Health Effects of Particulate Air Pollution: Time for Reassessment?

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Numerous studies have observed health effects of particulate air pollution. Compared to early studies that focused on severe air pollution episodes, recent studies are more relevant to understanding health effects of pollution at levels common to contemporary cities in the developed world. We review recent epidemiologic studies that evaluated health effects of particulate air pollution and conclude that respirable particulate air pollution is likely an important contributing factor to respiratory disease. Observed health effects include increased respiratory symptoms, decreased lung function, increased hospitalizations and other health care visits for respiratory and cardiovascular disease, increased respiratory morbidity as measured by absenteeism from work or school or other restrictions in activity, and increased cardiopulmonary disease mortality. These health effects are observed at levels common to many U.S. cities including levels below current U.S. National Ambient Air Quality Standards for particulate air pollution. *Key words*: air pollution, particulate pollution, health effects, respiratory disease. *Environ Health Perspect* 103:472–480 (1995)

Many investigators have reported associations between particulate air pollution and respiratory disease. Early studies focused on severe air pollution episodes including an episode in Meuse Valley, Belgium, in December 1930 (*1*); an episode in Donora, Pennsylvania, in 1948 (*2*); and several episodes in London, the most notable occurring in December 1952 (*3*). Although few data were available regarding concentrations of air pollutants during these episodes, large increases in sickness and death demonstrated severe health effects of air pollution.

Two other important observations were made. First, Martin noted that in the greater London region, overall annual respiratory mortality (as opposed to episodic mortality increases) was significantly related to smoke level (*4*). Second, Holland and Reid (*5*) 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 those in the metropolis. Accounting for cigarette smoking, significant decrements of FEV_1 (forced expiratory volume in 1 sec) in London employees compared to those in the provinces were reported. With our present knowledge of the remarkable predictive capability of FEV_1 for survival (*6*), this finding also suggests that longevity was adversely affected by pollution levels prevailing at that time. This type of air pollution from coal burning has been greatly reduced in the western industrialized nations, but it is still present in Eastern Europe and China. A recent study (*7*) of nonsmoking women in different areas around Beijing shows similar decrements of FEV_1 in areas of higher pollution as were first demonstrated by Holland and Reid (*5*).

By the 1970s, a link between respiratory disease and particulate air pollution and/or sulfur oxide pollution had been well established. There remained disagreement about what levels of pollution significantly affected human health. For example, Holland and several other prominent British scientists (*8*) reviewed research on the health effects of particulate pollution that had been published between 1968 and 1977. They concluded that particulate and related air pollution at high levels pose hazards to human health, but that health effects of particulate pollution at lower concentrations that existed in the United States and Britain by the 1970s could not be "disentangled" from health effects of other factors (*8*). Shy (*9*) responded that this review systematically discounted evidence of pollution-related health effects at contemporary pollution levels. Shy and other reviewers (*9–12*) contended that the cumulative weight of evidence suported the belief that particulate pollution may adversely affect human health even at relatively low concentrations. There has been a great increase in vehicular traffic over the past 20 years. The larger particles resulting from uncontrolled coal burning have been replaced in the urban environment by relatively high concentrations of much smaller particles, commonly 0.2 μm in size.

Much additional research has been conducted since the mid 1970s. While earlier research was useful in documenting the substantial health effects associated with large, dramatic pollution episodes, recent epidemiologic studies have provided more quantification of subtle health effects associated with particulate pollution common to contemporary cities in the developed world. Recent epidemiologic research has generally had better definitions and measures of pollution exposures and health endpoints. Advanced biostatistical and econometric techniques for longitudinal or cross-sectional analysis have greatly expanded opportunities to evaluate health effects of particulate pollution and have increased the analytical rigor of recent studies. For example, recent advances in autoregressive Poisson and logistic regression analysis have permitted the evaluation of pollution associations in panels or other small populations.

This review focuses on approximately 80 recently published epidemiologic studies, most since 1985, which evaluated effects of particulate pollution at concentrations commonly observed in contemporary cities in the developed world. For convenience, these studies are subdivided into general categories based on health endpoint and research methodology and are summarized in Tables 1–5. Separate critiques of each of the key papers are beyond the scope of this review. Although individual studies necessarily have limitations imposed by data deficiencies or by problems in analytical methods, when the whole body of contemporary research is viewed, it is possible to form a judgment concerning the validity of adverse health outcomes as a consequence of particulate pollution.

Acute Morbidity

Numerous studies evaluated acute morbidity effects of particulate pollution by examining short-term temporal associations between lung function measures and/or respiratory symptoms and pollution. Measures of lung function including forced vital capacity (FVC), FEV_1, and peak expiratory flow (PEF) were used. Most of these studies used formal daily time-series analysis, but some of them used periodic time-series analysis across one or more pollution episodes. A summary of the results of many of these studies is presented in Table 1.

Negative associations with particulate pollution and lung function measures were often observed. The particulate pollution effect on lung function was generally physiologically small but statistically signifi-

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This work was done partially while C.A.P. was on leave as a visiting scientist at the Environmental Epidemiology Program, Harvard School of Public Health, Boston, Massachusetts.

This work was supported in part by the Department of National Health and Welfare, Canada, contract no. 3237, project no. K281225 and project no. K281235.

Received 7 July 1994; accepted 23 February 1995.

cant. Because various measurements of particulate pollution were used, precise comparisons between the studies are difficult. Results of most of the studies suggest, however, that a 10 $\mu g/m^3$ increase in respirable particles (particulate matter ≤10 μm; PM_{10}) resulted in less than a 1% decline in lung function. Nevertheless, in several studies, 24-hr PM_{10} concentrations would occasionally exceed 150 $\mu g/m^3$. During such episodes lung function declined by as much as 7%. In addition to declines in lung function, many of these studies observed increases in respiratory symptoms. A 10 $\mu g/m^3$ increase in PM_{10} was typically associated with a 1–10% increase in symptoms such as cough, combined lower respiratory symptoms, and asthma attacks. These effects were also observed at comparable PM_{10} levels near or even below 150 $\mu g/m^3$.

An important limitation of these studies is that acute effects of particulate pollution on lung function are on average physiologically small and transient, remaining for a few days up to a few weeks. The importance of these small transient effects on a person's long-term well being is unclear. Furthermore, there is concern that these pollution effects may be due to confound-

Table 1. Selected time-series studies on acute effects of particulate pollution on lung function and respiratory symptoms

References	Health endpoints	Study area	Summary of findings
Braun-Fahrlander et al., 1992 (*13*)	Respiratory symptom episodes of 625 children	Basel and Zurich, Switzerland	Particulate pollution (TSP) was associated with incidence and duration of respiratory symptom episodes. No such associations were observed with SO_2 or ozone.
Dassen et al., 1986 (*14*)	Lung function (FVC, FEV_1, PEF) of 636 children	Ijmond, The Netherlands	Significant declines in lung function of 3–5% were observed during an episode of moderately elevated TSP and SO_2. Reductions remained for 16 (but not 25) days.
Dockery et al., 1982 (*15*); Brunekreef et al., 1991 (*16*)	Lung function (FVC, $FEV_{.75}$) of approx. 200 children	Steubenville, OH	Small, significant decreases in lung function were observed after TSP/SO_2 pollution episodes. The association was strongest with previous 5-day mean TSP concentrations.
Johnson et al., 1982 (*17*)	Lung function (FVC, FEV_1, FEF_{25-75}) of children	Missoula, MT	Declines in lung function of 1–3% were associated with a "normal" urban air pollution episode. Comparable declines were not associated with a volcanic ash episode.
Johnson et al., 1990 (*18*)	Lung function (FVC, FEV_1, FEF_{25-75}, PEF) of children	Five Montana cities	Transient declines in lung function were associated with particles. In some cities sources were mostly wood smoke and entrained dust with low levels of SO_2 or O_3.
Hoek and Brunekreef, 1993 (*19*)	Lung function (FVC, FEV_1, PEF, MMEF) of children	Wageningen, The Netherlands	Negative associations between lung function and particulate pollution were observed. Consistent associations with respiratory symptoms were not observed.
Koening et al., 1993 (*20*)	Lung function (FVC, FEV_1) of 326 children	Seattle, WA	Lung function declines were associated with fine particulate air pollution for asthmatic children, but not for nonasthmatic children.
Kinney et al., 1989 (*21*)	Lung function (FVC, $FEV_{.75}$, MMEF, $Vmax_{75}$) of 154 children	Kingston/Harriman, TN	Small decrements in lung function were associated with O_3 but not with particulate pollution, which had low concentrations with little variability.
Krupnick et al., 1990 (*22*)	Respiratory symptoms of 1000+ children/adults	Los Angeles, CA	Respiratory symptoms in both adults and children were associated with particulate pollution. An association with O_3 was observed for adults but not children.
Lebowitz et al., 1985 (*23*)	Lung function (PEF) and symptoms of 229 children/adults	Tucson, AZ	Declines in PEF were associated with elevated concentrations of TSP and O_3. Associations with smoking, gas stove use, and outdoor NO_2 concentrations were also observed.
Ostro et al., 1991 (*24*)	Respiratory symptoms of 207 adult asthmatics	Denver, CO	Several respiratory symptoms including cough and shortness of breath were associated with airborne acidic particulate pollution (H^+). Cough was also associated with $PM_{2.5}$.
Pope et al., 1991 (*25*); Pope and Dockery, 1992 (*26*)	Lung function (PEF) and symptoms of 100+ children and asthma patients	Provo/Orem, UT	Elevated PM_{10} levels were associated with significant declines in PEF, increases in respiratory symptoms, and increased use of asthma medication. Lagged associations were observed for up to 5 days. Particle acidity, SO_2, and O_3 levels were low.
Pope and Kanner, 1993 (*27*)	Lung function (FVC, FEV_1) of smokers with COPD	Salt Lake City, UT	Small transient negative associations between PM_{10} levels and lung function (FEV_1, FEV_1/FVC) were observed. This association was not entirely obscured by participants' smoking habit.
Raizenne et al., 1989 (*28*)	Lung function (PEF, FEV_1) in 112 girls	Girl's camp in Ontario	Maximum average declines in FEV_1 and PEF equal to 3.5 and 7%, respectively, were associated with elevated acid aerosol episodes.
Schwartz et al., 1994 (*29*)	Respiratory symptoms in children	Six U.S. cities	Cough and lower respiratory symtoms were positively associated with PM_{10}.
Whittemore and Korn, 1980 (*30*)	Asthma attacks of 443 asthmatics	Los Angeles, CA	Increased asthma attacks were observed on days with elevated levels of TSP and/or O_3.

Abbreviations: TSP, total suspended particulates; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 sec; PEF, peak expiratory flow; FEF, forced expiratory flow; PM_{10}, particulate matter ≤10 μm; COPD, chronic obstructive pulmonary disease.

ing by weather or some other factor that is not adequately accounted for in the analysis. This concern is partially mitigated by the fact that similar effects have been observed in locations with differing weather conditions including locations where particulate concentrations are high in the summer and where they are high in the winter. For example, effects were observed in studies from Switzerland, the Netherlands, Ohio, Montana, southern California, Arizona, Colorado, Utah, and southern Ontario. Effects were observed in communities where most of the pollution was from wood burning, steel mills, and related industry, or was composed of a complex mixture of aerosols and other particles that are characteristic of urban air pollution. Effects were observed in studies both with and without high concentrations of acid aerosols, sulfur dioxide, and ozone. Effects were observed for both children and adults. Effects were generally observed across areas where the primary source of particulate pollution was combustion, but very small or no effects were associated with large volcanic ash particulate concentrations (*17*).

Numerous studies have also evaluated acute morbidity effects of particulate pollution by examining short-term temporal associations between particulate air pollution and hospital admissions, health care visits, or other measures of restricted activity due to illness (Table 2). These studies usually used formal time-series analytical methods. Statistically significant associa-

Table 2. Selected studies on acute effects of particulate pollution on respiratory morbidity as measured by hospital admissions, health care visits, or other measures of restricted activity due to illness

References	Health endpoints	Study area	Summary of findings
Bates and Sizto, 1987, 1989 (*31,32*); Lipfert and Hammerstrom, 1992 (*33*)	Hospital admissions for 79 hospitals	Southern Ontario	Statistically significant associations between respiratory hospital admissions and sulfates and ozone were observed during summer months. No such associations with nonrespiratory admissions were observed.
Bates et al., 1990 (*34*)	Hospital emergency visits to 9 hospitals	Vancouver, British Columbia	Particulate concentrations were low, and associations with pollution variables were inconsistent. For ages 15–60, asthma and all respiratory visits were significantly correlated in summer with SO_2 and SO_4 levels.
Burnett et al., 1995 (*35*)	Admissions for 168 hospitals	Ontario	Significant positive associations were observed between respiratory and cardiac hospital admissions and previous-day sulfate levels.
Schwartz et al., 1993 (*36*)	Asthma emergency visits	Seattle, WA	Asthma visits were associated with PM_{10} (but not SO_2 or O_3) even at PM_{10} levels below 100 $\mu g/m^3$. An increase in PM_{10} equal to 30 $\mu g/m^3$ was associated with a 12% increase in asthma visits.
Thurston et al., 1992 (*37*)	Respiratory emergency visits	Buffalo, Albany, New York, NY	Associations between elevated summer haze pollution, including acid particles, particulate sulfate, and ozone, and total respiratory and asthma admissions were observed.
Lutz, 1983 (*38*)	Outpatient clinic visits	Salt Lake City, UT	Strong positive associations were observed between weekly particulate pollution levels and the percentage of patients with a diagnosis of respiratory tract or cardiac illnesses.
Ponka, 1991 (*39*)	Hospital admissions for asthma attacks	Helsinki, Finland	Hospital admissions for asthma were associated with NO_2, NO, SO_2, CO, O_3, and TSP. Associations were strongest for adults of working age, followed by the elderly.
Pope, 1989, 1991 (*40,41*)	Respiratory hospital admissions	Provo/Orem, UT	Strong, statistically significant associations between PM_{10} and respiratory admissions (especially children's bronchitis and asthma admissions) were observed.
Samet et al., 1981 (*42*)	Emergency room visits	Steubenville, OH	Statistically significant but small increase in respiratory emergency room visits were associated with elevated levels of TSP and SO_2.
Schwartz, 1994 (*43*)	Hospital admissions for elderly	Birmingham, AL	Admissions for pneumonia and COPD were associated with particulate air pollution and less strongly associated with ozone.
Schwartz, 1994 (*44*)	Hospital admissions for elderly	Minneapolis/St. Paul, MN	Admissions for pneumonia and COPD were associated with both particulate and ozone air pollution.
Schwartz et al., 1991 (*45*)	Medical visits for croup or obstructive bronchitis	Five areas in Germany	Associations between croup cases and TSP and NO_2 were observed. An increase in TSP from 10 to 70 $\mu g/m^3$ was associated with a 27% increase in croup cases. No associations with obstructive bronchitis and pollution were observed.
Schwartz, 1994 (*46*)	Hospital admission for elderly	Detroit, MI	Admissions for pneumonia and COPD (other than asthma) were associated with particulate and ozone air pollution.
Sunyer et al., 1991 (*47*)	Hospital emergency room visits for COPD	Barcelona, Spain	Emergency visits for COPD were consistently associated with particulate pollution (black smoke) and SO_2, even at 24-hr levels less than 100 $\mu g/m^3$.
Ostro, 1983, 1987, 1990 (*48–50*); Ostro and Rothschild, 1989 (*51*)	Restricted activity days of up to 12,783 adult workers	Cities in U.S. Health Interview Survey (HIS)	Respiratory morbidity was consistently associated with particulate pollution. Morbidity was often more strongly associated with the fine, respirable, or sulfate component of particulate pollution. Lagged pollution effects of 2–5 weeks were observed.
Ransom and Pope, 1992 (*52*)	Grade school absences	Provo/Orem, UT	Significant robust associations between grade-school absenteeism and PM_{10} were observed. These effects persisted for up to 3–4 weeks.

Abbreviations: PM_{10}, particulate matter ≤10 μm; TSP, total suspended particulates; COPD, chronic obstructive pulmonary disease.

tions between hospital/health care visits for respiratory illnesses and particulate pollution were observed in most, but not all, of these studies. Most of the studies suggested that a 10 $\mu g/m^3$ increase in PM_{10} on the day of the visit or 1 or 2 days before the visit was typically associated with a 1–4% increase in hospital visits. Significant associations between respiratory hospital admissions or related health care visits and particulate pollution were observed in many study areas including southern Ontario, British Columbia, Washington, Utah, Finland, New York, Ohio, Germany, and Spain.

A major concern about using hospital databases to evaluate effects of air pollution is the reliability of diagnoses and other information. Some studies have concluded that when only broad diagnostic classes are used, hospital databases provide reliable information for research on air pollution effects (*53*). Nevertheless, most air pollution studies have used existing databases without specifically evaluating data reliability.

Another concern about interpreting these studies is that the length of the lead-lag relationship of particulate pollution effects differed across studies. These differences may be partially due to disparities in type of health care visit and health care delivery systems across study areas. It may also be due to data analysis that only evaluated short-term effects. The study of inpatient admissions for respiratory disease in Utah Valley (*40,41*) found associations between admissions and air pollution levels up to a month or more before the visit. Several studies that used other measures of respiratory morbidity also observed long lead-lag times. Associations between particulate pollution in Utah Valley and absences of elementary schoolchildren had lead-lag relationships up to 4 weeks (*52*). Also, a series of studies by Ostro (*48–51*) observed that the association between particulate air pollution and days of respiratory morbidity serious enough to restrict activity (including loss of work, confinement to bed, or other restrictions) had a lead-lag time of 2 or more weeks.

Chronic Morbidity

Measures of lung function and incidence rates of respiratory symptoms have also been compared across communities or neighborhoods with different levels of particulate air pollution. Given the cross-sectional design of these studies and because pollution measures are averages over relatively long periods of time (1 year or more), these studies are often interpreted as evaluating chronic or cumulative effects of exposure rather than acute effects. Approximately 35 cross-sectional studies of lung function and/or respiratory symptoms were initially reviewed. Most reported associations between particulate pollution and either respiratory symptoms, lung function, or both. However, many of these studies included only a small number of communities and did not have individual data but relied only on aggregate measures of illness, limiting the amount of confidence that can be given to their results. In this paper, only studies using more sophisticated analysis and individual data for several or more study areas are included and are summarized in Table 3.

Small deficits in lung function (FVC, FEV_1, PEF) were generally associated with higher levels of particulate pollution and were often statistically significant. The results suggest that a 10 $\mu g/m^3$ increase in PM_{10} was typically associated with a decline of less than a 2% in lung function. Respiratory disease, including emphysema and chronic bronchitis, and the incidence of respiratory symptoms were also associated with particulate pollution. The results suggest that a 10 $\mu g/m^3$ increase in PM_{10} was typically associated with a 10–25% increase in bronchitis or chronic cough.

The major limitation of these studies may be the lack of true long-term individual exposure data. An individual's cumulative or long-term exposure to particulate pollution can only be estimated by using available data for the individual's area of residence. Even when available pollution databases allow for adequate estimation of pollution concentrations for a given area, there may be bias in exposure estimates due to selective migration from or into more polluted areas. For example, if persons most sensitive to pollution are more likely to move from polluted areas to less polluted areas, pollution effects would be underestimated.

Acute Mortality

Some of the most striking studies of health effects of particulate air pollution are those that observed changes in daily death counts associated with short-term changes in particulate air pollution (Table 4). Because various measurements of particulate pollution were used, precise comparisons between studies is difficult, but results of most of the studies suggest that a 10 $\mu g/m^3$ increase in

Table 3. Selected cross-sectional studies on chronic effects of particulate pollution on respiratory morbidity

References	Health endpoints	Study areas	Summary of findings
Chestnut et al., 1991 (*54*)	Lung function (FVC, FEV_1) of adults	49 U.S. cities from NHANES I	Small, statistically significant associations between lung function and TSP were observed.
Schwartz, 1989 (*55*)	Lung function (FVC, FEV_1, PEF) age 6–24	44 U.S. cities from NHANES II	Lung function was negatively associated with TSP, NO_2 and O_3, but not with SO_2
Vedal et al., 1991 (*56*)	Lung function and symptoms in children	Port Alberni, British Columbia	Particulate pollution was associated with prevalence of chronic respiratory symptoms, but not lung function.
Dockery et al., 1989 (*57*); Ware et al., 1986 (*58*); Speizer, 1989 (*59*)	Lung function (FVC, FEV_1, $FEV_{.75}$, MMEF), respiratory symptoms of 5422 children	Portage, WI; Topeka, KS; Watertown, MA; Kingston, TN; St. Louis, MO; Steubenville, OH	Chronic cough, bronchitis, and chest illness were associated with particulates. Associations were stronger for children with a history of wheeze or asthma. Associations with lung function were negative but statistically insignificant.
Euler et al., 1987 (*60*)	Nonsmoking adult COPD symptoms	Areas in California	COPD symptoms were associated with particulate pollution and less strongly with SO_2 pollution.
Portney and Mullahy, 1990 (*61*)	Chronic respiratory disease	Cities in U.S annual Health Interview Survey (HIS)	Particulate pollution was associated with emphysema, chronic bronchitis, and asthma. Ozone was more associated with sinusitis and hay fever.
Schwartz, 1993 (*62*)	Chronic respiratory disease	53 U.S. Cities from NHANES I	Chronic bronchitis and respiratory diagnosis by a physician were associated with particulate pollution.

Abbreviations: FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 sec; NHANES, National Health and Nutrition Examination Survey; TSP, total suspended particulates; PEF, peak expiratory flow; MMEF, maximal midexpiratory flow rate; COPD, chronic obstructive pulmonary disease.

PM_{10} was associated with an increase in daily mortality equal to 0.5–1.5%. In some studies, lagged pollution effects of up to approximately 5 days were observed.

A few studies divided mortality by cause of death. Figure 1 presents relative risk ratios of mortality associated with similar increases in particulate air pollution in Philadelphia (*69*) and Utah Valley (*77*). Respiratory disease deaths were most strongly associated with particulate pollution levels, but statistical associations were also observed for cardiovascular disease deaths. Why cardiovascular mortality is associated with particulate air pollution is unclear. Reasons may include diagnostic misclassification, acute bronchiolitis precipitating heart failure, and/or effects of pollutants on lung permeability. A recent detailed examination of cardiovascular deaths on days with high particulate air pollution reported that most of the increase in cardiovascular deaths also had respiratory disease as a contributing factor (*70*).

These daily time-series studies have been partially summarized and reviewed (*81,82*). The daily time-series studies suggest that the association between particulate pollution and mortality are not due to confounding by weather, SO_2, or ozone. They also provide information on the age pattern of early deaths and causes of death. Most of them used Poisson regression analysis, allowing a comparison of effect-size estimates on a common scale. Time-series studies have observed effects in varied locations such as California, Utah, Michigan, Missouri, Tennessee, and Alabama in the United States, as well as England, Germany, Greece, and Brazil. It is highly unlikely that such concordance across so many locations could have occurred due to confounding or by chance. Many studies are in locations where particulate concentrations peak in the summer while others are in areas with winter peaks. In locations with winter peaking of particulate concentrations, ozone can be eliminated as a potential confounding factor. Most of the studies examined SO_2. The relationship between mortality and particles was generally independent of SO_2, while the SO_2 relationship disappeared when particles were considered. In Utah Valley and Santa Clara, California, SO_2 concentrations were low. Almost all the studies examined nonlinear relationships with weather factors. Both warm and cold climates and dry and humid locations have reported positive associations between air-

Table 4. Selected daily time-series studies on acute effects of particulate pollution on mortality

References	Study area	Summary of findings
Ostro, 1984 (*63*); Schwartz and Marcus, 1990 (*64*); Ito et al., 1993 (*65*)	London	Daily mortality was associated with particulate pollution (British smoke) and SO_2. The association seemed to be primarily due to particulate pollution but the overall air pollution effect could not be assigned to a specific pollutant with certainty. No threshold level was observed.
Schwartz, 1993 (*66*)	Birmingham, AL	Daily mortality was associated with PM_{10}. The association was strongest for respiratory deaths. An increase in PM_{10} equal to 100 μg/m^3 was associated with an 11% increase in mortality.
Ozkaynak and Spengler, 1985 (*67*)	New York, NY	Daily mortality was associated with particulate pollution (COH) and SO_2. Data limitations provided little opportunity to estimate separate effects of particles and SO_2.
Wyzga, 1978 (*68*)	Philadelphia, PA	An association between daily mortality and particulate pollution (COH) was observed. The estimated total deaths due to pollution equaled approximately 6%.
Schwartz and Dockery, 1992 (*69*) Schwartz, 1993 (*70*)	Philadelphia, PA	A 100 μg/m^3 increase in TSP was associated with an increase in mortality due to COPD, pneumonia, and cardiovascular disease equal to 19, 11, and 10%, respectively. On high pollution days, COPD, pneumonia, and dead-on-arrival deaths were disproportionately increased.
Shumway et al., 1988 (*71*) Kinney and Ozkaynak, 1991 (*72*)	Los Angeles, CA	Associations between daily mortality and particulate pollution were observed. Because of multicollinearity between pollutants, independent effects could not be estimated but mortality was not significantly associated with SO_2.
Mazumdar and Sussman, 1983 (*73*)	Three areas in Pittsburgh, PA	Small associations between daily mortality and particulate pollution (COH) were observed only for the area with the highest pollution levels. Emergency hospital admissions were also significantly associated with particulate pollution.
Dockery et al., 1992 (*74*)	St. Louis, MO; Kingston, TN	Mortality was associated with PM_{10}. The association was statistically significant only in St. Louis, yet in both areas an increase in PM_{10} of 100 μg/m^3 was associated with an approximately 17% increase in mortality. Associations with SO_2, aerosol acidity, or O_3 levels were not observed.
Schwartz, 1991 (*75*)	Detroit, MI	Daily mortality was associated with TSP levels. The association seemed to be independent of SO_2 and existed even at very low levels of pollution. A 100 μg/m^3 increase in PM_{10} was associated with a 6% increase in mortality.
Fairley, 1990 (*76*)	Santa Clara County, CA	Daily mortality was associated with particulate pollution (COH) at levels below 150 μg/m^3. Lagged effects were observed for at least 2 days. The association was stronger for respiratory mortality than for mortality due to other causes.
Pope et al., 1992 (*77*)	Provo/Orem, UT	Daily mortality was associated with PM_{10} pollution. The strongest association was with 5-day moving average PM_{10}. An increase in PM_{10} equal to 100 μg/m^3 was associated with an increase in deaths/day equal to 16%. The association was largest for respiratory disease deaths, next largest for cardiovascular deaths, and smallest for all other deaths.
Schwartz and Dockery, 1992 (*78*)	Steubenville, OH	An association between daily mortality and TSP was observed. This association seemed to be independent of SO_2 and was observed at particulate levels below current standards.
Saldiva et al., 1995 (*79*)	Sao Paulo, Brazil	Mortality of elderly persons was associated with PM_{10}, NO_x, SO_2, and CO. Only the association with PM_{10} was independent of other air pollutants.
Wichmann et al., 1989 (*80*)	North Rhine-Westfalia Germany	During a moderate pollution episode, mortality in the more polluted area was elevated by 8%. Hospital admissions were also elevated. Effects on cardiovascular diseases were larger than on respiratory disease.

Abbreviations: PM_{10}, particulate matter ≤10 μm; TSP, total suspended particulates; COPD, chronic obstructive pulmonary disease.

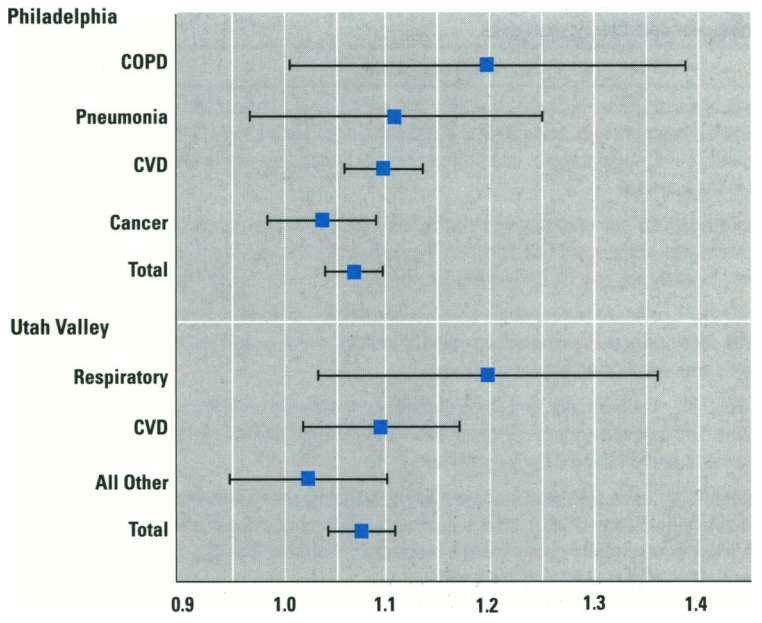

Figure 1. Relative risks of mortality in Philadelphia associated with a 100 μg/m^3 increase in total suspended particulates and in Utah Valley associated with a 50 μg/m^3 increase in suspended particles ≤10 μm diameter. COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease.

borne particles and mortality. They also covered over an order of magnitude range in airborne particle concentrations. Despite substantial variations in all of the potential confounding factors, the quantitative relationships between particles and daily mortality were essentially the same.

A particulate pollution threshold was not generally observed in these studies. Regression results remained relatively consistent even when pollution episodes that exceed air quality standards were excluded. Several studies, such as those in St. Louis and eastern Tennessee, were conducted in locations that never exceeded two-thirds of the ambient air quality standard, and all provided evidence of an exposure-dependent increase in mortality with particle concentration.

Chronic Mortality

Mortality effects of long-term or chronic exposure to particulate air pollution have been studied using two basic cross-sectional study designs. Population-based (ecologic) cross-sectional studies have correlated city-specific mortality rates with particulate air pollution (Table 5). These studies generally observe a positive association between mortality and various measures of particulate pollution. Most of the population-based cross-sectional studies observed strongest associations with fine particulate pollution or sulfate particulate matter. One of these studies evaluated health effects based on sources of particulate pollution and suggested that particles from the iron/steel industry or coal combustion are relatively more hazardous than soil-derived particles (*87*). These studies typically estimate that 2–9% of total mortality was associated with particulate pollution.

The major limitation of the cross-sectional population-based studies is their ecologic design, which does not permit direct control of individual differences in cigarette smoking and other risk factors. The strength of the relationship between mortality and particulate pollution was often sensitive to model specification, socioeconomic, demographic, and other risk factors included in the analysis and the choice of study areas included in the analysis.

Cross-sectional differences in mortality and air pollution were also studied in a prospective cohort study of 8,111 adults in 6 cities (*92*) and a larger study of over 500,000 adults in 151 cities (*93*). The prospective cohort design allowed for direct control of individual differences in age, sex, cigarette smoking, and other risk factors. In both studies fine particulate air pollution or sulfate particle concentrations were associated with mortality. Adjusted risk of mortality was approximately 15–25% higher in cities with the highest levels of fine particulate pollution compared to cities with the lowest levels. The results suggest that a 10 μg/m^3 increase in average PM_{10} exposure was associated with an increase in daily mortality equal to 3% or more. The strongest associations were observed with cardiopulmonary disease and lung cancer deaths, with only small, insignificant associations with death due to other causes.

Discussion

There are important concerns pertaining to these studies that reflect legitimate skepticism about inherent limitations imposed upon epidemiologic studies. Limitations and concerns relating to these studies tend to fall in three categories: 1) issues related to methodological or analytical bias, 2) issues relating to biological significance or plausibility, and 3) concerns about confounding.

It is unlikely that the overall effects of particulate air pollution are due to systematic methodological or analytical bias because the reasonably consistent findings from many differing study designs, data sets, and analytical techniques used. Many of the studies used simple, straightforward comparative statistical analysis coupled with more sophisticated statistical modeling techniques. Generally, the simple and the more sophisticated analysis observed similar associations between particulate air pollution and the health endpoint. Furthermore, recent reviews have noted considerable consistency across studies, especially the daily time-series mortality studies (*81,82,94*).

The epidemiologic studies, taken individually or as a whole, are severely limited with regard to establishing biological plausibility or providing information on specific biological mechanisms responsible for the observed effects (*95*). Recently, Bates (*96*) has noted the importance of biological plausibility but suggested that the coherence of epidemiologic studies of the health effects of particulate air pollution provide a convincing pattern. A recent review of the acute health effects of particulate air pollution also noted substantial coherence across various health endpoints (*94*). Clearly, biological plausibility is enhanced by the observation of a coherent cascade of respiratory health effects and by the fact that non-cardiopulmonary health endpoints were not typically associated with particulate pollution. Also, several authors have offered biological explanations for the observed relationship between fine-particulate air pollution and cardiopulmonary disease (*6,97*).

The most fundamental concern about the validity of these epidemiologic studies pertains to issues of confounding. Confounding may result when another risk factor that is correlated with both exposure and disease is not adequately controlled for in the analysis, resulting in spurious correlations. One proposed confounder is cigarette smoking. Although cigarette smoking contributes to baseline or underlying respiratory disease rates in a population, it could not be a common confounder across all the studies. For example, cigarette smoking would not be a confounder in the short-term time-series studies because 1) lung function, respiratory symptoms, and school absences studies were generally conducted among nonsmoking children; 2) the largest association between respiratory hospitalizations and pollution was often

Table 5. Selected cross-sectional studies on chronic effects of particulate pollution on mortality

References	Study areas	Summary of findings
Lave and Seskin, 1970 (*83*); Chappie and Lave, 1982 (*84*); Lipfert, 1984 (*85*); Evans et al., 1984 (*86*)	U.S. SMSAs	Statistical associations between mortality and particulate pollution were observed. The strength of the relationship between mortality and particulate pollution was sensitive to model specification, choice of social, demographic, and other variables included in the models, and the choice of SMSAs used in the analysis.
Ozkaynak and Thurston, 1987 (*87*)	U.S. SMSAs	Associations between mortality and particulate concentrations were relatively strong and consistent with sulfate and fine particles. Particles from the iron/steel industry and coal combustion seemed to be larger contributors to human mortality than soil-derived particles.
Mendelsohn and Orcutt, 1979 (*88*)	U.S. county groups	Statistically significant associations between mortality and sulfate particulates were observed. Smaller, less consistent associations with CO and SO_2 were observed. An estimated 9% of total mortality was associated with air pollution.
Lipfert et al., 1988 (*89*)	U.S. cities	SO_4, SO_2, NO_x, fine particles, and particulate trace metals (Fe and Mn) were associated with mortality. The data did not allow estimation of independent effects of these pollutants, but effects of SO_4 and fine particles were fairly consistent.
Bobak and Leon 1992 (*90*)	Czech Republic districts	Infant mortality, especially post-neonatal infant mortality, was consistently associated with particulate air pollution (PM_{10}). After adjusting for differences in socioeconomic characteristics, the relative risk of respiratory post-neonatal respiratory mortality was approximately 3.00 for most polluted areas versus least polluted areas.
Archer, 1990 (*91*)	Three counties in Utah	Spatial and longitudinal differences in death rates in three counties with low smoking rates and the introduction of a major pollution source were evaluated. It was estimated that 30–40% of respiratory disease deaths (approximately 5% of all deaths) were associated with the air pollution in the most polluted county.
Dockery et al., 1993 (*92*)	Six U.S. cities	Prospective cohort study directly controlled for individual differences in age, sex, cigarette smoking, and other risk factors. Statistically significant and robust associations between particulate air pollution and mortality were observed.
Pope et al., 1995 (*93*)	151 U.S. cities	Prospective cohort study included over >500,000 subjects followed up for 8 years. After controlling for individual differences in age, sex, cigarette smoking, and other risk factors, fine and sulfate particulate pollution was associated with mortality (mostly cardiopulmonary mortality).

Abbreviations: SMSA, standard metropolitan statistical area; PM_{10}, particulate matter ≤10 μm.

between young, nonsmoking children; and 3) cigarette smoking does not change day-to-day, week-to-week, or month-to-month in positive correlation with air pollution. Cigarette smoking is a more plausible confounder in some of chronic morbidity and mortality studies. However, even in these studies, smoking is an unlikely common confounder because the estimated pollution effects were observed after analytically controlling for cigarette smoking or restricting the analysis to never-smokers.

Another set of proposed confounders are socioeconomic factors. As with cigarette smoking, socioeconomic status in a population does not change day-to-day in correlation with air pollution. Therefore, socioeconomic status was not a potential confounder in the short-term time-series studies looking at lung function, respiratory symptoms, school absences, outpatient visits, and mortality.

Temporal multicollinearity makes confounding by weather and seasonal variables a concern. The studies often observed various weather and seasonal effects. Several observations pertaining to the studies as a whole mitigate the prospect of weather and/or seasonal variables being common confounders: 1) daily, seasonal, or annual changes in weather were not potential confounders in the chronic mortality and morbidity studies; 2) in most of the shorter-term time-series studies, at least some attempts to control for weather and/or seasonal effects were part of the analysis; 3) the study period for some of the acute studies were conducted only during single seasons, eliminating potential confounding by seasonal or annual changes in weather; and 4) the estimated pollution effects are reasonably consistent for areas with different climates and weather conditions.

It is extremely unlikely that several different confounders for the different studies would coincidentally cause spurious correlations that were coherent across the different studies and different health endpoints. The most likely common confounder that could be responsible for the effects observed is another pollutant or combination of pollutants that are highly correlated with particulate pollution. However, it is difficult to determine which other pollutant(s) may be the confounder. Similar particulate-related health effects have been observed in areas where sulfur dioxide, ozone, and aerosol acidity levels are low or poorly correlated with particulate pollution compared with areas with relative high levels of these pollutants. Given current data, proposing additional potential confounding pollutants is largely speculative. It may be that the true culprit pollutant is a constituent of particulate mass such as combustion particles, sulfate particles, fine- or ultra-fine particles. It may also be possible that various measures of particulate exposure are serving as proxies for an unknown or unmeasured pollutant or combination of pollutants.

Conclusions

There is substantial body of contemporary epidemiologic research that has explored health effects of particulate air pollution at levels common to contemporary cities in the developed world. Observed health effects of respirable particulate pollution include: increased incidence of respiratory symptoms, decreased lung function, increased hospitalizations and other health care visits for cardiopulmonary disease, increased respiratory morbidity as measured by absenteeism from work or school or other restrictions in activity, and increased cardiopulmonary disease mortality. Health effects are observed at levels common to many U.S. and Canadian cities, including levels well below current U.S. National Ambient Air Quality Standards. There is no clear evidence of a safe threshold level. Many studies observe that health effects increase monitonically with pollution levels, often with a near-lin-

ear dose–response relationship.

When a substantial body of epidemiologic evidence indicates that a material to which people are commonly exposed may be having serious adverse health effects the burden of proof may be deemed to have shifted from those who draw a causal inference, to those who maintain no causal inference is possible (*98*). The latter should be required to explain the consistency and coherence of the large body of evidence and put forward alternative hypotheses to explain the findings.

Based on our evaluation of this recent research, there is enough consistency and coherency of results across a large number of studies and a wide range of expected outcomes, methodologies, study areas, and researchers to merit a reassessment of the importance of fine and/or respirable particulate pollution on cardiopulmonary health. A research emphasis should be directed at elucidating the mechanisms behind the epidemiological data. It is unclear why morbidity and mortality should be so closely linked to respirable particulate pollution. Nonetheless, Sir Austin Bradford Hill (*99*), in his famous lecture in 1965, warned us that we should not require mechanistic understanding before making the inference of causality from associative epidemiological studies.

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