EPIDEMIOLOGICAL EVIDENCE OF HEALTH EFFECTS OF COMBUSTION-SOURCE PARTICULATE AIR POLLUTION

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INTRODUCTION

Many epidemiological studies have investigated the health effects of particulate air pollution. Various researchers with differing training, interests, and research skills have conducted a wide variety of studies. This paper provides a simple framework to catagorize the basic study designs of most of the currently available epidemiological studies of the health effects of particulate air pollution and reviews the basic results of these studies. Currently there are nearly 100 relevant and published epidemiological studies on particulate air pollution. All of these studies cannot be referenced in this brief paper, but there have been several recent reviews of many of these studies. (1-12). In this paper, key studies will be referred to in parentheses by author and year of publication. For more detailed discussions and full references, see Dockery and Pope 1996, and Pope and Dockery 1996 (11, 12).

BASIC STUDY DESIGNS

Currently available studies typically fall within two broad classifications: 1) acute exposure studies, and 2) chronic exposure studies (See Figure 1). The acute exposure studies use short-term temporal changes in pollution as their source of exposure variability. These studies evaluate short-term changes in health endpoints associated with short-term changes in pollution. These studies may be as simple as observing changes in health over a pollution episode that lasts for one or more days, or they may be highly formal daily time-series studies. Because these studies typically evaluate only short-term temporal relationships (usually 1-5 days), the observed pollution effects are typically interpreted as the health effects of acute exposure.

Available chronic exposure studies primarily use spatial differences in pollution as their source of exposure variability. Chronic exposure studies, therefore, compare various health outcomes across communities or neighborhoods with different levels of pollution. These studies are principally cross-sectional in design and use longer-term pollution data (usually one year or more). These studies are often interpreted as evaluating the chronic and/or cumulative effects of exposure.

Nearly all of the currently published acute and chronic exposure studies can also be subdivided as population-based studies or cohort-based studies. The population-based studies are often referred to as ecological studies where the units of comparison are entire populations of communities or neighborhoods. The cohort-based studies include studies descriptively referred to as panel studies or sample-based studies. Although, central-site community-based monitoring is typically used to estimate pollution exposure in the cohort-based studies, the units of comparison for health outcomes and co-risk factors are individuals enrolled in a well-defined cohort, panel, or sample.

These studies can be further subdivided by the specific health outcomes evaluated. An appraisal of the strength of the overall epidemiological evidence of health effects of air pollution requires an evaluation of coherency. Effects of pollution should be evaluated across a range of related health outcomes. Cardiopulmonary health outcomes that have been evaluated include mortality, hospitalizations or health care visits for respiratory and/or cardiovascular disease, respiratory symptoms, measures of lung function, and restricted activity due to illness.

ACUTE EXPOSURE, POPULATION-BASED, MORTALITY STUDIES

Early studies focused on severe air pollution episodes, often in narrow industrial valleys such as the Meuse River in Belgium (Firket 1931) and Donora, PA (Ciocco & Thompson 1961). The most dramatic of these documented air pollution episodes occurred in London, England (Logan 1953). Several later studies in London reported associations between daily mortality air pollution at much lower pollution levels (Ostro 1984, Schwartz and Marcus 1990, Ito et al. 1993). Elevated respiratory and cardiovascular disease morbidity and mortality have also been reported for a more moderate increase in pollution in the North Rhine--Westfalia area of Germany (Wichmann et al. 1989).

The severe air pollution episodes have been frequently reviewed (Ellison & Waller 1978, Holland et al. 1979, Shy 1979, Bates 1980). They demonstrated an important link between cardiopulmonary disease mortality and morbidity with extremely elevated concentrations of particulate and/or sulfur oxide air pollution. They also suggested effects at lower levels. Although the biological mechanisms involved were poorly understood, there remained little disagreement that, at very high levels, ambient air pollution can be an important risk factor associated with increased cardiopulmonary disease and early mortality.

A series of recent studies analyzed the temporal distribution of deaths and particulate air pollution at current levels. The U.S. EPA has reviewed these studies in the recent criteria document on the health affects of particulate air pollution and other reviews of these studies have been made (1-12). These studies observed changes in daily death counts associated with short-term changes in particulate air pollution. A particulate pollution threshold was not generally observed in these studies. The relative risk of mortality increased monotonically with particulate concentrations--usually in a near linear fashion.

These studies have observed similar particulate air pollution effects in varied locations. Because various measurements of particulate pollution were used, precise comparisons between studies are difficult. But when particulate measurements are converted to PM_{10}, there is remarkable consistency in the estimated effect of PM10 across these studies. The esimated effect ranges between a 0.5 percent and 1.6 percent in daily mortality for each 10 $\mu g/m^3$ increase in PM_{10} concentration with a weighted mean of about 0.8 percent.

Several studies also provided a breakdown of mortality by broad cause-of-death categories. Particulate air pollution generally had the largest effect on respiratory disease mortality but effects on cardiovascular mortality were also observed. An examination of cardiovascular deaths in Philadelphia reported that on days with high particulate air pollution there was a substantial increase in respiratory factors as contributing causes for death, with cardiovascular disease reported as the underlying cause of death.

ACUTE EXPOSURE, POPULATION-BASED, HOSPITALIZATION STUDIES

The results of a unique natural experiment that occurred in the Utah Valley have been reported (Pope 1989, 1991). During the winter of 1986-1987 a labor dispute resulted in the closure of the local steel mill, the largest single source of particulate air pollution in the valley. During this winter, PM_{10} concentrations averaged 51 $\mu g/m^3$ with a high of 113 $\mu g/m^3$ compared with a mean of 90 $\mu g/m^3$ with a high of 365 $\mu g/m^3$ during the previous winter. During this winter, children's hospital admissions for respiratory disease dropped by more than 50 percent, compared with adjacent years. Regression analysis estimated a 4.2 percent decrease in asthma and bronchitis admissions of children associated with a 10 $\mu g/m^3$ increase in 2-month mean PM_{10}.

Several studies have found that increased rates of respiratory hospital admissions in southern

Ontario are associated with increased sulfate and ozone concentrations (Bates and Sizto 1987, 1989; Burnett et al. 1994). Burnett et al (1995) also evaluated hospital admissions data for 168 hospitals in Ontario and observed significant positive associations between respiratory and cardiac hospital admissions and sulfate concentrations. Thurston and colleagues have reported similar associations in Toronto, Ontario (Thurston et al. 1993) and for several cities in New York State (Thurston et al. 1992). The focus of these studies was the effects of acid aerosols, but estimates were reported for various measures of particle exposure. Taken together, these studies found an increase in hospital admissions for respiratory diagnoses ranging from approximately 0.8 percent to 3.4 percent for each 10 $\mu g/m^3$ increase in daily mean PM_{10}.

Several studies have also analyzed emergency department visits and found them to be associated with particulate air pollution. For example, particulate air pollution was associated with emergency department visits for asthma in Seattle, WA (Schwartz et al. 1993), emergency department visits for chronic obstructive pulmonary disease in Barcelona (Sunyer et al. 1991, 1993), and emergency department visits in Steubenville, OH (Samet et al. 1981). The estimated percent increase in emergency visits associated with a 10 $\mu g/m^3$ increase in PM_{10} ranged from 0.5 percent to 3.4 percent with a weighted mean of approximately 1.0 percent.

Given the associations between particulate pollution and emergency department visits, it would be expected that associations would also be observed for outpatient visits for respiratory illness. There is less availability of outpatient data to researchers than there is for hospitalization data. However, based on a limited study of outpatient data from a clinic in Salt Lake City, UT, Lutz (1983) reported that strong positive associations were observed between weekly particulate pollution levels and the percentage of patients with a diagnosis of respiratory tract or cardiac illness.

ACUTE EXPOSURE, COHORT-BASED, SYMPTOM/DISEASE STUDIES

Studies of upper and lower respiratory symptoms have been conducted in the Utah Valley (Pope et al. 1991, Pope and Dockery 1992), the Netherlands (Hoek & Brunekreef 1993, 1994), a study of six U.S. cities (Schwartz et al. 1994), and Southern California (Ostro et al. 1993). Very small, often statistically insignificant associations between particulate pollution and upper respiratory symptoms were observed. Association with lower respiratory disease were larger and usually statistically significant. Based on these studies, the estimated percent increase in reported lower respiratory symptoms associated with a 10 $\mu g/m^3$ increase in PM_{10} was as high as 15 percent, but the weighted mean was approximately 3.0 percent.

Cough was analyzed separately in three of these studies as well as in another diary study in the Netherlands (Roemer et al. 1993), a study of two Swiss cities (Braun-Fahrlander et al. 1992), and a study in Uniontown, Pennsylvania (Neas et al. 1992). Cough was typically associated with particulate pollution, with the estimated percent increase in reported cough associated with a 10 $\mu g/m^3$ increase in PM_{10} as high as 28 percent but with a weighted mean of approximately 1.2 percent

Evidence from hospital admissions and emergency visit studies suggests that exposures to particulate air pollution may be directly associated with asthma attacks. Several investigators have considered less severe asthmatic attacks as reported by panels of asthma patients. Winter studies of asthmatic children with chronic respiratory symptoms in The Netherlands (Roemer et al. 1993) and of asthmatic adults in Denver, Colorado, (Ostro et al. 1991) both found substantial increases in reported asthmatic attacks associated with particle exposures. An earlier study in the Los Angeles area (Whittemore and Korn 1980) reported increased attacks associated with particle exposures but the effect was much

lower than in the more recent studies. The weighted mean of these three studies gives an effect estimate of 3 percent increase in asthmatic attacks associated with 10 $\mu g/m^3$ increase in PM_{10}.

Bronchodilator use has also been evaluated as a measure of exacerbation of asthma in a panel of asthmatics in the Netherlands (Roemer et al. 1993) and in the Utah Valley (Pope et al. 1991). Based on the reported results of these studies, the estimated percent increase in asthma attacks or use of bronchodilator associated with a 10 $\mu g/m^3$ increase in PM_{10} range from 1.1 percent to 12 percent with a weighted mean of approximately 3.0 percent.

Associations between particulate air pollution and more general measures of acute disease have also been observed. For example, Ostro (1983, 1987, 1990) and Ostro and Rothschild (1989) evaluated the timing of restricted activity days of U.S. adult workers. Restricted activity due to respiratory morbidity was consistently associated with particulate pollution. Morbidity was often more strongly associated with the fine, respirable, or sulfate component of particulate pollution. Ransom and Pope (1992) reported similar associations between PM_{10} and grade-school absences in children in the Utah Valley, Utah. Lagged pollution effects of up to several weeks were observed for both restricted activity in adults and in school absences.

ACUTE EXPOSURE, COHORT-BASED, LUNG FUNCTION STUDIES

Several studies have observed negative associations between particulate pollution and lung function. Panels of elementary school children in Steubenville, OH had their lung function measured weekly before, during, and after particulate and sulfur oxide episodes during four periods in 1978 through 1980 (Dockery et al. 1982). Declines in forced expired volume in 0.75 seconds ($FEV_{.75}$) were observed following these episodes. In a re-analysis of the Steubenville data, Brunekreef et al. (1991) found the strongest association with the mean particle concentrations over the previous 5 days. Similar decreases in forced expired volume in 1 second (FEV_1) were observed in school children following a particulate and sulfur oxide pollution episode in January 1985 in the Netherlands (Dassen et al. 1986). Subsequent studies of panels of school children in the Netherlands with weekly lung function measurements (Hoek & Brunekreef 1993, 1994) have also shown decreased FEV_1 associated with daily PM_{10} concentrations. Lagged effects of up to seven days were observed.

Pope and Kanner (1993) analyzed repeated FEV_1 measurements in a panel of adults with chronic pulmonary disease who were participating in the Lung Health Study. Measurements were taken 10 to 90 days apart. FEV_1 levels were found to be associated with PM_{10} concentrations. Koenig and colleagues (1993) studied the lung function [forced vital capacity (FVC) and FEV_1] of children in Seattle, WA with relatively low particulate air pollution levels. Lung function declines were associated with fine particulate air pollution for asthmatic children, but not for non-asthmatic children. Overall, these studies generally observed a decrease of up to 0.35 percent in FEV_1 associated with each 10 $\mu g/m^3$ increase in daily mean PM_{10}, with a weighted average of 0.15 percent.

Several studies have used peak flow measurements as an indicator of acute changes in lung function including studies in the Netherlands (Hoek and Brunekreef 1993, 1994; Roemer et al. 1993), the Utah Valley (Pope et al., 1991; Pope and Dockery 1992), and Uniontown, PA (Neas et al. 1992). In these studies a 10 $\mu g/m^3$ increase in PM_{10} was associated with a 0.04 percent to 0.25 percent decreases in peak flow measurements. As with FEV_1, the strongest associations with peak flow included particulate pollution over the previous several days, allowing for a lag in effect.

CHRONIC EXPOSURE, POPULATION-BASED MORTALITY STUDIES

There have been many studies that have suggested mortality effects of chronic exposure to air pollution. Martin (1964) reported that in the Greater London region overall annual respiratory mortality (as opposed to episodic mortality) was significantly related to smoke (or particulate pollution) levels. In 1970 Lave and Seskin reported the results of one of the first serious attempts to measure the long-term mortality effects of air pollution in the U.S. The work of Lave and Seskin has been followed by many other similar studies that have tried to replicate or refine their use of population-based (ecologic) cross-sectional study designs. Most of these studies observed that mortality rates tended to be higher in cities with higher fine or sulfate particulate pollution levels. Formal regression modeling techniques to evaluate cross-sectional differences in air pollution and mortality and to control for other ecological variables were used. In an attempt to control for other risk factors, population average values for demographic variables and other factors such as smoking rates, education levels, income levels, poverty rates, housing density, and others were often included in the regression models. The basic conclusions from the population-based cross-sectional studies include: 1) Mortality rates are associated with air pollution; 2) Mortality rates are most strongly associated with fine or sulfate particulate matter; and 3) An average mortality effect of 3 to 9 percent of total mortality can be estimated.

Although these population-based cross-sectional studies suggest that air pollution contributes to human mortality, these studies have severe limitations and have been largely discounted for several reasons. An overriding concern of these studies was that these population-based cross-sectional studies could not directly control for individual differences in cigarette smoking and other risk factors. They could only try to control for them by using population-based averages --making potential confounding a concern.

CHRONIC EXPOSURE, COHORT-BASED MORTALITY STUDIES

Recently the results of two prospective cohort mortality studies have been reported. Because of their improved study design these studies brought some of the most compelling evidence about mortality effects of chronic exposure to air pollution. The first of these recently reported prospective-cohort mortality studies was the "Six Cities study" (Dockery et al. 1993). This study involved a 14-16 year prospective follow-up of 8,111 adults living in 6 U.S. cities. The data were then analyzed using survival analysis, including multivariate Cox proportional hazards regression modeling. Although TSP concentrations dropped over the study periods, fine particulate and sulfate pollution concentrations were relatively constant. Mortality risks were most strongly associated with cigarette smoking, but after controlling for individual differences in age, sex, cigarette smoking, body mass index, education, and occupational exposure, differences in relative mortality risks across the six cities were strongly associated with pollution levels in those cities. Associations between mortality risk and air pollution were stronger for respirable particles and sulfates, as measured by PM_{10}, $PM_{2.5}$, and SO_4, than for TSP, SO_2, acidity (H^+), or ozone. The association between mortality risk and fine particulate air pollution was consistent and nearly linear, with no apparent "no effects" threshold level above the ambient level in the least polluted city (Portage). The adjusted total mortality-rate ratio for the most polluted of the cities compared with the least polluted was 1.26 with 95% confidence interval (CI) from 1.08 to 1.47. Fine particulate pollution was associated with cardiopulmonary mortality and lung cancer mortality (not statistically significant) but not with the mortality due to other causes analyzed as a group.

Similar results were observed in a much larger prospective cohort study (Pope et al. 1995). In this study approximately 500,000 adults drawn from the American Cancer Society (ACS) Cancer Prevention Study II (CPS-II) who lived in 151 different U.S. metropolitan areas

were followed prospectively from 1982 through 1989. Individual risk-factor data and 8 years of vital status data were collected. Ambient concentrations of sulfates and fine particles, were used as indices of exposure to combustion-source ambient particulate air pollution. Exposure was estimated from national data bases. Pollution exposure also was assessed for a time period just prior to entry into the cohort. An association between mortality and air pollution was observed after adjusting for age, sex, race, cigarette smoking, pipe and cigar smoking, exposure to passive cigarette smoke, occupational exposure, education, body mass index, and alcohol use. Mortality-rate ratios (and 95 percent confidence intervals) of total mortality for the most polluted areas compared with the least polluted equaled 1.15 (1.09-1.22) and 1.17 (1.09-1.26) when using sulfate and fine particulate measures, respectively. For total, cardiopulmonary, and lung cancer mortality, the associations with sulfate particles were highly statistically significant ($P < 0.01$). For total and cardiopulmonary mortality, significant associations were also found using fine particulate matter as the index of air pollution levels. The association between air pollution and all-cause and cardiopulmonary mortality was observed for both men and women and for smokers and nonsmokers.

CHRONIC EXPOSURE, COHORT-BASED, SYMPTOMS/DISEASE STUDIES

There have been several studies that have evaluated associations between particulate air pollution and chronic respiratory symptoms and disease. These studies include the Harvard six-cities study (Dockery et al 1989), analysis of chronic obstructive pulmonary disease (COPD) symptoms of never-smoking Seventh-Day Adventists in California (Euler et al., 1987), analysis of data from the 1979 version of the U.S. National Health Interview Survey (NHIS) (Portney and Mullahy, 1990), analysis using data from the first National Health and Nutrition Examination Survey (NHANES I) (Schwartz 1993), and analysis of the symptoms data from the 24-cities study (Dockery et al, 1993). The effects of air pollution on respiratory disease or symptoms were estimated while adjusting for individual differences in various other risk factors. In all of these studies, statistically significant associations were observed between particulate air pollution and respiratory symptoms. Particulate air pollution was most consistently associated with bronchitic symptoms. The results suggest that a 10 $\mu g/m^3$ increase in PM_{10} was typically associated with a 10 to 25 percent increase in bronchitis or chronic cough.

CHRONIC EXPOSURE, COHORT-BASED, LUNG FUNCTION STUDIES

Holland and Reid (1965) made a cross-sectional comparison of British male postal employees in London and in smaller country towns, where levels of SO_2 and particulate pollution were about half of those in the metropolis. Accounting for cigarette smoking levels, significant decrements of FEV_1 in London employees compared to those in the provinces were reported. There have been several more recent studies that have evaluated associations between measures of lung function (FVC, FEV_1, PEF) and particulate pollution levels in the U.S. These studies include analysis of children's lung function data from the Harvard six-city study (Dockery et al, 1989), analysis of data from both the first and second National Health and Nutrition Examination Surveys (NHANES I and NHANES II) (Chestnut et al, 1991 and Schwartz, 1989), analysis of children's lung function from 24 U.S. cities (Raizenne et al, 1993) and analysis from eight different areas in Switzerland (Ackermann-Liebrich et al, 1987). Each of these studies had information on individual persons in the samples. The effects of air pollution on lung function were estimated after adjusting for individual differences in age, race, sex, height, and weight and controlling for smoking or restricting the analysis to never-smokers.

All of these studies observed small negative associations between lung function and particulate air pollution. In the six-cities study, which had the least statistical power, the association was very weak and statistically

insignificant. In each of the other studies, the association was small, but statistically significant. The results suggest that a 10 $\mu g/m^3$ positive difference in PM_{10} was typically associated with less than a two percent decline in lung function. However, lung function measures have been shown to be important measures of health with remarkable predictive capacity for survival (Bates 1989). Furthermore, as reported in the 24-city study, the risk of relatively large deficits in lung function (15 percent or more) was much higher in the more polluted cities, suggesting detrimental effects of respirable particulates or particulate acidity on normal lung growth and development.

SUMMARY AND CONCLUSIONS

Table 1 presents ranges of effect estimates relating particulate exposure to various health end points. Although the biological linkages remain poorly understood, the results of the acute and chronic exposure studies are complementary. The current epidemiologic evidence suggests that respirable particulate air pollution, at levels common to many urban and industrial areas in the United States, contributes to human morbidity and mortality. Long-term, repeated exposure increases the risk of chronic respiratory disease and the risk of cardiorespiratory mortality. Short-term exposures can exacerbate existing cardiovascular and pulmonary disease and increase the number of persons in a population who become symptomatic, require medical attention, or die. The pattern of cardiopulmonary health effects associated with particulate air pollution that has been observed by epidemiological studies is the strongest evidence of the health effects of this pollution. Nevertheless, the epidemiological studies have important limitations that stem largely from the use of people who are living in uncontrolled environments, and who are exposed to complex mixtures of particulate air pollution.

In addition to providing limited information about biological mechanisms, current epidemiological studies provide relatively meager information regarding linkages between ambient and personal exposures, and are unable to fully explore the relative health impacts of various constituents of air pollution. Furthermore, the relationships between chronic versus acute exposures remain unclear. Much of the recent epidemiological effort has focused on effects of acute exposure, primarily because of the relative availability of relevant time-series data sets. However, the effects of chronic exposure may be more important in terms of overall public health relevance.

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Figure 1: Basic Study Designs of Currently Published Studies of Health Effects of Particulate Air Pollution

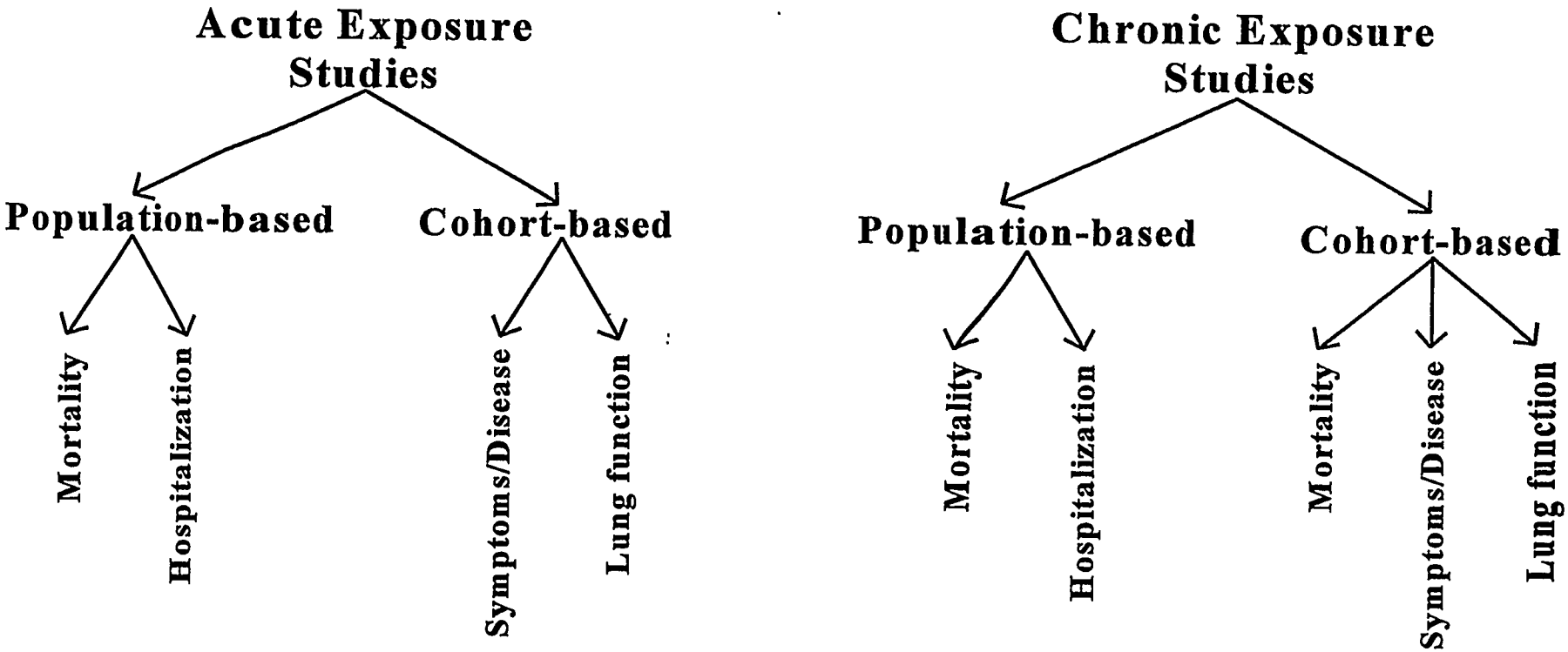

Table 1. Approximate range of estimated effects measure as percent change in health endpoint per 10 $\mu g/m^3$ increase in PM_{10} for the different basic study designs.

Health Endpoints	Acute Exposure		Chronic Exposure	
	Population-Based	**Cohort-Based**	**Population-Based**	**Cohort- or Sample-Based**
Mortality	Total: 0.5 - 1.5 Resp: 1.5 - 4.0 Cardio: 0.5 - 2.0		Total: 0 - 5	Total: 3 - 6 Cardiopulmonary: 5 - 9 Lung cancer: 0 - 9
Respiratory Health Care	Hospit. Admit: 0.5 - 4.0 Emergency Visits: 0.5 - 3.5			
Decrease in Lung Function		FEV_1: 0.05 - 0.35 PEF: 0.04 - 0.25		Lung function 0 - 2
Respiratory Symptoms, Disease		Lower: 0 - 15 Upper: 0 - 7 Cough: 0 - 25 Asthmatic attacks: 1 - 12		Emphysema, Chronic bronchitis or cough 10 - 25
Restricted Activity	Grade school absences: 1.0 - 4.0	Restricted activity days: 1.0 - 5.0		