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ORIGINAL PAPER

Geographies of uncertainty in the health benefits of air quality improvements

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Abstract Assessing the long-term benefits of marginal improvements in air quality from regulatory intervention is methodologically challenging. In this study, we explore how the relative risks (RRs) of mortality from air pollution exposure change over time and whether patterns in the RRs can be attributed to air quality improvements. We employed two-stage multilevel Cox models to describe the association between air pollution and mortality for 51 cities with data from the American Cancer Society (ACS) cohort (N = 264,299, deaths = 69,819). New pollution data were computed through models that predict yearly average fine particle ($PM_{2.5}$) concentrations throughout the follow-up (1982–2000). Average $PM_{2.5}$ concentrations from 1999 to 2000 and sulfate concentrations from 1980 were also examined. We estimated the RRs of mortality associated with air pollution separately for five time periods (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000). Mobility models were implemented with a sub-sample of 100,557 subjects to assist with interpreting the RR estimates. Sulfate RRs exhibit a large decline from the 1980s to the 1990s. In contrast, $PM_{2.5}$ RRs follow the opposite pattern, with larger RRs later in the 1990s. The reduction in sulfate RR may have resulted from air quality improvements that occurred through the 1980s and 1990s in response to the acid rain control program. $PM_{2.5}$ concentrations also declined in many places, but toxic mobile sources are now the largest contributors to PM in urban areas. This may account for the heightened RR of mortality associated with $PM_{2.5}$ in the 1990s. The paper concludes with a three alternative explanations for the temporal pattern of RRs, each emphasizing the uncertainty in ascribing health benefits to air quality improvements.

Keywords Fine particulate matter · Risk assessment · Air pollution · Multilevel Cox regression model · Health benefits assessment

Abbreviations

NRC	National Research Council
ACS	American Cancer Society
TSP	Total suspended particulate
PM_{10}	Particles less than or equal to 10 μm in diameter
$PM_{2.5}$	Particles less than or equal to 2.5 μm in diameter

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RR	Relative risk
CR	Concentration-response
MSAs	Metropolitan statistical areas
CVD	Cardiovascular disease
GAM	Generalized additive model
SO_4	Sulfate
EPA	Environmental Protection Agency

1 Introduction

There has been considerable interest in quantifying the health benefits from government interventions to improve air quality (NRC 2002). In particular, the Health Effects Institute (HEI 2003) has developed an ''accountability'' framework to evaluate the impact of improvements in air quality. Such evaluations have often proven difficult—with a few exceptions—because air quality regulations exert impacts through complex incremental changes. This paper uses the American Cancer Society (ACS) Cancer Prevention II prospective cohort to illustrate the uncertainties in assessing the health benefits of air quality improvements in the United States.

An analysis of residential mobility patterns is used to further indicate the complexities of attributing health benefits to air quality improvements. Specifically, if mobility is pervasive and subjects move between zones of the country with different pollution concentrations, previously unmeasured ''population mixing'' effects (Stiller and Boyle 1996; Koushik et al. 2001) may exert a large influence on the exposure experience of the cohort. Further complications arise when migration intermingles with population susceptibility. As a consequence, attributing health benefits to long-term improvements in air quality raises many methodological issues, which we term the ''geography of uncertainty.'' The paper is intended to generate hypotheses for identifying important aspects of the spatial and temporal uncertainties in air pollution–mortality relations and subsequent benefits assessment, rather than to supply specific empirical information for benefits estimation. Such benefits assessments should be based on other published literature (Pope et al. 2002; Krewski et al. 2000) where the emphasis is on deriving epidemiologic estimates rather than illustrating methodological and conceptual issues. The paper thus concludes with three possible explanations for the observed risk patterns and for understanding why risks from air pollution may change over time.

2 Methods

2.1 Health and exposure data

We employed two-stage multilevel models with new imputed exposure data for different periods of follow-up in the ACS prospective cohort. This cohort was enrolled in 1982 and included over 1.1 million participants. New pollution data were computed using predictive models to impute $PM_{2.5}$ concentrations from measured total suspended particulates (TSP) and particles less than or equal to 10 μm in diameter (PM_{10}) (Lall et al. 2004). This resulted in estimates of the average annual concentrations $PM_{2.5}$ in 83 cities during the period 1972–2000. These estimates relied on sites with co-located TSP, PM_{10}, and $PM_{2.5}$ monitors to derive estimates capable of predicting over 43% of the variation in $PM_{2.5}$ at locations not included in the model calibration. Some 51 of these cities were included in previous analyses with measured $PM_{2.5}$ concentrations from 1999 to 2000 and sulfate concentrations from 1980 (N = 264,299 with 69,819 deaths). The 51 cities included here were selected because of the availability of previously used and new exposure models. Cities used here were mapped in Fig. 1 in the context of cities included in previous $PM_{2.5}$ and sulfate analyses (Pope et al. 2002; Krewski et al. 2000). Of note, there were fewer cities in the Ohio River Valley, where the RRs of mortality due to air pollution were shown to be highest in previous analyses (Jerrett and Finkelstein 2005).

2.2 Statistical model relating mortality to air pollution exposure

The association between ambient concentrations of air pollution and mortality is examined by a survival model in which the probability of dying at any given time or age is related to known risk factors for death, such as smoking and diet, and ambient air pollution. This instantaneous probability of death, or hazard function, is mathematically related to the risk factor via the model

$$h_{ic}^{(s)}(t) = h_0^{(s)} \exp(\beta' X_{ic}^{(s)}),$$

where $h_{ic}^{(s)}(t)$ is the hazard function for the ith subject in the cth community in the sth strata. The model assumes that the baseline hazard function, $h_0^{(s)}$, is common to all subjects within a strata. The risk of death is modeled by modulating the baseline hazard by the regression equation, $\exp(\beta' X_{ic}^{(s)})$, which distinguishes risk among subjects within a strata and community. The risk factor information is contained in the matrix $X_{ic}^{(s)}$, and related to the hazard function by the regression vector β. Strata are defined by single year age groups, gender, and race. For example, we follow the survival experience of all white females, aged 54 at the beginning of the study in 1982 and relate their air pollution exposure to their longevity. This process is repeated for all possible age-gender-race combinations. The association between the risk factors is then summarized among strata and represented by the single regression vector β. This

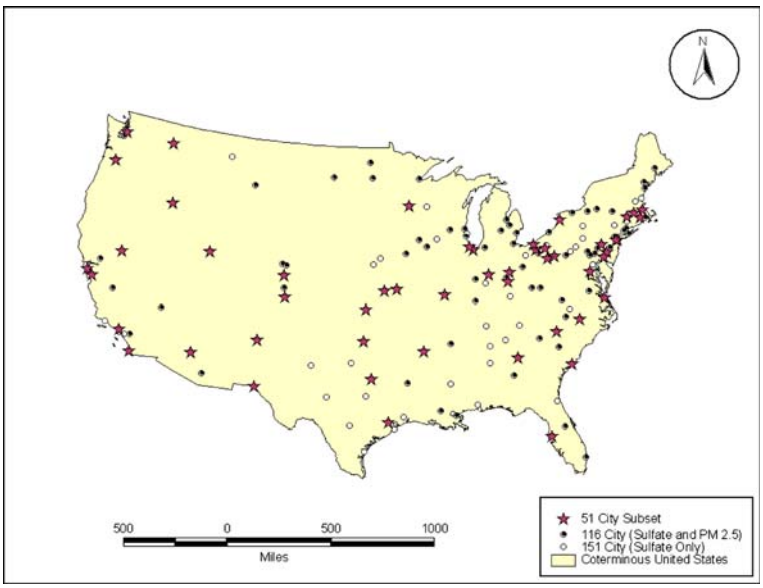

Fig. 1 Map of 51 cities in the context of cities used in previous ACS studies

model also assumes that the association between the risk factors, including air pollution, and mortality can be represented by a single value, β, which is constant over the follow up period. Since differences in values of the risk factors modulate the hazard function, this model is called the proportional hazards model.

The proportional hazards model assumes that the survival experience among all subjects is statistically independent. However, subjects living in the same community intrinsically have some risk factors in common that are not included in our model. These unmeasured factors tend to correlate the survival experience of subjects within geographic areas. To accommodate this potential correlation or spatial clustering of survival within a community we extend the hazard model to

$$h_{ic}^{(s)}(t) = h_0^{(s)} \exp(\eta_c + \beta' X_{ic}^{(s)}),$$

where η_c is a random variable which represents the unexplained survival experience of all subjects within the cth community. It has zero expectation and common variance among communities, σ^2. It is also possible that subjects living in communities close together will share some lifestyle and environmental risk factors, which are not as strongly shared between subjects living in communities farther apart. To capture this type of spatial autocorrelation we assume that the correlation between the random effects of adjacent communities if positive, ρ say, and zero otherwise. Here, adjacency is assumed if two city-specific Thessien polygons are connected.

Statistical estimates of the regression parameters β and dispersion parameters σ^2 and ρ are made by a two-stage process. In stage one, estimates of the random effects were obtained controlling for all risk factors except air pollution (Cakmak et al. 2003). These random effect estimates are the average residual mortality among subjects in each community after controlling for all available risk factors. The role of air pollution in predicting mortality is then examined in stage two using a linear simultaneous autoregressive model in which the variance of the estimated random effects is $\sigma^2\rho + v_c$, where v_c is the statistical error in estimating the random effect for the cth community. The correlation between the estimated random effects between communities is assumed to be modeled by ρ if communities are adjacent and zero otherwise. This first stage produced a random effect estimate for each city indexed to the City of Chicago, which had $PM_{2.5}$ levels in the central part of the distribution of pollution levels among cities. This second stage estimation process is described by Jerrett et al. (2003).

Our analysis focused on five time periods (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000). Following previous research on this cohort, RRs were estimated for all-cause, cardiopulmonary, and lung cancer mortality, as well as mortality from all other causes (Pope et al. 2002). In this study, RR was estimated separately for each period and for each cause of death with a two-stage random effects model (Cakmak et al. 2003) that controlled for 44 individual covariates in the first stage. These individual-level covariates remained the same as those described in earlier studies, comprehensively covering smoking, other lifestyle, diet, demographic, occupational exposure, and social confounders (Pope et al. 2002).

2.3 Exposure models

We used three exposure metrics for this analysis of 51 cities: (1) sulfate concentrations measured in 1980 as reported earlier (Krewski et al. 2000); (2) $PM_{2.5}$ concentra-

tions measured in 1999–2000 (Pope et al. 2002); and (3) imputed $PM_{2.5}$ exposures that had either matched the time windows of follow-up (e.g., 1982–1986 exposure and follow-up data) or lagged the exposure for the previous 5-year period (e.g., 1982–1986 mortality data and average $PM_{2.5}$ concentrations from 1977 to 1981). Details of prediction on the historical $PM_{2.5}$ estimates for time-matched and lagged pollution metrics are given elsewhere (Lall et al. 2004). Briefly the historic $PM_{2.5}$ estimates were derived based on assessing MSA-specific ratios of $PM_{2.5}/PM_{10}$ (particles with diameter less than or equal 10 μ) for co-located sites in 1999–2000, defined as b_1 and similar ratios for PM_{10}/TSP for 1987–1998 defined as b_2. The ratio of $PM_{2.5}$/TSP equals $b_1 \times b_2$. This estimation procedure predicted 43% of the variation of 1980 $PM_{2.5}$ measured values at sites excluded from the ratio model.

To ensure comparability with earlier results (e.g., Krewski et al. 2000; Pope et al. 2002) we also computed RR estimates for the entire follow-up period using each of the exposure metrics. For the imputed $PM_{2.5}$ data, exposure for the entire time period was assumed to begin in 1972 (the earliest date with pollution estimates), as many of the subjects in the ACS study had residence in the same city for many years before enrollment of the cohort in 1982 (Krewski et al. 2000).

2.4 Residential mobility analysis

For 100,557 of the individuals included in the ACS cohort, zip code of residence was available in 1982, particular archived dates (up to six through the follow-up), and in 2003. These zip codes were converted to either metropolitan statistical areas (MSAs) or state of residence at the beginning and end of the period to examine patterns of mobility in this subset. The residential mobility information was in the form of zip codes, which were converted to either MSAs or state of residence at the beginning and end of the period, creating a dataset with 100,557 observations for which mobility information was available.

Using this dataset of 100,557 subjects, the number of in-migrants, out-migrants, net-migrants and the respective rates of migration were calculated, at both the state and metropolitan scale. In-migrants were defined as individuals who have moved into a specific MSA or state, while out-migrants were defined as individuals who have moved out of a specific MSA or state (Newbold 2001). Net-migration was the number of in-migrants minus the number of out-migrants to a specific state or MSA, providing an overall indicator of regional population loss or gain. In- and out-migration rates were calculated as the number of in- and out-migrants divided by the size of the population that is ''at-risk'' of moving. The at-risk population for in-migrants was defined as the total sample size minus the number of individuals who were initially in the MSA or state. The at-risk population of out-migrants was the number of individuals who were initially in the MSA or state.

Logit analyses were undertaken to examine the likelihood of out-migration from both the 1982 state and MSA of residence while controlling for other covariates affecting migration. Based upon several individual characteristics, the analyses essentially allowed for testing whether or not the ACS respondents followed general migration patterns observed within the broader literature (Stiller and Boyle 1996; Koushik et al. 2001). For example, were the better educated and the young more likely to migrate? Were individuals in the Northeastern US more likely to out-migrate than those in the South or West? This information could provide an assessment of whether certain subgroups were likely to be subject to greater air pollution exposure misclassification.

Models for each time period stratified for age (<65, 65+ years) and for education (less than or equal to high school, greater than high school) were used to further interpret the temporal patterns in the RRs.

3 Results

3.1 Health effects

The RRs of mortality across the period of follow-up based on the subset of the 51 cities considered were smaller than in the full air pollution cohort considered in the previously full ACS cohort (Krewski et al. 2000; Pope et al. 2002). For example, all-cause mortality was significantly elevated by 6% in the larger cohort, but generally was not significantly elevated in these sub analyses. For cardiopulmonary, RRs were significantly increased in both the present and previous studies, but slightly larger in the earlier, larger study (see Fig. 2).

Although overall health effects were somewhat lower in the present as compared to the previous analysis, there was a marked difference in the temporal pattern of RRs between sulfates and $PM_{2.5}$ (measured, imputed, and lagged) for all-cause and cardiopulmonary deaths (Fig. 3a, b). Sulfate RRs exhibited a large decline moving from follow-up in the 1980s to the 1990s. In the 1990's, sulfate RRs were no longer elevated for these causes of death. In contrast, $PM_{2.5}$ RRs generally followed the opposite pattern, with RRs for all three $PM_{2.5}$ exposures showing larger RRs in the later periods than the earlier ones for cardiopulmonary deaths. Lagged $PM_{2.5}$ followed a similar pattern to the other PM models. Lung cancer displayed a different pattern, with the effects for sulfate and $PM_{2.5}$ following an inverted ''U'' shape with the smallest effects in the first and last time window.

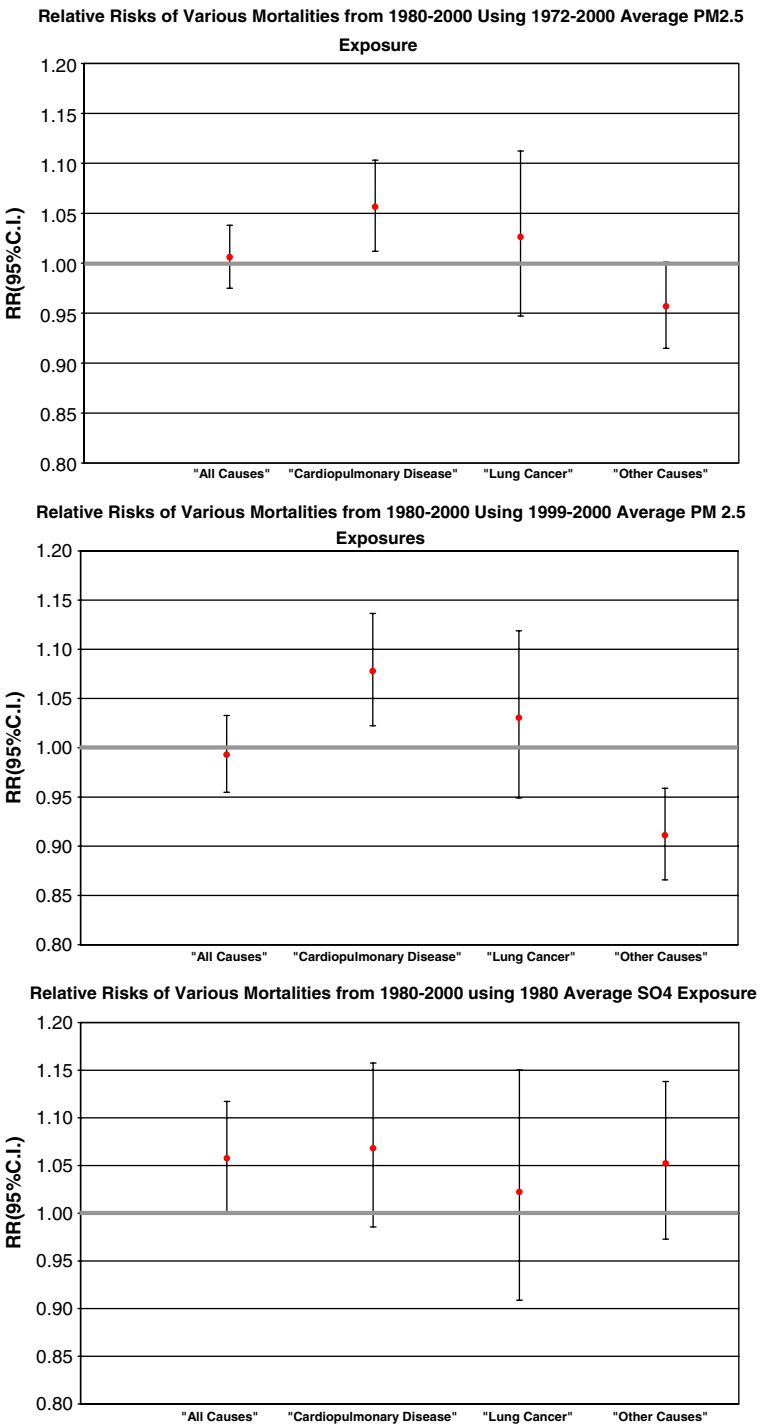

Fig. 2 Summary of risks for different exposures over the entire follow-up

3.2 Mobility results

Overall, logit mobility models supported the broader research findings from demography, suggesting that individuals in the ACS cohort were mobile, with movers in this cohort demonstrating similar characteristics to those observed in the larger population. An important consequence of mobility in the cohort was the temporal variation in exposure that occurred when subjects move among areas with different air pollution levels (see Tables 1, 2).

The likelihood of out-migration between 1982 and 2003 at the state and MSA scales was similar in that all variables except for 'female' (for both state and MSA analysis) were statistically significant at the 1–2% level. In terms of personal characteristics, those who were aged 55 or greater at baseline were less likely to make an interstate/inter-MSA

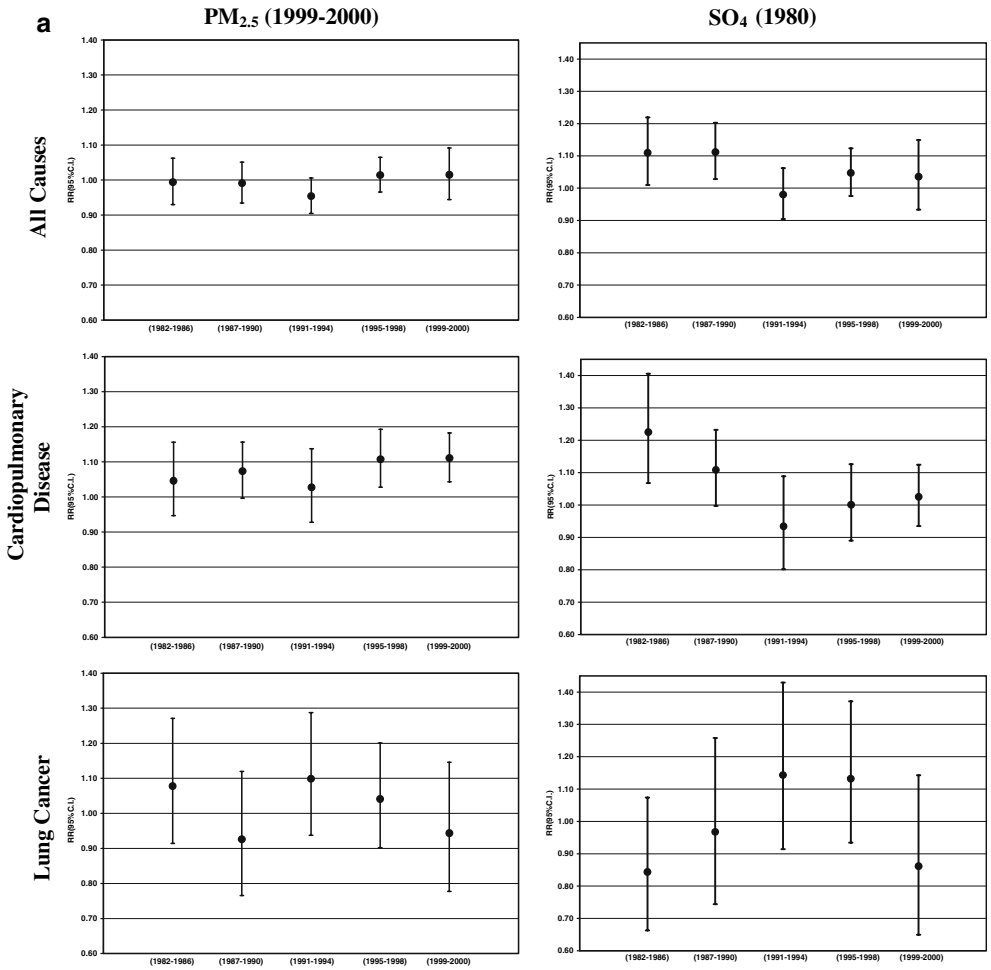

Fig. 3 **a** Relative risks for all-cause, cardiopulmonary and lung cancer deaths estimated for five time periods of the follow-up (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000) with measured exposures. **b** Relative risks for all-cause, cardiopulmonary and lung cancer deaths estimated for five time periods of the follow-up (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000) with imputed exposures

move than their younger counterparts. This finding was supported in the literature, since the young were able to achieve increased benefits to migration (Long 1988). The education variables showed that there was a higher likelihood of migration among those with greater education than those with high school education or less (the 'reference' category). The education variables supported the notion that those with higher levels of education might be able to achieve greater benefits from migration due to the potential of increased returns to education and decreased costs to access pertinent origin and destination information. Those who were not married were less likely to undertake an interstate migration than those who were married. Consistent with the broader literature, those living in the New England, Middle Atlantic or East North Central states were more likely than those living in the rest of the United States to undertake an interstate migration. Although not visible in this table, southwestern and southeastern states were the beneficiaries of these migrants.

3.3 Effect modification

We undertook further analyses for each time period stratified by age and education level (see Fig. 4a–c).

For long-term exposure to $PM_{2.5}$ during the period 1972–2000, we saw larger RRs in the later periods dominated by individuals who were <65 years of age at enrollment, which was consistent with past evidence on effect modification (Krewski et al. 2000). RRs were generally larger in the lower education groups. This was evident in the higher RRs for the group that was younger at enrollment, where RRs were generally larger for the later periods of follow-up. These findings were noteworthy because they indicated higher RRs by age and by lower education, when examination of the aggregate RRs for the entire follow-up indicated relatively few effects. For the $PM_{2.5}$ 1999–2000 estimates, there was a less consistent pattern, but individuals who were older at enrollment were somewhat more likely to have higher RRs in earlier

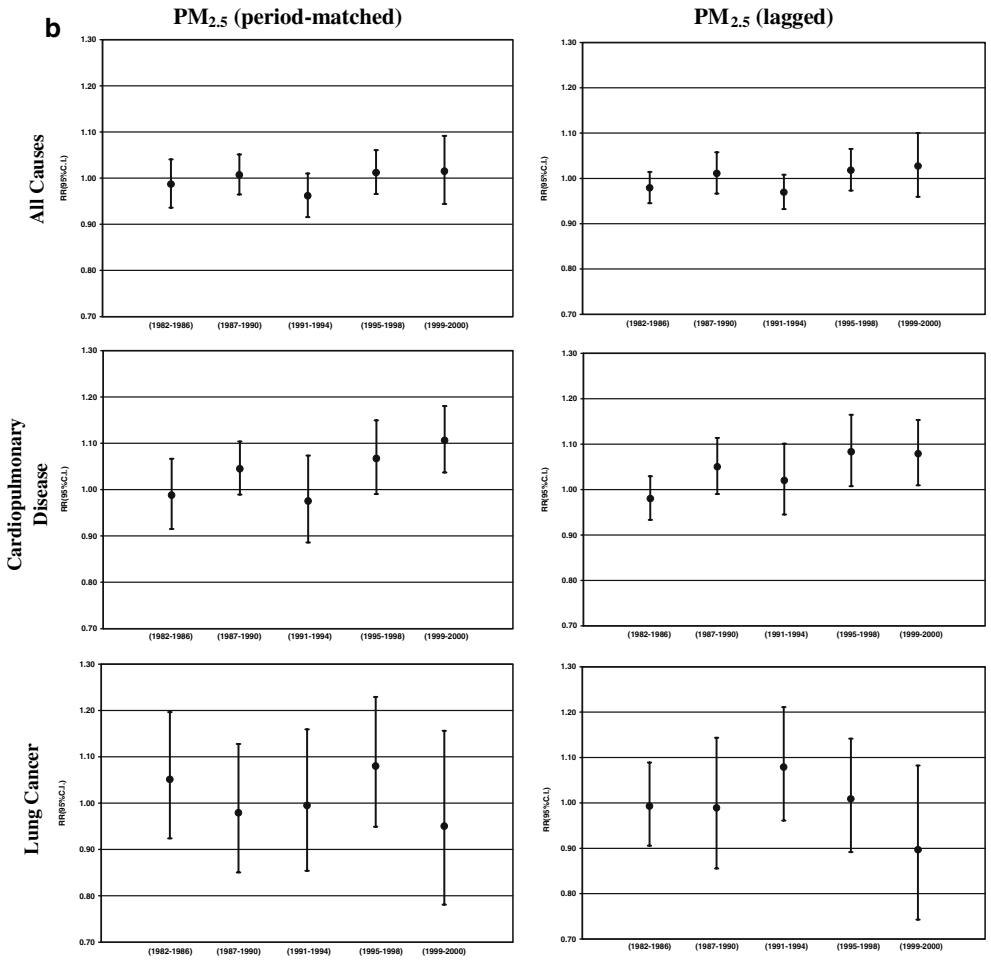

Fig. 3 continued

periods, particularly those with higher education. The opposite was true for those <65 years of age at enrollment, with larger RRs in the later follow-up periods, and higher RRs concentrated in the low-education group. With the exception of the older high education group, nearly all subgroups had higher RRs in the earlier periods. Those who were older at enrollment with lower education had the largest RRs.

Table 1 Logit results of out-migration from a state, 1982–2003

Parameter	Estimate	Error	Pr > χ^2
Intercept	–2.0821	0.0261	<0.0001
Aged 55 and older	–0.1884	0.0190	<0.0001
Vocational/trade school or some college	0.3275	0.0249	<0.0001
College degree	0.3382	0.0267	<0.0001
Graduate school	0.4319	0.0272	<0.0001
Female	0.000600	0.0189	0.9746
Non-married: single, divorced, separated, or widowed	–0.0961	0.0387	0.0131
Out-migration from New England states	0.5961	0.0363	<0.0001
Out-migration from Mid Atlantic states	0.0574	0.0219	0.0088
Out-migration from East North Central states	0.2194	0.0254	<0.0001
N	100,557		
Rho-squared	0.00896		
Likelihood ratio	733.3871		
% Predicted	54.4		

New England states: New England: Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut. Middle Atlantic States: New York, Pennsylvania, New Jersey. East North Central states: Wisconsin, Illinois, Michigan, Indiana, Ohio. Source: Derived from CPS and ACS nutritional sub cohort merged datasets

Table 2 Logit model results of out-migration from a metropolitan area, 1982–2003 (with regional effects)

Parameter	Estimate	SE	Pr > χ^2
Intercept	–2.6412	0.0281	<0.0001
Aged 55+	–0.1176	0.0243	<0.0001
Some College	0.3655	0.0325	<0.0001
University Degree	0.3606	0.0347	<0.0001
Graduate Degree	0.4806	0.0346	<0.0001
Not married	0.1183	0.0457	0.0096
North East US	0.0738	0.0251	0.0032
Rho-squared	0.007		
Likelihood Ratio	274.68		
N	91,652		
% Concordant	48.8		

4 Discussion

Overall estimated RRs in the 51 cities used in this study were lower than in previous national studies. The lower RR estimates probably resulted from the exclusion of cities in the Ohio River Valley, which tended to demonstrate larger RRs from air pollution than other geographic regions (Krewski et al. 2000; Pope et al. 2002). Given the difference between our overall risk estimates for the entire period and those of earlier national studies, we also investigated the same five exposure windows using the larger set of 151 cities with sulfate measurements and 116 cities with $PM_{2.5}$, which were used in earlier studies. In both instances, we observed larger RRs than in the subset of cities used here. The temporal pattern in the risks was similar although less pronounced in the larger sets of cities used earlier (cf. Krewski et al. 2000; Pope et al. 2002). Although the risks in the 51 cities used in this analysis were attenuated, we continued to see significant associations with mortality for most of the exposure estimates, but these had measurable variation over time.

Sulfate effects on all-cause and cardiopulmonary mortality appeared to be larger and more significant in earlier than in later periods of follow-up. In contrast, $PM_{2.5}$ displayed an opposite pattern, with larger health effects in the later periods. Although RRs generally had overlapping confidence intervals for the periods under investigation, the opposite patterns between the two pollutants raise some interesting possibilities for interpretation, which we expand upon below.

Unlike the other causes of death, the RRs for lung cancer mortality followed an inverted U-shaped pattern, especially for sulfate. This different RR pattern for cancer may reflect the protracted multifactorial process of disease formation and was consistent with recent studies investigating the temporal dose-response functions in other mortality cohorts (Laden et al. 2006).

While ambient $PM_{2.5}$ levels declined in many parts of the United States (Lall et al. 2004), mobile sources were now the largest contributors to pollution in urban areas (Park and Kim 2005). Mobile source emissions contained more toxicologically active transition metals, polycyclic aromatic hydrocarbons, quinones, and ultrafine particles (Nel 2005). The decline in sulfate effects may have been the result of dramatic reductions that occurred through the 1990s in response to the acid rain control program (EPA 2005). From the perspective of assessing accountability, this combination of events might be interpreted as government programs to reduce sulfate partly achieving their goal. In contrast, the relatively larger contributions from transportation sources to $PM_{2.5}$ may have increased the toxicity of ambient particles and led to the larger effects observed here in later periods.

Drawing such conclusions from the data, however, is complicated by uncertainties that prevented direct attribution of the health effects from changes in government regulations or societal patterns of emissions. We offer three alternative explanations for the changing temporal patterns of RRs.

4.1 Robust survivor explanation

Mortality in the early portion of the follow-up may have concentrated in areas of high susceptibility and high exposure. Sulfate pollution tended to be highest in areas of relatively low educational achievement (Jerrett and Finkelstein 2005). Our subgroup analysis supported the conclusion that subjects in the low education-higher age group had the largest RR from air pollution (RR: 1.37, 95% CI: 1.11–1.69 over a 10 $\mu g/m^3$ contrast). Assessment of effect modification by age and education indicated higher RRs at older ages (whether this was for the early follow-up for those greater than 65 years of age at enrollment, or the later follow-up for subjects <65 in 1982). For sulfate, there was also evidence that older individuals with low education had much higher RRs earlier in the follow-up, and with the exception of the high education older group, all other groups had higher RRs earlier in the follow-up. The combination of heightened risk in the low education group due to various health threats may have combined with higher exposure to affect more subjects in the earlier part of the follow-up. This explanation did not account for the increases in the RRs from $PM_{2.5}$ over the follow-up, but would explain the declining risks for sulfate.

4.2 Environmental inequality-mobility explanation

We have explored the mobility of subjects within a subset of the ACS cohort where complete tracking of residential location was available ($N \sim 100{,}557$). This analysis

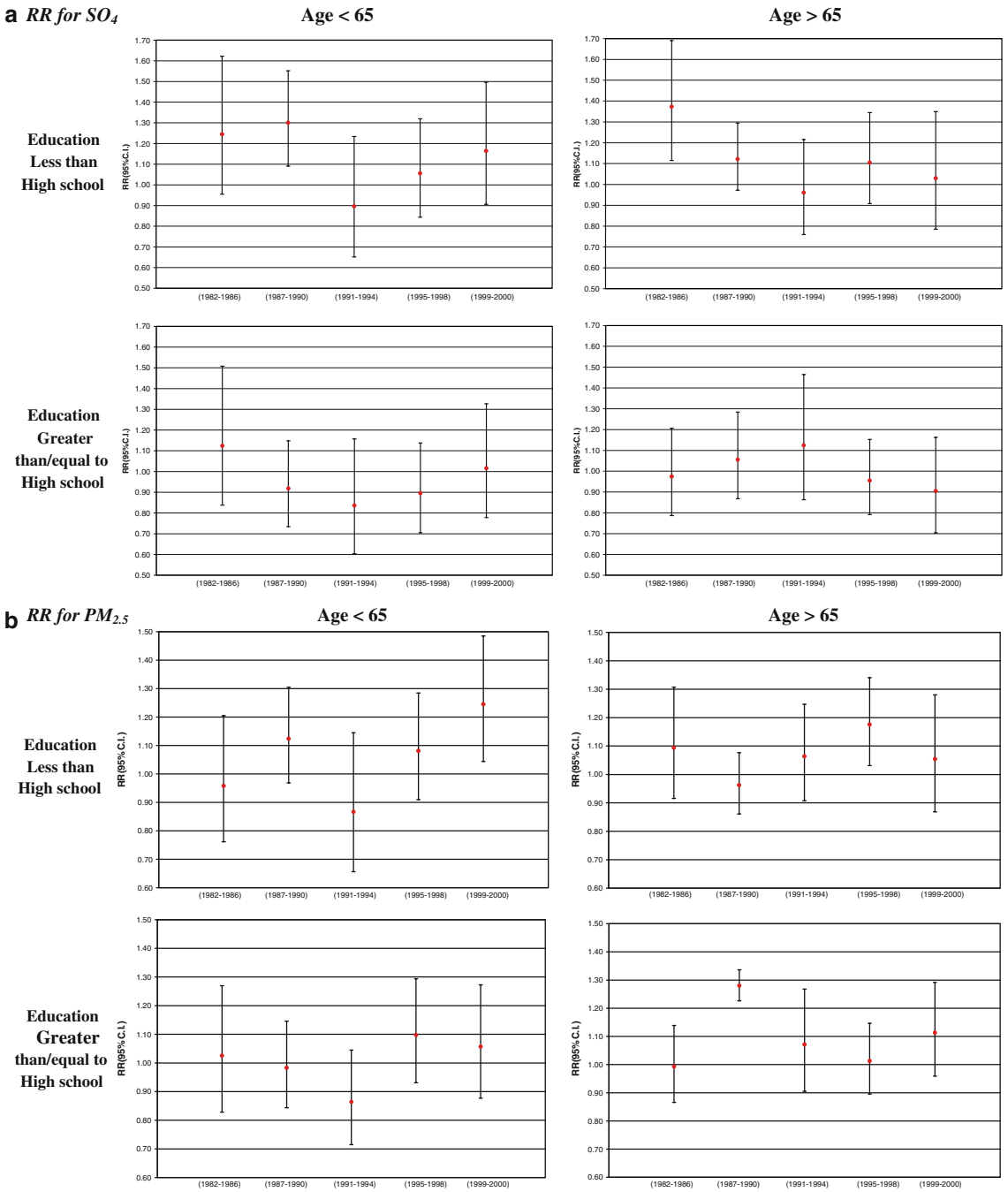

Fig. 4 **a** Relative risks using SO_4 exposures for cardiopulmonary outcome stratified by age and education for five time periods. **b** Relative risks using $PM_{2.5}$ (1999–2000) exposures for cardiopulmonary outcome stratified by age and education for five time periods. **c** Relative risks using average $PM_{2.5}$ (1972–2000) exposures for cardiopulmonary outcome stratified by age and education for five time periods

revealed that many areas of the country with the highest sulfate pollution levels were also subject to large out-migration, particularly out of the Midwestern and Northeastern states of the ''rust belt'' (Getis and Getis 1995). Thus, exposure misclassification may have increased over time, as the ACS cohort only had complete residential histories for the initial enrollment period in 1982. In predicting the propensity to migrate, older persons and those with lower education appeared less likely to migrate. These subjects may have had less exposure measurement error than other subjects in the ACS cohort, potentially contributing to larger health effects for sulfate in the earlier periods. For $PM_{2.5}$, many of the areas receiving migrants also experienced relatively little improvement in $PM_{2.5}$ and

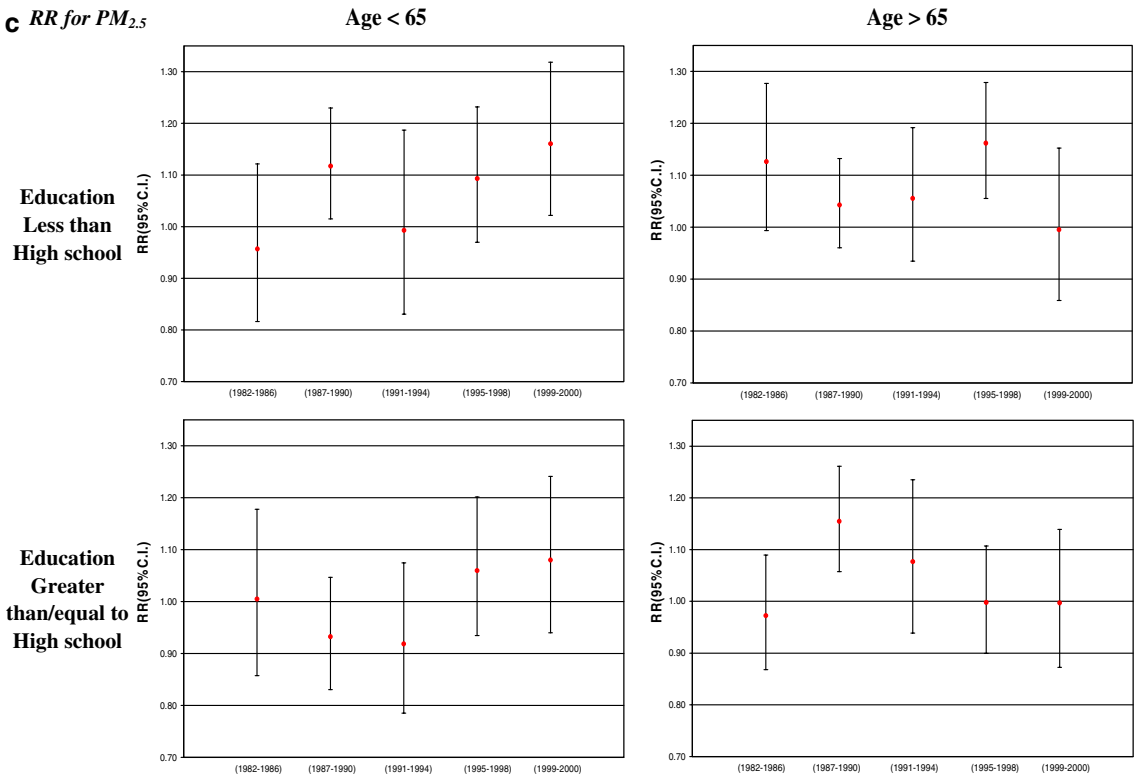

Fig. 4 continued

were to some extent worsening compared to other parts of the country (Lall et al. 2004). Those areas in the southeast, southwest, and southern California experienced both higher in-migration and lower overall improvements in $PM_{2.5}$ levels. This may have in part explained why $PM_{2.5}$ RRs increased through the 1990s.

Due to data constraints we were unable to assess either mobility or exposure at the within-city scale. It seems likely that some greater level of movement may have occurred within cities, but this is not taken into account here. Likewise, the within-city exposure contrasts, which have been associated with even larger risks (Jerrett et al. 2005), were not controlled in this analysis. For most locations, sulfate and $PM_{2.5}$ will vary only slightly within cities compared to the between city variation, but for the larger MSAs such as New York and Los Angeles, there may be additional error that is not taken into account in this analysis. Future studies will need to address this within-city phenomenon if health benefits are to be linked to air quality improvements.

4.3 Temporal measurement error explanation

In most instances, we have observed the largest health effects for the time windows closest to the actual monitoring period. Sulfate RRs were largest in the earlier periods closest to the 1980 measurement, while the $PM_{2.5}$ RRs were generally largest in the latest period closest to the actual monitoring period of 1999–2000. A similar effect was present in the imputed data, which was calibrated against the 1999–2000 data, and the data for this window were virtually the same as the measured values (Lall et al. 2004). We could not test this explanation directly due to lack of direct monitoring data for the entire period. The pattern across all RRs nonetheless indicated this may have been another plausible explanation for the observed temporal pattern in the RRs.

5 Conclusion

Growing interest in measuring health benefits from air quality improvements resulting from government regulations has prompted a series of ''intervention'' studies (Jaakkola et al. 1999; Heinrich et al. 2000; Clancy et al. 2002; Hedley et al. 2002; Heinrich et al. 2002; Pope et al. 2002; Frye et al. 2003). With few exceptions, these studies have examined the short-term or acute benefits of air pollution regulations or of natural experiments such as labor strikes at steel mills. Although important, findings from these studies may not apply directly to most of the air quality improvements that result in gradual decreases over many years. However, when the follow-up period is long, many other factors can obfuscate the linkage of air quality improvements to health benefits.

First, the survivor-harvesting explanation seems germane for explaining whether the dynamics of individual vulnerability in the cohort itself lead to observed RR patterns over time. Second, the environmental exposure-mobility hypothesis illustrates how more susceptible individuals may be less likely to move and therefore experience less measurement error. Finally, the temporal exposure misclassification explanation would alternatively imply a classical or non-differential error structure that may explain why larger health effects are observed closer to the period of pollution measurement.

This high susceptibility in the low education group due to various health threats may combine with higher exposure to harvest more subjects in the earlier part of the follow-up. These subjects would be more susceptible and receive high exposures, possibly leading to early onset of death. Studies attempting to ascribe the health benefits of incremental air quality improvements, which constitute the majority of cases, will have to examine closely the inter-correlations among these variables. In particular, understanding the interplay among education, age, mobility, and subsequent exposure error constitutes a priority for future research. All these factors can potentially influence the estimation of health effects from air pollution, sometimes directly and other times through mediating variables. The complexities of these relationships and the subsequent myriad of potential explanations underscore the uncertainties of ascribing mortality reductions to air quality improvements.

This paper has investigated the spatial and temporal patterns of RRs from exposure to four different air pollution metrics in the ACS cohort. We found higher RRs for sulfate exposure in the earlier periods of the follow-up, and a lower RR in the 1990s for this pollutant. In contrast, the RRs for $PM_{2.5}$ (measured directly in 1999–2000 and imputed for time-matched and lagged windows) increase through the follow-up period. The potential susceptibilities of underlying populations and the measurement error that results from mobility in the cohort have been explored. These analyses suggest a complicated picture and at least three possible explanations for the changing risk patterns. By exploring these issues though an empirical analysis of the ACS cohort, we have illustrated the uncertainties of interpreting changing risk patterns over time and of ascribing these patterns to changes in environmental regulations and in ambient air quality. In future research on the benefits of air quality, more emphasis will have to be placed on understanding the interplay of mobility, education, susceptibility, and age structures in the formation of health effects from air pollution.

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