Fine Particulate Matter and Mortality

A Comparison of the Six Cities and American Cancer Society Cohorts With a Medicare Cohort

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Background: The American Cancer Society study and the Harvard Six Cities study are 2 landmark cohort studies for estimating the chronic effects of fine particulate air pollution ($PM_{2.5}$) on mortality. Using Medicare data, we assessed the association of $PM_{2.5}$ with mortality for the same locations included in these studies.

Methods: We estimated the chronic effects of $PM_{2.5}$ on mortality for the period 2000–2002 using mortality data for cohorts of Medicare participants and average $PM_{2.5}$ levels from monitors in the same counties included in the 2 studies. We estimated mortality risk associated with air pollution adjusting for individual-level (age and sex) and area-level covariates (education, income level, poverty, and employment). We controlled for potential confounding by cigarette smoking by including standardized mortality ratios for lung cancer and chronic obstructive pulmonary disease.

Results: Using the Medicare data, we estimated that a 10 $\mu g/m^3$ increase in the yearly average $PM_{2.5}$ concentration is associated with 10.9% (95% confidence interval = 9.0–12.8) and with 20.8% (14.8–27.1) increases in all-cause mortality for the American Cancer Society and Harvard Six Cities study counties, respectively. The estimates are somewhat higher than those reported by the original investigators.

Conclusion: Although Medicare data lack information on some potential confounding factors, we estimated risks similar to those in the previously published reports, which incorporated more extensive information on individual-level confounders. We propose that the Medicare files can be used to construct on-going cohorts for tracking the risk of air pollution over time.

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Epidemiologic studies have provided evidence that long-term exposure to airborne fine particulate matter, as indexed by the concentration of particulate matter less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$), is associated with chronic health effects including cardiovascular and respiratory diseases, and also with increased mortality.[1–6] Chronic effects of air pollution potentially encompass both the cumulative effects of long-term exposures and persistent effects of acute exposures.[7,8] Chronic effects of air pollution on human health have been estimated primarily with prospective cohort studies, but also with the case–control design (using retrospective estimation of exposure), particularly for lung cancer.[9,10]

The question of whether long-term exposure to air pollution increases risk for mortality has been addressed in cohort study data by testing whether the hazard is positively associated with time-averaged indicators of pollution exposure. The study data have typically included individual-level covariate information on potential confounding and modifying factors [eg, age, smoking, socioeconomic status (SES), and obesity], and exposure has been classified for geographically defined groups based on common residence location. For example, in the Harvard Six Cities Study (SCS), individual-level data were collected at baseline from samples of residents of 6 US cities and at periodic follow-up; in the initial report on mortality, pollution exposures were assigned to participants based on mean concentrations for the 6 cities over a 17-year follow-up.[1] The design of the American Cancer Society's (ACS) Cancer Prevention Study II was similar, but covariate data were collected only on enrollment, and exposure was assigned to the 50 metropolitan areas based on pollution concentrations measured during 1979–1983, over a follow-up interval that extended initially from 1982 to 1989. In the more recent follow-up reports of both cohorts, exposure information has been updated and the chronic effects of pollution over time have been re-estimated to assess whether the risk had changed.[3,5] Other cohort studies on long-term exposure to air pollution and mortality have been carried out.[11–14] However, the analyses reported to date from these studies have assessed the pollution-mortality relationship cross-sectionally, as did the initial analyses of data from the Six Cities and ACS Studies.[6]

We have used the Medicare files for 2000–2002 to create a cohort of persons age 65 years and older to assess

TABLE 1. Comparison of Characteristics of the Medicare Study Versus the American Cancer Society (ACS) Study and the Six Cities Study (SCS)

	Medicare	ACS and SCS
Study design	Open to enrollment	Closed to enrollment
Geographical areas	Counties	Metropolitan statistical areas
Population age	≥65 yrs	>25 yrs
Exposure	Measured $PM_{2.5}$ only	Measured $PM_{2.5}$ and estimated $PM_{2.5}$ from PM_{10}
Time scale of exposure	Concurrent with the study period	Preceding and concurrent with the study period
Individual-level risk factors	Age, sex	Age, race, sex, education, smoking, and more
Statistical model	Log-linear regression	Cox proportional hazards regression

morbidity and mortality risks associated with air pollution.[15] We have previously shown its potential utility in investigating acute exposure to $PM_{2.5}$ and risk for hospitalization.[15] Using this large data set, we have constructed 2 cohorts for the locations corresponding to those included in the ACS and Six Cities Studies, denoted as Med-ACS and Med-SCS, respectively. These 2 cohorts differ from the original analyses with respect to study design, study period, availability of individual and area-level confounders, and modeling approach (Table 1). The original cohorts were "closed" so that new members were not added after their inception, whereas Medicare has new enrollees each month and the Med-ACS and Med-SCS cohort populations are dynamic. In this paper we compare findings from these 2 new cohorts, drawn from Medicare participants, with the results from the 2 earlier cohort studies.

METHODS

From the Medicare enrollment files, we have constructed a cohort of about 40 million people with individual-level information on age, sex, race, and county of residence for the period 2000–2002. To account for residential history, we have included in the analysis only enrollees who did not change their address during the study period 1999–2002. The cohort is dynamic, including all new enrollees to Medicare during this interval. Using county of residence, we linked the Medicare participants to air pollution monitoring data from the US Environmental Protection Agency Air Quality System on $PM_{2.5}$. We calculated the mortality rates for the same geographical locations included in the original studies.

Table 2 summarizes the numbers of geographic locations, numbers of deaths and people at risk, mean levels of $PM_{2.5}$, and exposure periods of the Med-ACS, ACS, Med-SCS, and Harvard Six Cities. For the Med-ACS, we identify the 110 counties corresponding to the 50 metropolitan areas in the ACS.[2] These were identified from the list of counties that includes the cities and towns within the metropolitan areas' boundaries as given by Krewski et al.[16] For the Med-SCS, we identified the counties that include the 6 cities in the Harvard Six Cities.[1]

Figure 1 shows the locations of the 6 and 110 counties included in the Med-SCS and Med-ACS, respectively. We estimated yearly county-specific averages of $PM_{2.5}$ using only data based on measurements for at least 10 months of the year and at least 4 days per month, for the years 2000–2002. Specifically, we computed the 10% trimmed mean of the monitor-specific $PM_{2.5}$ concentrations for each county (excluding source-based monitors) and then computed the average of these concentrations across the study interval. For the ACS counties, $PM_{2.5}$ concentrations were not available for Chattanooga, TN and Omaha, NE. We assigned to these counties the $PM_{2.5}$ concentrations measured in the neighboring coun-

TABLE 2. Study Characteristics: Med-ACS, ACS,[3] Med-SCS, and SCS[5]

Characteristics	Med-ACS	ACS	Med-SCS	SCS
No. counties	110*	50†	6‡	6
No. subjects§	7,333,040	295,223	341,099	8096
No. deaths¶	1,122,311	62,000	54,160	2732
$PM_{2.5}$ ($\mu g/m^3$); mean (SD)	13.6 (2.8)	17.7 (3.7)	14.1 (3.1)	16.4‖ (5.6)‖
Range	6.0–25.1	9–33.5	9.6–19.1	10.2–29.0‖
Study period	2000–2002	1982–1998	2000–2002	1974–1998
Period of measured exposure	2000–2002	1979–1983, 1999–2000	2000–2002	1979–1988, 1990–1998

*Counties identified by the Reanalysis team[16] as being within the 50 metropolitan statistical areas included in the ACS.[2]
†These are metropolitan statistical areas.
‡The 6 counties that include the 6 cities in the SCS.
§The number of subjects for the Med-ACS and Med-SCS datasets is the number of persons at risk in year 2000. For ACS and SCS, it is the number of persons enrolled at the beginning of the study period.
¶Total deaths occurred during the entire study period. For ACS,[3] the number of deaths is approximately triple the number of deaths in the original ACS.[2]
‖Calculated based on Table 1 and Figure 1 from Laden et al.[5]
SD indicates standard deviation.

FIGURE 1. Locations of the counties included in the Med-ACS and Med-SCS. The diamonds represent the 110 locations corresponding to the 50 metropolitan areas included in the American Cancer Society study,[2] and the letters represent the 6 cities included in the Six Cities Study[1] Topeka KS (T), St. Louis MO (L), Steubenville OH (S), Watertown MA (W), Harriman TN (H), and Portage, WI (P).

ties: McMinn County, TN, and Polk County, IA. For the Harvard Six Cities counties, $PM_{2.5}$ concentrations were not available for Roane County, TN and Columbia County, WI, which include Harriman, TN and Portage, WI, respectively. For these 2 counties, we assigned the $PM_{2.5}$ values in the neighboring counties of Knox County, TN and Dane County, WI, respectively. As a sensitivity analysis, we estimated the chronic effects using the SMA as the geographical unit by aggregating the 110 Med-ACS counties to constitute the 50 metropolitan areas used in the ACS.

As indicators of area-level SES, we used: (1) the proportion of women and men with a college degree or higher; (2) the proportion of women and men with a high school degree or higher educational attainment; (3) the proportion of women and men who are unemployed; (4) the proportion of individuals below the poverty level in each age-group; and (5) the median income in the county, from the 2000 US Census. We selected these covariates to maximize comparability with the SES area-level covariates that were used in ACS and Harvard Six Cities.

As surrogates for area-level long-term smoking exposure, we calculated county-specific age-sex-race adjusted standardized mortality rates for chronic obstructive pulmonary disease (COPD) and lung cancer for the period 1992–2002 from the National Center Health Statistics.[17]

For each year, county of residence, and age-sex stratum, we calculated the number of all-cause deaths and the number of people at risk (Table 2). We stratified the study population in 6 strata defined by sex and 3 age groups (65–74, 75–84, and ≥85 years). Let Y^{sc} and μ^{sc} be the observed and expected number of all-cause deaths, and let N^{sc} be the number of people at risk in county c and age-sex stratum s. Let $\bar{x}^c$ be the average $PM_{2.5}$ for the 2000–2002 period. We fit the following log-linear regression model, allowing for age-sex stratum-specific intercepts and including the SES factors z^{sc}:

$$\log(\mu^{sc}) = \theta_0^s + \theta\bar{x}^c + \gamma z^{sc} + log(N^{sc}) \qquad (1)$$

The parameter $10 \times \theta$ denotes the log relative risk of mortality associated with a 10 $\mu g/m^3$ increase in longer-term average $PM_{2.5}$ adjusted for socioeconomic factors. We fit Model 1 to the Med-ACS and Med-SCS data, separately for each year and also for all 3 years combined. Estimation of Model 1 needs to account for 2 sources of correlation due to the repeated observations by age and sex within a county, and for the clustering of county-specific observations within geographical regions (spatial correlation). Robust standard errors were calculated to account for the correlation due to the repeated measures.[18] Poisson regression models with random effects were fitted to account for clustering of county-level observations within larger geographical regions.

As a sensitivity analysis, we explored the impact of exposure period on the results separately by year, regressing county-specific average of $PM_{2.5}$ for the period 1999–2001 on mortality rates for the period 2000–2002.

Data manipulation and analyses were performed using R, version 2.2.1 (R Development Core Team, 2005) and SAS software, version 9.1 (SAS Institute Inc., Cary, NC 2000).

RESULTS

Figure 2 shows the average $PM_{2.5}$ concentrations used in the ACS for the 1979–1983 period, plotted against the average $PM_{2.5}$ concentrations over the 2000–2002 time interval in the Med-ACS. As expected, in most counties average $PM_{2.5}$ was higher in the earlier ACS data compared with the later Med-ACS data. We found agreement among these measurements except for the noticeable outlier of Fresno, CA, which experienced an increase in $PM_{2.5}$ concentration.[19]

Figure 3 shows age- and sex-adjusted mortality rates plotted against average $PM_{2.5}$ over the 2000–2002 period for the 6 and 110 counties included in the Med-SCS and Med-ACS, respectively. These adjusted mortality rates were obtained by fitting Model 1 without including $PM_{2.5}$ and the SES covariates in the model. For both studies, the mortality rates tend to be higher in counties with higher average $PM_{2.5}$ values, although the 2 counties with the highest $PM_{2.5}$ values among the Med-ACS counties have relatively low mortality rates.

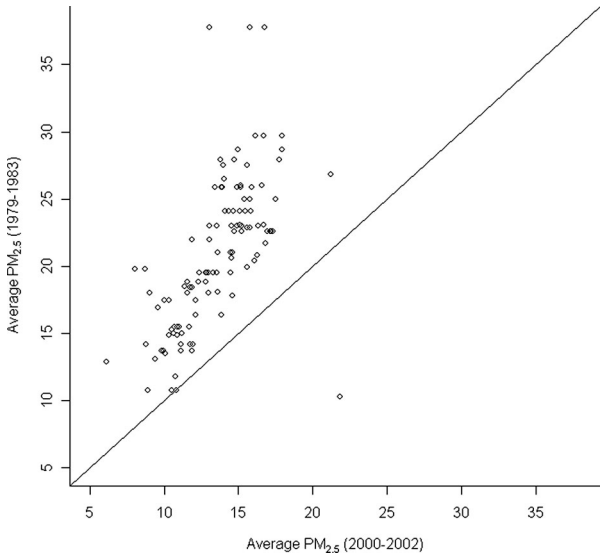

FIGURE 2. Average $PM_{2.5}$ over the years 1979–1983[2] versus average $PM_{2.5}$ over the years 2000–2002, for 110 U.S. counties.

Table 3 compares the results of the analyses of Med-SCS and Med-ACS with the first reports of the Harvard Six Cities and ACS, the reanalyses conducted for the Health Effects Institute, and the follow-up of the Harvard Six Cities and ACS. In the Med-SCS, we found that a 10 $\mu g/m^3$ increase in average $PM_{2.5}$ is associated with a 20.8% increase in the overall mortality rate [95% confidence interval (CI) = 14.8–27.1], adjusted for age and sex. In the Med-ACS, we estimated that a 10 $\mu g/m^3$ increase in average $PM_{2.5}$ is associated with a 10.8% increase in the mortality rate (8.6–13.0), adjusted for age and sex. Without adjustment for area-level covariates, the Med-SCS and Med-ACS provide results similar to the ACS and Harvard Six Cities. In the Med-ACS, with adjustment for area-level covariates, we estimated a 10.9% increase in the mortality rate (9.0–12.8), slightly larger than the ACS estimates from the reanalysis.[16] Estimates from the Med-ACS with the 50 SMAs as geographical units were smaller than from the Med-ACS with the 110 counties and much closer to the ACS estimates.

Table 4 summarizes the results of the Med-SCS and Med-ACS by year and for all years combined, with and without adjustment for area-level SES covariates and with and without adjustment for the SMRs for COPD and lung cancer. The results were similar across years and robust to adjustment for these area-level variables. We also used the average $PM_{2.5}$ over the period 1999–2001 as the exposure measure, and found that the results were unchanged (results not included). Table 5 gives the sensitivity of the estimates to alternative models for the adjustment of area-level SES covariates. Results were not sensitive to the adjustment.

DISCUSSION

We have compared risk estimates from 2 well-known cohort studies (ACS and Harvard Six Cities) with estimates from 2 cohorts drawn from Medicare enrollees in the same

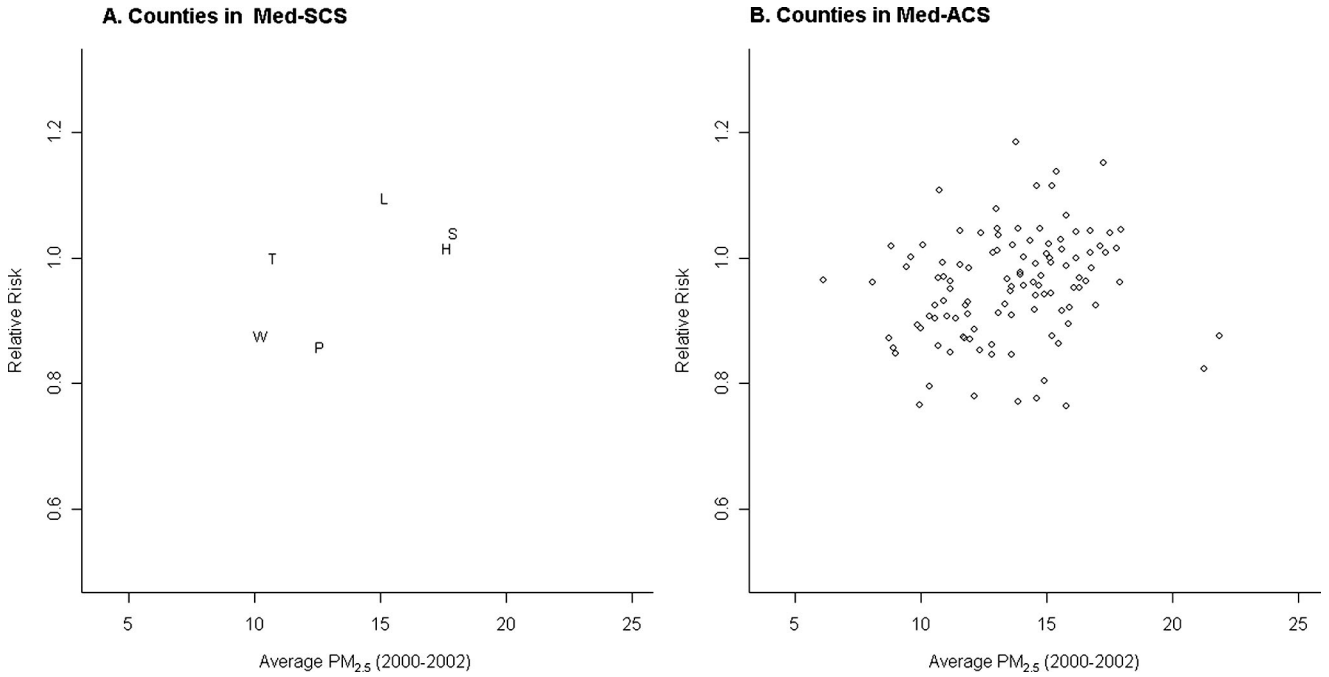

FIGURE 3. Adjusted mortality relative risk estimates plotted against average $PM_{2.5}$ for (A) the 6 Med-SCS and (B) the 110 Med-ACS counties. T denotes Topeka, KS (the reference city for all plots); W Watertown, MA; L St. Louis, MO; S Steubenville, OH; H Harriman, Tennessee; P Portage, Wisconsin.

TABLE 3. Comparison of Results Across Studies: Estimated Percent Increase in Mortality Rate per 10 $\mu g/m^3$ Increase in $PM_{2.5}$

Study	Primary Source	Duration of Measured Exposure ($PM_{2.5}$)	Change in Mortality Risk per 10 $\mu g/m^3$ Increase in Average $PM_{2.5}$ (95% CI)
SCS*	Dockery et al.[1]	1979–1988	13.2 (4.2–23.0)
SCS†	Krewski et al.[16]	1979–1988	16.6 (7.3–26.1)
SCS*	Laden et al.[5]	1979–1988, 1990–1998	16.0 (7.0–26.0)
Med-SCS†		2000–2002	20.8 (14.8–27.1)
ACS‡	Pope et al.[2]	1979–1983	6.6 (3.5–9.8)
ACS§	Krewski et al.[16]	1979–1983	10.2 (7.0–13.7)
ACS¶	Krewski et al.[16]	1979–1983	7.4 (4.4–10.6)
ACS‖	Pope et al.[3]	1979–1983, 1999–2000	6.2 (1.6–11.0)
Med-ACS†		2000–2002	10.8 (8.6–13.0)
Med-ACS**		2000–2002	10.9 (9.0–12.8)
Med-ACS††		2000–2002	6.3 (3.8–8.9)
Med-ACS**††		2000–2002	8.9 (6.9–10.9)

*Adjusted for individual-level age, sex, cigarette smoking, BMI, education.
†Adjusted for individual-level age and sex.
‡Adjusted for individual-level age, sex, cigarette smoking, BMI, education, race, alcohol consumption, and occupational exposure.
§Adjusted for individual-level age, race, and sex.
¶Adjusted for population change, income, poverty, income disparity, unemployment, and education See Table 47, Part II.[10]
‖Adjusted for age, sex, race, cigarette smoking, body-mass index, education, alcohol consumption, marital status, diet, and occupational exposure.
**Adjusted for individual-level age and sex, and for area-level education, income, poverty, and employment.
††Includes the 50 original SMAs form ACS, aggregated from the 110 locations in Med-ACS.

geographic locations (Med-SCS and Med-ACS). In comparison with the original studies, the Med-SCS and Med-ACS cohorts differed in the exposure data used and in the timing of data collection in relation to outcome events. Risk estimates for the Medicare cohorts were adjusted only for age and sex at the individual level and for smoking and SES at the county level. As surrogate measures of area-level exposure to smoking, we constructed age- and sex-adjusted SMRs for

TABLE 4. Estimated Percent Increase in Mortality Rate per 10 $\mu g/m^3$ Increase in $PM_{2.5}$ by Year and for Exposure Period 2000–2002

Model	Overall % Increase (95% CI)	Years		
		2000 % Increase (95% CI)	2001 % Increase (95% CI)	2002 % Increase (95% CI)
Med-ACS*	10.8 (8.6–13.0)	10.9 (7.3–14.6)	9.1 (5.3–12.7)	10.1 (6.0–14.3)
Med-SCS*	20.8. (14.8–27.1)	17.8 (9.8–26.4)	16.5 (7.4–25.0)	33.5 (19.2–49.3)
Med-ACS†	10.9 (9.0–12.8)	11.4 (8.5–14.3)	8.7 (5.4–11.5)	10.4 (6.8–14.0)
Med-ACS†‡	8.1 (4.7–11.8)	13.8 (7.6–20.4)	8.3 (3.3–14.6)	10.4 (4.5–16.6)
Med-ACS* + COPD	10.4 (8.2–12.6)	10.6 (7.1–14.3)	8.6 (4.9–12.1)	9.5 (5.5–13.7)
Med-ACS* + LC	10.4 (8.2–12.6)	10.5 (7.0–14.1)	8.6 (4.9–12.2)	9.6 (5.6–13.7)
Med-ACS† + COPD	10.6 (8.7–12.5)	11.2 (8.3–14.1)	8.3 (5.1–11.2)	10.0 (6.4–13.6)
Med-ACS† + LC	10.6 (8.7–12.6)	11.1 (8.3–14.1)	8.4 (5.2–11.3)	10.0 (6.5–13.7)
Med-ACS*§	6.3 (3.8–8.9)	6.4 (2.4–10.7)	5.0 (0.7–9.2)	5.6 (1.0–10.4)
Med-ACS†§	8.9 (6.9–10.9)	10.6 (7.7–13.6)	7.0 (3.5–9.9)	8.8 (5.0–12.8)

*Adjusted for individual-level age and sex.
†Adjusted for individual-level age and sex, and for area-level education, income, poverty, and employment.
‡Random effects model accounting for the clustering of counties within regions.
§Includes the 50 original SMAs form ACS, aggregated from the 110 locations in Med-ACS.

TABLE 5. Estimated Percent Increase in Mortality Rate per 10 $\mu g/m^3$ Increase in $PM_{2.5}$ by Year and for Exposure Period 2000–2002 Under Several Models for the Adjustment of Area-Level Covariates

Model	Overall % Increase (95% CI)	Years		
		2000 % Increase (95% CI)	2001 % Increase (95% CI)	2002 % Increase (95% CI)
PM only	7.5 (−4.0 to 20.3)	7.4 (−10.2 to 28.5)	6.3 (−13.3 to 27.1)	6.6 (−13.9 to 32.1)
* + Phigh	8.4 (6.2 to 10.7)	9.7 (6.2 to 13.2)	6.5 (2.8 to 10.0)	5.9 (1.7 to 10.2)
* + Phigh + Pdeg	8.3 (6.4 to 10.3)	9.9 (6.8 to 13.1)	6.2 (2.9 to 9.9)	6.3 (2.8 to 9.9)
* + Phigh + Pdeg + Punem	8.6 (6.6 to 10.6)	10.1 (7.1 to 13.2)	6.4 (3.1 to 9.4)	6.6 (3.1 to 10.3)
* + Phigh + Pdeg + Punem + mincome	10.1 (8.1 to 12.0)	11.0 (8.1 to 14.0)	7.8 (4.5 to 10.8)	9.0 (5.4 to 12.7)

*Adjusted for individual-level age and sex.

Phigh indicates the proportion of women and men with a college degree or higher; Pdeg, the proportion of women and men with a high school degree or higher educational attainment; Punem, the proportion of women and men who are unemployed; mincome, the proportion of individuals below the poverty level in each age-group.

COPD and lung cancer.[17] Both diseases reflect the long-term use of tobacco by the population.[20]

Additionally, the time periods for follow-up were not the same. Nonetheless, the risk estimates were reasonably close and CIs were overlapping (Table 3). Notably, the estimates were comparable even though the estimates for the Medicare cohorts were not adjusted for confounding at the same individual level of detail as in the ACS and Harvard Six Cities analyses.

Prospective cohort studies of air pollution and health with collection of data from individual participants, including the original ACS, have the advantage of collecting extensive information on individual-level covariates. However, they are expensive and time consuming to carry out. In addition, their results continue to be challenged by critics because of imprecise effect estimates and the potential for residual confounding at individual- and area-levels. Because data from Medicare, the EPA, and the census are available nationally, we were able to construct a data set on outcome, air pollution exposure, and confounders for the same geographical locations included in the ACS and Harvard Six Cities. With this data set, we investigated whether Medicare data provide evidence on the chronic effects of air pollution similar to the original ACS and Harvard Six Cities studies, even though confounding cannot be controlled as tightly at the individual level. In general, the estimates from the 2 Medicare cohorts were similar to those from the original cohorts. A useful next step will be a similar replication of other US cohorts.

Strengths of the Medicare data are its size and full representativeness of the target population of elderly persons and, because it is dynamic, successive cohorts can be readily selected so that changes in risk can be tracked. Studies based on the Medicare files, however, are potentially limited by lack of individual-level covariate information on residual confounding and modifying factors.

Several risk factors are of particular concern as potential confounding factors in epidemiologic studies of long-term exposure to air pollution; these include cigarette smoking, and obesity and its correlates. The prevalence rates for both risk factors vary spatially and they are strongly associated with risk for multiple causes of death. However, in the original Harvard Six Cities and ACS analyses, estimates of the effects of air pollution measures on mortality were robust to confounder adjustment, including adjustment for smoking, and effect modification was not found. In the reanalysis of data from these studies, more comprehensive treatment of potential confounding in these studies, including use of time-dependent variables in the Harvard Six Cities, showed insensitivity of the findings to the degree of control of potential confounders.[21] The reanalysis found effect modification by educational level, with lesser risk at higher levels of education. Because the Medicare data do not include individual-level information on education, we could not assess whether there was similar effect modification in the Med-SCS and Med-ACS cohorts.

In the Medicare cohort, the potential for individual-level confounding may be low because of the older age of Medicare participants. At older ages, the strength of several risk factors for mortality declines, including smoking and obesity.[22,23] These considerations regarding confounding in the elderly and the comparability of estimates from the Medicare and original cohorts imply that cohorts of Medicare participants can provide valid estimates of the effect of air pollution on mortality. We show that the population mortality rates from lung cancer and COPD can be used as indicators of smoking at the population level. We suggest that Medicare enrollees represent a population that can be used to create successive cohorts for tracking the risks of air pollution, on both hospitalization and mortality. We have demonstrated the feasibility of creating such cohorts and comparability of estimates of the effect of particulate air pollution to those from cohorts with better characterization of participants at the individual level.

With adjustment for area-level covariates, in addition to the individual-level risk factors, the Med-ACS estimates were

slightly larger than reported in the ACS. Several factors might contribute to the differences. First, chronic effects of $PM_{2.5}$ on mortality might be underestimated when using exposure indicators aggregated at the larger metropolitan area-level.[6] In other words, aggregation bias may have resulted from the differing sizes of geographic units in which estimates of exposure were based. The Med-ACS is based on smaller geographical areas (110 counties) than the ACS (50 metropolitan areas). In the Netherlands cohort study,[11] risk estimates almost doubled when local sources of pollution were used in the estimation process versus community-wide concentration. To provide further evidence toward this hypothesis, we have conducted additional analyses using the SMA as the geographical unit instead of the county. Results are presented in Tables 3 and 4. When we used the SMA as the geographical unit, the effect estimates of Med-ACS were similar to the effect estimates from ACS.

Second, the study population in Med-ACS is older than the populations of the ACS and the Harvard Six Cities. The average ages at enrollment in the ACS and Harvard Six Cities were 59 and 50 years, respectively.[24] The Medicare cohort comprises only people over 65 years of age, and therefore may represent a more sensitive population to the chronic effects of ambient $PM_{2.5.}$ Previous studies have shown that when pollution levels are high, older people are more likely to be hospitalized for heart and lung problems, and some may die prematurely.[25] In contrast, chronic effect estimates in the Harvard Six Cities were actually larger in the younger half of the cohort.[1]

Third, the estimates from Med-ACS could be biased upward due to the lack of adjustment for individual-level risk factors. Fourth, larger effect estimates observed at lower exposure levels could indicate that the relationship between $PM_{2.5}$ and mortality is nonlinear.

A further limitation of our analysis is the lack of adjustment for spatially correlated unmeasured confounders. This is an issue of concern in epidemiologic studies that compare adjusted mortality rates with longer-term air pollution exposure across different locations. The Health Effects Institute reanalysis[16,24,26–28] developed statistical methods for analyses of spatially correlated data aimed at minimizing the autocorrelation in the residuals.[29–32] The original results were confirmed, but the CIs were larger, suggesting that there was substantial residual autocorrelation in the data, a possibility for our analyses as well.

In summary, we have used the Medicare files to assemble cohorts for the same geographic locations included in the Harvard Six Cities and ACS cohorts. Although the analyses of the Med-SCS and Med-ACS cohorts considered only age and sex as individual-level covariates, risk estimates were comparable for the original and Medicare cohorts. We suggest that the periodic assembly of cohorts from Medicare participants can provide tracking of the risks of air pollution in a large, representative, and susceptible population. The Medicare cohorts could provide ongoing evidence to complement data obtained from the small number of fixed-population prospective cohort studies.

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