to the increased mortality and morbidity risks observed in the epidemiology studies. Figure C-1, from the PM Staff Paper (1996b), illustrates the consistency and coherence of the relative risk findings for PM_{10}.

Relative risk estimates shown in Table C-2 for mortality and morbidity effects associated with short-term ambient PM exposures provided the key bases for derivation of the new 65 $\mu g/m^3$ $PM_{2.5}$ (24-hr) NAAQS set by EPA in 1997 to protect sensitive human population groups from adverse effects of short-term exposures to fine particles. Of particular importance in substantiating the need for fine particle standards were analyses of Harvard Six City Study data reported by Schwartz et al. (1996a) showing stronger, more consistently statistically significant, associations between acute (24-h) $PM_{2.5}$ concentrations and increased mortality risks than for 24-h concentrations of inhalable coarse fraction particles ($PM_{15-2.5}$) in the same cities (see Figure C-2).

However, as indicated in Chapter 5 of this document, there is little evidence substantiating the occurrence of health effects due to acute ($\leq$24-hr) exposures to diesel emissions containing DPM at ambient or near-ambient concentrations. Note that 300 $\mu g/m^3$ is the lowest DPM concentration at which mild irritation and inflammation of respiratory tract tissues (but not pulmonary function decrements) were observed with 1-hr controlled human exposures of healthy adult volunteers to diesel exhaust (see Chapter 5). In contrast, various noncancer (respiratory system) effects have been shown to occur in numerous mammalian species as the result of controlled long-term (subchronic, chronic) exposures to DPM. Thus, key elements forming the basis for derivation of the 15 $\mu g/m^3$ $PM_{2.5}$ annual-average NAAQS set in 1997 to protect against health effects associated with long-term fine particle exposures are far more germane here in attempting to relate ambient fine particle health risk estimates to potential ambient DPM exposure risks.

As noted in Chapter 6 of this document, the derivation of the 15 $\mu g/m^3$ $PM_{2.5}$ annual-average standard was based, in part, on the assumption that increased mortality and morbidity effects associated with acute (24-h) $PM_{2.5}$ exposures were most likely due to $PM_{2.5}$ concentrations above the annual mean values for the cities evaluated. Also, it was noted in Chapter 6 that annual mean $PM_{2.5}$ values typically exceeded 15 $\mu g/m^3$ for cities where 24-h $PM_{2.5}$ levels were found to be statistically significantly related to increased mortality and/or morbidity risks, as shown by several key studies (Schwartz et al., 1996; Thurston et al., 1994; Neas et al., 1995).

Other key elements contributing to the derivation of the annual average $PM_{2.5}$ NAAQS were several new prospective cohort studies (published in the 1990's) that evaluated associations between long-term exposures to ambient PM and increased risks of mortality or morbidity. The most salient points of the PM CD (U.S. EPA, 1996a) assessment of such prospective cohort

studies are summarized in Section C.2 below. These are augmented by discussion of pertinent findings from recent new follow-up analyses for one of the subject prospective cohort studies.

C.2. Prospective Cohort Studies of Long-Term Ambient PM Exposure Effects

Newer prospective cohort studies (Abbey et al., 1991; Dockery et al., 1993; and Pope et al., 1995) were considered in the PM CD (1996a) as providing more credible evidence on PM-health effects relationships than numerous previous cross-sectional studies. Salient features of those three key prospective studies are summarized in Table C-4 (reproduced from Chapter 12 of the 1996 PM CD).

C.2.1. Harvard Six U.S. Cities Study

Dockery et al. (1993) analyzed survival probabilities among 8,111 adults first recruited in the mid-1970s in mid-western and eastern U.S. cities, including: Topeka, KS; Portage, WI (a small town north of Madison); St. Louis, MO; Steubenville, OH; (an industrial community on W. VA-PA border); Kingston-Harriman, TN (small towns southwest of Knoxville) and Watertown, MA (western suburb of Boston). These locations comprise a transect across the Northcentral and Northeastern United States, from the upper Midwest through Appalachia, to suburban Boston. In each community, about 2,500 adults (white, aged 25 to 74, at enrollment) were selected randomly, but the final cohorts numbered 1,400 to 1,800 persons in each city. Follow-up periods ranged from 14 to 16 years, during which 13 to 22% of the enrollees died. Of the 1,430 death certificates, 98% of the decedents were located, including persons who had moved away and died elsewhere, but no information was provided on actual locations of death. The analyses reported were mainly based on all-cause mortality; no mention was made of subtracting external causes.

Air monitoring data obtained from routine sampling stations and special instruments set up by the research team were used. Individual characteristics of the cohort subjects (and thus of the decedents) considered in statistical analyses included: smoking habits, an index of occupational exposure, body mass index, and completion of high school education. The Cox proportional hazards model was used to estimate coefficients for individual risk factors after stratifying by gender and age (5-year groups). The effects of air pollution were evaluated (a) by estimating the relative risks of residence in each city relative to Portage (the city with the lowest pollution levels for most indices) and (b) by including the community-average air quality levels directly in the models. Since only six different long-term average values were available for each pollutant, the effective degrees of freedom are small. Most of the air quality measures were averaged over the period of study, in an effort to study long-term (chronic) exposure effects; the specific averaging

periods varied by pollutant. Steubenville, Kingston-Harriman, and St. Louis were the most polluted cities and also had the oldest and least educated cohorts and the heaviest rates of smoking among the six cities.

No consideration was given to possible independent effects of occupation classification, other personal lifestyle variables such as diet or physical activity, migration, or income. Presumably, each subject was characterized by his status at entry to the study; follow-up data on possible changes in risk factors over time were not mentioned. Since the air quality data used in this study were largely obtained from "private" monitoring rather than from public archives, comparisons of the average levels with routine monitoring data were of some interest; and no serious disagreements were found, except that it might have been preferable to consider peak rather than average levels of ozone, as is more typical in most studies of acute O_3 effects on mortality. Also, it is notable that collection of size-classified PM data began in 1980, whereas TSP data began in 1974 and from 1974 to 1980 there were large reductions in TSP (and likely the size-classified particles as well), so that the size-classified data may be less representative than TSP of cumulative exposures. Sulfate appeared to be intermediate in this regard.

A more complete breakdown of relative risk estimates by city, sex, smoking status, education, and body mass index is given in Table C-5. The mean $PM_{2.5}$ values are provided for reference, but the adjusted relative risks used only age, smoking, education, and body mass as covariates. The RR values for men and women combined are plotted in Figure C-3 for each pollutant. Note that the apparently linear relationship between fine particles and risk is less linear if plotted separately for men and for women, and the confidence intervals also become wider due to smaller sample sizes.

Substantial differences in survival rates (expected based on statewide mortality data) were observed across the study's transect of the Northcentral and Northeastern U.S. The long-term average mortality rate in Topeka was 9.7 deaths per 1,000 person-years and in Steubenville was 16.2, yielding a range in average (crude) relative risk of 67% among the six cities. After individual adjustment for age, smoking status, education, and body-mass index, the range in average relative risk was reduced to 26%. The relative importance of adjustments for age, smoking, education, and body mass in determining the final ranks of the cities may be seen from the Table C-5. Also, there is more scatter for men and women separately than when combined, presumably because of the reduction in sample size.

Dockery et al. (1993) report that "mortality was more strongly associated with the levels of fine, inhalable, and sulfate particles" than with the other pollutants, which they attributed

primarily to factors of particle size. They provided relative risk estimates and confidence limits based on the differences between air quality in Steubenville and in Portage for these three PM indicators. However, it is relatively simple to independently estimate coefficients from the adjusted risks and pollutants levels in each of the six communities. These estimates obtained (see Table C-6) correspond well to those of Dockery et al. (1993), based on output from the Cox proportional hazards model. However, because there are only 6 different values for the air quality data, the resulting confidence limits are considerably wider than those for the risk factors having individual data. The estimates given in Table C-6, allow comparisons of results for various pollutants and combination of pollutants. As in the original paper, the relative risks are based on the difference in air pollution between Steubenville and Portage. The data for 1970 TSP (corresponding to a lag of about 12 years) were obtained from Lipfert (1978), assuming that Madison could represent Portage, WI, as was done in the analysis of Schwartz et al. (1996b).

Table C-6 shows only small differences among many pollutants, including SO_2 and NO_2, owing in part to the strong collinearity present. Note that relative risk elevations for the PM_{15} and fine particle indicators ($PM_{2.5}$, SO_4) were statistically significant. The non-sulfate portion of $PM_{2.5}$ had the tightest confidence limits. In contrast, TSP and the coarse particle variables created by subtracting PM_{15} from TSP and $PM_{2.5}$ from PM_{15} were not significant, suggesting that particles ≥ 15 μm in aerodynamic diameter may be less important; this outcome may reflect in part greater spatial variability within the communities for coarse versus fine particles. Note also that the estimated 1970 TSP variable performed slightly better than the TSP data (ca. 1982) used by Dockery et al., thus suggesting a role for previous pollution exposure. Dockery et al. noted that mean ozone levels varied little among cities; but this may have been less so if a measure of peak (e.g., 1- or 8-hr) O_3 levels had been used instead of daily (24-h) averages. Also, no relationship was found for aerosol acidity (H^+), but only limited data were available. Both sulfate and non-sulfate fine particles effects seem rather similar, as shown in Figure C-2, making it plausible that there may be PM effects related to particle size independent of sulfate content or particle acidity.

In comparing the most and least polluted cities, Dockery et al. also reported elevated risks for cardiopulmonary causes (RR 1.37; 95% CL 1.11 to 1.68) and lung cancer (RR 1.37; 95% CL 0.81 to 2.31, not significant). The relative risk for all other causes of death was 1.01 (0.79 to 1.30). When the six cities were considered individually, only Steubenville showed a statistically significant ($p < 0.05$) elevated risk with respect to the least polluted city (Portage).

Comparison of pollution risks among the various cohort subsets considered is one of the most useful outcomes of a study on individuals. Such comparisons must account for the higher variability among subgroups, however, and the study was not capable of distinguishing excess risks between subgroups less than about 18% (i.e., an excess risk of 1.18 cannot be distinguished

from one of 1.36, for example). Although none of these subgroup differences were statistically significant, the mortality risks associated with area of residence (and thus air pollution) were higher for females and for smokers, as were risks for those occupationally exposed compared to the nonexposed. Because of reduced uncertainties about exposures of non-smokers and non-occupationally exposed persons to air pollution not reflected in the outdoor monitoring data used in this study, the relative risk estimates for those subgroups might be the most reliable estimates (1.19 and 1.17, respectively).

Issues concerning possible residual confounding, age adjustment, and smoking controls were raised, and Dockery and Pope (1994) agreed that confounding is a potential concern but did not address the possibility that variables other than the ones they considered might be important. They dealt with the age adjustment issue quantitatively and pointed out that the air pollution risk estimates were reasonably stable over different subgroups by smoking status. Age is a potentially important covariate because it measures both susceptibility to health effects and cumulative exposure to pollutants. There is also a possible interaction involving age, air pollution, and time of death, since air pollution concentrations in some communities such as Steubenville and St. Louis decreased substantially during the years preceding and during the period of the study.

The authors of the Harvard Six City Study were cautious in their conclusions, stating only that the results suggest that fine-particulate air pollution "contributes to excess mortality in certain U.S. cities." One further caveat is warranted before placing quantitative reliance on the specific relative risk values generated by the study. If the responses to air pollution truly are chronic in nature, it is logical to expect that cumulative exposure would be the preferred metric. Pollution levels 10 years before the Six City study began were much higher in Steubenville and St. Louis, as indexed by TSP from routine monitoring networks; and atmospheric visibility data suggest that previous fine particle levels may have been higher in winter, but not necessarily in summer. These uncertainties argue for caution in accepting and using the quantitative regression results based solely on coincident monitoring data. For example, annual average TSP in 1965 in Steubenville was about three times the value used by Dockery et al.; inclusion of older data in the exposure indices would have reduced implied regression coefficients and relative risk estimates.

C.2.2. American Cancer Society (ACS) Study

Pope et al. (1995) analyzed 7-year survival data (1982 to 1989) obtained by the American Cancer Society (ACS) for about 550,000 adult volunteers. The Cox proportional hazards model was used to define individual risk factors for age, sex, race, smoking (including passive smoke exposure), occupational exposure, alcohol consumption, education, and body-mass index. The deaths (about 39,000 in all) were assigned to geographic locations using 3-digit zip codes for residences listed at enrollment into the ACS study in 1982. Relative risks were then computed for

151 metropolitan areas defined by these zip codes and compared to corresponding air quality data (ca. 1980). The sources of air quality data used were (a) the EPA AIRS system data for sulfates, obtained from high-volume sampler filters for 1980, and (b) the Inhalable Particulate Network data for fine particles ($PM_{2.5}$) obtained from dichotomous samplers during 1979-81. Pope et al. used the values from this data base reported by Lipfert et al., 1988, but only 50 $PM_{2.5}$ locations could be matched with the death data. The correlation between the two pollutants was 0.73. Causes of death considered included all causes, cardiopulmonary causes (ICD-9 401-440, 460-519), lung cancer (ICD-9 162), and all other causes.

This study took great care with potential confounding factors for which data were available. Several different active smoking measures were considered, as was time exposed to passive smoke. The occupational exposure variable was specific to (any of) chemicals/solvents, asbestos, coal or stone dusts, coal tar/pitch/asphalt, diesel exhaust, or formaldehyde. The education variable was an indicator for having less than a high-school education, and alcohol use and body-mass index were considered as linear predictors of survival. Pope et al. (1995) did not report relative risk coefficients they obtained for these cofactors, which does not allow comparison of findings for the non- pollution variables with exogenous estimates from independent studies. Risk factors not considered by Pope et al. (1995) include: income, employment status, dietary factors, drinking water hardness and physical activity levels (all shown to affect longevity); and they did not discuss possible influences of other air pollutants.

The ACS cohort is not a random sample of the U.S. population; it is 94% white and better educated than the general public, with a lower percentage of smokers than in the Six City Study. The (crude) death rate during the 7.25 years of follow-up was just under 1% per year, which is about 20% lower than expected for the white population of the U.S. in 1985, at the average age reported by Pope et al. In contrast, the corresponding rates for the Six- Cities Study (Dockery et al., 1993) discussed above tended to be higher than the U.S. average. In spite of these differences, the cause specific ratios for smoking are not significantly different between the ACS and Six-Cities studies.

No mention was made of residence histories for the decedents; matching was done on residence location at time of study entry. The 1979 to 1981 pollution values were assumed to be representative of long-term cumulative exposures, in keeping with the goal of analyzing chronic effects. However, the previous decade was one of extensive pollution cleanup in most of the nation's dirtiest cities (TSP dropped by a factor of 2 in New York City, for example); but PM levels remained relatively constant in cities that already met the standards. Thus, it is reasonable to expect that the contrast between "clean" and "dirty" cities would have been greater in 1970 than in 1980. For example, the ranges of TSP and SO_4 across the U.S. in 1970 were from 40 to 224 and from 3 to 28 $\mu g/m^3$, respectively (Lipfert, 1978). In 1980, these ranges decreased to

41-142 and 2-17 $\mu g/m^3$ (Lipfert, 1984), suggesting that the dirtiest cities became cleaner while the "clean" cities stayed about the same. The change in pollution range is about a factor of 1.8. If the excess mortality found in the ACS study were in fact due to cumulative exposures, the regression coefficients would have been biased upward (in terms of relative risk per $\mu g/m^3$) by only using the more recent data. The typically long latency period for lung cancer (ca. 20 yr.) suggests that data on prior exposures may be particularly important for this cause of death.

The adjusted total mortality risk ratios (computed for the range of the pollution variables) were 1.15 (95% CL = 1.09 to 1.22) for sulfates and 1.17 (95% CL = 1.09 to 1.26) for $PM_{2.5}$, suggesting that particle chemistry may be relatively unimportant as an independent risk factor. Pope et al. (1995) found that the PM pollution coefficients were reduced by 10 to 15% when variables for climate extremes were added to the model. No significant excess mortality for the "other" causes of death was attributed to air pollution in this study. Note that Pope et al. found very consistent pollution risks for males and females and for ever-smokers and never-smokers for all-cause mortality. However, the relative risks for air pollution were slightly higher for females for cardiopulmonary causes of death and the sulfate-lung cancer association was only statistically significant for males, except for male never-smokers.

The results of the ACS prospective study were qualitatively consistent with those of the Six City Study with regard to their findings for sulfates and fine particles; but relative standard errors were smaller, as expected because of the substantially larger ACS database. However, no other copollutants (e.g., O_3, CO, NO_2, etc.) were investigated in the ACS analysis, so that it was not possible to provide an analogous type of pollutant comparison given earlier in Table C-6 for the Six Cities Study. In addition, the ACS regression coefficients were about 1/4 to 1/2 of the corresponding Six City values and were much closer to the corresponding values obtained in various acute mortality studies.

C.2.3. California Seventh-Day Adventists Study

In the Abbey et al. (1991) prospective study (the Adventist Health Study of Smog or "AHSMOG"), 6,338 long-term California residents (all white, non-Hispanic, and nonsmoking) were followed for 6 to 10 years, beginning in 1976. Ambient air quality data dating back to 1966 were used in analyses restricted to those who lived within 5 miles of their current residence for at least 10 years. Subjects lived either within the 3 major California air basins (San Diego, Los Angeles, or San Francisco) or else were part of a random 10% sample of Adventist Health Study participants in the rest of California. Individual exposure profiles (duration of exposure to specific minimum concentration levels) were created for each participant, by interpolating to their zip code centroids based on the 3 nearest monitoring stations. Monitored pollutants were mainly limited to TSP and O_3 in this paper; but, total oxidant concentrations were used in the early part

of the monitoring record. Health endpoints evaluated and the numbers of cases included: (a) newly diagnosed cancers (incidence at any site) for males, 115; (b) any cancer site for females, 175; (c) respiratory cancer, 17; (d) definite myocardial infarction, 62; (e) mortality from any external cause, 845; and (f) respiratory symptoms, 272. The Cox proportional hazards model was used, considering age, sex, past smoking, education, and presence of definite symptoms of asthma, chronic bronchitis, or emphysema of airway obstructive disease (AOD) in 1977 as individual risk factors, together with various exposure indices for TSP or O_3 (considered separately). Data on occupational exposures and history of high blood pressure were available but not used in the mortality model; nor were data available on climate, body mass, income, migration, physical activity levels or diet.

Of the above endpoints, only respiratory symptoms and female cancers (any site) were reported by Abbey et al. (1991) to be statistically associated with TSP exposure. Neither heart attacks or nonexternal mortality were associated with either TSP or O_3 / oxidants. The authors stated that possible errors in their estimated exposures to air pollution may have contributed to the lack of significant findings, and a later version of the data base included estimates of attenuation resulting from time spent indoors (Abbey et al., 1993), but mortality was not considered in the 1993 paper. Follow-up analyses (Abbey et al., 1995) considered exposures to PM_{10} (estimated from site-specific regressions on TSP), $PM_{2.5}$ (estimated from visibility), sulfates (SO_4), and visibility per se (extinction coefficient). No significant associations with nonexternal mortality were reported, and only high levels of TSP or PM_{10} were associated with AOD or bronchitis symptoms.

This study used an unique air quality data base developed explicitly for studying effects of long-term cumulative exposures to community air pollution. The technique provided spatial interpolations that were somewhat better for O_3 than for TSP, in keeping with the regional nature of O_3. TSP may have been an inadequate index of exposure to inhalable particles, especially in this relatively arid region where a large fraction of non-inhalable crustal particles could be expected. Also, no attention was given to temporal matching of air quality and health; the analyses using this data base were intended to evaluate the hypothesis that health is affected by cumulative long-term pollution exposure at some undetermined time, as opposed to acute or coincident exposures. Note that the data base began in 1966 and the mortality follow-up began 10 years later. Because air quality generally improved during this period, highest pollutant concentrations likely occurred in the earlier part of the record; and one would not expect spatially-based correlations to also reflect the sum of acute effects, as when air quality and health data are also matched in time.

The PM CD (U.S. EPA 1996a) noted that the finding of Abbey et al. (1991, 1995) of no association between long-term cumulative exposure to ambient TSP or O_3 (or to SO_4 or estimated

PM_{10} or $PM_{2.5}$) concentrations and all natural-cause mortality could be interpreted as showing the absence of chronic responses after 10 years but not necessarily the absence of (integrated) acute responses, since coincident air pollution exposures or integrated exposures over the preceding few years were not considered. It is also possible that the exposure measurements or estimates used were inadequate or that the latency period for chronic effects may exceed 10 years and that additional follow-up might still reveal chronic effects.

Further such follow-up analyses of the same California AHSMOG database have been reported recently by Abbey et al. (1999). These analyses (not considered in the 1996 PM CD or 1997 PM NAAQS decisions) do provide some evidence indicative of increased risk of mortality from contributing non-malignant respiratory causes being associated with long-term PM exposures. Other recent AHSMOG analyses reported by Abbey et al. (1999) and Beeson et al. (1998) are also suggestive of increased risk of mortality from lung cancer possibly being associated with long-term PM_{10} exposures, as summarized below.

Abbey et al. (1999) evaluated the mortality status of AHSMOG subjects after ca. 15-years of follow-up (1977-1992), finding 1,628 deaths (989 female, 639 male) in the cohort. There were 1,575 deaths from all natural (non-external) causes, of which 1,029 were cardiopulmonary deaths, 135 were non-malignant respiratory deaths (ICD9 codes 460-529), and 30 were lung cancer deaths (ICD9 code 162). Abbey et al. (1999) also created an additional death category, "contributing respiratory causes" (CRC). CRC included any mention of nonmalignant respiratory death as either an underlying cause or a contributing cause on the death certificate CRC coded by an exposure-blinded nosologist (the other groups listed only underlying causes), with 410 deaths (246 female and 164 male) being found. Numerous analyses were done for the CRC category, due to the large numbers and relative specificity of respiratory causes as a factor in the deaths. Education was used as an index of socio-economic status, rather than income. Physical activity and occupational exposure to dust were also used as covariates. Migration was not a major concern in this residentially stable cohort.

A number of exposure indicators were used: mean values of PM_{10} (imputed from TSP in the earlier years of the study), SO_4, SO_2, O_3, and NO_2; and "threshold" indicators (i.e., days per year with $PM_{10} > 100\ \mu g/m^3$; and hours per year with $O_3 > 100$ ppb). In summary tables that follow below, the "standard" increments used for PM_{10} and SO_4 are (a) the same as used earlier for the short-term mortality studies (50 $\mu g/m^3$ for PM_{10} and 15 $\mu g/m^3$ for SO_4) and (b) 30 days per year for exceedances of PM_{10} above 100 $\mu g/m^3$. The mean values for PM_{10} and SO_4 during the study period were 51 and 7.2 $\mu g/m^3$ respectively, and 31 days per year for PM_{10} exceedances over 100 $\mu g/m^3$. The means were much larger than the inter-quartile ranges (IQR) of 24 and 3.0 $\mu g/m^3$. IQR is the increment used for other variables. RR and confidence limits using IQR

from Abbey et al. (1999) are shown to 2 decimal places; those estimated for standard increments are shown to 3 decimal places.

Cox proportional hazard models adjusted for a variety of covariates, or stratified by sex, were used in the models. The "time" variable used in most of the models was survival time from date of enrollment, except that age on study was used for lung cancer effects due to the expected lack of short-term effects. A large number of covariate adjustments were evaluated, as shown in Table C-7 and described by Abbey et al. (1999).

The CRC RR estimates for 30 days per year with $PM_{10} > 100\ \mu g/m^3$ for males and females combined are shown in Table C-7. Positive and statistically significant effects are found for almost all models that include age, pack-years of smoking, and body-mass index (BMI) as covariates. Subsets of the cohort also often had elevated risks. Former smokers had higher relative risks than never-smokers (RR for PM_{10} exceedances for never-smokers was marginally significant by itself, in spite of the reduced sample size). Subjects with low intake of anti-oxidant vitamins A, C, E had significantly elevated risk of response to PM_{10} whereas those with adequate intake did not, suggesting that dietary factors (or possibly other socio-economic or life style factors for which they are a surrogate) may be important covariates. There also appears to be a gradient of PM_{10} risk with respect to time spent outdoors, with individuals who had spent at least 16 hours per week outside at distinctly elevated risk from PM_{10} exceedances. The extent to which time spent outdoors is a surrogate for other variables or is a modifying factor reflecting temporal variation in exposure to ambient air pollution is not certain. For example, males spend about twice as much time outdoors as females, so that outdoor exposure time is confounded with gender.

A considerably different picture is shown when the analyses are broken down by gender. Table C-8 shows much lower RR for female CRC deaths for all co-pollutants, with all female RR positive, but not statistically significant. The CRC for males remains significant only for PM_{10} exceedances, but not for other air pollution metrics. The PM_{10} exceedance effect for CRC for both sexes is roughly the average of that for males and females. Personal monitoring was not conducted on this part of the cohort, and other factors (e.g., occupational exposure) for which the questionnaire was not adequate may also account for male vs. female differences, along with gender differences in the amount of time spent outdoors. Finally, it is not surprising that individuals reporting respiratory symptoms in 1977 may be at greater risk to PM_{10} or other environmental insults presumably involved in subsequent CRC deaths, and prior health status may also be gender-related.

Table C-9 shows much lower RR for female non-external deaths for all co-pollutants, with no female RR positive nor statistically significant. Deaths from non-external causes for males

remains statistically significant for PM_{10} exceedances, but not for other air pollution metrics. However, the RR estimates for males for other air pollutant metrics are relatively large.

Table C-10 shows much lower RR for female cardio-pulmonary deaths for all co-pollutants, with only the female RR for mean SO_2 positive and none statistically significant. The RR for deaths from cardiopulmonary causes for males is no longer statistically significant for PM_{10} exceedances, nor for other air pollution metrics (although the RR estimates for males for air pollutant metrics are relatively large).

Table C-11 shows a confusing welter of results obtained for lung cancer mortality. For example, the RR's for lung cancer deaths are significant for males for PM_{10} and O_3 metrics, but not for females. In contrast lung cancer deaths are significant for mean NO_2 for females, but not for males, but lung cancer metrics for mean SO_2 are significant for both males and females. This pattern is not readily interpretable, but may be attributable to the very small numbers of cancer-related deaths (18 for females; 12 for males), resulting in wide RR confidence intervals.

In general, this study (Abbey et al., 1999) suggests a pattern of mortality from diverse causes (e.g., CRC, lung cancer) in males, but provides little evidence for female mortality from these causes. The male causes primarily appear to be associated with exposures to PM_{10} and especially to $PM_{10} > 100\ \mu g/m^3$. Some other air pollutants (SO_2, NO_2) appear to be associated with lung cancer deaths in females.

The analyses reported here attempted to separate PM_{10} effects from those of the other pollutants by use of two-pollutant models, but none of the quantitative findings from these models were reported. The Abbey et al. (1999) text mentions that the PM_{10} coefficient for CRC remained stable or increased when other pollutants were added to the model. Lung cancer mortality models for males were evaluated for co-pollutant effects in detail. NO_2 remained nonsignificant in all two-pollutant models, and the other pollutant coefficients were stable in magnitude. The PM_{10} and O_3 effects remained stable when SO_2 was added, suggesting that their effects are independent. However, the effects of PM_{10} and O_3 were hard to separate because these pollutants were highly correlated in this study. When both exceedances $PM_{10} > 100\ \mu g/m^3$ and $O_3 > 100$ ppb were used in the model, both RR were reduced in magnitude, but the O_3 exceedance RR remained more significant than the RR for the PM_{10} exceedance. The possibility that the finding of a significant PM_{10} effect is partially attributable to correlation with other pollutants such as O_3 cannot be precluded. The SO_2 coefficient for lung cancer mortality in females remained stable in two-pollutant models when PM_{10} and O_3 exceedances were included. This suggests that the significance of the SO_2 effect for females may not be an artifact wholely attributable to collinearity with these co-pollutants.

Beeson et al. (1998)

This study used essentially the same data as did Abbey et al. (1999), but concentrates on lung cancer incidence (1977-1992) as an endpoint. There were only 20 female cases and 16 male cases of lung cancer among the 6,338 AHSMOG subjects. The exposure metrics were constructed to be specifically relevant to cancer, being the annual average of the monthly exposure indices from January, 1973 through the following months, but ending 3 years before the date of diagnosis of the case. This represents a 3-year lag between exposure and diagnosis of lung cancer, allowing for a latency period. Therefore, statistical indices for exposure have somewhat different statistics than in Abbey et al. (1999), such as the IQR and mean.

The covariates in the Cox proportional hazards model were pack-years of smoking and education, and the time variable was attained age. A number of additional covariates were evaluated for inclusion in the model, but only 'current use of alcohol' met the criteria for inclusion in the final model. Individual pollutants evaluated were PM_{10}, SO_2, NO_2, and O_3. No interaction terms with the pollutants proved to be significant, including outdoor exposure times. Gender-specific relative risk estimates were reported for the various risk factors. Results are shown in Table C-12 for males and Table C-13 for females. Standard increments were used for PM_{10} mean (50 $\mu g/m^3$) and exceedances of PM_{10} > 100 $\mu g/m^3$ (30 d/y). The RR estimates and confidence limits using IQR from Beeson et al. (1998) are shown to 2 decimal places, those estimated for standard increments are shown to 3 decimal places.

The RR estimates for the male lung cancer cases are: positive and statistically significant for all PM_{10} indicators; positive and predominantly significant for O_3 indicators, except for mean O_3, number of O_3 exceedances > 60 ppb, and in former smokers; and are positive and significant for mean SO_2, except when restricted to proximate monitors. The RR for mean NO_2 is positive but not significant. The very high RR for mean PM_{10} for males (31.1) may be attributable to the small number of cases (N = 16) and the large standard increment (50 $\mu g/m^3$) used. When data are restricted to subjects with at least 80 percent A/B quality data (within 32 km of the residence), the RR is reduced to 9.26 over 50 $\mu g/m^3$. The RR over the IQR of 24 $\mu g/m^3$ in the full data set is 5.21, so that the use of the IQR may be more appropriate for the exposure in long-term studies.

The female lung cancer RR estimates reported by Beeson et al. (Table C-13) are much smaller than those for males, not being statistically significant for any indicator of PM_{10} or O_3 and statistically significant only for mean SO_2.

Extensive multi-pollutant analyses were also carried out. Regression coefficients for PM_{10} and SO_2 were not reduced when O_3 or NO_2 were added to the single-pollutant models for males. The regression coefficients for the two-pollutant model with PM_{10} and SO_2 remained highly positive and significant, which the authors suggest may be associated with independent effects of PM_{10} and SO_2 on lung cancer incidence. PM_{10} was more strongly correlated with lung cancer in males than the other pollutants. For females, the SO_2 coefficient remained significant when

co-pollutants were added one at a time, and was the air pollutant most strongly associated with female lung cancer cases.

The results of Abbey et al. (1999) and Beeson et al. (1998) are somewhat different than those of earlier studies using the same cohort. Abbey et al. (1991) reported completely non-significant relationships between total ('all natural causes') mortality and air pollution. The RR for 1000 h/y of TSP > 200 $\mu g/m^3$ was 0.99 (CI 0.87-1.13), and for 500 h/y of O_3 > 100 ppb was 1.00 (CI 0.89-1.12), after 10 years of follow-up. Also, Abbey et al. (1991) reported no statistically significant increases in all malignant neoplasms for males attributable to air pollution. The RR for 1000 h/y of TSP > 200 $\mu g/m^3$ was 0.96 (CI 0.68-1.36), and for 500 h/y of O3 > 100 ppb was 1.09 (CI 0.80-1.47), after 10 years of follow-up. However, there was a statistically significant increase in all malignant neoplasms for females. The RR for females attributed to 1000 h/y of TSP > 200 $\mu g/m^3$ was 1.37 (CI 1.05-1.80). Neoplasms in females attributed to 500 h/y O_3 > 100 ppb were much less significant, with RR = 1.03 (CI 0.81-1.32).

C.2.4. Relationship of AHSMOG to Six Cities and ACS Study Findings

The results of the recent AHSMOG mortality studies (Abbey et al., 1999) are compared below with the earlier Six Cities Study (Dockery et al., 1993) and ACS Study (Pope et al., 1995). Tables C-14, C-15, and C-16 compare the estimated RR for total, cardiopulmonary, and lung cancer mortality, respectively, among the studies. The PM indices used are the mean PM_{10} concentration for the Six Cities and AHSMOG studies (increment 50 $\mu g/m^3$), and the mean $PM_{2.5}$ and SO_4 concentrations (increments 25 and 15 $\mu g/m^3$ respectively) for the ACS study. The comparisons for the Six Cities and ACS studies have been translated from published RR for the most polluted vs. least polluted city for PM_{10}, $PM_{2.5}$, and SO_4. Results are shown by sex and smoking status. The AHSMOG subjects are classified as 'non-smokers', although some former smokers are included. The ACS study combines past and current smokers into an 'ever smoker' category, although long-term past smokers are at much lower risk than current smokers. The number of subjects in these studies varies greatly (6,338 AHSMOG subjects, 8,111 Six Cities Study subjects; compared to 295,223 subjects in the 50 fine particle cities and 552,138 subjectsin the 151 sulfate cities of the ACS study), and may partially account for differences among their results.

Table C-14 shows relative risks for total mortality at comparable standard increments. RR is generally highest for the Six Cities Study. The AHSMOG Study found a much smaller RR for women than did the other studies, whereas the effect for males was similar to non-smokers in the ACS Study and marginally significant. RR among the three studies varied substantially with sex and smoking categories. Six of the 16 independent analyses showed significant positive RR (LCL $\geq$ 1.0), but subsetting the data allowed less power to detect effects than the whole data sets would

have allowed. Neither of the AHSMOG RR were significant using the mean as the PM_{10} index, but another PM_{10} index (exceedances over 100 $\mu g/m^3$) was significant for males.

Table C-15 shows relative risks for cardiopulmonary mortality at comparable standard increments. RR is highest for the Six Cities Study, which did not report separate effects by sex and smoking status. The AHSMOG Study found a much smaller cardiopulmonary RR for women than did the other studies. However, the RR for male non-smokers was much more similar to the ACS results than for female non-smokers. RR for the AHSMOG endpoint CRC ('contributing respiratory causes') was more similar to the ACS findings for women, but higher in men, although the confidence intervals are very wide. Seven of 13 of the independent analyses showed significant positive RR (LCL $\geq$ 1.0). The AHSMOG cardiopulmonary RRs using mean PM_{10} were not significant for either males or females. However, the 100 $\mu g/m^3$ exceedance index for males was nearly so.

Table C-16 shows relative risks for lung cancer mortality at comparable standard increments for PM-related variables. The lung cancer mortality RR estimates were highest for males in the AHSMOG study, and statistically significant. The AHSMOG study also found a larger RR for women than did the other studies. The only other statistically significant finding for lung cancer mortality was for past and current male smokers in the ACS 151-city sulfate study. The overall pattern of results for lung cancer, then, is a somewhat conflicting set of findings across the three prospective cohort studies assessed here, providing only somewhat suggestive evidence at best for possible ambient PM relationship to increased lung cancer risk.

There is no obvious statistically significant relationship between PM effect sizes, gender, and smoking status across these studies. The AHSMOG studies show no statistically significant relationships between PM_{10} and total mortality or cardiovascular mortality for either sex, and only for male lung cancer incidence and lung cancer deaths in a predominantly non-smoking sample. The ACS results, in contrast, show similar and significant associations with total mortality for both "never smokers" and "ever smokers", although the ACS cohort may include a substantial number of long-term former smokers with much lower risk than current smokers. The Six Cities Study cohort shows the strongest evidence of a higher PM effect in current smokers than in non-smokers, with female former smokers having a higher risk than male former smokers. This study suggests that smoking status is "effect modifier" for ambient PM, just as smoking may be a health effect modifier for ambient ozone (Cassino et al., 1999).

It is interesting to note, in relation to the above discussion, that a comparison of the Six-Cities Study non-smoker RRs with the Six-Cities results in Table C-14 for smokers indicates that larger and more significant effects of ambient PM pollution are found for smokers than non-smokers. This suggests that smoking is an effect modifier that increases the adverse effects of ambient pollution. This trend is consistent with air pollution effect causality, as smokers

represent a compromised population, logically more likely to be adversely affected by air pollution. This may also explain why the reported AHSMOG study RRs are generally not significant, in contrast with the overall Six-Cities Study results (but consistent with the Six-Cities nonsmoker results), as there are no identified smokers among the AHSMOG study group to "drive up" the overall significance of the air pollution effect. This again indicates that more years of follow-up may be required to see any statistically significant total mortality effects in both the AHSMOG and Six-Cities studies' non-smoking populations.

C.2.5. Studies by Particulate Matter Size-Fraction and Composition

Particulate matter mass varies widely over time and from place to place in size and chemical composition, and this likely affects the toxicity of that mass. The semi-individual cohort studies assessed here investigated the relative roles of various PM components in the air pollution association with mortality. As shown in Table C-17, the Harvard Six-Cities study (Dockery et al., 1993) results indicated that the $PM_{2.5}$ and SO_4 RR associations (as indicated by their respective 95% CI's and t-statistics) were stronger than those for the coarser mass components. However, the effects of sulfate and non-sulfate $PM_{2.5}$ are indicated to be quite similar. Acid aerosol (H^+) exposure was also considered by Dockery et al. (1993), but only less than one year of measurements collected near the end of the follow-up period were available in most cities, so the Six-Cities results were much less conclusive for the acidic component of PM than for these other PM metrics (that, in contrast, were measured over many years during the study). The Six-Cities Study also yielded total mortality RR estimates for the reported range across those cities of $PM_{2.5}$ and SO_4 concentrations that, although not statistically different, were roughly double analogous RRs for the TSP-PM_{15} and $PM_{15-2.5}$ mass components.

Table C-18 presents comparative $PM_{2.5}$ and SO_4 results from the ACS study that indicate that, although the RR differences were not statistically significant across pollutants, the SO_4 RRs were in every case more strongly significant than those for the $PM_{2.5}$ across the various mortality cause classifications considered, especially for lung cancer (SO_4 t=2.92 vs. t=0.38 for $PM_{2.5}$).

The most recent AHSMOG study analysis (Abbey et al., 1999) employed PM_{10} as its PM mass index, finding some significant associations with total and by-cause mortality, even after controlling for potentially confounding factors (including other pollutants). This analysis also considered SO_4 as a PM index for all health outcomes studied except lung cancer, but SO_4 was not as strongly associated as PM_{10} with mortality, and was not found to be statistically significant for any mortality category. The significant mortality associations found for PM_{10} contrasts with previously published AHSMOG study PM analyses that found weaker mortality associations with TSP (Abbey et al., 1991). Although the longer follow-up time in this new analysis may have also contributed, the greater strength of association by PM_{10} vs. TSP is consistent with the Harvard

Six-City study results presented in Table C-17, as well as with the Özkaynak and Thurston (1987) cross-sectional comparisons of mortality associations with the various PM fractions.

Single-pollutant results about PM components are informative, however, as shown in Table C-19 for total mortality, and in Table C-20 for cardiopulmonary causes. The t-statistics are compared for studies where appropriate: mean PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, and sulfate for the Six Cities (Dockery et al., 1993); mean $PM_{2.5}$ and sulfate for ACS (Pope et al., 1995); mean PM_{10} and sulfate, and PM_{10} exceedances of 100 $\mu g/m^3$ for AHSMOG (Abbey et al., 1999).

Estimates for Six Cities parameters were calculated in two ways: (1) mortality RR for most versus least polluted city in (Table 3, Dockery et al., 1993) adjusted to standard increments; (2) ecological regression fits in (Table 12-18, U.S. Environmental Protection Agency, 1996). The eastern and mid-western Six Cities suggest a strong and highly significant relationship for fine particles and sulfates, a slightly weaker but still highly significant relationship to PM_{10}, and a marginal relationship to $PM_{10-2.5}$. The ACS study looked at a broader spatial representation of cities, and found a stronger statistically significant relationship to $PM_{2.5}$ than to sulfate (no other pollutants were examined).

Overall, the prospective cohort studies conducted to-date collectively confirm cross-sectional study indications that, as opposed to the more coarse mass fractions, the fine mass component of PM (and sometimes including its acidic sulfate constituent) are strongly correlated with mortality.

The credibility of the above findings of increased risk of mortality being associated with chronic, long-term exposures to fine particles is enhanced by analogous findings of increased risk of respiratory symptoms and lung function decrements being associated with long-term exposures to fine particles, as illustrated in Figure C-4. That figure graphically depicts results from the study reported on by Razienne et al. (1996), which demonstrate strong positive relationships between decrements in children's lung function and long-term exposure to fine particles (indexed by $PM_{2.1}$), but not to inhalable thoracic coarse particles ($PM_{10-2.1}$).

C.2.6. Conclusions

A review of the prospective cohort studies summarized in the previous PM AQCD (U.S. Environmental Protection Agency, 1996) indicates that past epidemiologic studies of chronic PM exposures collectively indicate increases in mortality to be associated with long-term exposure to airborne particles of ambient origins. The PM effect size estimates for total mortality from these studies also indicate that a substantial portion of these deaths reflected cumulative PM impacts above and beyond those exerted by acute exposure events.

The new AHSMOG study (Abbey et al., 1999) provides all-cause mortality RR estimates for adult males that are quantitatively and qualitatively consistent with prior semi-individual prospective cohort studies, especially the similarly designed 6-Cities study. Extensive new by-gender, by-cause, and multiple pollutant sensitivity analyses, as well as a more comprehensive analyses of numerous potentially uncontrolled factors in this study (such as of the effects of variations in the time spent outdoors) provide important new evidence that is largely supportive of the mortality associations with PM of ambient origins previously reported by the Six-Cities and ACS studies.

With regard to the role of various PM constituents in the PM-mortality association, cross-sectional studies have generally found that the fine particle component, as indicated either by $PM_{2.5}$ or sulfates, was the PM constituent most consistently associated with mortality. In addition, the Six-Cities prospective semi-individual study also indicates that the fine mass components of PM are more strongly associated with the mortality effects of PM than the coarse PM components.

The recent analyses of the long-term AHSMOG study provide some evidence indicative of health effects being associated with ambient PM_{10} exposure for which a substantially greater level of individualized ambient PM_{10} information is available, but also demonstrates some differences with the earlier Six Cities and ACS studies (Dockery et al., 1993; Pope et al., 1995). Statistically significant increases in lung cancer incidence (Beeson et al., 1998) and statistically significant increases in lung cancer deaths and deaths associated with any contributing respiratory causes (Abbey et al., 1999) were found in AHSMOG males, but not females. The results were generally robust to different confounder specifications, population subsets, and inclusion of co-pollutants, and were larger for and more significant for PM exceedance indices (number of days per year with PM_{10} greater than a cut point, typically 100 $\mu g/m^3$) than with the mean PM_{10} concentration. However, PM_{10} was estimated from TSP rather than measured in the earlier part of the AHSMOG study and, therefore, the AHSMOG results may not be as credible as those from the other two prospective cohort studies where direct PM_{10}, $PM_{2.5}$, or SO_4 measurements data were used.

Using the same mean PM_{10} increment of 50 $\mu g/m^3$, total mortality attributable to long-term ambient PM_{10} RR was similar to that of the ACS study for $PM_{2.5}$ for male nonsmokers (1.24) and smaller than that for the Six Cities study (1.57), albeit only significant for the ACS study (Table C-13). The AHSMOG RR for females (Table 6-31) is smaller and non-significant (0.88), whereas the ACS RR for female non-smokers is significant and only somewhat smaller than the male RR (1.22 in the 50-city $PM_{2.5}$ study, 1.15 in the 151-city SO_4 study) and 1.28 in the Six Cities.

The AHSMOG findings for cardiopulmonary mortality attributable to long-term ambient PM_{10} are positive for males, but not statistically significant, whereas the ACS findings are

significant for female nonsmokers in both studies and in male nonsmokers for the 151-city study (Table C-14). However, the male RR in AHSMOG (1.22 for cardiopulmonary deaths, 1.54 for CRC deaths) is similar to that of ACS male non-smokers (1.24 for the 50-city study, 1.21 for the 151-city study) and smaller than that for all Six Cities subjects (1.74, includes smokers and non-smokers). The ACS female non-smokers have RR of 1.58 and 1.32 respectively, both significant, compared to 0.84 in AHSMOG.

Lung cancer mortality attributable to long-term ambient PM_{10} is not significant for females in any of the studies, nor for male nonsmokers in ACS, but was reported to be statistically significant for male nonmokers in AHSMOG and male smokers in ACS 151-city. Lung cancer mortality attributable to long-term ambient $PM_{2.5}$ was not significant for either gender in the ACS and Six Cities studies. Thus, the available overall evidence, from the three prospective cohort studies of PM effects assessed here, definitely is not conclusive and can, at best, be viewed as indicative of possible ambient PM associations with increased risk of lung cancer or associated mortality.

Table C-1. Effect estimates per 50 $\mu g/m^3$ increase in 24-h PM_{10} concentrations from U.S. and Canadian studies

Study Location	RR (± CI) Only PM in Model	RR (± CI) Other Pollutants in Model	Reported PM_{10} Levels Mean (Min/Max)[†]
Increased Total Acute Mortality			
Six Cities[a]		—	
Portage, WI	1.04 (0.98, 1.09)	—	18 (±11.7)
Boston, MA	1.06 (1.04, 1.09)	—	24 (±12.8)
Topeka, KS	0.98 (0.90, 1.05)	—	27 (±16.1)
St. Louis, MO	1.03 (1.00, 1.05)	—	31 (±16.2)
Kingston/Knoxville, TN	1.05 (1.00, 1.09)	—	32 (±14.5)
Steubenville, OH	1.05 (1.00, 1.08)	—	46 (±32.3)
St. Louis, MO[c]	1.08 (1.01, 1.12)	1.06 (0.98, 1.15)	28 (1/97)
Kingston, TN[c]	1.09 (0.94, 1.25)	1.09 (0.94, 1.26	30 (4/67)
Chicago, IL[h]	1.04 (1.00, 1.08)	—	37 (4/365)
Chicago, IL[g]	1.03 (1.02, 1.04)	1.02 (1.01, 1.04)	38 (NR/128)
Utah Valley, UT[b]	1.08 (1.05, 1.11)	1.19 (0.96, 1.47)	47 (11/297)
Birmingham, AL[d]	1.05 (1.01, 1.10)	—	48 (21, 80)
Los Angeles, CA[f]	1.03 (1.00, 1.055)	1.02 (0.99, 1.036)	58(15/177)
Increased Hospital Admissions (for Elderly > 65 yrs.)			
Respiratory Disease			
Toronto, CAN[i]	1.23 (1.02, 1.43)[‡]	1.12 (0.88, 1.36)[‡]	30-39[*]
Tacoma, WA[j]	1.10 (1.03, 1.17)	1.11 (1.02, 1.20)	37 (14, 67)
New Haven, CT[j]	1.06 (1.00, 1.13)	1.07 (1.01, 1.14)	41 (19, 67)
Cleveland, OH[k]	1.06 (1.00, 1.11)	—	43 (19, 72)
Spokane, WA[l]	1.08 (1.04, 1.14)	—	46 (16, 83)
COPD			
Minneapolis, MN[n]	1.25 (1.10, 1.44)	—	36 (18, 58)
Birmingham, AL[m]	1.13 (1.04, 1.22)	—	45 (19, 77)
Spokane, WA[l]	1.17 (1.08, 1.27)	—	46 (16, 83)
Detroit, MI[o]	1.10 (1.02, 1.17)	—	48 (22, 82)

Table C-1. Effect estimates per 50 $\mu g/m^3$ increase in 24-h PM_{10} concentrations from U.S. and Canadian studies (continued)

Study Location	RR (± CI) Only PM in Model	RR (± CI) Other Pollutants in Model	Reported PM_{10} Levels Mean (Min/Max)[†]
Pneumonia			
Minneapolis, MN[n]	1.08 (1.01, 1.15)	—	36 (18,58)
Birmingham, AL[m]	1.09 (1.03, 1.15)	—	45 (19, 77)
Spokane, WA[l]	1.06 (0.98, 1.13)	—	46 (16, 83)
Detroit, MI[o]	—	1.06 (1.02, 1.10)	48 (22, 82)
Ischemic HD			
Detroit, MI[p]	1.02 (1.01, 1.03)	1.02 (1.00, 1.03)	48 (22, 82)
Increased Respiratory Symptoms			
Lower Respiratory			
Six Cities[q]	2.03 (1.36, 3.04)	Similar RR	30 (13,53)
Utah Valley, UT[r]	1.28 (1.06, 1.56)[τ]	—	46 (11/195)
	1.01 (0.81, 1.27)[π]		
Utah Valley, UT[s]	1.27 (1.08, 1.49)	—	76 (7/251)
Cough			
Denver, CO[x]	1.09 (0.57, 2.10)	—	22 (0.5/73)
Six Cities[q]	1.51 (1.12, 2.05)	Similar RR	30 (13, 53)
Utah Valley, UT[s]	1.29 (1.12, 1.48)	—	76 (7/251)
Decrease in Lung Function			
Utah Valley, UT[r]	55 (24, 86)[**]	—	46 (11/195)
Utah Valley, UT[s]	30 (10, 50)[**]	—	76 (7/251)
Utah Valley, UT[w]	29 (7,51)[***]	—	55 (1,181)

References:

[a]Schwartz et al. (1996a).
[b]Pope et al. (1992, 1994)/O_3.
[c]Dockery et al. (1992)/O_3.
[d]Schwartz (1993).
[f]Kinney et al. (1995)/O_3, CO.
[g]Ito and Thurston (1996)/O_3.
[h]Styer et al. (1995).
[i]Thurston et al. (1994)/O_3.
[j]Schwartz (1995)/SO_2.
[k]Schwartz et al. (1996b).
[l]Schwartz (1996).
[m]Schwartz (1994e).
[n]Schwartz (1994f).
[o]Schwartz (1994d).
[p]Schwartz and Morris (1995)/O_3, CO, SO_2.
[q]Schwartz et al. (1994).
[r]Pope et al. (1991).
[s]Pope and Dockery (1992).
[t]Schwartz (1994g)
[w]Pope and Kanner (1993).
[x]Ostro et al. (1991)
[†]Min/Max 24-h PM_{10} in parentheses unless noted otherwise as standard deviation (± S.D), 10 and 90 percentile (10, 90). NR = not reported.
[τ]Children.
[π]Asthmatic children and adults.
[*]Means of several cities.
[**]PEFR decrease in ml/sec.
[***]FEV_1 decrease.
[‡]RR refers to total population, not just>65 years.

Table C-2. Effect estimates per variable increments in 24-h concentrations of fine particle indicators ($PM_{2.5}$, $SO_4^=$, H^+) from U.S. and Canadian studies

Acute Mortality	Indicator	RR (± CI) per 25 $\mu g/m^3$ PM Increase	Reported PM Levels Mean (Min/Max)[†]
Six City[a]			
Portage, WI	$PM_{2.5}$	1.030 (0.993, 1.071)	11.2 (±7.8)
Topeka, KS	$PM_{2.5}$	1.020 (0.951, 1.092)	12.2 (±7.4)
Boston, MA	$PM_{2.5}$	1.056 (1.038, 1.0711)	15.7 (±9.2)
St. Louis, MO	$PM_{2.5}$	1.028 (1.010, 1.043)	18.7 (±10.5)
Kingston/Knoxville, TN	$PM_{2.5}$	1.035 (1.005, 1.066)	20.8 (±9.6)
Steubenville, OH	$PM_{2.5}$	1.025 (0.998, 1.053)	29.6 (±21.9)
Increased Hospitalization			
Ontario, CAN[b]	$SO_4^=$	1.03 (1.02, 1.04)	R = 3.1-8.2
Ontario, CAN[c]	$SO_4^=$	1.03 (1.02, 1.04)	R = 2.0-7.7
	O_3	1.03 (1.02, 1.05)	
NYC/Buffalo, NY[d]	$SO_4^=$	1.05 (1.01, 1.10)	NR
Toronto[d]	H^+ ($Nmol/m^3$)	1.16 (1.03, 1.30)*	28.8 (NR/391)
	$SO_4^=$	1.12 (1.00, 1.24)	7.6 (NR, 48.7)
	$PM_{2.5}$	1.15 (1.02, 1.78)	18.6 (NR, 66.0)
Increased Respiratory Symptoms			
Southern California[e]	$SO_4^=$	1.48 (1.14, 1.91)	R = 2-37
Six Cities[f] (Cough)	$PM_{2.5}$	1.19 (1.01, 1.42)**	18.0 (7.2, 37)***
	$PM_{2.5}$ Sulfur	1.23 (0.95, 1.59)**	2.5 (3.1, 61)***
	H^+	1.06 (0.87, 1.29)**	18.1 (0.8, 5.9)***
Six Cities[f] (Lower Resp. Symp.)	$PM_{2.5}$	1.44 (1.15-1.82)**	18.0 (7.2, 37)***
	$PM_{2.5}$ Sulfur	1.82 (1.28-2.59)**	2.5 (0.8, 5.9)***
	H^+	1.05 (0.25-1.30)**	18.1 (3.1, 61)***

Table C-2. Effect estimates per variable increments in 24-h concentrations of fine particle indicators ($PM_{2.5}$, $SO_4^=$, H^+) from U.S. and Canadian studies (continued)

Acute Mortality	Indicator	RR (± CI) per 25 $\mu g/m^3$ PM Increase	Reported PM Levels Mean (Min/Max)[†]
Decreased Lung Function			
Uniontown, PA[g]	$PM_{2.5}$	PEFR 23.1 (-0.3, 36.9) (per 25 $\mu g/m^3$)	25/88 (NR/88)

References:
[a]Schwartz et al. (1996a)
[b]Burnett et al. (1994)
[c]Burnett et al. (1995) O_3
[d]Thurston et al. (1992, 1994)
[e]Ostro et al (1993)
[f]Schwartz et al. (1994)
[g]Neas et al. (1995)

[†]Min/Max 24-h PM indicator level shown in parentheses unless otherwise noted as (± S.D.), 10 and 90 percentile (10,90) or R = range of values from min-max, no mean value reported.
[*]Change per 100 nmoles/m^3
[**]Change per 20 $\mu g/m^3$ for $PM_{2.5}$; per 5 $\mu g/m^3$ for $PM_{2.5}$ sulfur; per 25 nmoles/m^3 for H^+.
[***]50th percentile value (10,90 percentile)

Table C-3. Effect estimates per increments[a] in annual average levels of fine particle indicators from U.S. and Canadian studies

Type of Health Effect & Location	Indicator	Change in Health Indicator per Increment in PM[a]	Range of City PM Levels Means ($\mu g/m^3$)
Increased total chronic mortality in adults		Relative Risk (95% CI)	
Six City[b]	$PM_{15/10}$	1.42 (1.16-2.01)	18-47
	$PM_{2.5}$	1.31 (1.11-1.68)	11-30
	$SO_4^=$	1.46 (1.16-2.16)	5-13
ACS Study[c] (151 U.S. SMSA)	$PM_{2.5}$	1.17 (1.09-1.26)	9-34*
	$SO_4^=$	1.10 (1.06-1.16)	4-24
Increased bronchitis in children		Odds Ratio (95% CI)	
Six City[d]	$PM_{15/10}$	3.26 (1.13, 10.28)	20-59
Six City[e]	TSP	2.80 (1.17, 7.03)	39-114
24 City[f]	H^+	2.65 (1.22, 5.74)	6.2-41.0
24 City[f]	$SO_4^=$	3.02 (1.28, 7.03)	18.1-67.3
24 City[f]	$PM_{2.1}$	1.97 (0.85, 4.51)	9.1-17.3
24 City[f]	PM_{10}	3.29 (0.81, 13.62)	22.0-28.6
Southern California[g]	$SO_4^=$	1.39 (0.99, 1.92)	—
Decreased lung function in children			
Six City[d,h]	$PM_{15/10}$	NS Changes	20-59
Six City[e]	TSP	NS Changes	39-114
24 City[i,j]	H^+ (52 nmoles/m^3)	3.45% (-4.87, -2.01) FVC	—
24 City[i]	$PM_{2.1}$ (15 $\mu g/m^3$)	3.21% (-4.98, -1.41) FVC	—
24 City[i]	$SO_4^=$ (7 $\mu g/m^3$)	3.06% (-4.50, -1.60) FVC	—
24 City[i]	PM_{10} (17 $\mu g/m^3$)	2.42% (-4.30, -.0.51) FVC	—

[a]Estimates calculated annual-average PM increments assume: a 100 $\mu g/m^3$ increase for TSP; a 50 $\mu g/m^3$ increase for PM_{10} and PM_{15}; a 25 $\mu g/m^3$ increase for $PM_{2.5}$; and a 15 $\mu g/m^3$ increase for $SO_4^=$, except where noted otherwise; a 100 nmole/m^3 increase for H^+.

[b]Dockery et al. (1993)
[c]Pope et al. (1995)
[d]Dockery et al. (1989)
[e]Ware et al. (1986)
[f]Dockery et al. (1996)
[g]Abbey et al. (1995a,b,c)
[h]NS Changes = No significant changes.
[i]Raizenne et al. (1996)
[j]Pollutant data same as for Dockery et al. (1996)

*Range of annual median values for subset of 50 cities.

Table C-4. Prospective cohort mortality studies

Source	Health Outcome	Population	Time Period/ No. Units	PM Indicators	PM Mean ($\mu g/m^3$)	PM Range/ (Std. Dev.)	Sites Per City	Total Deaths	Model Type	PM Lag Structure	Other Pollutants	Other Factors	Relative Risk[a] at SO_4 = 15, PM_{15} = 50, $PM_{2.5}$ = 25	RR. Confidence Interval	Elasticity
Abbey et al. (1991)	Total mortality from disease	Calif. 7th Day Adventist	1977-82 Defined by air monitoring sites	24 h TSP >200	102	25-175 (annual avg)	NA	845	Cox proportional hazards	10 yrs	none	age, sex, race, smoking, education, airway disease	0.99 TSP[a]	(0.87-1.13)[a]	NS[b]
Dockery et al. (1993)	Total mortality	White adult volunteers in 6 U.S. cities[c]	1974-91	PM_{15} $PM_{2.5}$ SO_4	29.9 18 7.6	18-47 11-30 5-13	1	1429	Cox proportional hazards	none	none	age, sex, smoking, education, body mass, occup. exposure hypertension[d], diabetes[d]	1.42 PM_{15} 1.31 $PM_{2.5}$ 1.46 SO_4	(1.16-2.01) (1.11-1.68) (1.16-2.16)	0.25 0.22 0.23
Pope et al. (1995)	Total mortality	American Cancer Society, adult volunteers in U.S.	1982-89 $PM_{2.5}$ 50 cities SO_4 151 cities	$PM_{2.5}$	18.2	9-34	1	20,765	Cox proportional hazard	none	none	age, sex, race, smoking, education, body mass, occup. exposure, alcohol consumption, passive smoking, climate	1.17 $PM_{2.5}$	(1.09-1.26)	0.117
				SO_4	11[e]	4-24	1	38,963					1.10 SO_4	(1.06-1.16)	0.077

[a]For 1,000 h/yr > 200 $\mu g/m^3$.
[b]NS = non significant, confidence limits not shown.
[c]Portage, WI; Topeka, KS; Watertown, MA; Harrisman-Kingston, TN; St. Louis, MO; Steubenville, OH.
[d]Used in other regression analyses not shown in this table.
[e]Value may be affected by filter artifacts.

Source: PM CD (U.S. EPA, 1996a).

Table C-5. Relative mortality risks in six U.S. cities

Risk Factor	$PM_{2.5}$ Data ($\mu g/m^3$)	Crude Risk	Adjusted Risks		
			All[a]	Men[a]	Women[a]
Residence					
Portage	11.0 (1980-7)3[b]	1.0[c]	1.0	1.0	1.0
Topeka	12.5 (1980-8)	0.90	1.01	1.04	0.97
Watertown	14.9 (1980-5)	1.16	1.07	0.94	1.22
Harriman	20.8 (1980-7)	1.16	1.17	1.21	1.07
St. Louis	19.0 (1980-6)	1.48	1.14	1.15	1.13
Steubenville	29.6 (1980-7)	1.51	1.26	1.29	1.23
Smoking Status					
Current			1.59	1.75	1.54
Previous			1.20	1.25	1.18
No high school education			1.19	1.22	1.13
Body mass index of 4.5			1.08	1.03	1.11

[a]Adjusted for age, smoking, education, and body mass.

[b]Period of $PM_{2.5}$ air monitoring.

[c]Baseline annual crude death rate = 10.73 per thousand population.

Source: Dockery et al. (1993)

Table C-6. Estimated relative risks of mortality in six U.S. cities associated with a range of air pollutants

Species	Regr. Coeff.	Standard Error	Pollutant Range	Rel. Risk	95% CIs (n=6)
PM_{15}	0.0085	(0.0026)	28.3	1.27	(1.04-1.56)
$PM_{2.5}$	0.0127	(0.0034)	18.6	1.27	(1.06-1.51)
SO_4^{2-}	0.0297	(0.0081)	8.5	1.29	(1.06-1.56)
TSP	0.0037	(0.0014)	55.8	1.22	(0.99-1.53)
TSP-PM_{15}	0.0042	(0.0032)	27.5	1.12	(0.88-1.43)
PM_{15}-$PM_{2.5}$	0.0178	(0.0098)	9.7	1.19	(0.91-1.55)
$PM_{2.5}$-SO_4	0.0255	(0.0029)	8.4	1.24	(1.16-1.32)
PM_{15}-SO_4	0.0121	(0.0034)	18.1	1.24	(1.05-1.48)
SO_2	0.0093	(0.0032)	19.8	1.20	(1.01-1.43)
NO_2	0.0126	(0.0046)	15.8	1.22	(1.00-1.49)
1970 TSP	0.0014	(0.00044)	154.0	1.25	(1.03-1.50)

Source: U.S. EPA (1996a) recalculations based on results of Dockery et al. (1993).

Table C-7. Relative risk of mortality from contributing nonmalignant respiratory causes, for 30 days per year with PM_{10} > 100 $\mu g/m^3$

PM Covariate Model	RR	LCL	UCL
BASE (age, sex)	1.069	0.978	1.168
BASE + pack-years	1.096	1.000	1.201
BASE + pack-years + body-mass-index cats.	1.122	1.022	1.233
BASE + pack-years + body-mass-index cats.+ exercise cats.	1.122	1.017	1.239
STANDARD (age, pack-y., y. lived with smoker, occup., educ., BMI)	1.122	1.017	1.239
STANDARD w. PM_{10} (100) over last 4 years only	1.102	1.001	1.214
STANDARD, subset for former smokers	1.155	0.937	1.424
STANDARD, subset for never smokers	1.116	0.999	1.246
STANDARD, subset for low anti-oxidant vitamin intake	1.175	1.008	1.370
STANDARD, subset for high anti-oxidant vitamin intake	1.055	0.917	1.214
STANDARD, subset for < 4 h/wk outdoors	1.048	0.896	1.227
STANDARD, subset for 4-16 h/wk outdoors	1.122	0.928	1.358
STANDARD, subset for 16+ h/wk outdoors	1.207	1.015	1.436
STANDARD, subset for reported respiratory symptoms	1.321	1.079	1.616

LCL = Lower 95% Confidence Limit.
UCL = Upper 95% Confidence Limit.

Source: Abbey et al. (1999).

Table C-8. Relative risk of mortality from contributing nonmalignant respiratory causes, by sex and air pollutant, with alternative covariate model

		Females			Males		
Pollution Index	**Pollution Incr.**	**RR**	**LCL**	**UCL**	**RR**	**LCL**	**UCL**
PM_{10}>100, d/yr	30 days/yr	1.069	0.936	1.220	1.188	1.030	1.370
PM_{10} mean	50 $\mu g/m^3$	1.219	0.739	2.011	1.537	0.879	2.688
SO_4 mean	15 $\mu g/m^3$	1.105	0.396	3.086	1.219	0.411	3.619
O_3>100 ppb, h/yr	551 h/yr (IQR)	1.01	0.77	1.33	1.20	0.88	1.64

LCL = Lower 95% Confidence Limit UCL = Upper 95% Confidence Limit.

Source: Abbey et al. (1999).

Table C-9. Relative risk of mortality from all nonexternal causes, by sex and air pollutant, for an alternative covariate model

		Females			Males		
Pollution Index	**Pollution Incr.**	**RR**	**LCL**	**UCL**	**RR**	**LCL**	**UCL**
PM_{10}>100, d/yr	30 days/yr	0.958	0.899	1.021	1.082	1.008	1.162
PM_{10} mean	50 $\mu g/m^3$	0.879	0.713	1.085	1.242	0.955	1.616
SO_4 mean	15 $\mu g/m^3$	0.732	0.484	1.105	1.279	0.774	2.116
O_3>100 ppb, h/yr	551 h/yr (IQR)	0.90	0.80	1.02	1.140	0.98	1.32
SO_2 mean	3.72 (IQR)	1.00	0.91	1.10	1.05	0.94	1.18

LCL = Lower 95% Confidence Limit UCL = Upper 95% Confidence Limit.

Source: Abbey et al. (1999).

Table C-10. Relative risk of mortality from cardiopulmonary causes, by sex and air pollutant, for an alternative covariate model

		Females			Males		
Pollution Index	**Pollution Incr.**	**RR**	**LCL**	**UCL**	**RR**	**LCL**	**UCL**
PM_{10}>100, d/yr	30 days/yr	0.929	0.857	1.007	1.062	0.971	1.162
PM_{10} mean	50 $\mu g/m^3$	0.841	0.639	1.107	1.219	0.862	1.616
SO_4 mean	15 $\mu g/m^3$	0.857	0.498	1.475	1.279	0.002	1018
O_3>100 ppb, h/yr	551 h/yr (IQR)	0.88	0.76	1.02	1.06	0.87	1.29
O_3 mean	10 ppb	0.975	0.865	1.099	1.066	0.920	1.236
SO_2 mean	3.72 (IQR)	1.02	0.90	1.15	1.01	0.86	1.18

LCL = Lower 95% Confidence Limit UCL = Upper 95% Confidence Limit.

Source: Abbey et al. (1999).

Table C-11. Relative risk of mortality from lung cancer, by sex and air pollutant, for an alternative covariate model

			Females			Males		
Pollution Index	Pollution Incr.	Smoking Category	RR	LCL	UCL	RR	LCL	UCL
PM_{10}>100, d/yr	30 days/yr	All[a]	1.055	0.657	1.695	1.831	1.281	2.617
PM_{10} mean	50 $\mu g/m^3$	All	1.808	0.343	9.519	12.385	2.552	60.107
NO_2 mean	19.78 (IQR)	All	2.81	1.15	6.89	1.82	0.93	3.57
O_3>100 ppb, h/yr	551 h/yr (IQR)	All	1.39	0.53	3.67	4.19	1.81	9.69
		never smoker				6.94	1.12	43.08
		past smoker				4.25	1.50	12.07
O_3 mean	10 ppb	All	0.805	0.436	1.486	1.853	0.994	3.453
SO_2 mean	3.72 (IQR)	All	3.01	1.88	4.84	1.99	1.24	3.20
		never smokers	2.99	1.66	5.40			

[a]All = both never smokers and past smokers.

LCL = Lower 95% Confidence Limit. UCL = Upper 95% Confidence Limit.

Source: Abbey et al. (1999).

Table C-12. Relative risk of lung cancer incidence in males, by air pollutant, for Adventist health study

Pollution Index	Pollution Incr.	Covariate Model or Sub-Group	RR	LCL	UCL
PM_{10}>40 $\mu g/m^3$	139 d/y (IQR)	standard	4.50	1.31	15.44
PM_{10}>50 $\mu g/m^3$	149 d/y (IQR)	standard	4.96	1.54	16.00
PM_{10}>60 $\mu g/m^3$	132 d/y (IQR)	standard	4.72	1.69	13.18
PM_{10}>80 $\mu g/m^3$	78 d/y (IQR)	standard	3.43	1.71	6.88
PM_{10}>100 $\mu g/m^3$	30 d/y	standard	2.127	1.454	3.112
PM_{10} mean	50 $\mu g/m^3$	standard	31.147	3.978	243.85
SO_2 mean	3.7 ppb	standard	2.66	1.62	4.39
NO_2 mean	2.0 ppb	standard	1.45	0.67	3.14
O_3>60 ppb	935 h/y	standard	2.14	0.82	5.62
O_3>80 ppb	756 h/y	standard	2.96	1.09	8.04
O_3>100 ppb	556 h/y	standard	3.56	1.35	9.42
O_3>120 ppb	367 h/y	standard	3.75	1.55	9.90
O_3>150 ppb	185 h/y	standard	3.61	1.78	7.35
O_3 mean	2.1 ppb	standard	2.23	0.79	6.34
PM_{10}>100 $\mu g/m^3$	30 d/y	never smokers	2.102	1.325	3.335
O_3>100 ppb	556 h/y	never smokers	4.48	1.25	16.04
O_3>100 ppb	556 h/y	past smokers	2.15	0.42	10.89
PM_{10}>100 $\mu g/m^3$	30 d/y	high population density	2.865	1.794	4.574
O_3>100 ppb	556 h/y	high population density	10.18	2.44	42.45
SO_2 mean	3.7 ppb	high population density	3.22	1.87	5.54
PM_{10} mean	50 $\mu g/m^3$	> 80% data from monitors within 20 miles of residence	9.256	1.135	75.516
SO_2 mean	3.7 ppb	> 80% data from monitors within 20 miles of residence	2.18	0.92	5.20

LCL = Lower 95% Confidence Limit.
UCL = Upper 95% Confidence Limit.

Source: Beeson et al. (1998).

Table C-13. Relative risk of lung cancer incidence in females, by air pollutant, for Adventist health study

Pollution Index	Pollution Incr.	Covariate Model or Sub-Group	RR	LCL	UCL
PM_{10}>50 $\mu g/m^3$	149 d/y (IQR)	standard	1.21	0.55	2.66
PM_{10}>60 $\mu g/m^3$	132 d/y (IQR)	standard	1.25	0.57	2.71
SO_2 mean	3.7 ppb	standard	2.14	1.36	3.37
O_3>100 ppb	556 h/y	standard	0.94	0.41	2.16
PM_{10}>100 $\mu g/m^3$	30 d/y	high population density	1.089	0.726	1.633
SO_2 mean	3.7 ppb	high population density	2.11	1.32	3.38
PM_{10} mean	50 $\mu g/m^3$	> 80% data from monitors within 20 miles	2.425	0.310	19.004
SO_2 mean	3.7 ppb	> 80% data from monitors within 20 miles	2.52	1.19	5.33

LCL = Lower 95% Confidence Limit.
UCL = Upper 95% Confidence Limit.

Source: Beeson et al. (1998).

Table C-14. Relative risk (RR) of total mortality in three prospective cohort studies, by sex and smoking status

Sex	Smoking Status	Study	PM Index	PM Inc.	RR	LCL	UCL
F	NON-SMOKER	Six Cities	PM_{10}	50	1.280	0.704	2.345
		ACS	$PM_{2.5}$	25	1.215	1.020	1.440
			SO_4	15	1.147	1.045	1.261
		AHSMOG	PM_{10}	50	0.879	0.713	1.085
	PAST	Six Cities	PM_{10}	50	1.999	0.704	5.632
	PAST + CURRENT	ACS	$PM_{2.5}$	25	1.102	0.898	1.338
			SO_4	15	1.104	0.977	1.240
	CURRENT	Six Cities	PM_{10}	50	1.442	0.719	3.166
M	NON-SMOKER	Six Cities	PM_{10}	50	1.568	0.674	3.678
		ACS	$PM_{2.5}$	25	1.245	1.000	1.554
			SO_4	15	1.104	0.977	1.247
		AHSMOG	PM_{10}	50	1.242	0.955	1.616
	PAST	Six Cities	PM_{10}	50	1.611	0.930	2.825
	PAST + CURRENT	ACS	$PM_{2.5}$	25	1.164	1.051	1.297
			SO_4	15	1.104	1.037	1.176
	CURRENT	Six Cities	PM_{10}	50	1.858	1.090	3.166

LCL = Lower 95% Confidence Limit. UCL = Upper 95% Confidence Limit.

Sources: Dockery et al. (1993); Pope et al. (1995); Abbey et al. (1999).

Table C-15. Relative risk (RR) of cardiopulmonary mortality in three prospective cohort studies, by sex and smoking status

Sex	Smoking Status	Study	PM Index	PM Inc.	RR	LCL	UCL
F	NON-SMOKERS	ACS	$PM_{2.5}$	25	1.585	1.235	2.039
			SO_4	15	1.316	1.147	1.518
		AHSMOG	PM_{10}	50	0.841	0.639	1.107
		AHSMOG - CRC	PM_{10}	50	1.219	0.739	2.011
	PAST + CURRENT	ACS	$PM_{2.5}$	25	1.276	0.918	1.760
			SO_4	15	1.219	1.008	1.465
M	NON-SMOKERS	ACS	$PM_{2.5}$	25	1.245	0.929	1.668
			SO_4	15	1.205	1.023	1.412
		AHSMOG	PM_{10}	50	1.219	0.862	1.616
		AHSMOG - CRC	PM_{10}	50	1.537	0.879	2.688
	PAST + CURRENT	ACS	$PM_{2.5}$	25	1.235	1.061	1.440
			SO_4	15	1.126	1.037	1.233
F+M	ALL	Six Cities	PM_{10}	50	1.744	1.202	2.501

LCL = Lower 95% Confidence Limit. UCL = Upper 95% Confidence Limit.

Sources: Dockery et al. (1993); Pope et al. (1995); Abbey et al. (1999).

Table C-16. Relative risk (RR) of lung cancer mortality in three prospective cohort studies, by sex and smoking status

Sex	Smoking Status	Study	PM Index	PM Inc.	RR	LCL	UCL
F	NON-SMOKERS	ACS	$PM_{2.5}$	25	0.644	0.203	2.091
			SO_4	15	1.432	0.731	2.800
		AHSMOG	PM_{10}	50	1.808	0.343	9.519
	PAST + CURRENT	ACS	$PM_{2.5}$	25	0.949	0.563	1.595
			SO_4	15	1.074	0.781	1.479
M	NON-SMOKERS	ACS	$PM_{2.5}$	25	0.483	0.086	2.714
			SO_4	15	1.261	0.501	3.190
		AHSMOG	PM_{10}	50	12.385	2.552	60.107
	PAST + CURRENT	ACS	$PM_{2.5}$	25	1.123	0.827	1.533
			SO_4	15	1.316	1.104	1.577
F+M	ALL	Six Cities	PM_{10}	50	1.744	0.689	4.390
		ACS	$PM_{2.5}$	25	1.031	0.796	1.338
			SO_4	15	1.261	1.082	1.465

LCL = Lower 95% Confidence Limit. UCL = Upper 95% Confidence Limit.

Sources: Dockery et al. (1993); Pope et al. (1995); Abbey et al. (1999).

Table C-17. Comparison of estimated relative risks (RR) for all-cause mortality in six U.S. cities associated with the reported inter-city range of concentrations of various PM metrics

PM Species	Concentration Range ($\mu g/m^3$)	Relative Risk Estimate	RR 95% CI	Relative Risk t-Statistic
SO_4=	8.5	1.29	(1.06-1.56)	3.67
$PM_{2.5}$ - SO_4=	8.4	1.24	(1.16-1.32)	8.79
$PM_{2.5}$	18.6	1.27	(1.06-1.51)	3.73
$PM_{15-2.5}$	9.7	1.19	(0.91-1.55)	1.81
TSP-PM_{15}	27.5	1.12	(0.88-1.43)	1.31

Source: Dockery et al. (1993); U.S. Environmental Protection Agency (1996).

Table C-18. Comparison of reported $SO_4^=$ and $PM_{2.5}$ relative risks (RR) for various mortality causes in the ACS study

Mortality Cause	$SO_4^=$ (Range = 19.9 $\mu g/m^3$)			$PM_{2.5}$ (Range = 24.5 $\mu g/m^3$)		
	Relative Risk	RR 95% CI	RR t-Statistic	Relative Risk	RR 95% CI	RR t-Statistic
All Cause	1.15	(1.09-1.22)	4.85	1.17	(1.09-1.26)	4.24
Cardiopulmonary	1.26	(1.15-1.37)	5.18	1.31	(1.17-1.46)	4.79
Lung Cancer	1.35	(1.11-1.66)	2.92	1.03	(0.80-1.33)	0.38

Source: Pope et al. (1995).

Table C-19. Comparison of total mortality relative risk (RR) estimates and T-statistics for PM components in three prospective cohort studies

PM Index	Study	Subgroup	Relative Risk	t Statistic
PM_{10} (50 $\mu g/m^3$)	Six Cities	All	1.504[a]; 1.530[b]	**2.94**[a]; **3.27**[b]
		Male Nonsmoker	1.280[a]	0.81[a]
	AHSMOG	Male Nonsmoker	1.242	1.616
$PM_{2.5}$ (25 $\mu g/m^3$)	Six Cities	All	1.364[a]; 1.379[b]	**2.94**[a]; **3.73**[b]
		Male Nonsmoker	1.207[a]	0.81[a]
	ACS (50 cities)	All	1.174	**4.35**
		Male Nonsmoker	1.245	**1.96**0
SO_4= (15 $\mu g/m^3$)	Six Cities	All	1.504[a]; 1.567[b]	**2.94**[a]; **3.67**[b]
		Male Nonsmoker	1.359	0.81[a]
	ACS (151 cities)	All	1.111	**5.107**
		Male Nonsmoker	1.104	1.586
	AHSMOG	Male Nonsmoker	1.279	0.960
Days/y with PM_{10}>100 (30 days)	AHSMOG	Male Nonsmoker	1.082	**2.183**
$PM_{10-2.5}$ (25 $\mu g/m^3$	Six Cities	All	1.814[a]; 1.560[b]	**2.94**[a,c]; 1.816[b]
		Male Nonsmoker	1.434[a]	0.81[a]

[a]Method 1 compares Portage vs. Steubenville (Table 3, Dockery et al., 1993).
[b]Method 2 is based on ecologic regression models (Table 12-18, U.S. Environmental Protection Agency, 1996).
[c]Method 1 not recommended for PM10-2.5 analysis due to high concentration in Topeka.

Table C-20. Comparison of cardiopulmonary mortality relative risk (RR) estimates and T-statistics for PM components in three prospective cohort studies ("Male Non. - CRC" identifies subjects who died of any contributing nonmalignant respiratory cause in the AHSMOG study)

PM Index	Study	Subgroup	Relative Risk	t Statistic
PM_{10} (50 $\mu g/m^3$)	Six Cities	All	1.744[a]	**2.94**[a]
	AHSMOG	Male Nonsmoker	1.219	1.120
		Male Non. - CRC	1.537	**2.369**
$PM_{2.5}$ (25 $\mu g/m^3$)	Six Cities	All	1.527[a]	**2.94**[a]
	ACS (50 cities)	All	1.317	**4.699**
		Male	1.245	**3.061**
		Male Nonsmoker	1.245	1.466
SO_4= (15 $\mu g/m^3$)	Six Cities	All	1.743[a]	**2.94**[a]
	ACS (151 cities)	All	1.190	**5.470**
		Male	1.147	**3.412**
		Male Nonsmoker	1.205	**2.233**
	AHSMOG	Male Nonsmoker	1.279	0.072
		Male Non. - CRC	1.219	0.357
Days/y with PM_{10}>100 (30 days)	AHSMOG	Male Nonsmoker	1.082	1.310
		Male Non. - CRC	1.188	**2.370**
$PM_{10-2.5}$ (25 $\mu g/m^3$	Six Cities	All	2.251[a]	**2.94**[a,b]

[a]Method 1 compares Portage vs. Steubenville (Table 3, Dockery et al., 1993).
[b]Method 1 not recommended for PM10-2.5 analysis due to high concentration in Topeka.

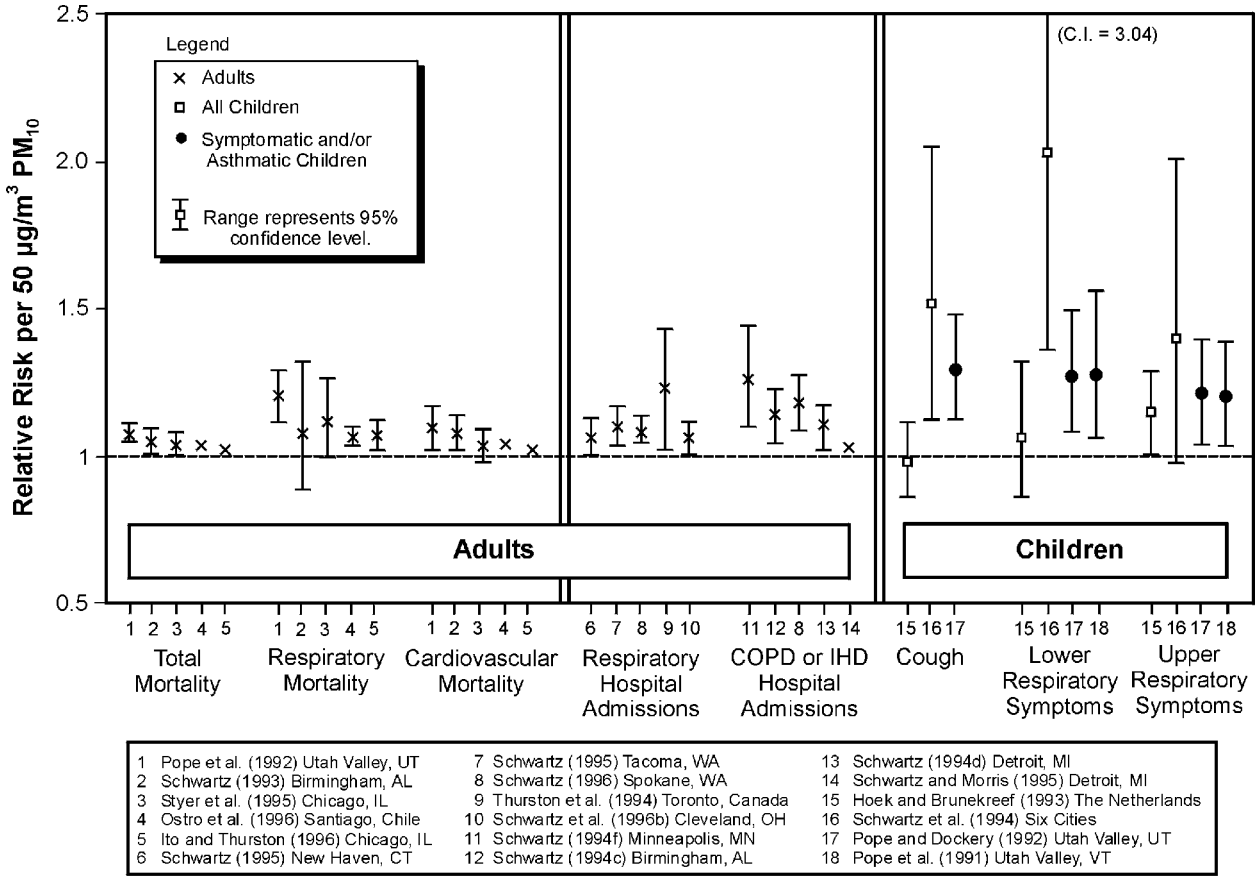

Figure C-1. Relative risk (RR) estimates for increased mortality and morbidity endpoints associated with 50 μg/m^3 increments in PM_{10} concentrations as derived from studies cited by numbers listed above each given type of health endpoint. Note the consistency of RR elevations across studies for given endpoint and coherence of RR estimates across endpoints, e.g., higher RR values for symptoms versus hospital admissions and cause-specific mortality.

Source: PM Staff Paper (1996b). See U.S. EPA (1996b) for full reference citations for each study identified in figure.

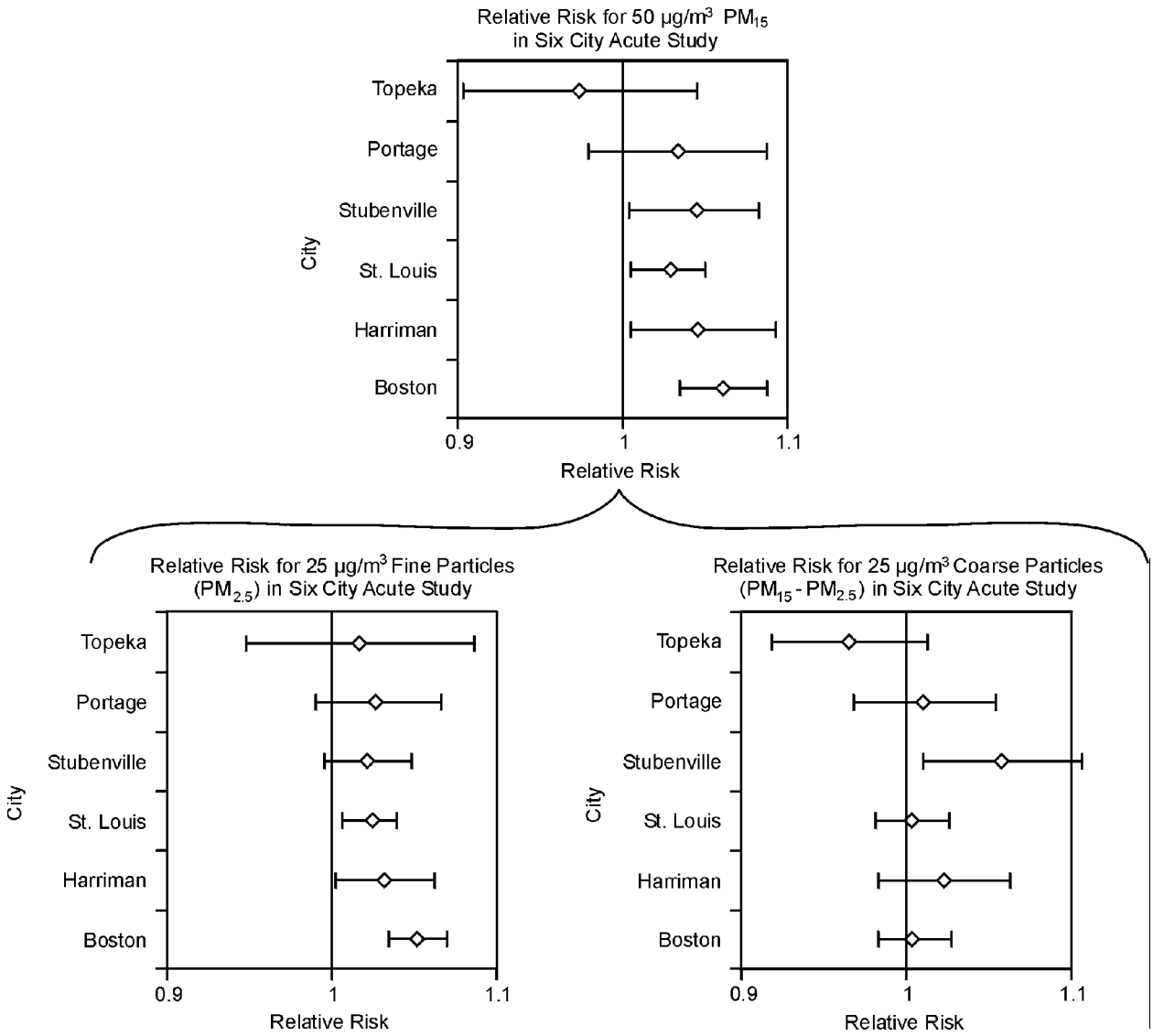

Figure C-2. Relative risks of acute mortality in Harvard Six Cities Study, for inhalable thoracic particles (PM_{15}/PM_{10}), fine particles ($PM_{2.5}$), and coarse fraction particles (PM_{15}-$PM_{2.5}$). Note that the coarse fraction effects are smaller and statistically non-significant (i.e., lower 95% confidence intervals do not exceed relative risk of 1.0), except in Steubenville where there is high correlation between fine and coarse particles ($R^2 = 0.69$).

Source: PM CD (U.S. EPA, 1996a) graphical depiction of results from Schwartz et al. (1996).

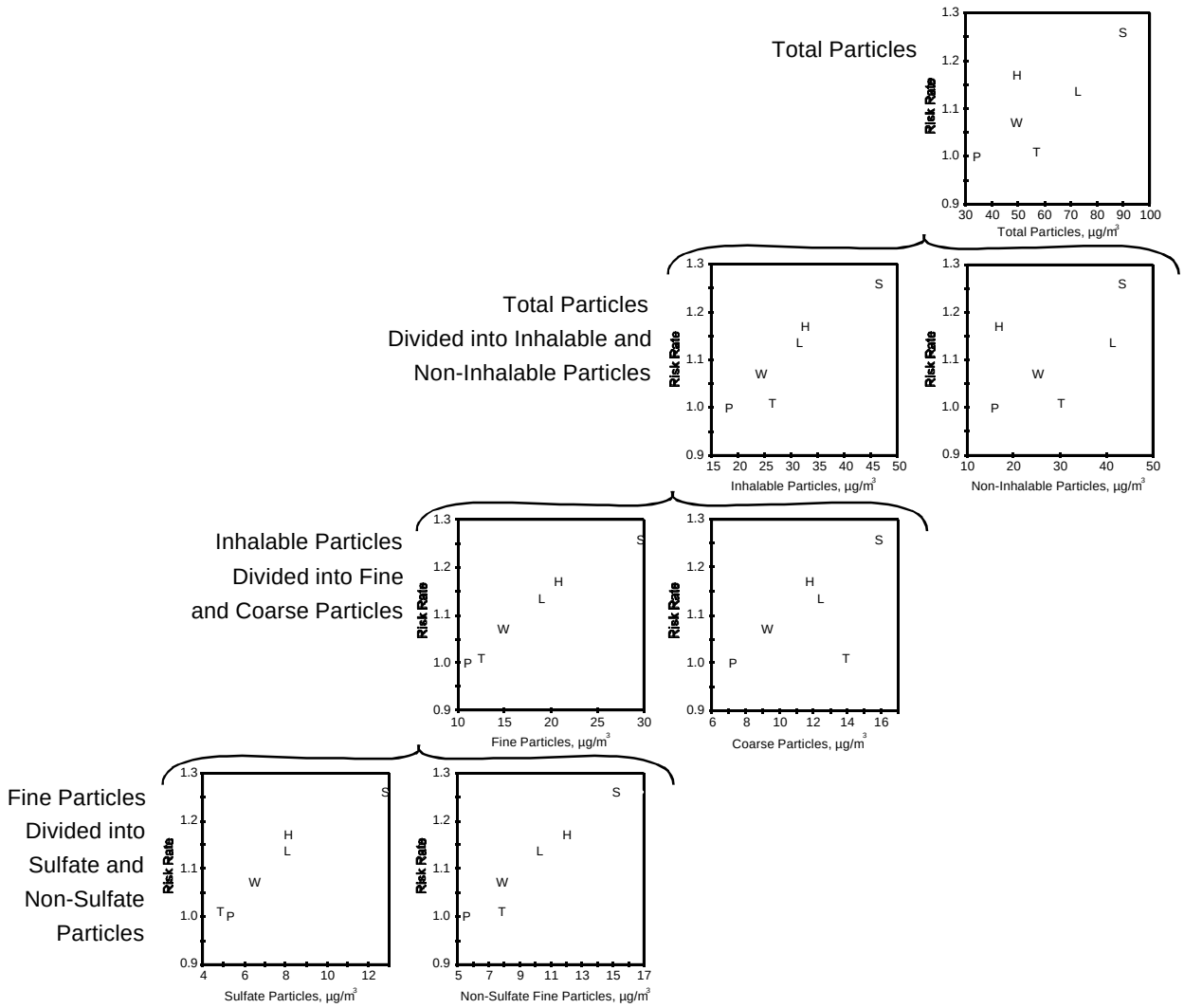

Figure C-3. Adjusted relative risks for mortality are plotted against each of seven long-term average particle indices in the Harvard Six City Study, from largest range (total suspended particles, upper right) through sulfate and nonsulfate fine particle concentrations (lower left). Note that a relatively strong linear relationship is seen for fine particles, and for its sulfate and non-sulfate components. Topeka, which has a substantial coarse particle component of inhalable (thoracic) particle mass, stands apart from the linear relationship between relative risk and inhalable particle concentration.

Source: U.S. EPA (1996a) replotting of results from Dockery et al. (1993).

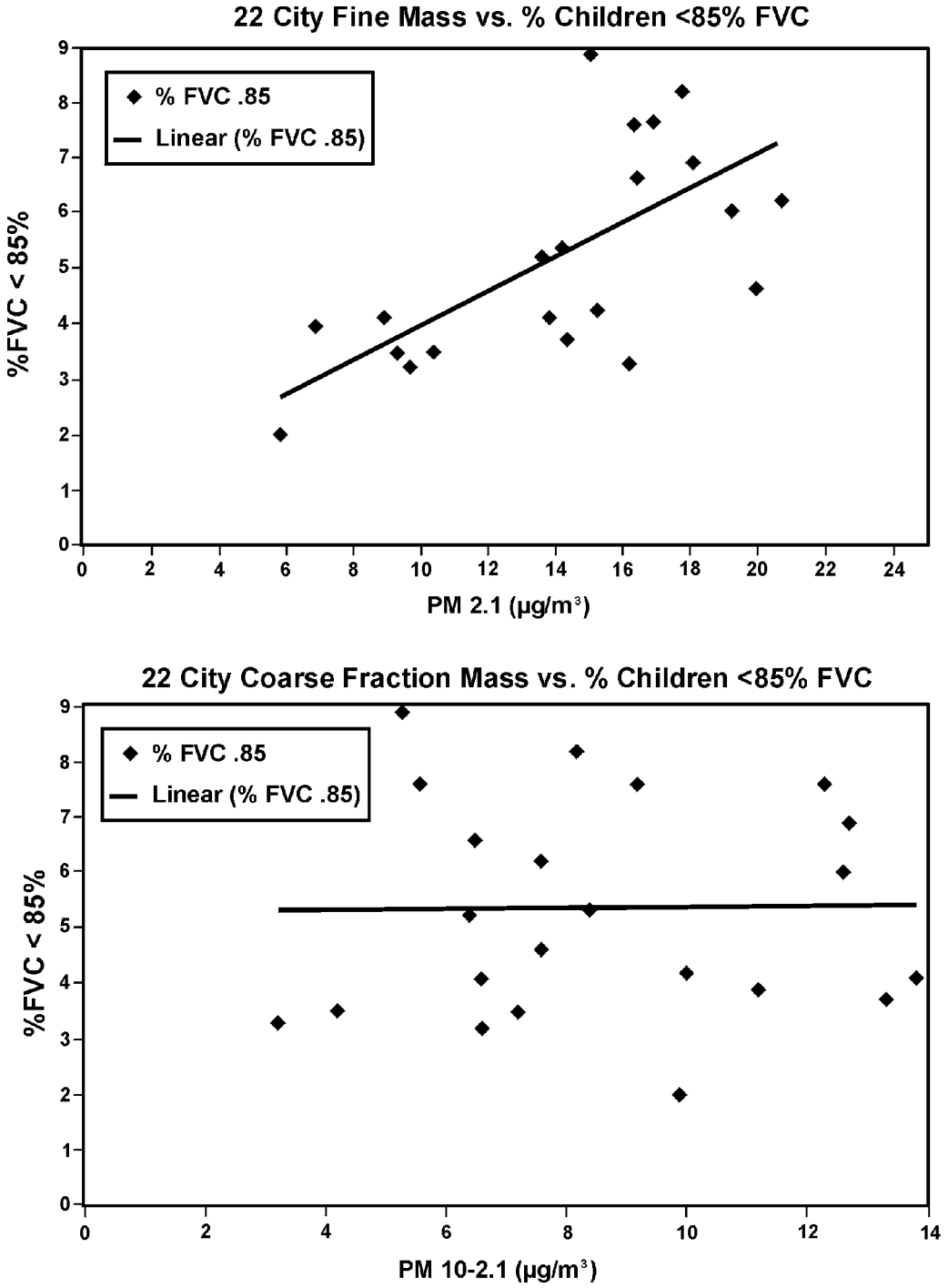

Figure C-4. Percent of children with <85% normal FVC versus annual-average fine ($PM_{2.1}$) particle concentrations and coarse fraction ($PM_{10-2.1}$) levels for 22 North American cities. Note much stronger relationship of fine particles to lung function decrements (top panel) versus for coarse fraction particles (bottom panel).

Source: PM Staff Paper (1996b) graphical depiction of results from Razienne et al. (1996).

C.3. REFERENCES

Abbey, DE; Mills, PK; Petersen, FF; et al. (1991) Long-term ambient concentrations of total suspended particulates and oxidants as related to incidence of chronic disease in California Seventh-Day Adventists. Environ Health Perspect 94:43-50.

Abbey, DE; Hwang, BL; Burchette, RJ; et al. (1995) Estimated long-term ambient concentrations of PM_{10} and development of respiratory symptoms in a nonsmoking population. Arch Environ Health 50:139-152.

Abbey, DE; Nishino, N; McDonnell, WF; et al. (1999) Long-term inhalable particles and other air pollutants related to mortality in nonsmokers. Am J Respir Crit Care Med 159:373-382.

Beeson, WL; Abbey, DE; Knutsen, SF. (1998) Long-term concentrations of ambient air pollutants and incident lung cancer in California adults: results from the AHSMOG study. Environ Health Perspect 106:813-823.

Dockery, DW; Pope, CA, III; Xu, X; et al. (1993) An association between air pollution and mortality in six U.S. cities. N Engl J Med 329:1753-1759.

Federal Register. (1987) Revisions to the national ambient air quality standards for particulate matter. F R 52:24,634-24,669.

Federal Register. (1997) National ambient air quality standards for particulate matter; final rule. F R 62:38,652-38,752.

Lipfert, FW. (1978) The association of human mortality with air pollution: statistical analyses by region, by age, and by cause of death. Mantua, NJ: Eureka Publications.

Lipfert, FW. (1984) Air pollution and mortality: specification searches using SMSA-based data. J Environ Econ Manage 11:208-243.

Neas, LM; Dockery, DW; Koutrakis, P; et al. (1995) The association of ambient air pollution with twice daily peak expiratory flow rate measurements in children. Am J Epidemiol 141:111-122.

Özkaynak, H; Thurston, GD. (1987) Associations between 1980 U.S. mortality rates and alternative measures of airborne particle concentration. Risk Anal 7:449-461.

Pope, CA, III; Thun, MJ; Namboodiri, MM; et al. (1995) Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. Am J Respir Crit Care Med 151:669-674.

Raizenne, M; Neas, LM; Damokosh, AI; et al. (1996) Health effects of acid aerosols on North American children: pulmonary function. Environ Health Perspect 104:506-514.

Schwartz, J; Dockery, DW; Neas, LM. (1996) Is daily mortality associated specifically with fine particles? J Air Waste Manage Assoc 46:927-939.

Schwartz, J. (1996b) Air pollution and hospital admissions for respiratory disease. Epidemiology 7:20-28.

Thurston, GD; Ito, K; Hayes, CG; et al. (1994) Respiratory hospital admissions and summertime haze air pollution in Toronto, Ontario: consideration of the role of acid aerosols. Environ Res 65:271-290.

U.S. Environmental Protection Agency (U.S. EPA). (1996) Review of the national ambient air quality standards for particulate matter: policy assessment of scientific and technical information. OAQPS staff paper. Research Triangle Park, NC: Office of Air Quality Planning and Standards; report no. EPA/452/R-96-013. Available from: NTIS, Springfield, VA; PB97-115406REB.