



Original Contribution

Individual-Level Modifiers of the Effects of Particulate Matter on Daily Mortality

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Consistent evidence has shown a positive association between particulate matter with an aerodiameter of less than or equal to 10 μm (PM_{10}) and daily mortality. Less is known about the modification of this association by factors measured at the individual level. The authors examined this question in a case-crossover study of 20 US cities. Mortality events (1.9 million) were obtained for nonaccidental, respiratory, heart disease, and stroke mortality between 1989 and 2000. PM_{10} concentrations were obtained from the US Environmental Protection Agency. The authors examined the modification of the PM_{10} –mortality association by sociodemographics, location of death, season, and secondary diagnoses. They found different patterns of PM_{10} –mortality associations by gender and age but no differences by race. The level of education was inversely related to the risk of mortality associated with PM_{10} . PM_{10} -related, out-of-hospital deaths were more likely than were in-hospital deaths, as were those occurring during spring/fall versus summer/winter. A secondary diagnosis of diabetes modified the effect of PM_{10} for respiratory and stroke mortality. Pneumonia was a positive effect modifier for deaths from all causes and stroke, while secondary stroke modified the effects for all-cause and respiratory deaths. The findings suggest that more attention must be paid to population characteristics to identify greater likelihood of exposures and susceptibility and, as a result, to improve policy making for air pollution standards.

air pollution; effect modifiers (epidemiology); mortality

Abbreviations: CI, confidence interval; PM_{10} , particulate matter with an aerodiameter of less than or equal to 10 μm .

Particles in air have been shown to increase morbidity and mortality (1–7). These effects could not be explained by high concentrations of other co-pollutants, weather, or seasonal patterns (4, 5, 8–11), thus strengthening the ground for a causal relation. Nevertheless, much remains to be understood about individual-level factors that might modify these risks, including sociodemographic factors, medical conditions, and modifiers of exposure. Better knowledge of these modifiers will increase the power to detect risk in future studies and also help to identify the potential mechanisms of the particulate matter effects (12). In addition, a better understanding of differential risks will aid in public policy determinations and, hence, benefit risk assessment and the making of air pollution standards.

Although many studies have examined the effects of particles on human health, only a limited number of studies have explored the differences in these effects among population subgroups defined by group-level (5, 13–15) or individual-level modifying factors (16–25). Different factors, including sociodemographics, location of death, specific medical conditions, season and ventilation characteristics, and the focus of the present work, have all been described as potential modifiers of air pollution effects on morbidity and mortality events (5, 13–26). Many of these earlier studies were conducted in only a limited number of cities and examined only some of the potential modifiers. Most studies of socioeconomic status have used area-level, including city-level, ecologic data rather than individual-level variables (5, 15, 27). The present study examined these factors at the

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individual level in a case-crossover design across 20 cities in the United States.

MATERIALS AND METHODS

Study data

Daily mortality. We obtained detailed mortality files of the US population between 1989 and 2000 from the National Center for Health Statistics. We defined all-cause daily mortality after excluding any deaths from accidental causes (*International Classification of Diseases*, Tenth Revision, codes V01–Y98). Specific causes of death included mortality from heart disease (codes I01–I51), acute myocardial infarction (codes I21 and I22), respiratory disease (codes J00–J99), and stroke (codes I60–I69).

Air pollution data. Air pollution data for particulate matter with an aerodiameter of equal to or less than 10 μm (PM_{10}) were obtained from the US Environmental Protection Agency Aerometric Information Retrieval System for the same years (28). This system retrieves data from multiple monitors in each county for both daily and hourly average measurements. The sampling method for hourly data uses monitors that are susceptible to a greater loss of semi-volatile particles from traffic than the integrated 24-hour monitors (29, 30). Therefore, we used the integrated PM_{10} data for our analyses.

Exposure assignment in our study was done for each city (a city may include more than one county). Such assignment required that the different monitored daily values in each city be averaged to one daily value. Because not all monitors in a city work every day, the average daily values for that city could vary because of the number of included monitors and not just because of true concentration variability. To avoid such a problem, we applied an algorithm described by Schwartz (15) that removes monitor influence in the city daily values.

Although we selected cities with daily PM_{10} monitoring, daily concentrations of PM_{10} were occasionally missing. Even small numbers of missing data can present a problem when examining multiple lags of exposure in a model. We used regression models to predict missing PM_{10} daily values utilizing local meteorologic data obtained from the US Surface Airways and Airways Solar Radiation hourly data (including extinction coefficient (31), a measure of light scattering by fine particles) and PM_{10} concentrations the day before and the day after. We included only those months missing less than 25 percent of the days and PM_{10} daily values of less than or equal to 300 $\mu\text{g}/\text{m}^3$. On average, 9.5 percent of missing data were filled in.

We focused on 20 cities in the United States with sufficient series of mortality and daily air pollution data: Birmingham, Alabama; Boulder, Colorado; Canton, Ohio; Chicago, Illinois; Cincinnati, Ohio; Cleveland, Ohio; Colorado Springs, Colorado; Columbus, Ohio; Denver, Colorado; Detroit, Michigan; Honolulu, Hawaii; Minneapolis, Minnesota; Nashville, Tennessee; New Haven, Connecticut; Pittsburgh, Pennsylvania; Provo, Utah; Salt Lake City, Utah; Seattle, Washington; Terra Haute, Indiana; and Youngstown, Ohio.

An earlier case-crossover study (32) used distributed-lag models (33) to examine the temporal effects of PM_{10} concentrations on the same day and 1 and 2 days before the event on the risk of mortality, using the same data as the present study. This previous study reported the persistent effects of PM_{10} concentrations over several days for all-cause mortality (1 and 2 days prior to the event), respiratory disease (across all 3 days), and heart disease mortality (1–2 days before the event). For deaths from myocardial infarction, the effect of PM_{10} was mainly on the same day as the event and, for stroke mortality, mainly with exposures the day before the event (32). Because the focus of the present paper was effect modification, we had to reduce these observed associations to a simple measure of PM_{10} . For those associations where the effects persisted for more than 1 day, the average concentration of PM_{10} over those days was used, while for those with PM_{10} concentrations for only 1 day, that day's exposure concentration was used in the analyses.

Effect modification

Detailed mortality files included individual-level data on the secondary causes of death and the individual characteristics of the event cases. This information was used to examine effect modification of the mortality– PM_{10} association by sociodemographic factors, location of death, season, and contributing causes of death.

Sociodemographic characteristics. Variability in the effects of particulate matter on mortality could be attributed to differences in individual-level characteristics, for example, gender, race, and age group. Analyses were stratified by gender (males and females), race (White and Black), and age group (>0–65 years, >65–75 years, and >75 years).

We used education as an indicator of socioeconomic status. We used three levels of education: *low education* for less than 8 years of schooling, *medium education* for 8–12 school years, and *high education* for 13 years or more.

Location of death. Different patterns of mortality from air pollution have been described for different placement of death (24, 25). In our study, we defined location of death as “in-hospital deaths,” which included hospital, clinic, or medical center inpatients, as well as outpatients admitted to the emergency room; and “out-of-hospital deaths” defined as all other deaths.

Season. The effect of PM_{10} was examined for winter, summer, and transition period (spring and fall). The effect of season may be related to an interaction between temperature and other weather conditions with particulate matter (34, 35) or to differences in level of exposure due to the rate of ventilation of indoor environments with outdoor concentrations (36–38).

Contributing causes of death. Poor health has been shown to increase the risk of death from increased concentrations of PM_{10} (12, 16–18, 24, 39), because of increased susceptibility. For example, among those affected with cardiac disease, increased lung inflammation may lead to the release of inflammatory mediators, exacerbation of lung conditions, and increased blood coagulability, leading to exacerbation of cardiovascular disease (12, 17, 22).

Diabetes as a secondary condition has been hypothesized to increase the susceptibility of the capillary system to influences from exposures to particulate matter (20, 21, 40).

We examined secondary diagnoses of pneumonia, heart failure, stroke, and diabetes as modifiers of the PM₁₀ effects on daily mortality.

Statistical method of analysis

The study used a case-crossover design to examine the association between daily mortality and PM₁₀. The case-crossover design is similar in concept to that for a case-control study (41), except that now the case and its controls are the same subject, but in different times. The time (day) of the event defines a case, and the times (days) free of the event are its controls. To control for confounding by season or confounding by time trends, we selected control days to be close to the event day, using a time-stratified approach (the same month of the same year as the event) (8, 9, 42, 43).

Controls were selected as every third day within each stratum (month/year of the event) to eliminate any serial correlation. As in a case-control study, conditional logistic regression was applied to the matched strata, to compare different characteristics between the case day and its controls.

We tested for statistically important differences between effect estimates of the strata of a potential effect modifier (e.g., the difference between males and females) by calculating the 95 percent confidence interval as shown below:

$$(\hat{Q}_1 - \hat{Q}_2) \pm 1.96 \sqrt{\hat{S}\hat{E}_1 + \hat{S}\hat{E}_2},$$

where \hat{Q}_1 and \hat{Q}_2 are the estimates for the two categories (e.g., males and females), and $\hat{S}\hat{E}_1$ and $\hat{S}\hat{E}_2$ are their respective standard errors (44, 45). Regardless of significance, we considered modification of effect by a factor of two or more to be important, and discuss as such.

Two-level analyses

Analyses were carried out in two hierarchical stages. All analyses were stratified on each modifying factor being examined. For example, when examining the effect of PM₁₀ by gender, separate analyses were carried out for males and females. In the *first stage*, the effects of PM₁₀ on mortality risk were estimated through city-specific models. These models additionally included indicator variables for "day of week" and quadratic functions for apparent temperature (46, 47) on the same day and the day before the event to control for the effect of weather (32, 48, 49).

We estimated the overall effects across all cities in the *second-stage* analyses, applying random-effect meta-regression models to allow for heterogeneity in the city-specific response (50), using the estimates from the city-specific models of the *first stage*.

Sensitivity analyses

We carried out sensitivity analyses using a common lag structure of PM₁₀ (average PM₁₀ concentration on 3 days)

for all-cause and heart disease mortality, to compare with main analyses. We then examined effect modification by education, age, and season.

To test the sensitivity of our results to filling in missing PM₁₀ data, we used multiple imputation methods in several large cities with the greatest number of days with missing data and compared the results with those of the main analyses.

For age, education, and season, we carried out trend analyses and report two-sided *p* values of these.

The estimates of the PM₁₀-mortality association reported in this paper refer to the percentage of increase in mortality per any 10-μg/m³ increment of PM₁₀ concentration. SAS software (SAS Institute, Inc., Cary, North Carolina) was used for statistical analyses of the first stage, and S-PLUS software (Insightful Corporation, Seattle, Washington) was used to implement random meta-regression analyses.

RESULTS

Average annual mortality events per 100,000 were higher in Birmingham, Alabama; Minneapolis, Minnesota; Nashville, Tennessee; Pittsburgh, Pennsylvania; and Terra Haute, Indiana (table 1). Deaths from any respiratory disease were about 10 percent of all-cause mortality. One third of all deaths were from heart disease, and about a third of these (26 percent) were deaths from myocardial infarction. Mortality from stroke was about 7 percent of all-cause mortality. In total, the study included 1,896,306 deaths.

Higher summer apparent temperature was seen for Birmingham, Alabama; Cincinnati and Columbus, Ohio; Nashville, Tennessee; and Terra Haute, Indiana. The overall mean concentration of PM₁₀ varied by city and across time within each city. The large variation of PM₁₀ concentrations within strata ensured sufficient power for this study.

All-cause mortality increased 0.42 percent (95 percent confidence interval (CI): 0.26, 0.58) for PM₁₀ concentrations 1 and 2 days prior (figure 1). For respiratory deaths, the effect was doubled at 0.87 percent (95 percent CI: 0.38, 1.36).

Sociodemographic factors

PM₁₀-associated mortality from all causes and the broad groupings of respiratory and heart disease did not differ by gender or race (table 2). Although dividing by cause and gender reduced numbers and precision, the effect estimate for stroke was more than five times higher in females than in males, and for myocardial infarction it was more than double, although neither difference was statistically significant. An approximately fourfold increase for deaths from myocardial infarction was seen among Blacks, while stroke deaths were mainly among Whites.

Those aged 75 or more years were significantly more affected by PM₁₀ for all-cause mortality (table 2). However, the specific grouping of mortality causes showed differences in the magnitude and trend of the effects in the three age groups. For respiratory mortality, the effect was essentially

TABLE 1. Daily mortality, temperature, and particulate concentration in the 20 US cities included in the study of the association between PM₁₀* and daily mortality between 1989 and 2000†

City	All-cause mortality‡		Respiratory disease (% of all-cause mortality)	Heart disease (% of all-cause mortality)	Stroke (% of all-cause mortality)	Minimum summer apparent temperature (°C)	Maximum winter apparent temperature (°C)	Mean PM ₁₀ (µg/m ³)	Mean variance of PM ₁₀ by strata (µg/m ³)§
	Total deaths	Deaths/100,000¶							
Birmingham, Alabama	41,398	1,401	9	32	8	29.3 (3.3)#	6.7 (5.8)	31.9 (18.0)	300.7 (227.2)
Boulder, Colorado	9,551	441	12	31	8	20.1 (3.3)	−1.2 (5.4)	22.1 (11.3)	114.0 (127.4)
Canton, Ohio	34,061	1,055	11	35	7	22.5 (4.6)	−3.0 (5.5)	26.6 (11.5)	113.0 (90.8)
Chicago, Illinois	534,793	921	9	36	6	23.6 (5.3)	−3.5 (4.9)	33.7 (16.4)	257.0 (196.2)
Cincinnati, Ohio	82,455	1,136	10	33	7	25.1 (4.5)	−0.5 (6.0)	31.4 (13.9)	165.4 (131.3)
Cleveland, Ohio	188,434	1,192	8	38	6	23.2 (4.8)	−2.2 (5.7)	37.5 (18.7)	331.7 (247.1)
Colorado Springs, Colorado	17,518	508	14	28	9	18.3 (3.6)	−0.9 (5.3)	24.0 (13.2)	135.3 (193.8)
Columbus, Ohio	33,472	886	8	34	6	24.6 (4.7)	−1.4 (4.7)	28.5 (12.5)	132.0 (82.6)
Denver, Colorado	41,313	1,049	13	29	7	20.1 (3.6)	−0.9 (5.6)	28.5 (12.8)	153.1 (250.3)
Detroit, Michigan	213,352	1,024	8	39	6	23.2 (4.9)	−3.1 (4.4)	32.1 (17.7)	322.8 (236.2)
Honolulu, Hawaii	17,255	663	10	32	10	29.0 (1.3)	24.9 (1.9)	15.9 (6.8)	42.1 (153.0)
Minneapolis, Minnesota	155,078	1,265	10	27	8	22.3 (4.9)	−6.6 (4.5)	24.7 (12.3)	148.3 (142.8)
Nashville, Tennessee	64,187	1,254	10	33	8	28.7 (3.8)	3.8 (6.0)	30.1 (12.1)	129.5 (101.4)
New Haven, Connecticut	94,502	1,019	10	35	6	23.1 (4.6)	−2.0 (4.2)	25.4 (14.4)	216.9 (217.7)
Pittsburgh, Pennsylvania	169,098	1,387	9	37	7	23.3 (4.4)	−1.5 (5.3)	30.2 (18.5)	302.2 (256.9)
Provo, Utah	15,289	392	11	31	9	22.4 (4.3)	−2.0 (4.1)	33.7 (22.2)	370.3 (629.5)
Seattle, Washington	101,626	709	11	31	8	17.0 (3.6)	3.1 (3.5)	26.4 (14.7)	188.1 (194.4)
Salt Lake City, Utah	54,825	579	10	28	7	22.4 (4.4)	−2.1 (4.1)	35.0 (20.8)	354.2 (457.0)
Terra Haute, Indiana	5,035	1,352	9	37	8	24.8 (4.4)	−3.6 (5.4)	29.2 (14.6)	159.4 (143.4)
Youngstown, Ohio	23,064	1,122	8	38	8	22.1 (4.7)	−2.9 (4.8)	30.8 (13.9)	164.0 (120.1)

* PM₁₀, particulate matter with an aerodiameter of less than or equal to 10 µm.

† All descriptive statistics for weather and PM₁₀ concentrations were extracted from the available data between 1989 and 2000.

‡ The primary cause of death from injuries was excluded.

§ Strata were defined by each event case (day of event), and its control days were selected every third day of the same month and year as the case day.

¶ Numbers represent the average annual mortality per 100,000.

Numbers in parentheses, standard deviation.

identical across age groups. In contrast, deaths from heart disease (between >75 and ≤65 years: difference = 0.62 percent, 95 percent CI: 0.01, 1.12) and stroke showed higher effects in the oldest age group, while for myocardial infarction events, the effect on those aged 65–75 years was several times larger than that in older or younger age groups, although the difference of effect estimates of age strata was imprecise.

We tested the hypothesis that postmenopausal women had a different risk from premenopausal women, in particular for heart disease mortality, by further stratifying deaths among females by age (<60 years vs. older). The magnitude of the PM₁₀-associated risk for females aged 60 or more years for heart disease (0.50 percent, 95 percent CI: 0.17, 0.83) was fivefold that of the younger group (0.10 percent, 95 percent CI: −1.31, 1.51). In comparison, the effect in

males aged 60 or more years was only twice (0.62 percent, 95 percent CI: 0.27, 0.97) that of the younger group (0.29 percent, 95 percent CI: −0.36, 0.94).

As with age, deaths from respiratory disease showed no trend across educational categories. In contrast, for all-cause mortality, the increase in the PM₁₀-associated risk was about 72 percent, comparing *low* with *medium* education, and about 130 percent, comparing *low* with *high* education, although again power issues resulted in an insignificant trend ($p = 0.29$).

Location of death

More than a threefold effect on all-cause mortality from high concentrations of PM₁₀ was observed for deaths occurring out of hospital, when compared with in-hospital deaths

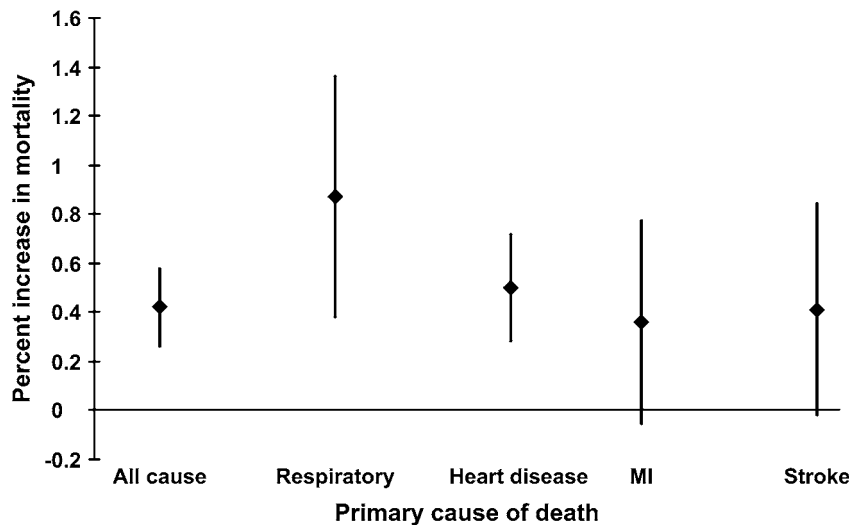


FIGURE 1. Percent increase in mortality per 10- $\mu\text{g}/\text{m}^3$ increase in PM₁₀ in 20 US cities between 1989 and 2000. The association for all-cause mortality and PM₁₀ is for average concentrations on the day before and 2 days before the event. The respiratory mortality–PM₁₀ association is evaluated for concentrations on all 3 days. The association between heart disease mortality and PM₁₀ is for the 2 days before the event, the myocardial infarction (MI)–PM₁₀ association is evaluated for concentrations on the same day as the death, and the association for stroke mortality and PM₁₀ concentrations is for the day prior. The diamonds represent percent increase in mortality, and the vertical bars indicate the 95 percent confidence intervals. PM₁₀, particulate matter with an aerodiameter of less than or equal to 10 μm .

(table 3) (difference of estimates: 0.49 percent, 95 percent CI: 0.23, 0.75). This effect appeared driven by heart disease and stroke.

Season

PM₁₀-associated deaths from all causes, especially from respiratory disease, showed higher effects during the transition periods (spring/fall) than in the winter or summer (table 4). Heart disease risk seemed consistent across season. Only the respiratory death seasonal differences showed a significant trend ($p = 0.03$).

Contributing causes of death

We found that the risk of mortality associated with PM₁₀ for all causes doubled by the presence of a secondary diagnosis of pneumonia and positive evidence for modification by coexisting stroke (difference of estimates: 0.53 percent, 95 percent CI: –0.05, 1.11) (table 5).

There was about a twofold relative effect modification by heart failure, stroke, and diabetes for respiratory mortality, although the differences in effects were imprecise. No modifying effect of any secondary condition was observed for mortality from heart disease. The risk of mortality from myocardial infarction more than tripled in the presence of secondary pneumonia. This was also true for stroke deaths (difference of estimates: 1.45 percent, 95 percent CI: –0.01, 2.91), and there was a suggestive finding for coexisting diabetes (table 5). Important and suggestive findings are also illustrated in figure 2.

Sensitivity analyses

We found no difference in the effects using a similar lag pattern for all-cause and heart disease mortality compared with those of the main analyses. The level of uncertainty due to missing PM₁₀ data in our study results was not important.

DISCUSSION

In a case-crossover design, we assessed modification of the association of PM₁₀ with daily deaths by factors characterized at the individual level, in a study of 20 US cities for a period of 12 years. While a number of studies have examined modification of this association by several factors (5, 13–25), only a few of those have assessed this at the individual level, in a more limited geographic area and time of study (16–25). In the present study, we consider relative effect modification of a factor of two or more as important, and we have found such modification by individual socio-demographic factors, location of death, season, and coexisting medical conditions.

One key finding of this study was the substantial differences in the patterns of association with respiratory mortality versus other causes of death. Unlike all-cause mortality, respiratory mortality showed no difference in effect size estimate across age ranges or educational levels. However, the risk was more than doubled in persons with stroke or diabetes. These differences have not been reported previously. The other findings are discussed by category of effect modifiers.

TABLE 2. Effects of the demographic factors gender, race, and age as modifiers of the PM₁₀*—all-cause and cause-specific daily mortality associations in 20 US cities between 1989 and 2000

Primary cause of death	Gender				Race				Age			
	Male		Female		White		Black		<65 years		65–75 years	
	%†	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval
All cause	0.46	0.28, 0.64	0.37	0.17, 0.57	0.40	0.22, 0.58	0.37	–0.02, 0.76	0.25‡	0.01, 0.49	0.23‡	–0.06, 0.52
Respiratory disease	0.71	0.004, 1.42	1.04	0.33, 1.75	0.88	0.33, 1.43	0.71	–0.56, 1.98	0.94	–0.31, 2.19	0.87	–0.25, 1.99
Heart disease	0.54	0.23, 0.85	0.46	0.15, 0.77	0.50	0.25, 0.75	0.64	0.13, 1.15	0.04§	–0.45, 0.53	0.60	0.13, 1.07
Myocardial infarction	0.21	–0.40, 0.82	0.59	0.08, 1.10	0.24	–0.27, 0.75	0.99	0.05, 1.93	0.12	–0.76, 1.00	0.92	0.21, 1.63
Stroke	0.11	–0.58, 0.80	0.59	–0.04, 1.22	0.48	0.01, 0.95	0.13	–0.87, 1.13	0.09	–1.09, 1.27	–0.46¶	–1.42, 0.50

* PM₁₀, particulate matter with an aerodiameter of less than or equal to 10 μm .

† Estimates are presented as the percent increase in mortality per any 10- $\mu\text{g}/\text{m}^3$ increment of PM₁₀ concentration.

‡ Differences between >75 years and <65/65–75 years were significant at $\alpha = 0.05$.

§ The difference between >75 years and <65 years was significant at $\alpha = 0.05$.

¶ The difference between >75 years and 65–75 years was significant at $\alpha = 0.05$.

Sociodemographic factors

As reported previously, older persons were at greater risk for all-cause mortality in association with PM₁₀. The effect in those older than 75 years was more than double that of younger age groups, and that difference was statistically significant. Consideration of specific causes of death provided additional insights that have not been previously reported. There was no trend in the mortality risk with age for respiratory disease, whereas myocardial infarction deaths peaked in the middle age group. Stroke mortality was mainly among those aged over 75 years.

The main modification in the effect of PM₁₀ on mortality from heart disease by gender was the lower effect of PM₁₀ on women under 60 years of age than on men under 60 years, suggesting that hormonal status may play a role in modifying the effect of PM₁₀. This hypothesis has also been suggested in investigations of the long-term effects of particulate matter on atherosclerosis (51).

The study found no evidence that gender or race modified the all-cause mortality–PM₁₀ association or that for broad mortality groups. However, a suggestion of higher risk was seen among females for myocardial infarction and stroke mortality, and Blacks had a higher risk of myocardial infarction deaths and lower risk of stroke deaths.

Previous large multicity studies have examined the role of socioeconomic factors as modifiers of the PM₁₀ effect by use of county-level data, and they found little evidence of modification (4, 5). Our study, with individual-level data on education, showed evidence for an inverse trend, with more than a doubling of effect size in a comparison of low with higher educational level. This is consistent with results reported by cohort studies (52–54). Zanobetti and Schwartz (19) in an earlier study found a smaller difference by educational level; however, they only dichotomized education. The largest change in our data is for persons with less than 8 years of education. Another study with small area-based measures of socioeconomic position in Hamilton, Ontario, found important modification of the particle effects by social class (53, 54). The finding of a twofold difference in risk in our study suggests an important level of modification. This has important implications for social policy and for the US Environmental Protection Agency statutory mandate to set standards that protect sensitive populations.

Factors such as educational attainment, race, gender, and age may represent health status that conveys susceptibility, or they may be predictors of socioeconomic status (19, 55–58). Increased susceptibility to the effects of air pollution due to disadvantaged socioeconomic status may be related to factors such as reduced access to health care, poorer nutrition, or psychological stress and violence. Persons with lower socioeconomic status are more likely to live in poorer and more disadvantaged neighborhoods, with a higher likelihood of exposure as a result of living closer to roadways with increased traffic density and closer to more polluted areas and with a higher likelihood for coexposures due to either living conditions or occupation.

Relatively few studies have examined gender or racial differences in the association of airborne particles with daily

TABLE 3. Effects of the modifiers educational attainment and location of death on PM₁₀*–all-cause and cause-specific daily mortality associations in 20 US cities between 1989 and 2000

Primary cause of death	Education						Location of death (in or out of hospital)			
	Low (<8 years)		Medium (8–12 years)		High (>12 years)		In		Out	
	%†	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval
All cause	0.62	0.29, 0.95	0.36	0.12, 0.60	0.27	–0.004, 0.54	0.22‡	0.04, 0.40	0.71‡	0.51, 0.91
Respiratory disease	0.82	–0.32, 1.96	0.88	0.12, 1.64	0.88	–0.04, 1.80	0.78	0.17, 1.39	1.09	0.25, 1.93
Heart disease	0.72	0.23, 1.21	0.38	0.07, 0.69	0.54	0.13, 0.95	0.15‡	–0.14, 0.44	0.93‡	0.60, 1.26
Myocardial infarction	0.33	–0.83, 1.49	0.79	0.28, 1.30	–0.13	–0.82, 0.56	0.34	–0.11, 0.79	0.48	–0.23, 1.19
Stroke	0.07	–1.44, 1.58	0.29	–0.32, 0.90	0.52	–0.28, 1.32	0.06‡	–0.49, 0.61	0.87‡	0.05, 1.69

* PM₁₀, particulate matter with an aerodiameter of less than or equal to 10 μm .

† Estimates are presented as the percent increase in mortality per any 10- $\mu\text{g}/\text{m}^3$ increment of PM₁₀ concentration.

‡ The difference between in and out of hospital is significant at $\alpha = 0.05$.

deaths. Ito and Thurston (56) in a smaller study found mortality rate ratios associated with high concentrations of PM₁₀ to be greatest among Black women, compared with White women, Black men, and White men. Another study (19) of four US cities reported a slightly higher risk of all deaths for females, which we were unable to reproduce. Such differences by gender may be partly explained by variability in the particle deposition in men and women (59–61).

Our findings for race did not support hypotheses for racial differences in the effects of air pollution, with the higher effects among Blacks, based on the evidence that they represent a more disadvantaged group regarding socioeconomic and health status (62, 63).

Consistent with reports from numerous studies (16, 24, 64–66), our study found higher susceptibility to air pollution among the elderly. Interesting deviations from this pattern were seen for specific causes. In addition to the already

noted uniform pattern of respiratory mortality risk versus age, the risk of myocardial infarction in our study peaked in the middle age group (65–75 years of age).

Location of death

The evidence that out-of-hospital deaths carried higher risk supports previous reports of the same nature (24, 25). The difference in the effects of air pollution for the placement of death may reflect true exposure differences. Out-of-hospital deaths normally occur at home or in environments where the indoor/outdoor ratio of air pollution concentrations is not as small as may be the case of in-hospital deaths, since most US hospitals use air filtration. This difference may also be due to the accessibility to treatment and alleviation of air pollution effects as a result. Another explanation for this difference may be related to the

TABLE 4. Effects of the modifier season (ventilation) on PM₁₀*–all-cause and cause-specific daily mortality associations in 20 US cities between 1989 and 2000

Primary cause of death	Season					
	Winter		Summer		Transition (spring/fall)	
	%†	95% confidence interval	%	95% confidence interval	%	95% confidence interval
All cause	0.28	0.04, 0.52	0.19	–0.22, 0.60	0.49	0.25, 0.73
Respiratory disease	–0.007‡	–0.87, 0.86	0.69	–0.68, 2.06	1.57‡	0.86, 2.28
Heart disease	0.41	–0.002, 0.82	0.52	0.03, 1.01	0.56	0.13, 0.99
Myocardial infarction	0.32	–0.37, 1.01	0.30	–0.82, 1.42	0.38	–0.31, 1.07
Stroke	–0.09	–0.93, 0.75	0.67	–0.31, 1.65	0.51	–0.20, 1.22

* PM₁₀, particulate matter with an aerodiameter of less than or equal to 10 μm .

† Estimates are presented as the percent increase in mortality per any 10- $\mu\text{g}/\text{m}^3$ increment of PM₁₀ concentration.

‡ The difference is significant at $\alpha = 0.05$.

TABLE 5. Contributing causes of death as modifiers of PM₁₀*—all-cause and cause-specific daily mortality associations in 20 US cities between 1989 and 2000

Primary cause of death	Secondary pneumonia				Secondary heart failure				Secondary stroke				Diabetes			
	Present		Absent		Present		Absent		Present		Absent		Present		Absent	
	%†	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval	%	95% confidence interval
All cause	0.67	0.16, 1.18	0.34	0.16, 0.52	0.42	0.01, 0.83	0.37	0.19, 0.55	0.85‡	0.30, 1.40	0.32‡	0.14, 0.50	0.57	0.02, 1.12	0.34	0.14, 0.54
Respiratory disease	1.28	-0.33, 2.89	0.78	0.15, 1.41	1.48	0.07, 2.89	0.79	0.26, 1.32	1.95	-0.11, 4.01	0.80	0.29, 1.31	1.96	-0.22, 4.14	0.82	0.31, 1.33
Heart disease	0.66	-0.63, 1.95	0.49	0.27, 0.71	NA*				0.73	-0.05, 1.51	0.48	0.24, 0.72	0.34	-0.42, 1.10	0.52	0.28, 0.76
Myocardial infarction	1.54	-1.05, 4.13	0.42	0.05, 0.79	NA				0.50	-1.38, 2.38	0.36	-0.05, 0.77	0.70	-0.38, 1.78	0.41	0.04, 0.78
Stroke	1.74‡	0.35, 3.13	0.29‡	-0.16, 0.74	1.01	-0.77, 1.79	0.38	-0.05, 0.81	NA				1.02	-0.53, 2.57	0.37	-0.08, 0.82

* PM₁₀, particulate matter with an aerodynamic diameter of less than or equal to 10 µm; NA, nonapplicable.† Estimates are presented as the percent increase in mortality per any 10-µg/m³ increment of PM₁₀ concentration.‡ The difference is significant at $\alpha = 0.10$.

physiologic/pathologic mechanism of death. Many of the out-of-hospital deaths are sudden deaths, suggesting that particles may play a role in triggering such an event. For example, lower heart rate variability, increased C-reactive protein concentrations in plasma, and decreased plaque stability are risk factors for sudden death that have been associated with particle exposure (67–69).

Effect of season

One new finding in this study is the difference in the particle effects between the transitional seasons (spring/fall) and summer or winter, which could be the results of differences in exposure gradients and particle composition. Sarnat et al. (70, 71) reported that outdoor concentrations of particles were significantly associated with indoor concentrations, but that the slope of the relation varied strongly with ventilation. In particular, the slope was twice as high during periods when windows were open as when these were closed.

Spring and fall are the seasons most likely to have open windows. In summer, air-conditioning use is more common and, thus, there is less ventilation. Winter is also likely to have windows closed. Hence, the observed differences in effect size are consistent with the expected difference in ventilation. Supporting evidence for this hypothesis was reported from Janssen et al. (13), who found that cities with a higher prevalence of air conditioning had a lower effect of particles on hospital admissions, and by Zeka et al. (32), who found a greater effect of PM₁₀ in cities with larger summer temperature variability.

In addition, particle composition also varies seasonally. However, many other factors influence these patterns in different cities, making generalizations difficult. Overall, we believe the contrast likely reflects a gradient in the concentration-exposure relation.

A large study by Peng et al. (72) in an analysis by US geographic regions found strong seasonal patterns in the Northeast (with a peak in summer) and little seasonal variation in the southern regions of the country. Our study could not explore geographic variation because of the limited number of cities included. However, the difference in peak season (summer in the study by Peng et al. vs. transitional season in ours) requires comment. Several differences between the studies may explain the different results. First, in our study, each death is contrasted to control days chosen in the same month as the death. Hence, pollution concentrations for deaths in each city, by design, are compared with only concentrations in the same season as controls. In the analysis of Peng et al., all days of all years are effectively the controls for each day of death, with seasonal variations in death controlled by the use of splines. It is possible that this very different analytical approach leads to differences in seasonal interaction terms. Another difference is that Peng et al. report only seasonal differences for PM₁₀ concentrations the day before. Our examination of seasonal interactions is for a distributed lag model involving 3 days of PM₁₀ exposure. It is possible that the use of 3-day means, rather than single lags, results in a different pattern of effect modification by season.

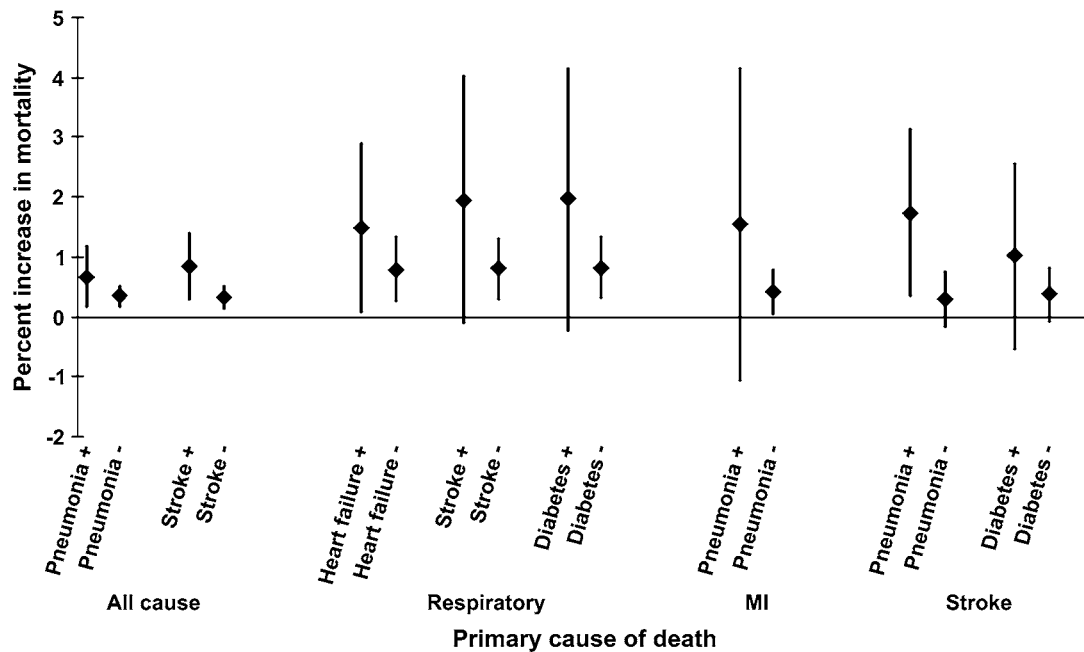


FIGURE 2. Modification of the mortality–PM₁₀ association by the presence of secondary diagnoses (on the abscissa) for all-cause, respiratory, myocardial infarction (MI), and stroke mortality in 20 US cities between 1989 and 2000. Estimates are presented as the percent increase in mortality per 10- $\mu\text{g}/\text{m}^3$ increase in PM₁₀. The presence or absence of a secondary condition is presented by “+” or “–,” respectively. The diamonds represent the percent increase in mortality, and the vertical bars indicate the 95 percent confidence intervals. PM₁₀, particulate matter with an aerodiameter of less than or equal to 10 μm .

Contributing causes of death

We found a greater effect of PM₁₀ for all-cause, myocardial infarction, and stroke mortality in the presence of pneumonia. Schwartz (24) reported in 1994 a higher association of particles for all-cause mortality in the presence of coexisting respiratory diseases. Consistent with this finding, Goldberg et al. (16) had reported higher effects of air pollution among those subjects with coexisting lower-respiratory infections.

Coexisting heart failure was not a modifier for all-cause mortality, in contrast to the single-city study reports of Goldberg et al. (17, 18) and Hoek et al. (73). However, persons with congestive heart failure had a twofold risk of respiratory deaths. A previous report by Zanobetti et al. (22) found congestive heart failure to be a modifier of the association of particle and hospital admissions for respiratory disease, adding support to this finding.

Subjects with secondary diagnoses of stroke had more than double the PM₁₀-associated risk for all-cause and respiratory deaths. To our knowledge, this is the first report that persons who have suffered a stroke are at increased risk of PM₁₀-associated deaths due to respiratory or other causes. Whether this represents generally poorer health or suggests a neurogenic component to the association of particles with mortality remains to be explored.

We found about a twofold increase in the effects for respiratory and stroke deaths in the presence of diabetes. Such a finding has not been reported to date, and we think it adds

to the general literature that suggests that diabetes may be an important modifier of the effect of particles (20, 21). Of particular interest is a recent paper by O’Neill et al. (40) reporting that only diabetics had impaired vascular function in response to particle exposure.

In summary, this study showed different effects of particulate matter on daily mortality in the presence of individual characteristics that may convey either differences in susceptibility or differences in the likelihood of exposure. Of particular interest are the strong findings for educational attainment; the difference in the effects for women aged more than 60 years versus those younger, suggesting an interaction with menopausal status; and the finding of a seasonal difference. The finding of a significant association with stroke mortality in the elderly and its possible role as an effect modifier are also noteworthy. We think that the study is an important contribution to the evidence on the association between particulate air pollution and mortality and to the identification of subpopulations at highest risk.

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