SPECIAL ARTICLE

Fine-Particulate Air Pollution and Life Expectancy in the United States

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ABSTRACT

BACKGROUND

Exposure to fine-particulate air pollution has been associated with increased morbidity and mortality, suggesting that sustained reductions in pollution exposure should result in improved life expectancy. This study directly evaluated the changes in life expectancy associated with differential changes in fine particulate air pollution that occurred in the United States during the 1980s and 1990s.

METHODS

We compiled data on life expectancy, socioeconomic status, and demographic characteristics for 211 county units in the 51 U.S. metropolitan areas with matching data on fine-particulate air pollution for the late 1970s and early 1980s and the late 1990s and early 2000s. Regression models were used to estimate the association between reductions in pollution and changes in life expectancy, with adjustment for changes in socioeconomic and demographic variables and in proxy indicators for the prevalence of cigarette smoking.

RESULTS

A decrease of 10 μg per cubic meter in the concentration of fine particulate matter was associated with an estimated increase in mean (±SE) life expectancy of 0.61±0.20 year (P=0.004). The estimated effect of reduced exposure to pollution on life expectancy was not highly sensitive to adjustment for changes in socioeconomic, demographic, or proxy variables for the prevalence of smoking or to the restriction of observations to relatively large counties. Reductions in air pollution accounted for as much as 15% of the overall increase in life expectancy in the study areas.

CONCLUSIONS

A reduction in exposure to ambient fine-particulate air pollution contributed to significant and measurable improvements in life expectancy in the United States.

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Since the 1970s, the United States has made substantial efforts and investments to improve air quality. As these efforts continue, a fundamental question remains: Do improvements in air quality result in measurable improvements in human health and longevity? Associations between long-term exposure to fine-particulate air pollution and mortality have been observed in population-based studies[1-3] and, more recently, in cohort-based studies.[4-11] Daily time-series and related studies,[12-15] natural intervention studies,[16-18] and cohort studies[10,19] all support the view that relatively prompt and sustained health benefits are derived from improved air quality.

We directly assessed associations between life expectancy and fine-particulate air pollution in 51 U.S. metropolitan areas, comparing data for the period from the late 1970s to the early 1980s with matched data for the period from the late 1990s to the early 2000s. We hypothesized that temporal changes in fine-particulate air pollution between 1980 and 2000 would be associated with changes in life expectancy. Specifically, we hypothesized that metropolitan areas with the largest declines in fine-particulate pollution would have the largest increases in life expectancy, even after adjustment for changes in various socioeconomic and demographic characteristics and proxy variables for status with regard to smoking.

METHODS

DATA COLLECTION AND STUDY AREAS

For the years 1979 through 1983, the U.S. Environmental Protection Agency (EPA) maintained the Inhalable Particle Monitoring Network for research purposes. The network sampled particulate matter in the air using dichotomous samplers with 15-μm and 2.5-μm cutoff points. On the basis of these data, from 1979 through 1983, mean concentrations of particulate matter with an aerodynamic diameter less than or equal to 2.5 μm ($PM_{2.5}$) were calculated for 61 U.S. metropolitan areas and used in the reanalysis and extended analyses of the American Cancer Society prospective cohort study.[6,7] (Metropolitan-area–specific means are presented in Appendix D of the American Cancer Society reanalysis report.[6]) After 1983, no broad-based monitoring network systematically and routinely collected $PM_{2.5}$ data until the promulgation of the National Ambient Air Quality Standard for $PM_{2.5}$ in 1997.[20] As required by the new $PM_{2.5}$ standard, many sites began measuring $PM_{2.5}$ in 1999. Daily $PM_{2.5}$ data were extracted from the EPA's Aerometric Information Retrieval System database for 1999 and the first three quarters of 2000. Data for the four quarters were averaged when more than 50% of the samples and 45 or more total sampling days were available for at least one of the two corresponding quarters in each year. Measurements were averaged first by monitoring site and then by metropolitan area. These calculated mean concentrations of $PM_{2.5}$ were available for 116 U.S. metropolitan areas and were used as part of the extended analysis of the American Cancer Society study.[7] There were 51 metropolitan areas with matching $PM_{2.5}$ data for the early 1980s and the late 1990s.

As part of a nationwide analysis of disparities in mortality across the counties, standard life-table techniques[21] were used to estimate annual life expectancies for more than 2000 individual or merged county units, on the basis of individual death records from national mortality statistics and population data from the U.S. Census, as described in more detail elsewhere.[22] For the purposes of this study, life expectancy for the 215 county units that were part of the 51 metropolitan areas with matching $PM_{2.5}$ data were included. The metropolitan areas were distributed throughout the United States (Fig. 1). For each county unit, life expectancy was calculated with the use of pooled death and population data for the 5-year periods 1978 through 1982 and 1997 through 2001. Because borough-specific death statistics were unavailable for the five boroughs of New York for the earlier period, the boroughs were treated as a single unit, resulting in 211 distinct county-level observations. As described elsewhere,[22] U.S. Census data were used to collect information on county-level socioeconomic and demographic variables, including population, income, and proportions of persons in the population who were high-school graduates, had urban residences, had not lived in their current county of residence 5 years before the census (5-year immigration), and reported that they were white, black, or Hispanic. Income was adjusted for inflation (base year, 2000).

In accordance with previous analyses,[23,24] age-standardized death rates for lung cancer and chronic obstructive pulmonary disease (COPD) were used as indicators of accumulated exposure

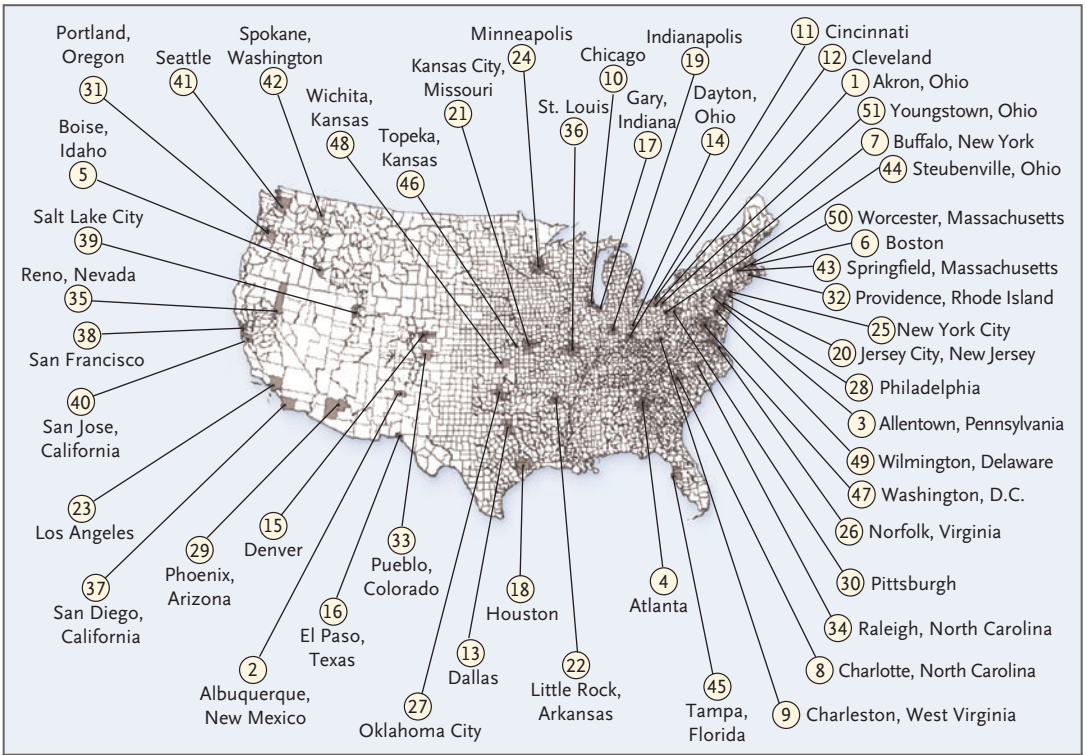

Figure 1. Distribution of Study Areas.

The locations of the counties included in the study are shown in gray, and the dots represent the approximate locations of the 51 metropolitan areas in the study. The metropolitan areas are coded by number as follows: 1 — Akron, Ohio; 2 — Albuquerque, New Mexico; 3 — Allentown, Pennsylvania; 4 — Atlanta; 5 — Boise, Idaho; 6 — Boston; 7 — Buffalo, New York; 8 — Charlotte, North Carolina; 9 — Charleston, West Virginia; 10 — Chicago; 11 — Cincinnati; 12 — Cleveland; 13 — Dallas; 14 — Dayton, Ohio; 15 — Denver; 16 — El Paso, Texas; 17 — Gary, Indiana; 18 — Houston; 19 — Indianapolis; 20 — Jersey City, New Jersey; 21 — Kansas City, Missouri; 22 — Little Rock, Arkansas; 23 — Los Angeles; 24 — Minneapolis; 25 — New York City; 26 — Norfolk, Virginia; 27 — Oklahoma City; 28 — Philadelphia; 29 — Phoenix, Arizona; 30 — Pittsburgh; 31 — Portland, Oregon; 32 — Providence, Rhode Island; 33 — Pueblo, Colorado; 34 — Raleigh, North Carolina; 35 — Reno, Nevada; 36 — St. Louis; 37 — San Diego, California; 38 — San Francisco; 39 — Salt Lake City; 40 — San Jose, California; 41 — Seattle; 42 — Spokane, Washington; 43 — Springfield, Massachusetts; 44 — Steubenville, Ohio; 45 — Tampa, Florida; 46 — Topeka, Kansas; 47 — Washington, D.C.; 48 — Wichita, Kansas; 49 — Wilmington, Delaware; 50 — Worcester, Massachusetts; 51 — Youngstown, Ohio.

to smoking. There were two reasons for using these indirect indicators of smoking. First, for most study areas, data on the prevalence of smoking are not available for the late 1970s and early 1980s, and second, the measures for lung cancer and COPD indicate the population's cumulative exposure to smoking. The *International Classification of Diseases, 10th Revision* (ICD-10) was used to calculate death rates for lung cancer (ICD-10 codes C33-C34 and D02.1-D02.2) and COPD (ICD-10 code J40-J44). The death rates were based on the underlying cause of death in individual death records from national mortality statistics and population data from the U.S. Census, pooled for the same 5-year periods as life expectancy. Death rates were calculated in 5-year age groups, and were age-standardized for the 2000 U.S. population of adults 45 years of age or older (rates of death from these diseases are unstable among younger adults because there is such a small number of cases). Additional estimates of changes in the prevalence of cigarette smoking were obtained from health surveys for use in sensitivity analyses of a subgroup of the metropolitan areas with data in both periods. The prevalence of smoking among adults in metropolitan areas for the years 1998 through 2002 could be estimated for 50 of the 51 metropolitan study areas from the Behavioral Risk Factor Surveillance System (www.cdc.gov/brfss/technical_infodata/surveydata.htm);

the prevalence for the years 1978 through 1980 could be estimated for 24 of the metropolitan study areas with data from the National Health Interview Survey (www.cdc.gov/nchs/nhis.htm). The change in the prevalence of smoking was estimated for each of 24 metropolitan areas on the basis of data from these sources for both periods.

STATISTICAL ANALYSIS

For both 5-year periods, life expectancies were plotted against $PM_{2.5}$ concentrations, and increases in life expectancy from the first period to the second were plotted against reductions in the $PM_{2.5}$ concentration. Cross-sectional regression models were estimated for both time periods, and first-difference regression models were estimated by regressing increases in life expectancy against reductions in monitored $PM_{2.5}$ concentrations. The sensitivity of the estimates on the pollution-related effect was explored with the use of five different approaches: including combinations of demographic, socioeconomic, and proxy variables for prevalence of smoking in the models, restricting the analysis to counties that had a population of 100,000 or more in 1986 or to the 51 largest counties in each metropolitan area, estimating population-weighted regression models, stratifying the analysis according to the pollution levels for 1979 through 1983 (in order to evaluate the influence of baseline pollution levels), and including direct measures of change in the prevalence of smoking for the subgroup of study areas with adequate survey data on smoking. Because of the potential for lack of statistical independence between counties in the same metropolitan area, clustered standard errors that were robust with regard to within-cluster correlation[25,26] (clustered by the 51 metropolitan areas) were estimated for all models except for the analysis that included only the 51 largest counties in each metropolitan area. Models were estimated with the use of PROC REG and PROC SURVEYREG in SAS, version 9.2 (SAS Institute).

RESULTS

Summary statistics for key study variables are listed in Table 1. In Figures 2 and 3, cross-sectional life expectancies are plotted against air-pollution data for the earlier and later time periods, respectively. At least five observations can be made on the basis of the data presented in these two

Table 1. Summary Characteristics of the 217 Counties Analyzed.*

Variable	Mean Value
Life expectancy (yr)	
1978–1982	74.32±1.52
1997–2001	77.04±1.82
Change	2.72±0.93
$PM_{2.5}$ ($\mu g/m^3$)	
1979–1983	20.61±4.36
1999–2000	14.10±2.86
Reduction	6.52±2.94
Per capita income (in thousands of $)	
1979	15.18±2.64
1999	23.67±5.05
Change	8.49±3.16
Population (in hundreds of thousands)	
1980	3.83±8.47
2000	4.82±10.13
Change	0.99±2.26
5-Year in-migration (proportion of population)†‡	
1980	0.25±0.10
2000	0.24±0.08
Change	–0.01±0.06
Urban residence (proportion of population)†	
1980	0.58±0.33
2000	0.78±0.22
Change	0.20±0.18
High-school graduates (proportion of population)†	
1980	0.68±0.11
2000	0.87±0.05
Change	0.19±0.15
Black population (proportion of population)†§	
1980	0.097±0.12
2000	0.115±0.13
Change	0.018±0.06
Hispanic population (proportion of population)†§	
1980	0.035±0.072
2000	0.068±0.093
Change	0.033±0.043
Deaths from lung cancer (no./10,000 population)	
1979–1983	14.38±2.95
1997–2001	16.73±3.27
Change	2.35±2.77
Deaths from COPD (no./10,000 population)	
1979–1983	7.92±1.85
1997–2001	12.37±2.71
Change	4.45±2.43

* Plus–minus values are means ±SD. COPD denotes chronic obstructive pulmonary disease, and $PM_{2.5}$ particulate matter with an aerodynamic diameter less than or equal to 2.5 μm.
† Proportions of the population are based on U.S. Census data.
‡ Five-year in-migration refers to the proportion of the population who did not reside in the county 5 years earlier.
§ Data on race and ethnic group were self-reported.

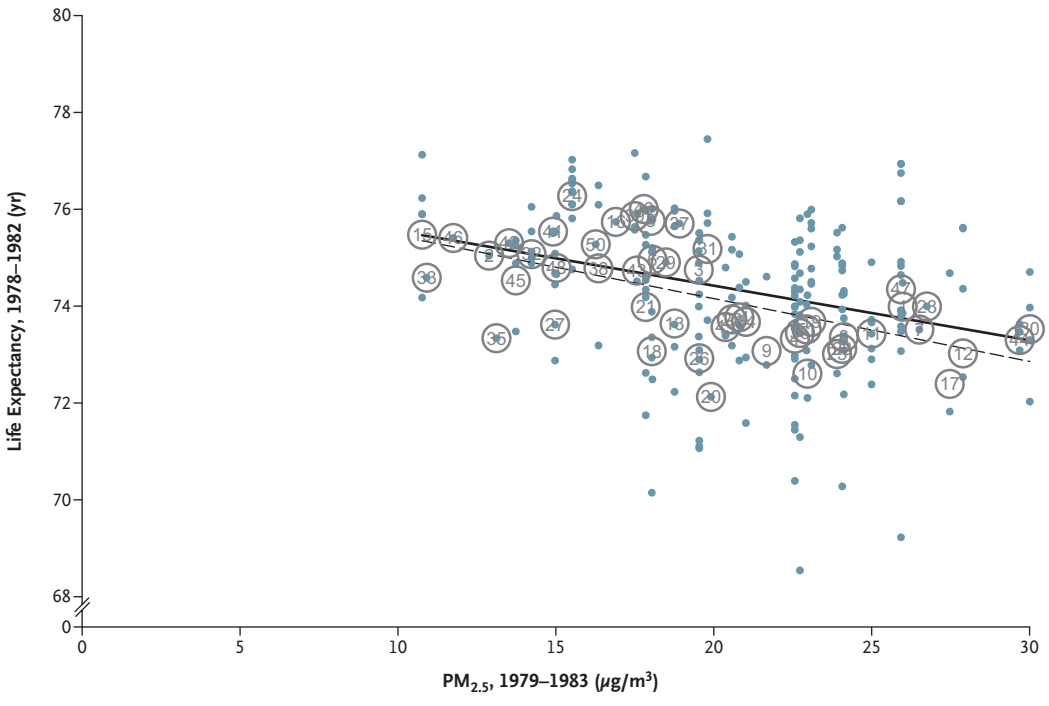

Figure 2. Cross-Sectional Life Expectancies for 1978–1982, Plotted against $PM_{2.5}$ Concentrations for 1979–1983.

Dots and circles labeled with numbers represent population-weighted mean life expectancies at the county level and the metropolitan-area level, respectively. The solid and broken lines represent regression lines with the use of county-level and metropolitan-area–level observations, respectively. The metropolitan areas are coded by number as follows: 1 — Akron, Ohio; 2 — Albuquerque, New Mexico; 3 — Allentown, Pennsylvania; 4 — Atlanta; 5 — Boise, Idaho; 6 — Boston; 7 — Buffalo, New York; 8 — Charlotte, North Carolina; 9 — Charleston, West Virginia; 10 — Chicago; 11 — Cincinnati; 12 — Cleveland; 13 — Dallas; 14 — Dayton, Ohio; 15 — Denver; 16 — El Paso, Texas; 17 — Gary, Indiana; 18 — Houston; 19 — Indianapolis; 20 — Jersey City, New Jersey; 21 — Kansas City, Missouri; 22 — Little Rock, Arkansas; 23 — Los Angeles; 24 — Minneapolis; 25 — New York City; 26 — Norfolk, Virginia; 27 — Oklahoma City; 28 — Philadelphia; 29 — Phoenix, Arizona; 30 — Pittsburgh; 31 — Portland, Oregon; 32 — Providence, Rhode Island; 33 — Pueblo, Colorado; 34 — Raleigh, North Carolina; 35 — Reno, Nevada; 36 — St. Louis; 37 — San Diego, California; 38 — San Francisco; 39 — Salt Lake City; 40 — San Jose, California; 41 — Seattle; 42 — Spokane, Washington; 43 — Springfield, Massachusetts; 44 — Steubenville, Ohio; 45 — Tampa, Florida; 46 — Topeka, Kansas; 47 — Washington, D.C.; 48 — Wichita, Kansas; 49 — Wilmington, Delaware; 50 — Worcester, Massachusetts; 51 — Youngstown, Ohio. $PM_{2.5}$ denotes particulate matter with an aerodynamic diameter less than or equal to 2.5 μm.

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figures: $PM_{2.5}$ concentrations generally declined during the 1980s and 1990s; life expectancies increased between the two periods; in both periods there were cross-sectional negative associations between life expectancies and pollution levels; similar negative associations were observed when analyses were performed with the use of county-level or metropolitan-area–level observations; and there was substantial variation, or scatter, around the regression line, indicating that the association with air pollution explains only part of the cross-sectional variation — clearly, other important factors influence life expectancy.

Estimates of the associations between $PM_{2.5}$ and life expectancies with the use of cross-sectional regression models were sensitive to the inclusion of socioeconomic and demographic variables and proxy variables for the prevalence of cigarette smoking and especially the proportion of high-school graduates, which was highly correlated with per capita income. For example, the association between $PM_{2.5}$ concentrations and life expectancy was stronger in the period with less pollution, without adjustment for any covariates. On the basis of regression models without any covariates, an increase in the $PM_{2.5}$ concen-

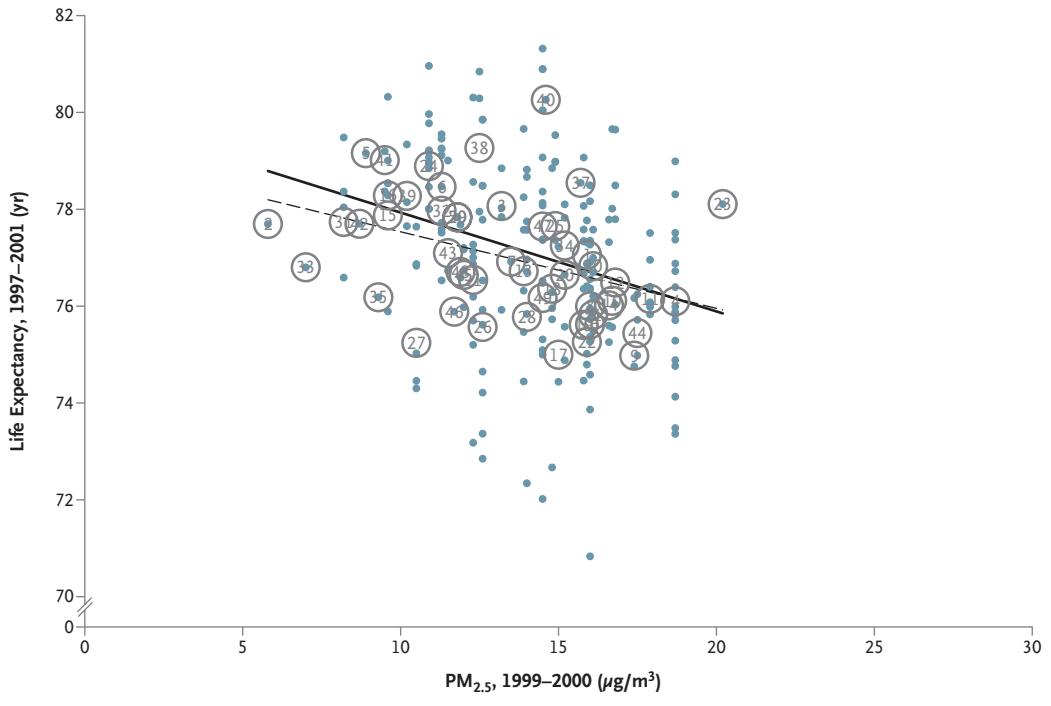

Figure 3. Cross-Sectional Life Expectancies for 1997–2001, Plotted against $PM_{2.5}$ Concentrations for 1999–2000.

Dots and circles labeled with numbers represent population-weighted mean life expectancies at the county level and the metropolitan-area level, respectively. The solid and broken lines represent regression lines with the use of county-level and metropolitan-area–level observations, respectively. The metropolitan areas are coded by number as follows: 1 — Akron, Ohio; 2 — Albuquerque, New Mexico; 3 — Allentown, Pennsylvania; 4 — Atlanta; 5 — Boise, Idaho; 6 — Boston; 7 — Buffalo, New York; 8 — Charlotte, North Carolina; 9 — Charleston, West Virginia; 10 — Chicago; 11 — Cincinnati; 12 — Cleveland; 13 — Dallas; 14 — Dayton, Ohio; 15 — Denver; 16 — El Paso, Texas; 17 — Gary, Indiana; 18 — Houston; 19 — Indianapolis; 20 — Jersey City, New Jersey; 21 — Kansas City, Missouri; 22 — Little Rock, Arkansas; 23 — Los Angeles; 24 — Minneapolis; 25 — New York City; 26 — Norfolk, Virginia; 27 — Oklahoma City; 28 — Philadelphia; 29 — Phoenix, Arizona; 30 — Pittsburgh; 31 — Portland, Oregon; 32 — Providence, Rhode Island; 33 — Pueblo, Colorado; 34 — Raleigh, North Carolina; 35 — Reno, Nevada; 36 — St. Louis; 37 — San Diego, California; 38 — San Francisco; 39 — Salt Lake City; 40 — San Jose, California; 41 — Seattle; 42 — Spokane, Washington; 43 — Springfield, Massachusetts; 44 — Steubenville, Ohio; 45 — Tampa, Florida; 46 — Topeka, Kansas; 47 — Washington, D.C.; 48 — Wichita, Kansas; 49 — Wilmington, Delaware; 50 — Worcester, Massachusetts; 51 — Youngstown, Ohio. $PM_{2.5}$ denotes particulate matter with an aerodynamic diameter less than or equal to 2.5 μm.

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tration of 10 μg per cubic meter was associated with mean (±SE) reductions in life expectancy of 1.19±0.27 years from 1978 to 1982 and 2.02±0.50 years from 1997 to 2001 ($P<0.001$ for both comparisons). However, models that controlled for income, population, cross-county migration, and the proportion of the population that was black or Hispanic or had an urban residence and that also included proxy variables for the prevalence of smoking showed smaller associations, especially in the second period. An increase of 10 μg per cubic meter in the $PM_{2.5}$ concentration was associated with a reduction in life expectancy of 0.46±0.22 year ($P=0.039$) from 1978 to 1982 and 0.37±0.20 year ($P=0.091$) from 1997 to 2001.

In Figure 4, increases in life expectancies are plotted against reductions in $PM_{2.5}$ concentrations from approximately 1980 to 2000. Several additional important observations can be made on the basis of these data: on average, life expectancy increased more in areas with larger reductions in air pollution; similar positive associations were observed between gains in life expectancy and reductions in $PM_{2.5}$ concentrations at the county level and the metropolitan-area level; and there was substantial variation, or scatter, around the

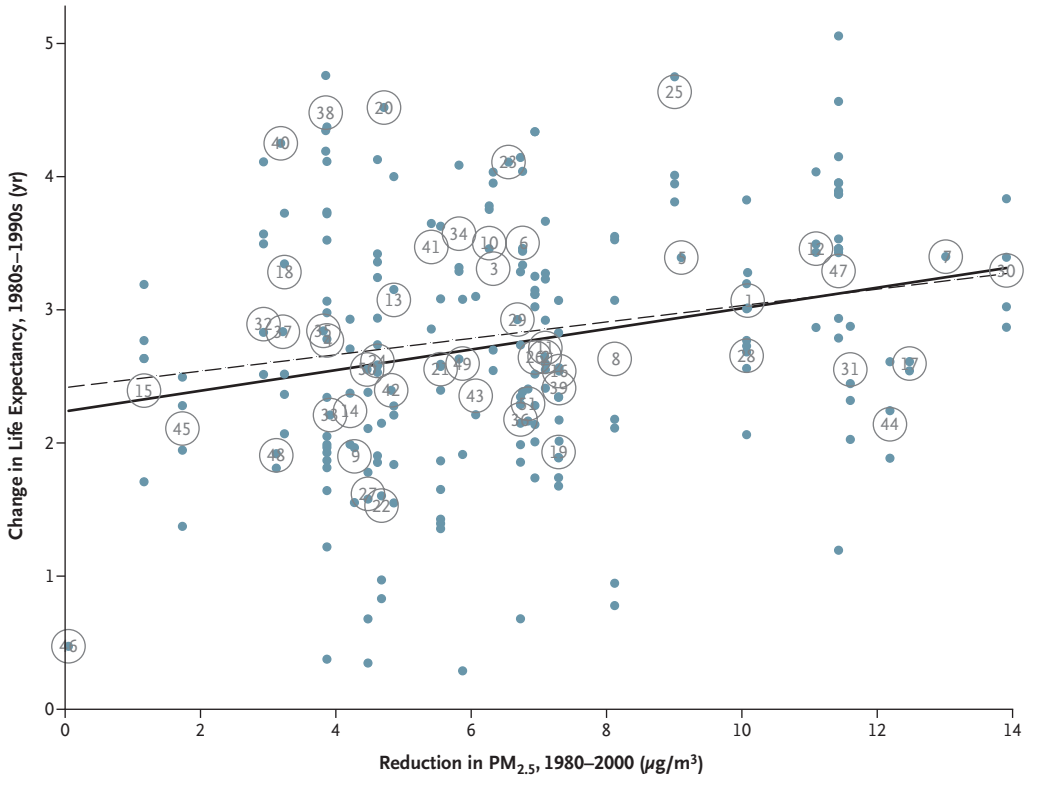

Figure 4. Changes in Life Expectancy for the 1980s–1990s, Plotted against Reductions in $PM_{2.5}$ Concentrations for 1980–2000.

Dots and circles labeled with numbers represent changes in population-weighted mean life expectancies at the county level and metropolitan-area level, respectively. The solid and broken lines represent regression lines with the use of county-level and metropolitan-area–level observations, respectively. The metropolitan areas are coded by number as follows: 1 — Akron, Ohio; 2 — Albuquerque, New Mexico; 3 — Allentown, Pennsylvania; 4 — Atlanta; 5 — Boise, Idaho; 6 — Boston; 7 — Buffalo, New York; 8 — Charlotte, North Carolina; 9 — Charleston, West Virginia; 10 — Chicago; 11 — Cincinnati; 12 — Cleveland; 13 — Dallas; 14 — Dayton, Ohio; 15 — Denver; 16 — El Paso, Texas; 17 — Gary, Indiana; 18 — Houston; 19 — Indianapolis; 20 — Jersey City, New Jersey; 21 — Kansas City, Missouri; 22 — Little Rock, Arkansas; 23 — Los Angeles; 24 — Minneapolis; 25 — New York City; 26 — Norfolk, Virginia; 27 — Oklahoma City; 28 — Philadelphia; 29 — Phoenix, Arizona; 30 — Pittsburgh; 31 — Portland, Oregon; 32 — Providence, Rhode Island; 33 — Pueblo, Colorado; 34 — Raleigh, North Carolina; 35 — Reno, Nevada; 36 — St. Louis; 37 — San Diego, California; 38 — San Francisco; 39 — Salt Lake City; 40 — San Jose, California; 41 — Seattle; 42 — Spokane, Washington; 43 — Springfield, Massachusetts; 44 — Steubenville, Ohio; 45 — Tampa, Florida; 46 — Topeka, Kansas; 47 — Washington, D.C.; 48 — Wichita, Kansas; 49 — Wilmington, Delaware; 50 — Worcester, Massachusetts; 51 — Youngstown, Ohio. $PM_{2.5}$ denotes particulate matter with an aerodynamic diameter less than or equal to 2.5 μm.

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regression line, indicating that factors other than changes in air pollution were influencing the changes in life expectancy.

Table 2 shows regression coefficients for the association between increases in life expectancy and reductions in $PM_{2.5}$ for models with various combinations of socioeconomic and demographic variables and proxy variables for the prevalence of smoking. Table 2 includes models that are restricted to counties with a population of 100,000 or more in 1986 or to the 51 largest counties in each metropolitan area. In all models, increased life expectancies were significantly associated with decreases in $PM_{2.5}$. According to model 4, a decrease of 10 μg per cubic meter in $PM_{2.5}$ was associated with an adjusted increase in life expectancy equal to 0.61±0.20 year. The estimated effect of reduced $PM_{2.5}$ on life expectancy was not highly sensitive after adjustment for changes in socioeconomic and demographic variables and

Table 2. Results of Selected Regression Models, Including Estimates of the Increase in Life Expectancy Associated with a Reduction in $PM_{2.5}$ of 10 μg per Cubic Meter, Adjusted for Socioeconomic, Demographic, and Proxy Indicators for Prevalence of Smoking.*

Variable	Model 1	Model 2	Model 3	Model 4	Model 5†	Model 6‡	Model 7‡
				years			
Intercept	2.25±0.21§	0.80±0.19§	1.78±0.27§	1.75±0.27§	2.02±0.34§	1.71±0.51§	2.09±0.36§
Reduction in $PM_{2.5}$ (10 μg/m³)	0.72±0.29¶	0.83±0.20§	0.60±0.20§	0.61±0.20§	0.55±0.24¶	1.01±0.25§	0.95±0.23§
Change in income (in thousands of $)	—	0.17±0.02§	0.13±0.02§	0.13±0.01§	0.11±0.02§	0.15±0.04§	0.11±0.02§
Change in population (in hundreds of thousands)	—	0.08±0.02§	0.05±0.02§	0.06±0.02§	0.05±0.02§	0.04±0.02	0.05±0.02¶
Change in 5-yr in-migration (proportion of population)‖	—	0.19±0.79	1.28±0.80	—	—	–0.02±1.83	—
Change in high-school graduates (proportion of population)‖	—	0.17±0.56	–0.11±0.53	—	—	–0.90±0.86	—
Change in urban residence (proportion of population)‖	—	–0.76±0.32¶	–0.40±0.25	—	—	0.03±1.88	—
Change in black population (proportion of population)‖	—	–1.94±0.58§	–2.74±0.58§	–2.70±0.64§	–2.95±0.78§	–5.06±2.12§	–5.98±1.99§
Change in Hispanic population (proportion of population)‖	—	1.46±1.23	1.33±1.10	—	—	2.44±2.22	—
Change in lung-cancer mortality rate (no./10,000 population)	—	—	–0.07±0.02§	–0.06±0.02§	–0.07±0.03¶	0.01±0.03	0.02±0.03
Change in COPD mortality rate (no./10,000 population)	—	—	–0.07±0.02§	–0.08±0.02§	–0.09±0.03§	–0.15±0.06§	–0.19±0.05§
No. of county units	211	211	211	211	127	51	51
R^2‡‡	0.05	0.47	0.55	0.53	0.60	0.76	0.74

* Plus–minus values are regression coefficients ±SE. COPD denotes chronic obstructive pulmonary disease, and $PM_{2.5}$ particulate matter with an aerodynamic diameter less than or equal to 2.5 μm.
† This model included only counties with populations of 100,000 or more in 1986.
‡ This model included only counties with the largest 1986 population in the statistical metropolitan area.
§ For these values, P<0.01.
¶ For these values, P<0.05.
‖ Proportions of the population are based on U.S. Census data.
** Five-year in-migration refers to the proportion of the population who did not reside in the county 5 years earlier.
†† Data on race and ethnic group were self-reported.
‡‡ R^2 denotes the coefficient of determination.

proxy variables for the prevalence of smoking or to data restricted to large counties.

In a variety of related sensitivity analyses, the effect estimate for a change in $PM_{2.5}$ was quite robust. In stepwise regressions, a reduction in $PM_{2.5}$ generally entered the model, after changes in per capita income and proxy indicators for prevalence of smoking were introduced; the effect estimate was stable with the inclusion of other variables. When models 4 and 7 in Table 2 were reestimated with the use of weighted regression (weighting by the square root of the average population for the two periods), similar results were observed, with a decrease of 10 μg per cubic meter in $PM_{2.5}$ associated with an estimated increase in life expectancy equal to 0.58±0.20 year for model 4 and 0.86±0.24 year for model 7. Stratified estimates of model 4 in Table 2 were calculated for the 44 counties in the 15 least-polluted metropolitan areas in the earlier period ($PM_{2.5}$, <17 μg per cubic meter) (Fig. 2) as compared with all the other, more-polluted areas. A reduction of 10 μg per cubic meter in $PM_{2.5}$ was associated with an increased life expectancy of 0.95±0.57 for the least-polluted areas and 0.57±0.26 year for other areas; there was no significant difference in the pollution effect for areas that initially had relatively low or high levels of pollution (P≥0.15).

Similarly, the effect estimate for the change in $PM_{2.5}$ was not highly sensitive to the inclusion of survey-based estimates of metropolitan-area–level changes in the prevalence of cigarette smoking. For example, when model 4 in Table 2 was reestimated with the use of data from the 136 counties in the 24 metropolitan areas with matching survey data for the prevalence of smoking, a reduction in $PM_{2.5}$ of 10 μg per cubic meter was associated with an estimated increase in life expectancy of 0.61±0.22 year without inclusion of the change in the variable for smoking prevalence (P=0.011) and 0.64±0.22 year with its inclusion (P=0.007). When model 7 in Table 2 was reestimated with data restricted to the 24 largest counties in the 24 metropolitan areas with matching survey data for the prevalence of smoking, a reduction of 10 μg per cubic meter in $PM_{2.5}$ was associated with an estimated increase in life expectancy of 0.94±0.32 year without inclusion of the change in the variable for smoking prevalence (P=0.007) and 1.00±0.34 years with its inclusion (P=0.008). When added to these models, the change in the prevalence of smoking was not significant (P>0.15), and the estimated effect of a change in the rate of death from COPD was largely unaffected. These results indicate that county-level changes in the rate of death from COPD were more robustly associated with county-level changes in life expectancy than metropolitan-area–level estimates of changes in the prevalence of smoking based on limited survey data.

DISCUSSION

Improvements in life expectancy during the 1980s and 1990s were associated with reductions in fine-particulate pollution across the study areas, even after adjustment for various socioeconomic, demographic, and proxy variables for prevalence of smoking that are associated with health through a range of mechanisms. Indirect calculations point to an approximate loss of 0.7 to 1.6 years of life expectancy that can be attributed to long-term exposure to fine-particulate matter at a concentration of 10 μg per cubic meter, with the use of life tables from the Netherlands and the United States and risk estimates from the prospective cohort studies.[27,28] In the present analysis, a decrease of 10 μg per cubic meter in the fine-particulate concentration was associated with an estimated increase in life expectancy of approximately 0.61±0.20 year — an estimate that is nearly as large as these indirect estimates.

For the approximate period of 1980 through 2000, the average increase in life expectancy was 2.72 years for the counties in this analysis. Reduced air pollution was only one factor contributing to increased life expectancies, with its effects overlapping with those of other factors. On the basis of the average reduction in the $PM_{2.5}$ concentration (6.52 μg per cubic meter) in the metropolitan areas included in this analysis and the effect estimate from model 4 in Table 2, the average increase in life expectancy attributable to the reduced levels of air pollution was approximately 0.4 year (6.52 × 0.061). Multicausality and competing risk issues make it difficult to quantify changes in life expectancy attributable to single risk factors, but these results suggest that the individual effect of reductions in air pollution on life expectancy was as much as 15% of the overall increase. In metropolitan areas where reductions in $PM_{2.5}$ were 13 to 14 μg per cubic meter, the contribution of improvements in air

quality to increases in life expectancy may have been as much as 0.82 year (13.5 × 0.061).

In previous cross-sectional analyses, investigators have observed associations between mortality rates and particulate-air pollution,[1-3] but the size of these associations was sensitive to efforts to control the analyses for potential confounders. Our analysis showed similar sensitivity for the strictly cross-sectional associations with life expectancy. The primary strength of this analysis, however, is the additional use of temporal variations. The availability of data on changes in pollution exposure across metropolitan areas from 1980 to 2000 provides the opportunity for an assessment that is similar to a natural experiment. Cross-sectional characteristics that do not change over time are controlled as if by design. Characteristics that affect life expectancy and that change over time — but not in correlation with changes in pollution — are unlikely to confound the results. Even with underlying spatial correlations, if the temporal changes in these characteristics are relatively less correlated, adjusted effect estimates from temporal regression models are likely to be more robust. In this analysis of differences in temporal changes, the estimated effects of reduced $PM_{2.5}$ exposure on increases in life expectancy were robust in analyses adjusted for socioeconomic, demographic, and proxy variables for the prevalence of smoking, as well as in an analysis restricted to large counties.

From an analytic perspective, it would have been informative if pollution had actually increased in some of the areas that were initially less polluted. However, pollution did not increase in any of the metropolitan areas, and the potential for reducing pollution was greater in the areas that were more polluted initially than in those that were less polluted. Stratified analyses showed no significant differences in pollution effects for the areas that initially had low or high pollution, which is consistent with previous findings on the effects of $PM_{2.5}$ even at relatively low concentrations.[7,10,11,15,19]

An appealing aspect of this analysis is that it is a simple, direct, and transparent exploration of the association between life expectancy and air pollution, with the use of available monitored data on $PM_{2.5}$ for both the first and second time periods. However, limited monitoring of data on $PM_{2.5}$ air pollution, especially for the period from 1979 through 1983, reduced both the number of metropolitan areas that could be included in the analysis and our ability to evaluate spatial and temporal associations with more specificity. Furthermore, because the analysis was population-based, we were limited in our ability to control for additional potential confounders, especially various individual and community risk factors that may have been affected by policies that were broadly related to environmental regulation.

For example, the three variables in the analysis that were most strongly associated with changes in life expectancy are all proxy variables. Increases in per capita income probably serve as a proxy variable for, or are highly correlated with, such factors as access to medical care, higher-quality diets, and healthier lifestyles. The use of rates of death from lung cancer and COPD as proxy variables was necessitated by the lack of reliable data on smoking, especially for the period from 1978 through 1982, yet these rates reflect the cumulative effects of smoking, which may similarly affect life expectancy. Although the large majority of deaths from lung cancer and COPD are attributable to smoking,[23] pollution may also have an effect (albeit much smaller) on these health outcomes,[7,8] potentially leading to conservative estimates of the effects of pollution when such proxies are used. The $PM_{2.5}$ variable may serve, in part, as a proxy variable for copollutants, and changes in $PM_{2.5}$ may represent estimates of changes in area-wide ambient concentrations based on fixed-site monitoring during the two time periods instead of being a direct measure of changes in personal exposures. Nevertheless, U.S. air-quality standards and related public policies are designed to restrict ambient pollutant concentrations in an effort to protect human health.[20] Previous prospective cohort studies, using measures of ambient concentrations of pollutants and controlling for smoking and other individual risk factors, have suggested similar improvements in survival and life expectancy, on the basis of indirect estimates.[4-11] The results of our population-based analysis, which showed similar improvements in life expectancy associated with public-policy–related reductions in ambient pollutant concentrations, corroborate these previous findings.

In conclusion, the results of this analysis are generally good news. Although multiple factors affect life expectancy, our findings provide evidence that improvements in air quality have con-

tributed to measurable improvements in human health and life expectancy in the United States.

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EDITORIALS

Cardiovascular Risks from Fine Particulate Air Pollution

Douglas W. Dockery, Sc.D., and Peter H. Stone, M.D.

More than a decade ago, prospective epidemiologic studies showed that mortality was increased among people living in communities with elevated concentrations of fine particulate air pollution.[1,2] Subsequent research has shown that particulate air pollution is statistically and mechanistically linked to increased cardiovascular disease.[3] New data are beginning to shed light on which persons are at heightened risk.

In this issue of the *Journal*, Miller et al.[4] report on data from the Women's Health Initiative (WHI) observational study, which greatly expands our understanding of how fine particulate pollution affects health. Earlier long-term prospective cohort studies showed an association between levels of air pollution consisting of particulate matter of less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) and an elevated risk of death from all causes and from cardiovascular disease.[1,2,5] The WHI study broadens the scope by finding that nonfatal cardiovascular events are also strongly associated with fine particulate concentrations in the community. Earlier work relied solely on death certificates to define the rate of death from cardiovascular disease. In the WHI study, cardiovascular events and mortality were defined by objective review of medical records. The earlier studies were designed to identify risk factors for respiratory disease[1] and cancer[2] and therefore had limited ability to adjust for cardiovascular risk factors. The WHI observational study was designed to assess the risk of cardiovascular events and therefore could exclude cardiovascular risk factors as explanations for the observed associations with air pollution.

Earlier studies did not include data on the full range of regulated community air pollutants — that is, $PM_{2.5}$ (and the larger particle fraction, PM_{10}), sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone. The WHI study considered all of these community air pollutants and found cardiovascular risk associated only with $PM_{2.5}$ concentrations. Whereas earlier work compared levels of air pollution and rates of death between various cities, the WHI investigators were also able to compare areas within individual cities. Their analysis demonstrated a relationship between increased levels of fine particulate pollution and higher rates of death and complications from cardiovascular and cerebrovascular disease, depending not only on which city a person lived in but also on where in that city she lived.

Perhaps most important, the WHI study established a stronger statistical association between fine particulate air pollution and death from coronary heart disease than that found in earlier studies. In the WHI study, Miller et al. found an increased relative risk of 1.76 for death from cardiovascular disease for every increase of 10 μg per cubic meter in the mean concentration of $PM_{2.5}$.[4] By comparison, a study by the American Cancer Society showed that each increase of 10 μg per cubic meter in the mean $PM_{2.5}$ concentration was associated with an increased relative risk of 1.12 for death from cardiovascular disease, 1.18 for death from ischemic heart disease (the largest proportion of deaths), and 1.13 for death from arrhythmia, heart failure, or cardiac arrest.[5]

Samples in previous studies consisted of subjects from the entire population of the cities being investigated. The WHI analysis was restricted to postmenopausal women with no history of cardiovascular health problems. A 22-year follow-up of a cohort of nonsmoking white adults in California showed an increased risk of death from coronary heart disease with rising levels of

fine particulate air pollution in women but not in men.[6] Does this suggest that the WHI population, or women in general, are more sensitive to the cardiovascular effects of particulate air pollution?

Women have a distinctly different profile of coronary disease. In the Women's Ischemia Syndrome Evaluation study, the cluster of conditions that increase the risk of vascular disease (e.g., hypertension, diabetes, obesity, and inactivity) was seen more frequently in postmenopausal women than in men.[7] Women's coronary arteries are smaller in size and tend to harbor more diffuse atherosclerosis than do men's arteries, and women's microvessels appear to be more frequently dysfunctional than those of men.[7] Indeed, in the Euro Heart Survey, although women were less likely than men to have fixed atherosclerotic obstructive disease, among patients undergoing elective diagnostic angiography for angina, women with confirmed coronary disease had twice the risk of death or myocardial infarction as that of men.[8] These findings suggest that sex may not define susceptibility to air pollution but, rather, may be an indicator of an underlying cardiac substrate that puts women at increased risk.

Characteristics that define increased cardiovascular susceptibility to particulate air pollution have also been identified in men. Stronger associations between fine particulate concentrations and abnormal variability in heart rate were reported in asymptomatic men with higher Framingham cardiovascular risk scores.[9] $PM_{2.5}$ was more strongly associated with impaired autonomic cardiovascular function in men with genotypic and phenotypic indicators of increased systemic inflammation and oxidative stress than in those without these markers.[10] However, the increased susceptibility was not found among men taking statins, which both improve lipid profiles and reduce systemic inflammation.

The mechanisms by which fine particulate air pollution influence the risk of cardiovascular disease are still under investigation. There is evidence that inhalation of particulate air pollution creates and exacerbates both pulmonary and systemic inflammation and oxidative stress, leading to direct vascular injury, atherosclerosis, and autonomic dysfunction.[3] Buildup of atherosclerotic plaque, measured by the carotid intima–media thickness, is higher in communities with higher mean $PM_{2.5}$ concentrations.[11] Particulate air pollution has been found to lead to rapid and significant increases in fibrinogen, plasma viscosity, platelet activation, and release of endothelins, a family of potent vasoconstrictor molecules.[3]

Taken together, these studies suggest that the status of cardiovascular risk factors has a substantial effect on susceptibility to the adverse effects of particulate air pollution. A particularly appealing aspect of the design of the WHI study is the range of data collected on all subjects, including demographic and lifestyle characteristics, cardiovascular risk factors, medical history, diet, and medications. With this wealth of data, the next generation of analyses should be able to focus risk stratification even further to identify the characteristics of persons who are most susceptible to the adverse effects of air pollution.

A multifaceted approach that encompasses both public health and medical interventions is needed to reduce the burden of cardiovascular disease attributable to air pollution. Comprehensive management of the harmful effects of fine particles must start with intensive efforts to reduce this destructive form of air pollution. Fine particulate air pollution results not only from the combustion of carbonaceous fuels in our vehicles, power plants, and factories but also from secondary particles produced by oxidation of gaseous pollutants emitted by these same sources. The evidence that has accumulated thus far regarding the health threat from $PM_{2.5}$ pollution is convincing enough to have prompted the Environmental Protection Agency (EPA) to lower the short-term (24-hour) standard for fine particulate concentration that communities must achieve. Unfortunately for public health, the EPA failed to follow the recommendation of its science advisers and reduce the long-term standard for fine particles.[12] The findings of the WHI study strongly support the recommendation for tighter standards for long-term fine particulate air pollution.

Even with tighter standards, people will continue to be exposed to fine particulate air pollution. Although the public health burden of cardiovascular disease attributable to air pollution is large, the evidence suggests that individual risks are modest. If the WHI and other studies can identify intrinsic and acquired individual factors that lead to increased adverse cardiovascular responses to air pollution, then it should be possible to offer focused interventions to persons who

are at greatest risk and thereby ameliorate at least some of the patient-specific damages of air pollution.

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The Healing Power of Listening in the ICU

Craig M. Lilly, M.D., and Barbara J. Daly, Ph.D, R.N.

Critical care services are highly valued because they can often restore function in patients with acute life-threatening illnesses. In this context, advances in medical science have led to increased expectations for favorable outcomes of episodes of critical illness, even when the patient has severe coexisting chronic disease. The growing demand for critical care has led both to increased numbers of patients who survived with desirable functional outcomes and to increased numbers of patients who die in the intensive care unit (ICU). Today, many deaths in the ICU occur after a decision has been made to discontinue or forgo advanced supportive technology.[1] Decisions to shift from apparently ineffective technology to a treatment plan that focuses primarily on the patient's comfort are usually made in discussions between caregivers and family members.[2] These discussions involve complex conversations and are important to families. Communication processes that have been shown to improve the well-being of patients and family members include proactive, multidisciplinary sessions that provide patients (when they are able to communicate) and family members with the opportunity to ask questions, articulate the patient's values, express painful emotions, discuss concerns, and obtain help with managing feelings of guilt.[3]

A clinical course that runs counter to the family's hopes and expectations is extraordinarily stressful and is an important contributor to ICU-related post-traumatic stress disorder (PTSD) among families.[4] A better understanding of how intensive care clinicians can support families as they make the transition from a goal of cure to one of comfort and acceptance of death is clearly needed. Recognition of the relationship between satisfaction, on the one hand, and expectations, perceptions, and prognosis, on the other hand, can lead to communication processes that synchronize the perceptions of family members with those of providers and close gaps between reality and expectations. Curtis and colleagues have described some of the components of a system of communication that is being increasingly recognized as an effective means of promoting harmony between critical care providers and families.[5] This five-part system, known by the mnemonic VALUE, includes the following elements: valuing and appreciating what the family mem-

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Long-Term Exposure to Air Pollution and Incidence of Cardiovascular Events in Women

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ABSTRACT

BACKGROUND

Fine particulate air pollution has been linked to cardiovascular disease, but previous studies have assessed only mortality and differences in exposure between cities. We examined the association of long-term exposure to particulate matter of less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) with cardiovascular events.

METHODS

We studied 65,893 postmenopausal women without previous cardiovascular disease in 36 U.S. metropolitan areas from 1994 to 1998, with a median follow-up of 6 years. We assessed the women's exposure to air pollutants using the monitor located nearest to each woman's residence. Hazard ratios were estimated for the first cardiovascular event, adjusting for age, race or ethnic group, smoking status, educational level, household income, body-mass index, and presence or absence of diabetes, hypertension, or hypercholesterolemia.

RESULTS

A total of 1816 women had one or more fatal or nonfatal cardiovascular events, as confirmed by a review of medical records, including death from coronary heart disease or cerebrovascular disease, coronary revascularization, myocardial infarction, and stroke. In 2000, levels of $PM_{2.5}$ exposure varied from 3.4 to 28.3 μg per cubic meter (mean, 13.5). Each increase of 10 μg per cubic meter was associated with a 24% increase in the risk of a cardiovascular event (hazard ratio, 1.24; 95% confidence interval [CI], 1.09 to 1.41) and a 76% increase in the risk of death from cardiovascular disease (hazard ratio, 1.76; 95% CI, 1.25 to 2.47). For cardiovascular events, the between-city effect appeared to be smaller than the within-city effect. The risk of cerebrovascular events was also associated with increased levels of $PM_{2.5}$ (hazard ratio, 1.35; 95% CI, 1.08 to 1.68).

CONCLUSIONS

Long-term exposure to fine particulate air pollution is associated with the incidence of cardiovascular disease and death among postmenopausal women. Exposure differences within cities are associated with the risk of cardiovascular disease.

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Exposure to air pollution has been associated with death and hospitalization from cardiovascular causes.[1] Uncertainty remains about the magnitude of these associations, the mechanisms, and the effects of long-term exposure to pollutants, as compared with short-term exposure. Although previous studies of daily increases in exposure to pollution have assessed both fatal and nonfatal events,[2] studies investigating long-term exposure — estimating average exposure during years of follow-up — have evaluated mortality only on the basis of death certificates.[3-8] The increase in mortality associated with long-term exposure to air pollution is larger than that seen in studies of short-term exposure, and long-term effects on death rates serve as the current basis for fiercely challenged environmental regulations in this country.[9-13]

In previous studies of the long-term effect of air pollution on cardiovascular disease, investigators have averaged exposures across a city and then compared health effects between cities.[3-5,14] However, gradients of exposure to pollutants within cities also affect the risk of death from cardiovascular causes[8,15] and may be associated with subclinical atherosclerosis.[16]

We evaluated long-term exposure to air pollution and the incidence of cardiovascular disease in the Women's Health Initiative (WHI) Observational Study, a prospective cohort study with medical-record review and classification procedures designed to document specific first cardiovascular events. We also examined how between-city and within-city gradients of exposure to particulate matter of less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) are associated with first cardiovascular events.

METHODS

STUDY SUBJECTS

The WHI enrolled postmenopausal women between the ages of 50 and 79 years in the study from 1994 to 1998. The study design and characteristics of the subjects have been described in detail elsewhere.[17,18] All subjects lived within commuting distance of one of 49 WHI clinical centers and satellite clinics in 36 U.S. Metropolitan Statistical Areas (referred to throughout as "cities"). Eligible subjects were those who planned to remain in the area and were free from conditions (including alcoholism, mental illness, and dementia) that might have precluded their participation in follow-up surveys. Baseline questionnaires assessed demographic and lifestyle characteristics, cardiovascular risk factors, medical history, diet, and medications. Written informed consent was obtained from all subjects. Anthropometric and blood-pressure measurements were performed at baseline.[18]

We restricted our study population to subjects without a history of physician-diagnosed cardiovascular disease, including previous myocardial infarction, congestive heart failure, coronary revascularization, and stroke. To establish a stable primary residence during follow-up, we included women who lived within 150 mi (241 km) of a clinic (and had not changed clinics) before either death or the year 2002. Institutional review boards at the University of Washington and the Fred Hutchinson Cancer Research Center approved the study.

DATA ON AIR POLLUTION EXPOSURE

We obtained data on the monitoring of air pollution from the Environmental Protection Agency's Aerometric Information Retrieval System with the use of AirData (www.epa.gov/oar/data). Such data are recorded for $PM_{2.5}$ and particulate matter of less than 10 μm in aerodynamic diameter (PM_{10}), sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone. We selected monitors on the basis of monitoring objectives and scale to represent ambient community-scale exposure and excluded those with data available from less than 50% of intended samples (see the Supplementary Appendix, available with the full text of this article at www.nejm.org). On the basis of a five-digit ZIP Code centroid, the nearest monitor to the location of each residence was identified and used to assign an average of annual pollutant concentrations to each study subject. Only women linked to a monitor within 30 mi (48 km) of their residence were included. The long-term average $PM_{2.5}$ concentration was the exposure of interest, and the annual average concentration in the year 2000 was the primary exposure measure, owing to the substantially increased network of monitors in place in that year, as compared with previous years.

CARDIOVASCULAR OUTCOMES

The WHI determined events on the basis of subjects' responses on annual questionnaires and

review of medical records (including hospital discharge summaries and diagnostic codes, results of electrocardiography, and reports on diagnostic tests and procedures) by physician adjudicators, following an established protocol.[19] Deaths were identified by proxy reports or by a review of the National Death Index. For deaths, WHI adjudicators reviewed all available records, including those from emergency, outpatient, and inpatient departments, and emergency medical services; autopsy and coroner records; and death certificates. We included outcomes adjudicated through August 2003.

The first cardiovascular event was the first occurrence of any of the following: myocardial infarction, coronary revascularization, stroke, and death from either coronary heart disease (categorized as "definite" or "possible") or cerebrovascular disease. These events were considered to be most consistent with an atherosclerotic disease process and most reliably verified by the WHI protocol.[20] Death from coronary heart disease (both definite and possible diagnoses) required documented myocardial infarction or angina or an antecedent procedure related to coronary artery disease during the follow-up period. Possible deaths from coronary heart disease were those consistent with the condition but without an identifiable nonatherosclerotic cause. Definite deaths from coronary heart disease were those with chest pain within the previous 72 hours or a history of chronic ischemic heart disease, without valvular disease or nonischemic cardiomyopathy. For some analyses, events were classified as coronary events (myocardial infarction, revascularization, and death from coronary heart disease) or cerebrovascular events (stroke and death from cerebrovascular causes). Although some women had more than one type of event, no analysis included multiple events per subject.

Our principal hypothesis concerned levels of $PM_{2.5}$. Single-pollutant and multipollutant models were fit to investigate possible independent or joint effects of other pollutants (see the Supplementary Appendix).

SENSITIVITY ANALYSES

We performed sensitivity analyses that excluded subjects living more than 10 mi (16 km) from a monitor or residing for fewer than 20 years in their current state. Other sensitivity analyses included and excluded coronary revascularization and other outcomes; examined a larger group of cardiovascular events, with the addition of angina pectoris, congestive heart failure, transient ischemic attack, other carotid artery disease, and deaths from all cardiovascular causes; and excluded cities with the highest variation of within-city exposure or the lowest exposure concentration (see the Supplementary Appendix).

STATISTICAL ANALYSIS

We used Cox proportional-hazards regression to estimate hazard ratios and 95% confidence intervals (CIs) for the time to the first cardiovascular event associated with an elevation of 10 μg per cubic meter in the level of long-term exposure to $PM_{2.5}$. In all models, we included factors that we hypothesized a priori could potentially confound the relationship between air pollution and cardiovascular disease. These factors included age, body-mass index (BMI), smoking status, the number of cigarettes smoked per day, the number of years of smoking, systolic blood pressure, educational level, household income, race or ethnic group, and presence or absence of diabetes, hypertension, or hypercholesterolemia. Models were stratified with use of separate baseline hazards according to current treatment for diabetes, age, and BMI. We also evaluated other characteristics previously associated with the risk of cardiovascular disease — including presence or absence of environmental tobacco smoke, occupation, physical activity, diet, alcohol consumption, waist circumference, waist-to-hip ratio, medical history, medications, and presence or absence of a family history of cardiovascular disease — as possible confounders in extended models.

Interactions between exposure and factors that could modify the association between air pollution and the incidence of cardiovascular disease were evaluated with partial-likelihood ratio tests. For tests of linear trend using the partial-likelihood method, potential effect modifiers measured as continuous variables (such as BMI, waist-to-hip ratio, and waist circumference) or as ordered categorical variables (such as household income, educational level, and years lived in state) were grouped into quintiles.

We created exposure variables to estimate between-city and within-city effects. Exposures for all women in a metropolitan area were averaged into a weighted citywide exposure. Two approaches were used to estimate the within-city effects as part of the overall exposure–effect relationship.

One approach fit indicator variables for each metropolitan area, which we term "city-adjusted." The other approach subtracted the weighted citywide mean exposure, which we termed "within-city" (see the Supplementary Appendix for details). Data were analyzed with the use of SAS software (version 8.0, SAS Institute) and Stata software (version 8.0, Stata).

RESULTS

STUDY SUBJECTS

Of the 93,676 subjects, 72,569 had no cardiovascular disease at baseline. Of those women, 65,893 (90.8%) returned a follow-up questionnaire, met our residence criteria, and were assigned $PM_{2.5}$ exposure data. We recorded 349,643 women-years of follow-up for the 58,610 women with complete information for the main analytical variables (88.9% of those who were eligible).

Most of the subjects were white (83.1%), and the median age at enrollment was 63 years. The characteristics of the subjects were similar in most respects across categories of $PM_{2.5}$ exposure (Table 1). Race and ethnic group and socioeconomic measures were distributed somewhat unevenly across exposure categories. Current smoking was rare (reported by 6.1% of the subjects), and half of the cohort reported never having smoked. Stable long-term residential location was typical; 85.7% of the subjects had lived for 20 years or more in their current state.

EXPOSURE TO POLLUTION

We linked each woman in the study to one of 573 $PM_{2.5}$ monitors operating in the year 2000, with

Table 1. Characteristics of Study Subjects and Events, According to the Quintile of Exposure to Fine Particulate Matter ($PM_{2.5}$).*

Characteristic	Quintile of Level of $PM_{2.5}$				
	3.4–10.9 $\mu g/m^3$ (N=12,906)	11.0–12.4 $\mu g/m^3$ (N=13,139)	12.5–14.2 $\mu g/m^3$ (N=13,568)	14.3–16.4 $\mu g/m^3$ (N=13,035)	16.5–28.3 $\mu g/m^3$ (N=13,245)
Cardiovascular and cerebrovascular events†	353	424	453	460	423
Age — yr	63.1±7.3	63.9±7.2	63.1±7.2	62.8±7.3	62.9±7.4
Race or ethnic group — %‡					
American Indian	0.6	0.5	0.2	0.3	0.2
Asian or Pacific Islander	10.4	1.1	1.9	1.2	2.3
Black	2.1	2.5	5.9	15.2	14.9
Hispanic	8.1	3.4	3.8	2.1	2.9
White	77.4	91.4	87.4	80.5	78.6
Other	1.5	1.1	0.8	0.8	1.2
Education — %					
Not high-school graduate	5.6	4.5	3.9	4.6	4.9
Graduate of high school or trade school or GED	27.8	27.4	24.4	24.5	23.3
Some college or associate degree	28.0	28.2	24.3	24.4	27.0
Bachelor's degree or higher	38.5	40.0	47.4	46.6	44.9
Household income — %					
<$20,000	15.2	13.4	11.5	14.6	14.4
$20,000–49,999	43.2	45.7	39.8	39.4	40.2
≥$50,000	38.5	37.9	46.0	43.4	42.0
Respondent did not know	3.2	3.1	2.8	2.7	3.4
Married — %	65.8	65.1	64.2	60.3	59.8
BMI	26.9±5.6	27.1±5.5	26.9±5.7	27.2±6.0	27.1±6.0
Smoking history — %					
Former smoker	40.9	43.6	44.0	42.3	41.4
Current smoker	5.7	5.6	5.5	7.0	6.7

a median of 20 monitors per city (range, 4 to 78) (Table 2). Most women lived within 6 mi (10 km) of a monitor. The overall median concentration of fine particle pollution was 13.4 μg per cubic meter (interquartile range, 11.6 to 18.3). The minimum concentration (3.4 μg per cubic meter) was observed in Honolulu, and the maximum (28.3 μg per cubic meter) in Riverside, California.

CARDIOVASCULAR EVENTS

A total of 1816 women had one or more cardiovascular events during the study (Table 3). An increase in exposure of 10 μg per cubic meter in the level of $PM_{2.5}$ was associated with an adjusted hazard ratio of 1.24 (95% CI, 1.09 to 1.41) for the time to the first cardiovascular event. Within-city estimates tended to be larger than between-city estimates, but the differences were not significant (P=0.07); the city-adjusted approach and the estimate of within-city effects yielded similar results (1.69 and 1.64, respectively). A similar pattern emerged for coronary heart disease and cerebrovascular events.

The magnitude of effects observed was largest for mortality end points (Table 3). The strongest overall association was with death definitely associated with coronary heart disease (hazard ratio, 2.21; 95% CI, 1.17 to 4.16), the fatal event characterized by greatest diagnostic certainty. The effect size increased across the range of exposure concentrations that were measured (Fig. 1). We did not observe associations between other pollutants and cardiovascular disease in single-pollutant models, and adjustment for other mea-

Table 1. (Continued.)

Characteristic	Quintile of Level of $PM_{2.5}$				
	3.4–10.9 μg/m³ (N=12,906)	11.0–12.4 μg/m³ (N=13,139)	12.5–14.2 μg/m³ (N=13,568)	14.3–16.4 μg/m³ (N=13,035)	16.5–28.3 μg/m³ (N=13,245)
Physical activity — MET/wk	14.3±14.9	14.3±14.6	14.6±14.5	14.0±14.6	13.5±14.4
Hypertension — %	29.8	29.3	28.1	30.0	30.8
Diabetes mellitus — %	5.0	3.8	3.7	4.9	4.8
Hypercholesterolemia — %	13.3	12.7	12.1	12.4	13.1
Waist circumference — cm	83.9±13.3	84.5±13.1	84.0±13.2	84.2±13.5	84.5±13.7
Hormone-replacement therapy — %					
Past use	19.8	20.5	20.0	19.4	20.1
Current use	53.2	49.6	43.4	48.8	51.1
Alcohol consumption — no. of drinks/wk	2.5±5.0	2.9±5.7	2.7±5.2	2.5±5.0	2.4±5.1
Time lived in current state — %					
≤9 yr	9.6	7.4	4.1	6.8	5.3
10–19 yr	10.0	7.6	5.7	7.9	7.3
≥20 yr	80.4	85.0	90.2	85.3	87.3
Time spent outdoors (summer) — %					
<30 min/day	31.7	30.8	30.2	31.5	33.7
30 min to 2 hr/day	49.0	49.8	49.6	49.6	49.6
>2 hr/day	19.4	19.5	20.2	18.9	16.7
Time spent outdoors (nonsummer) — %					
<30 min/day	37.2	37.8	38.2	37.9	38.2
30 min to 2 hr/day	50.4	50.0	50.8	51.0	50.7
>2 hr/day	12.5	12.2	11.0	11.1	11.0

* A total of 2113 events are listed for the 65,893 women in the study, even though 7283 of the women had missing data for at least one covariate. Therefore, the main analyses were conducted on data for only 1816 events among 58,610 women. Plus–minus values are means ±SD. Percentages may not total 100 because of rounding. GED denotes general equivalency diploma, BMI body-mass index (the weight in kilograms divided by the square of the height in meters), and MET metabolic equivalent.
† Events include myocardial infarction, revascularization, stroke, and death from coronary heart disease or cerebrovascular disease.
‡ Race or ethnic group was reported by the subjects.

Table 2. Average Concentrations of Fine Particulate Matter ($PM_{2.5}$) Measured near the Homes of 65,893 Subjects (Year 2000).*

$PM_{2.5}$ Exposure	Concentration		
	Mean	10th and 90th Percentiles	Range
		$\mu g/m^3$	
Individual exposure	13.5±3.7	9.1 to 18.3	3.4 to 28.3
Citywide average exposure	13.5±3.3	9.3 to 17.8	4.0 to 19.3
Difference between individual exposure and citywide average exposure	0±1.6	−1.6 to 1.7	−11.5 to 11.7

* Plus–minus values are means ±SD. The median distance between the location of monitors and the residences of subjects was 5.6 mi (9.0 km). A total of 573 monitors were used, with a median of 20 (range, 4 to 78) per city.

Table 3. Estimated Hazard Ratios for the Time to the First Cardiovascular Event or Death Associated with an Exposure Increase of 10 μg per Cubic Meter in the Level of Fine Particulate Matter ($PM_{2.5}$).*

Outcome	No. of Events	Hazard Ratio (95% CI)		
		Overall	Between Cities	Within Cities
First cardiovascular event				
Any cardiovascular event†	1816	1.24 (1.09–1.41)	1.15 (0.99–1.32)	1.64 (1.24–2.18)
Coronary heart disease‡	1268	1.21 (1.04–1.42)	1.13 (0.95–1.35)	1.56 (1.11–2.19)
Cerebrovascular disease§	600	1.35 (1.08–1.68)	1.20 (0.94–1.54)	2.08 (1.28–3.40)
Myocardial infarction	584	1.06 (0.85–1.34)	0.97 (0.75–1.25)	1.52 (0.91–2.51)
Coronary revascularization	949	1.20 (1.00–1.43)	1.14 (0.93–1.39)	1.45 (0.98–2.16)
Stroke	554	1.28 (1.02–1.61)	1.12 (0.87–1.45)	2.08 (1.25–3.48)
Death from cardiovascular cause				
Any death from cardiovascular cause	261	1.76 (1.25–2.47)	1.63 (1.10–2.40)	2.28 (1.10–4.75)
Coronary heart disease				
Definite diagnosis	80	2.21 (1.17–4.16)	2.22 (1.06–4.62)	2.17 (0.60–7.89)
Possible diagnosis	59	1.26 (0.62–2.56)	1.20 (0.54–2.63)	1.57 (0.29–8.51)
Cerebrovascular disease	122	1.83 (1.11–3.00)	1.58 (0.90–2.78)	2.93 (1.03–8.38)

* All analyses evaluated the time until the first event in the category. All estimates were adjusted for age, race or ethnic group, educational level, household income, smoking status, systolic blood pressure, body-mass index, and presence or absence of diabetes, hypertension, or hypercholesterolemia.
† Events include myocardial infarction, coronary revascularization, stroke, death from coronary heart disease (both definite and possible diagnosis), and cerebrovascular disease. The sum of events in each category may be greater than the total number of events, since some subjects had both coronary and cerebrovascular events.
‡ Events include myocardial infarction, coronary revascularization, and death from coronary heart disease.
§ Events include stroke and death from cerebrovascular disease.

sured pollutants did not attenuate the findings for $PM_{2.5}$.

SENSITIVITY ANALYSES

A sensitivity analysis incorporating a random-effect term for each city allowed for the possibility that effects might vary from city to city in the estimation of the main effect and its variance for each of the overall, between-city, and within-city effects. Results from this sensitivity analysis were consistent with the primary analysis. The effect estimates were not diminished, and in all cases, the lower confidence limits above 1 did not decrease (see the Supplementary Appendix). Adjustment for additional covariates (i.e., presence or absence of environmental tobacco smoke, occu-

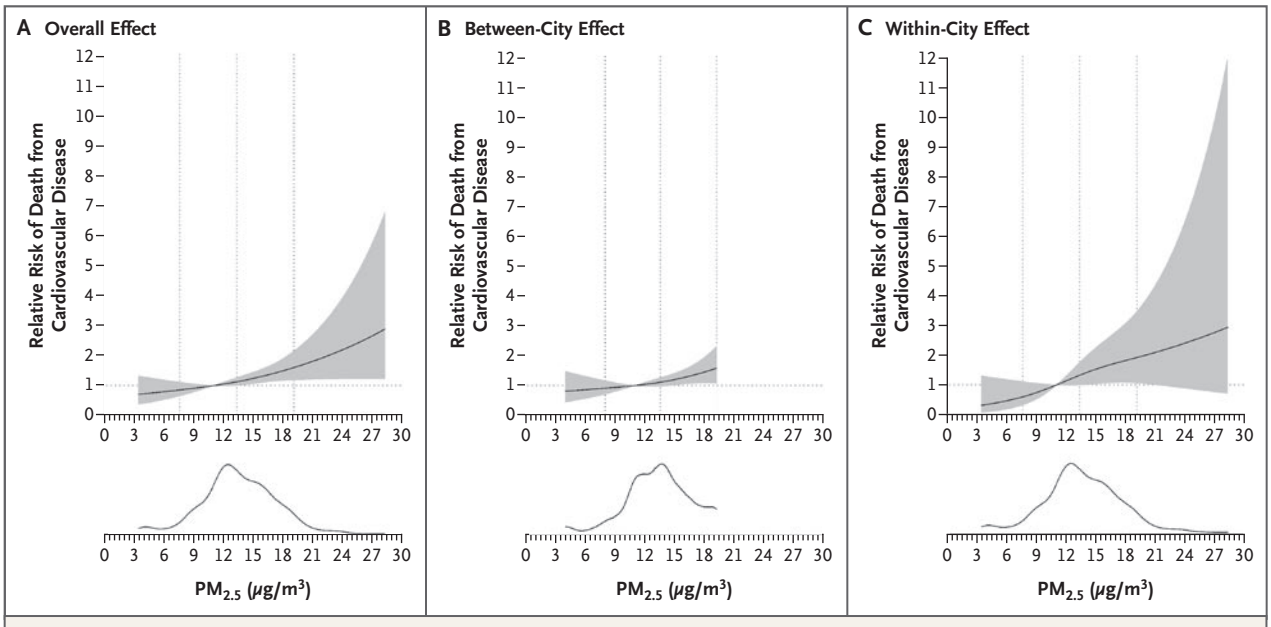

Figure 1. Level of Exposure to Fine Particulate Matter and the Risk of Death from Cardiovascular Causes in Women.

The graphs demonstrate the observed relationship between the risk of death from cardiovascular disease and the level of particulate matter of less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$), including both definite and possible deaths from coronary heart disease or cerebrovascular disease. Panel A shows the overall relationship between the $PM_{2.5}$ level and death, Panel B the effects between metropolitan areas, and Panel C the effects within metropolitan areas, with an indicator variable used to adjust for each city. These results suggest a generally linear relationship between exposure and risk, though the 95% confidence intervals (shaded areas) are wide at the extremes of exposure. Risk is depicted in comparison with a reference value of 11 μg per cubic meter. The histogram in each panel illustrates the density of exposure distribution for air pollution. All estimates are adjusted for age, race or ethnic group, educational level, household income, smoking status, systolic blood pressure, body-mass index, and presence or absence of a history of diabetes, hypertension, or hypercholesterolemia.

pation, physical activity, diet, the use or nonuse of dietary supplements, use or nonuse of alcohol, household income, waist circumference, waist-to-hip ratio, medical history, medications, and presence or absence of a family history of cardiovascular disease) did not substantially change the risk estimates.

SUSCEPTIBILITY TO EFFECTS OF AIR POLLUTION

Differences in the relationship between $PM_{2.5}$ and cardiovascular disease according to the characteristics of the subjects are summarized in Table 4. The association between cardiovascular events and the level of $PM_{2.5}$ increased with increasing categories of BMI and waist-to-hip ratio and with a shorter duration of residence in the current state.

DISCUSSION

In a large, prospective cohort of postmenopausal women, long-term (annual average) exposure to increased concentrations of fine particulate air pollution was associated with an increased risk of first cardiovascular events. The increased risk applied to nonfatal and fatal cardiovascular events, including both coronary and cerebrovascular events. We found that estimates of effects within cities were often larger than those of effects between cities; the latter had been the primary measure in previous U.S. studies of long-term exposure to pollutants.

The risk of death associated with higher levels of $PM_{2.5}$ was generally larger than the risk of all first events; it was also larger than mortality estimates reported in previous U.S. cohort studies that used only death certificates. For death from cardiovascular causes (including coronary heart disease and cerebrovascular disease), we estimated an overall 76% increase in risk with each increase of 10 μg per cubic meter in long-term $PM_{2.5}$ exposure — accounting for subjects in approximately the 10th to 90th percentiles for exposure.

Our measurement of the between-city effect is similar to that in the American Cancer Society's

Table 4. Estimated Hazard Ratios for Cardiovascular Events Associated with an Increase of 10 μg per Cubic Meter in the Level of Fine Particulate Matter ($PM_{2.5}$), According to Selected Characteristics.*

Characteristic	No. of Subjects with Event	Hazard Ratio (95% CI)	P Value	Hazard Ratio Adjusted for City (95% CI)†	P Value
Subjects with any cardiovascular event	1816	1.24 (1.09–1.41)		1.69 (1.26–2.27)	
Household income			0.64		0.81
<$20,000	388	1.30 (1.10–1.53)		1.75 (1.28–2.40)	
$20,000–49,999	886	1.23 (1.08–1.41)		1.69 (1.25–2.27)	
≥$50,000	542	1.20 (1.02–1.40)		1.66 (1.22–2.26)	
P for trend		0.34		0.54	
Education			0.22		0.31
Not high-school graduate	112	1.40 (1.11–1.75)		1.88 (1.32–2.67)	
Graduate of high school or trade school or GED	575	1.33 (1.14– 1.55)		1.79 (1.32–2.44)	
Some college or associate degree	514	1.26 (1.09–1.44)		1.74 (1.29–2.34)	
Bachelor's degree or higher	615	1.11 (0.94–1.31)		1.54 (1.13–2.10)	
P for trend		0.07		0.15	
Age			0.50		0.42
<60 yr	234	1.21 (0.84–1.73)		1.66 (1.05–2.61)	
60–69 yr	785	1.14 (0.93–1.39)		1.53 (1.09–2.14)	
≥70 yr	797	1.34 (1.11–1.63)		1.85 (1.34–2.56)	
P for trend		0.20		0.20	
Smoking status			0.36		0.38
Current smoker	150	1.68 (1.06–2.66)		2.28 (1.33–3.92)	
Former smoker	750	1.24 (1.01–1.52)		1.71 (1.23–2.39)	
Never smoked	916	1.18 (0.99–1.40)		1.60 (1.16–2.21)	
Living with smoker			0.55		0.51
Currently	158	1.28 (0.84–1.97)		1.65 (0.99–2.76)	
Formerly	1206	1.18 (1.00–1.38)		1.59 (1.16–2.16)	
Never	436	1.39 (1.07–1.80)		1.90 (1.31–2.78)	
Body-mass index			0.02		0.02
<22.5	227	0.99 (0.80–1.21)		1.35 (0.96–1.88)	
22.5–24.7	337	1.16 (0.96–1.40)		1.58 (1.14–2.19)	
24.8–27.2	359	1.24 (1.05–1.45)		1.69 (1.24–2.30)	
27.3–30.9	439	1.38 (1.18–1.61)		1.88 (1.38–2.56)	
>30.9	454	1.35 (1.12–1.64)		1.84 (1.33–2.55)	
P for trend		0.003		0.004	
Waist-to-hip ratio			0.05		0.04
<0.74	199	1.07 (0.90–1.29)		1.45 (1.05–2.00)	
0.74–0.77	272	1.12 (0.95–1.31)		1.51 (1.11–2.06)	
0.78–0.80	305	1.24 (1.07–1.44)		1.68 (1.23–2.27)	
0.81–0.86	482	1.30 (1.13–1.50)		1.76 (1.30–2.38)	
>0.86	558	1.29 (1.11–1.50)		1.75 (1.29–2.37)	
P for trend		0.008		0.007	

Table 4. (Continued.)

Characteristic	No. of Subjects with Event	Hazard Ratio (95% CI)	P Value	Hazard Ratio Adjusted for City (95% CI)†	P Value
Waist circumference			0.09		0.11
<73 cm	203	1.05 (0.86–1.27)		1.43 (1.02–1.99)	
73–78 cm	295	1.20 (1.02–1.41)		1.63 (1.19–2.23)	
79–85 cm	373	1.22 (1.05–1.41)		1.66 (1.22–2.24)	
86–95 cm	452	1.33 (1.15–1.53)		1.80 (1.33–2.43)	
>95 cm	493	1.27 (1.07–1.51)		1.73 (1.26–2.36)	
P for trend		0.06		0.07	
Hormone-replacement therapy			0.32		0.25
Current use	704	1.33 (1.09–1.61)		1.85 (1.32–2.58)	
No current use	1077	1.16 (0.98–1.39)		1.57 (1.14–2.17)	
Diabetes			0.13		0.08
Yes	219	0.96 (0.67–1.37)		1.24 (0.78–1.96)	
No	1597	1.28 (1.12–1.47)		1.75 (1.30–2.36)	
Hypertension			0.79		0.69
Yes	935	1.22 (1.02–1.45)		1.65 (1.09–2.27)	
No	881	1.26 (1.05–1.51)		1.74 (1.25–2.40)	
Hypercholesterolemia			0.92		0.94
Yes	333	1.25 (0.94–1.67)		1.71 (1.15–2.54)	
No	1483	1.23 (1.07–1.42)		1.69 (1.25–2.28)	
Family history of cardiovascular disease			0.19		0.19
Yes	1359	1.30 (1.12–1.51)		1.80 (1.32–2.44)	
No	436	1.07 (0.83–1.37)		1.46 (1.00–2.12)	
Time lived in current state			0.39		0.23
≥20 yr	1585	1.21 (1.06–1.39)		1.66 (1.23–2.23)	
10–19 yr	114	1.39 (1.12–1.72)		1.97 (1.40–2.79)	
≤9 yr	108	1.54 (1.06–2.26)		2.24 (1.39–3.59)	
P for trend		0.05		0.02	
Health insurance coverage			0.33		0.30
Yes	1763	1.22 (1.07–1.39)		1.71 (1.27–2.30)	
No	42	1.82 (0.81–4.10)		2.65 (1.12–6.28)	
Time spent outdoors			0.35		0.33
<30 min	510	1.09 (0.86–1.39)		1.56 (1.05–2.31)	
≥30 min	945	1.26 (1.05–1.50)		1.82 (1.29–2.57)	

* All estimates were adjusted for age, race or ethnic group, educational level, household income, smoking status, systolic blood pressure, body-mass index, and presence or absence of a history of diabetes, hypertension, or hypercholesterolemia. Data were missing for some subjects, so the number of subjects in each category may not total 1816.
† The city-adjusted models included an indicator variable for each metropolitan area.

Cancer Prevention Study II[4] and the Harvard Six Cities Study.[3] The between-city hazard ratio was 1.63 for death from cardiovascular causes as defined in our study and 1.42 for the broader definition similar to that used in the other two studies. In the independent reanalysis,[6] the estimated hazard ratio for death from all cardiovascular causes associated with an increase of 10 μg per cubic meter in long-term $PM_{2.5}$ exposure was 1.19 (95% CI, 1.05 to 1.34) in the Six Cities Study and

1.13 (95% CI, 1.08 to 1.18) in the American Cancer Society's study. However, subjects in those cohorts differed substantially from ours, especially by the inclusion of men and persons with previous cardiovascular disease. The larger effect sizes observed for levels of $PM_{2.5}$ in our study may be due to these factors or to our efforts to reduce misclassification of outcomes and exposures. However, other studies have suggested greater effects of particulate air pollution in women than in men.[16,21] The increased association we observed between the $PM_{2.5}$ level and death from cardiovascular causes, as compared with all cardiovascular events, could be related to methodologic considerations, such as a reduced misclassification of fatal events. Alternatively, fine particulate exposures could exert effects that disproportionately result in fatal events (such as arrhythmic events or hemorrhagic stroke), as compared with nonfatal cardiovascular events.

In addition to the increased risk of coronary heart disease, we identified an association between long-term exposure to air pollution and the incidence of cerebrovascular disease. For each increase of 10 μg per cubic meter of exposure, there was a 35% increase in the risk of cerebrovascular events and an 83% increase in the risk of death from cerebrovascular causes. Previous evidence in this area included ecologic studies suggesting that the rate of death from stroke may be elevated in areas near main roads or with increased pollution,[22,23] and short-term exposure has been linked to stroke, for example.[24]

We observed a stronger association between the $PM_{2.5}$ level and cardiovascular disease with increasing obesity, as measured by either the BMI or the waist-to-hip ratio. These findings require replication. In contrast to the findings in the American Cancer Society's study,[4,6] we observed a uniform pollution-related risk of cardiovascular events across age groups, possibly because of the greater homogeneity of subjects in our study.

Our study benefited from well-defined outcomes, extensive data regarding risk factors for cardiovascular disease, and long-term geographic stability of a cohort without previous cardiovascular disease. Critics of earlier studies have suggested that poorly measured or unmeasured confounding factors may vary from city to city and account, at least in part, for the observed city-to-city differences in death rates associated with air pollution.[25] We ascertained key characteristics of subjects that might confound the relationship with exposure, and study results were not sensitive to adjustment for these characteristics, although some residual confounding cannot be excluded. Aspects of our analytic approach also reduce the concern over confounding, such as our examination of the between-city and within-city components of exposure. We controlled for the factors that vary from city to city (e.g., imperfectly measured subject characteristics, the composition or toxicity of particulate matter, and particle infiltration) in the analysis, which included a city indicator variable. By investigating many potential covariates, and by including both within-city and between-city exposures, we provided confirmation of the observed association between long-term exposure to air pollution and cardiovascular disease.

The role of socioeconomic status has received attention in air-pollution epidemiology. Beyond controlling for educational level and household income, our results were not sensitive to further adjustment for occupation or Census-derived measures of income, wealth, or poverty on the basis of ZIP Code. Neither educational level nor household income significantly modified the relationship between air pollution and cardiovascular disease, although there was a trend toward greater effects among those with less education.

Since our study included a large number of women who lived in many locales, regional or smaller-scale differences in medical practice might have influenced our findings, particularly regarding coronary revascularization. However, the results did not change when revascularization procedures were not included in the analysis. Furthermore, it is possible that women living close to one another may be more similar than those living farther apart, which could affect the variance estimation. However, we found no evidence that such a bias influenced our results.

Our assessment of exposure remains necessarily limited, since exposure levels were assigned from one monitor with the use of the subjects' primary residential ZIP Codes, which could potentially introduce some inaccuracy. The degree to which ambient pollution monitors represent the exposures of the subjects is imperfect, though we took measures to exclude nonrepresentative monitors. We were unable to assess microclimate differences in exposure, whether some participants may have moved, or details regarding the

subjects' activity and location, such as time spent in traffic and indoors. These factors contribute to errors in measurement and misclassification of exposure but are unlikely to have introduced a bias that would explain the study's findings.

We used data regarding $PM_{2.5}$ levels from a single year at the midpoint of follow-up, rather than a baseline or multiyear average, because of the presence of a much greater number of measuring stations in the year 2000 than at other times. Concentrations of particulate pollution were stable during the period under study; year-to-year $PM_{2.5}$ values were very highly correlated during years available (Pearson's correlation, ≥0.92). Analysis in the American Cancer Society's study showed a strong correlation between the sites at a 20-year interval and no time dependence of the hazard function, indicating that fine particulate pollution measured at any time during follow-up is a reasonable surrogate for the relevant exposure (long-term exposure to particulate matter).[26]

The mechanism by which long-term exposure to fine particulate air pollution may increase the risk of cardiovascular disease remains uncertain and the subject of intensive speculation and investigation.[1,14,27] Accelerated atherosclerosis and vulnerability to plaque rupture have been documented in an experimental model,[28] and ambient pollution has been correlated with carotid intima–media thickness in humans.[16]

Our results were specific to fine particulate pollution; we did not observe robust effects with other sizes of particulate matter or with other measured air pollutants (see the Supplementary Appendix). Finally, since we investigated long-term exposure and first cardiovascular events, the results in this cohort cannot be ascribed primarily to the short-term effects of increases in levels of pollution occurring on a day-to-day basis or to effects of pollution limited to those who were already ill.

Our study provides evidence of the association between long-term exposure to air pollution and the incidence of cardiovascular disease. Our study confirms previous reports and indicates that the magnitude of health effects may be larger than previously recognized. These results suggest that efforts to limit long-term exposure to fine particulate pollution are warranted.

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No potential conflict of interest relevant to this article was reported.

The views expressed in this article do not necessarily reflect the views or policies of the Environmental Protection Agency.

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