Individual and neighborhood socioeconomic status, long term exposure to air pollution and risk of cardiovascular disease in the Women's Health Initiative Observational Study

Gloria Cheng-yu Chi

A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Public Health

University of Washington

2012

Committee:

Joel D. Kaufman

Sverre Vedal

Program Authorized to Offer Degree:

Public Health-Epidemiology

University of Washington

Abstract

Individual and neighborhood socioeconomic status, long term exposure to air pollution and risk of cardiovascular disease in the Women's Health Initiative Observational Study

Gloria Cheng-yu Chi

Chair of the Supervisory Committee:
Professor Joel D. Kaufman
Environmental and Occupational Health Sciences

Background: Previous studies have reported a positive association between exposure to higher levels of air pollution and cardiovascular mortality and morbidity. However, uncertainty remains regarding the potential confounding and effect modification of this association by socioeconomic status (SES). This study examined the roles that individual and neighborhood SES (at the Census tract level, NSES) may play in the association between particles less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) and incident cardiovascular disease.

Methods: We studied 48,067 women from the Women's Health Initiative Observational Study (WHI OS) who were free of cardiovascular disease at baseline. Outcomes of interest were time to first cardiovascular event and time to death from cardiovascular cause. Exposure data were obtained from nationwide monitors from the year 2000 and were used to predict annual average $PM_{2.5}$ concentrations at each subject's baseline geocoded address. Cox-proportional hazards regression was used. All models were adjusted for age, race, smoking, body mass index, diabetes, hypertension, hypercholesterolemia, systolic blood pressure, and physical activity. Individual and neighborhood SES were further adjusted for as covariates or modeled as linear interactions.

Results: A total of 2,446 cardiovascular events and 536 cardiovascular deaths were observed. In our fully adjusted models, each 10 $\mu g/m^3$ higher $PM_{2.5}$ exposure was associated with a 1.22 times

higher hazard (95% CI, 1.06 to 1.40) for cardiovascular events and a 1.31 times higher hazard (95% CI, 0.95 to 1.81) for cardiovascular deaths. In this cohort, neither individual nor neighborhood SES characteristics were strong confounders and individual SES characteristics also did not modify these associations. Only the following neighborhood SES variables: median family income, percent of adults over 25 years with high school degree, median home value, and the NSES score (a measure of overall deprivation of a neighborhood) were found to be significant effect modifiers. Greater effects tended to be observed among those residing in more disadvantaged neighborhoods.

Conclusions: Long term exposure to $PM_{2.5}$ was associated with increased risk of cardiovascular disease among a cohort of postmenopausal women and this effect cannot be explained by confounding by individual or neighborhood SES. In this cohort, women living in more disadvantaged neighborhoods were disproportionately affected by the adverse effects of $PM_{2.5}$ exposure on cardiovascular health. These results add to previously published research that tend to show greater effects among the less advantaged groups. Thus, a focus to reduce risks in these susceptible populations may be germane to public health and environmental policy.

INTRODUCTION

Landmark studies such as the American Cancer Society's Cancer Prevention Study II[1] and the Harvard Six Cities Study[2] have demonstrated that exposure to air pollution increases the risk of death from cardiovascular causes. Since then, mounting evidence has been published showing that air pollution not only increases risk of cardiovascular mortality, but morbidity as well.[2-6] Although low socioeconomic status (SES), both at the individual and neighborhood level, has consistently been identified as a risk factor for cardiovascular disease (CVD), much uncertainty still exists regarding how these two levels of SES affect the relationship between air pollution and CVD.

In the extant literature, there is evidence of effect modification by SES on the association between air pollution and mortality. It has been proposed that lower SES individuals may be more susceptible to the adverse effects of air pollution due to having fewer resources to cope, higher poverty, and higher psychosocial stress.[7, 8] Some researchers have found that particulate matter less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) had the greatest adverse effect on all-cause mortality among the least educated.[9, 10] However, the evidence has been inconsistent. Furthermore, few studies have assessed potential effect modification by both individual and neighborhood SES.

In addition to effect modification, there have been concerns that individual and neighborhood SES may confound the relationship between air pollution and adverse health outcomes. Some studies have found that individuals with low SES are more likely to be exposed to air pollution[7, 11-13] and are also more likely to suffer from CVD mortality.[14, 15] Thus, it is possible that a part of the observed negative effect of air pollution on health is due to the generally lower SES of highly exposed individuals, causing the observed effect of air pollution

on health to be spuriously high. Some researchers have found that higher neighborhood-level income attenuates the effect of air pollution on mortality.[16, 17] Furthermore, Naess et al observed that individual-level SES had less impact on the estimated effects of air pollution on mortality than neighborhood SES (NSES), suggesting the importance of looking at both individual and neighborhood SES.[17] However, to date, very few studies on air pollution effects on CVD risk have incorporated both individual and neighborhood SES in a multilevel framework.

Neighborhood and individual level SES are likely to have independent effects on health and susceptibility. Factors of individual SES such as income and education may affect health behaviors and one's ability to purchase health-related goods and services.[18] However, those with the same individual SES and different NSES may experience different chances of health outcomes depending on the SES of the area they reside in.[7] Factors such as crowding, traffic burden, neighborhood safety, and availability of clinics and fresh foods are all neighborhood level characteristics that may impact health.

In addition to assessing both levels of SES, it is also imperative to investigate the effects of the different domains of SES: education, income, wealth, and occupation. It is believed that although they are correlated, they represent distinct dimensions of SES.[18] Any single measure may not adequately capture SES in its entirety, nor can it fully account for the multidimensional effect of SES on health. Thus, in order to assess potential confounding or effect modification, we must look at multiple measures that represent different domains of SES.

A previously published epidemiological study by Miller and colleagues has investigated the relationship between fine particulate matter ($PM_{2.5}$) and cardiovascular disease in the Women's Health Initiative (WHI) observational study (OS). The authors reported a positive association between $PM_{2.5}$ exposure and risk of CVD events and mortality. In this study, we

focus on the role of individual and neighborhood SES in the relationship between $PM_{2.5}$ exposure and first cardiovascular events and mortality within the WHI OS. Specifically, we investigated how SES variables may confound or modify the effects of $PM_{2.5}$ and whether both levels of SES (individual and neighborhood) are relevant when studying the effects of air pollution on cardiovascular health. We were able to investigate all four domains of SES on the neighborhood level; but on the individual level, we did not have adequate information on wealth.

METHODS

Study population

We examined prospectively followed WHI OS subjects at baseline until the first cardiovascular event or until September 2005, which was the end of follow-up of the main cohort. The WHI participants include postmenopausal women between the ages of 50 and 79 years enrolled between 1994 and 1998.[19, 20] In the OS, 93,676 women were screened at baseline to obtain information about demographics, lifestyle characteristics, medical history, cardiovascular risk factors, and to obtain anthropometric and blood pressure measurements.[20] Annual updates on health outcomes were collected by mailed questionnaires. The women were mostly White (83%) and the cohort was generally better educated than same aged women in the overall U.S. Total family income decreased with increasing age, which may be attributable to parallel increases in widowhood and living alone. It may also be due to a cohort effect of inflation, where participants who were older had lower wages when their households were employed compared to younger participants.

Our study was restricted to participants who were free of clinically-apparent cardiovascular disease at baseline. Based on self-report, participants with a history of myocardial infarction, congestive heart failure, coronary revascularization, and stroke were excluded. Only participants with non-missing $PM_{2.5}$ predictions and predictions at the street level were included in the analyses. Participants who were missing data on any covariates of interest were also excluded. Institutional review boards at the University of Washington and Fred Hutchinson Cancer Research Center approved this study.

$PM_{2.5}$ exposures

$PM_{2.5}$ exposure concentration at each participant's address was predicted using a land use regression model (i.e., the mean model). Over 200 geographic covariates from the following categories were included: multiple indirect measures of traffic, population density, land use, satellite-based vegetative index (NDVI), nearby pollutant emissions based on emissions inventories, and distances to major sources of pollution. The nation was divided into three regions based on topography. Partial least squares (PLS) techniques were used to select relevant land use variables for the mean model. The model, in which monitor concentrations were regressed on the PLS components, was fit as a whole using maximum likelihood, with each region having its own set of estimated parameters. Universal kriging was used to model the remaining spatial structure in the residuals from the mean model.

The annual average of year 2000 monitoring data (obtained from the Environmental Protection Agency's Aerometric Information Retrieval System from AirData) was used to represent the long-term average at monitor locations throughout the US. This data was used to predict annual average $PM_{2.5}$ concentrations at each subject's baseline geocoded address. Data from the year 2000 was used because this represented an early year of complete national $PM_{2.5}$ monitoring, and a representative year during the follow-up period. Relative concentrations of particulate pollution were largely consistent for study locations throughout the period of study.[6] Furthermore, the year 2000 air pollution monitor data was chosen to facilitate comparisons with the Miller et al study, which used the same year.

Cardiovascular outcomes

The WHI identified CVD outcomes through annual follow-up questionnaires to

participants. If a participant reported an outcome, further details were ascertained via standardized questionnaire or physician adjudication of medical records.[21] Deaths were ascertained via proxy reports and data linkage with the National Death Index of the National Center for Health Statistics. Physician adjudicators reviewed all available records for deaths including hospitalization records, autopsy records, and death certificate diagnoses.[21]

Outcomes of interest in this study included time to first cardiovascular event (defined as myocardial infarction (MI), coronary revascularization, stroke, and death from coronary heart disease or cerebrovascular disease) and time to death from cardiovascular cause (including deaths from coronary heart disease (CHD) and cerebrovascular disease). An algorithm that incorporated elements of the medical history, electrocardiogram readings, and results of cardiac enzyme/troponin determinations were used to identify and categorize MI's into definite or possible MI's.[21] Coronary revascularization was defined as having documented coronary artery bypass graft (CABG) surgery, percutaneous transluminal coronary angioplasty (PTCA) or coronary stent or atherectomy. Strokes included persistent neurological deficit of more than 24 hour duration, due to obstruction or rupture in the brain arterial system. Deaths due to coronary heart disease include deaths due to definite MI's and to definite or possible CHD. Definite fatal CHD were those with no known non-atherosclerotic cause and chest pain within the 72 hours of death and/or a history of chronic disease (with no valvular heart disease or non-ischemic cardiomyopathy). Possible atherosclerotic cardiac disease death was defined as those with no known non-atherosclerotic cause that were consistent with CHD as an underlying cause.

Participant and neighborhood characteristics

The following participant characteristics were adjusted for in all models as potential

confounders: age, race/ethnicity, diabetes, hypertension, hypercholesterolemia, smoking (smoking status, cigarettes per day, years smoked), body mass index (BMI), systolic blood pressure (SBP), and physical activity. Age was a continuous variable measured in years. All analyses, however, were stratified in 5 year age categories. For this study, multiple categories of race/ethnicity were condensed into a binary indicator for non-Hispanic White or other race/ethnicity. Diabetes, hypertension, and cholesterol were binary variables indicating presence or absence of the condition and were obtained by self-report at baseline. Smoking status was a categorical variable indicating whether the participant smoked currently, in the past, or had never smoked. Cigarettes smoked per day and years smoking were measured as categorical variables and were condensed into 4 and 3 groups, respectively, for the analysis. All smoking variables were obtained at baseline from self-report. BMI was a continuous variable that was calculated from participant height and weight (kilograms/meters^2); BMI was broken into quartiles for analyses because its distribution was highly skewed. Systolic blood pressure was a continuous variable measured in mmHg and was an average of two measurements collected at the baseline examination. Physical activity was a continuous variable that measured energy expenditure from recreational physical activity (included walking, mild, moderate and strenuous physical activity) in total metabolic task (MET) hours per week. Physical activity had a highly skewed distribution and was categorized into quartiles for the analyses.

Individual SES measures that were obtained from the baseline questionnaire include: education (high school or less, some college/associate degree/trade school, and bachelor's degree or higher), family income (<$20,000, $20,000 - $34,999, $35,000 - $49,999, $50,000 - $74,999, and ≥$75,000), and occupation (managerial/professional, technical/sales/administrative, service/labor, and homemaker).

In addition to individual SES, we used data from the 2000 Census to assess NSES at baseline. Census data for each WHI participant was available at the tract level, a unit of geography small enough to be considered a reasonable proxy for neighborhood.[22] Variables included in this study are median family income, percentage of adults older than 25 with a high school degree, percentage unemployed, and median home value of owner-occupied housing units. All of these NSES variables were measured as continuous variables. These variables were selected *a priori* because they represent the major domains of SES: income, education, occupation and wealth. The "NSES score" was a composite measure of several Census tract-level variables selected from a confirmatory factor analysis. This index was comprised of (1) percent of adults older than 25 with less than a high school education; (2) percent male unemployment; (3) percent of households with income below the poverty line; (4) percent of households receiving public assistance; (5) percent of households with children headed only by a female; and (6) median household income.[23] In WHI, the NSES score interpolates Census data for the years between 1990 and 2000 and then assigned participants the NSES score based on their year of enrollment. Higher values on the score indicate higher NSES.

Statistical analysis

The relationship between long-term, annual average $PM_{2.5}$ exposure in 2000 and time until incident cardiovascular events was assessed in Cox proportional hazards models. Analyses were repeated for cardiovascular deaths. HR's with 95% confidence intervals were estimated. The analysis time used in this study was time from enrollment until first occurrence of events of interest, death, or loss of contact. All models were adjusted for the following confounders (decided *a priori*): age, race/ethnicity, diabetes, hypertension, hypercholesterolemia, BMI

(quartiles), systolic blood pressure (continuous), smoking status (3 categories), cigarettes smoked per day (4 categories), years smoked (3 categories), and physical activity (quartiles). All models were stratified on age (five year categories), BMI (four categories), and diabetes which allowed for different baseline hazards in each stratum in order to control for confounding more thoroughly.

Although the use of explanatory variables at both the individual and neighborhood level suggests a multilevel approach, multilevel Cox regression models are often computationally intensive and cumbersome.[24] Therefore, this study utilized the more tractable marginal method. Instead of the multilevel estimation of individual and neighborhood level coefficients and error terms for each individual, the marginal approach uses traditional estimation methods to estimate Cox regression coefficients. However, standard errors obtained by traditional estimation methods are biased downward due to the geographic clustering of individuals. To obtain unbiased estimates of the standard errors and p-values for the model coefficients, the marginal method adjusts the variance of these coefficients using a sandwich estimator.[25, 26]

To observe potential confounding by SES variables, we started with the basic model which adjusted for all non-SES covariates (age, race/ethnicity, diabetes, hypertension, hypercholesterolemia, BMI, systolic blood pressure, smoking, and physical activity). We then proceeded to adjust for SES variables one at a time, fitting separate models for each SES variable (individual or neighborhood). All NSES variables were measured as continuous variables and they were not transformed in the analyses for confounding. We then proceeded to fit three models using a combination of SES variables. The first model adjusted for all three individual SES variables (education, income, occupation). The second model adjusted for all four NSES variables (median family income, percentage of adults older than 25 with a high school degree,

percentage unemployed, and median home value of owner-occupied housing units). The third model adjusted for both individual and neighborhood SES variables. Lastly, analyses were conducted to observe potential confounding by the NSES score. Since this variable is a composite of several NSES variables, it was not necessary to adjust for other NSES factors. These models were first fit without adjusting for individual SES and subsequently fit while adjusting for only individual SES variables (in addition to the NSES score of interest and non-SES confounders such as age and BMI).

Potential effect modification by individual and neighborhood SES variables was investigated by fitting linear interaction terms with $PM_{2.5}$. Separate interaction models were fit for each individual and neighborhood SES variable. All models were adjusted for all individual and neighborhood SES variables in addition to the confounders such as age and race/ethnicity. Potential effect modifiers measured as continuous variables were grouped into quartiles and this form was used in the main effects and interaction terms. Trend tests were performed by modeling the SES variable quartiles as a single continuous variable. Overall effect modification was also assessed when SES variables and their interaction terms with $PM_{2.5}$ were included as factors (multiple indicator variables).

Statistical analyses were conducted using Stata software (version 11.2, Stata).

RESULTS

Subject Characteristics

Of the 93, 605 subjects with an OS baseline questionnaire, 18,562 had cardiovascular disease at baseline and were excluded from the study. Of the remaining women, 1,997 had missing cardiovascular disease status at baseline and were also excluded. 6,157 women were excluded due to missing baseline $PM_{2.5}$ predictions and 5,814 excluded due to poor geocodes (above the street level). Finally, 48,067 women had complete information for all the main analytical variables and a total of 364,762 women-years of follow-up time was available for analysis.

The mean age of subjects at enrollment was 63 years (Table 1). Most participants were non-Hispanic Whites (86.4%) and were never or past smokers (52.4% and 41.5%, respectively). Subjects who had cardiovascular events or deaths tended to be older, to be more likely to be current or past smokers, to have higher systolic blood pressure, to be more likely to have hypertension, hypercholesterolemia, and diabetes and to be less physically active. In terms of individual SES, those with CVD events or deaths tended to have lower education, lower income and were more likely to be homemakers or work in the service or labor sector. Those with events or deaths tended to live in neighborhoods with lower median family income, higher unemployment, lower education, lower median home values, and lower NSES scores.

$PM_{2.5}$ Exposure

The number of events in each quintile of $PM_{2.5}$ exposure is shown in Table 2. The overall mean concentration of $PM_{2.5}$ was 12.8 $\mu g/m^3$ (interquartile range, 4.0; Table 3). The minimum exposure was 2.2 $\mu g/m^3$ and the maximum was 25.1 $\mu g/m^3$. The 10^{th} and 90^{th} percentiles were

9.4 and 16.5 μg/m3, respectively. Predicted annual average $PM_{2.5}$ concentration by covariates and individual SES are shown in Table 3. Figure 1 shows scatter plots of $PM_{2.5}$ concentrations by various NSES characteristics with LOWESS curves. In general, areas with lower NSES tended to be exposed to higher levels of $PM_{2.5}$. However, the differences tended to be small.

Confounding by SES

Exposure to $PM_{2.5}$ was significantly associated with risk of cardiovascular events. The age-adjusted HR of a 10 $\mu g/m^3$ higher exposure to $PM_{2.5}$ was 1.25 (95% CI, 1.09 to 1.43) for the time to first cardiovascular event (Table 4). After additional adjustment for race/ethnicity, smoking, BMI, diabetes, hypertension, hypercholesterolemia, systolic blood pressure, and physical activity, the HR was 1.22 (95% CI, 1.06 to 1.40). Further adjustment for individual or neighborhood SES (singly or combined) did not change the HR materially.

The age-adjusted HR of a 10 $\mu g/m^3$ higher exposure to $PM_{2.5}$ was 1.38 (95% CI, 1.03 to 1.86) for the time to CVD death. The HR was attenuated and not statistically significant in the primary model, adjusted for race/ethnicity, smoking, BMI, diabetes, hypertension, hypercholesterolemia, systolic blood pressure, and physical activity (HR=1.31; 95% CI, 0.97 to 1.78). Similar to the analyses for CVD events, further adjustment for individual or neighborhood SES did not substantially change the HR.

Effect Modification

The association of $PM_{2.5}$ with CVD events or deaths by categories of different individual and neighborhood SES variables is shown in Table 5. None of the individual SES variables significantly modified the association between $PM_{2.5}$ and CVD events.

The association of $PM_{2.5}$ with CVD events increased as NSES decreased. The median family income, percent of adults over 25 years with high school degree, median home value of owner-occupied housing units, and NSES score all significantly modified the effect of $PM_{2.5}$ on CVD events (Table 5). Individuals residing in areas with the lowest quartile of NSES score had a HR of 1.73 (95% CI, 1.33 to 2.25). Those residing in areas with the highest NSES score had an HR of 0.91 (95% CI, 0.63 to 1.19). Similarly, those in the lowest quartile of median home value had a HR of 1.60 (1.21 to 2.11) which declined as family income increased.

There was weaker evidence of NSES affecting the association between long term $PM_{2.5}$ exposure and risk of CVD deaths. Individuals residing in the most advantaged neighborhoods had a much lower point estimate (HR=0.60; 95% CI, 0.15 to 1.04) than all of the other groups although the confidence intervals overlapped.

DISCUSSION

This study has confirmed previous studies that higher exposure to long term $PM_{2.5}$ is a risk factor for cardiovascular disease. The results suggest that individual and neighborhood SES are not important confounders of the association between $PM_{2.5}$ exposure and CVD in this cohort. However, NSES significantly modifies the association between $PM_{2.5}$ and cardiovascular events. NSES may also modify the association between $PM_{2.5}$ and cardiovascular deaths, but the evidence is weaker.

One previously published epidemiological study by Miller and colleagues has investigated the relationship between long-term exposure to fine particulate matter ($PM_{2.5}$) and cardiovascular disease incidence in the WHI OS.[6] The authors used the nearest monitor data from the participant's zip code centroid to assign exposures. The participants were followed from enrollment until August 2003 for outcome ascertainment. The authors found that each increase of 10 $\mu g/m^3$ of $PM_{2.5}$ was associated with a 24% increase in the risk of a cardiovascular event (hazard ratio [HR] = 1.24, 95% confidence interval [CI]: 1.09 to 1.41), adjusted for select demographic and individual level SES characteristics, and cardiovascular risk factors.[6] Furthermore, the HR associated with any death from cardiovascular disease was estimated to be 1.76 (95% CI: 1.25 to 2.47).

This study, which uses the same cohort with an extended period of follow-up and additional approach to exposure assessment, is consistent with the findings in the Miller et al study that long term exposure to $PM_{2.5}$ was significantly associated with an increased risk of CVD events, after adjustment for select demographics, SES, and cardiovascular risk factors. The observed associations are similar in magnitude; Miller et al reported an HR of 1.24 (95% CI,

1.09 to 1.41) compared to the fully adjusted HR of 1.22 (95% CI, 1.06 to 1.40) from this study. However, differences emerged in the analyses on time until CVD deaths.

Although this study did not find a significant association between $PM_{2.5}$ exposure and CVD deaths (fully adjusted HR=1.31, 95% CI, 0.95 to 1.81), the effect estimate is similar to that for total events suggesting an association does exist. The lack of statistical significance could be driven by the relatively small number of deaths in the cohort (n=536 or 1.1%), that is, limited power. In addition, our results may differ from those of Miller et al because of differences in exposure measurement between the two studies. This study employed a metric that was specific to the geocoded address of each participant whereas Miller at al used data from the nearest monitor to the participant. The method used in this paper likely produced an exposure with less measurement error. Also, this study had 2 more years of follow-up compared to the Miller study. This may introduce a source of measurement error if the baseline $PM_{2.5}$ exposure becomes less appropriate as a proxy for long-term $PM_{2.5}$ exposure as time goes on. Furthermore, the model used in this study differs from the one used in the Miller study due to slightly different selection and transformations of confounders. Our fully-adjusted estimate for the association between $PM_{2.5}$ and CVD deaths is close to those found in both the Harvard Six Cities Study (HR=1.19; 95% CI, 1.05 to 1.34) and the American Cancer Society study (HR=1.13; 95% CI, 1.08 to 1.18).[9] The slightly higher HR we observed may be due to differences in the subjects studied. Both the Harvard Six Cities Study and the American Cancer Society study included men and women. Prior research suggests that the effects of air pollution on health is larger in women than in men, which may explain our slightly larger point estimate.[27, 28]

Researchers generally adjust for some measure of SES in their models, because individuals with lower SES are at a greater risk of CVD but also tend to reside in areas with

higher air pollution.[7, 11-15] However, given the estimates in Table 4, we found no evidence of strong confounding by either individual or neighborhood SES in this cohort. Miller et al adjusted for confounding by individual-level household income and education. They reported that their results were not sensitive to further adjustment for occupation or Census-derived measures of income, wealth, or poverty on the basis of zip codes. Although previous research by Jerrett suggested that neighborhood SES consistently confounded the relationship between particulate air pollution and mortality, in their study none of the risk estimates changed more than 10% for exposure to 13 mg/m^3 higher total-suspended particles.[29] That is, NSES was not a strong confounder in the Jerrett et al study. A study by Brochu et al investigated whether particulate matter was associated with SES in the northeastern United States and found that lower SES populations were exposed to higher ambient PM compared with higher SES populations.[11] However, given that the percentage difference in annual average $PM_{2.5}$ and PM_{10} between the two groups was small, the authors concluded that SES was not likely a major source of confounding in epidemiological studies of PM. This is consistent with our results and with studies that reported small changes in estimates of relative risk after adjustment for SES variables including education and income.[1, 10, 29] However, it should be noted that the WHI cohort lives in higher SES neighborhoods relative to the U.S. as a whole. Relatively small SES variability in our data could also explain the lack of confounding by SES in our results. SES may still be an important confounder in populations where differences in air pollution between those with low and high SES are large.

According to the so-called triple jeopardy hypothesis, individuals with low SES may be disproportionately affected by the adverse health effects of air pollution.[7, 8] Researchers have documented that groups with low SES and racial minorities have higher exposure to air

pollution.[30, 31] In addition, as a result of poverty and psychosocial stress in poor communities, these groups suffer from worse health outcomes.[14, 15] The combination of greater exposure to air pollution and fewer resources to cope with the effects of air pollution may result in increased susceptibility to air pollution related health outcomes.[7, 8] Our study provides support for this hypothesis, as our data show that individuals living in more disadvantaged neighborhoods may be more susceptible to the harmful effects of $PM_{2.5}$.

In this study, NSES variables were found to significantly modify the association between $PM_{2.5}$ and time until first CVD events. HR's were higher in individuals residing in areas with lower NSES, as measured by the median family income, median home value of owner-occupied housing units, and NSES score. In the analyses of CVD deaths, only the NSES score was a significant effect modifier. This suggests that NSES is a more relevant effect modifier than individual SES. Miller et al did not find significant effect modification by individual level household income or education, although there is a trend of greater effect among the least educated. They did not assess effect modification by NSES. In addition, our results suggest that for this cohort, three of the four domains of SES: income, wealth, and education affect the association between $PM_{2.5}$ and CVD on a neighborhood level. Occupation (as measured by percentage unemployed) was not significant although individuals residing in areas with the highest unemployment had the highest HR estimate of 1.43 (95% CI, 1.05 to 1.81). The overall deprivation of a neighborhood, as reflected by the NSES score, was the most significant effect modifier of all, providing further evidence that the effect of overall SES cannot be captured by a single measure of SES alone.

Previous research provides mixed results regarding whether SES modifies the effect of air pollution on health. Some researchers have found that $PM_{2.5}$ had the greatest adverse effect on

all-cause mortality among the least educated.[9, 10, 32] Additionally, Finkelstein et al observed that total suspended particulate had a greater effect on all-cause mortality among those with lower neighborhood household income.[33] In Rome, there is also evidence that the harmful effects of PM_{10} exposure on mortality were greater in individuals with lower census block income and lower census block SES index (based on education, working category, unemployment, crowding, home ownership).[34] Researchers in Hong Kong found that the greatest effects of PM_{10} on mortality was observed in blue-collar workers and individuals living in public housing rather than private housing.[35] The extant literature also provides evidence that the largest effects of various gaseous pollutants on mortality[36] and respiratory health[37] were observed in individuals residing in areas with low NSES. However, some studies have found no effect modification by SES on the association between air pollution and adverse effects. Some studies of the effect of PM_{10} on mortality did not find effect modification by NSES.[4, 38] NSES[39] and individual SES[39, 40] were not found to influence the effect of air pollution on cardiac morbidity. Differences in these results may be due to the heterogeneity of the study subjects, location, and SES indicators (individual or neighborhood) investigated. This study supports results that suggest individuals with lower NSES carry a greater burden of the adverse effects of air pollution than those living in wealthier neighborhoods.

It has been hypothesized that individuals with low SES are more susceptible to air pollution effects because some conditions and traits linked to vulnerability are also associated with SES[7,41]. For example, chronic medical conditions, health care access, nutrition, fitness, other pollutant exposures, psychosocial stress, and addictions to drugs or alcohol may all affect individual susceptibility to the harmful effects of air pollution. Those with low individual SES may not have the income to purchase nutritious foods rich in antioxidants that may help to

alleviate the adverse effects of air pollution. Low SES individuals may have reduced access to healthcare and medications which may alleviate health conditions caused by or aggravated by air pollution. Furthermore, factors such as violence and psychosocial stress may be more prevalent in low SES individuals and can increase susceptibility. Although individual and neighborhood SES are correlated, they are likely to be independently associated with factors that affect susceptibility.[7] In other words, NSES may affect susceptibility independent of or in addition to the effects of individual SES. Individuals living in disadvantaged neighborhoods may not have access to fresh and healthy foods. This may be in addition to low individual income preventing them from buying healthier foods that are more expensive. Disadvantaged neighborhoods may also have less neighborhood communication and collaboration due to higher traffic density, thereby reducing social network and support. Furthermore, disadvantaged neighborhoods may be more likely to have higher concentrations of other environmental pollutants such as tobacco smoke, which may weaken the health of inhabitants and render them more vulnerable to additional insults by air pollution.[7]

There are several limitations to this study. First, there may be unobserved confounders, such as self-selection into certain neighborhoods that may confound our analysis. Because these potential confounders are unmeasured, their impact on the analyses is hard to decipher. However, we have adjusted for many demographic, socioeconomic, and health characteristics and our estimates are robust to these adjustments. Secondly, the study relies on exposure data that is based on ambient $PM_{2.5}$ concentrations measured at baseline, which may be a source of measurement error. We do not have information on indoor air pollution or individual time-activity patterns leading to participants spending time in different microenvironments that have different exposures. None of these are captured in our analysis which is focused on outdoor

concentrations. In addition, baseline $PM_{2.5}$ concentrations based on the year 2000 monitor data may not capture the true underlying long term $PM_{2.5}$ exposure. However, there is evidence that particulate pollution was stable and highly correlated over the years.[6] Third, we do not have access to potentially more relevant measures of individual SES in an elderly cohort (e.g., property values). However, we were able to look at median home value at the neighborhood level. Finally, subjects of this study were postmenopausal women over 50 years old at baseline, thus limiting our ability to generalize our results to the general population.

This study has several strengths. First, analyses were conducted using a large sample size and a long follow-up time. Second, outcomes were adjudicated based on protocol-based review of medical records, thereby reducing outcome misclassification. Third, we were able to resolve $PM_{2.5}$ exposures to the level of the individual's residence based on geocodes, reducing exposure misclassification. Finally, this study investigated the roles of both individual and neighborhood SES on the association between air pollution and cardiovascular disease. Previous research suggests that individual and neighborhood SES may have independent effects on health. However, few studies had been able to look at individual SES, NSES, air pollution, and cardiovascular health in a single framework. This study may help fill in part of the gap of knowledge in this area.

In conclusion, these results provide confirmation of the observed detrimental effects of long term exposure to $PM_{2.5}$ on cardiovascular health. Our results show that individual and neighborhood SES were not important confounders of the relationship between $PM_{2.5}$ and CVD in this cohort. Researchers who continue work in this area should still evaluate individual and neighborhood SES as potential confounders of the air pollution-CVD association given that the literature has previously found strong associations between air pollution and SES as well as CVD

and SES. Importantly, however, our study provides evidence that individuals living in more disadvantaged neighborhoods may be more susceptible to the harmful effects of $PM_{2.5}$. Further studies are needed to reach a definitive conclusion that NSES modifies the effect of air pollution on cardiovascular health. However, this study brings to light the importance of continued investigation on this topic. The collective results may have important public health and environmental policy implications and may inform decisions about resource allocation and where to focus our efforts to reduce air pollution.

Table 1. Demographic, socioeconomic (SES) and health characteristics of study subjects, overall, by cardiovascular event and by death from cardiovascular disease.*

Characteristic	Overall N=48,067	Cardiovascular event		Death from cardiovascular cause	
		Yes	No	Yes	No
Adjustment Covariates					
Age (yr)	63.4 ± 7.3	67.6 ± 6.7	62.7 ± 7.2	69.9 ± 6.6	62.9 ± 7.2
Race or ethnicity – n (%)					
Non-Hispanic White	41,547 (86.4)	2,175 (88.9)	39,372 (86.3)	468 (87.3)	41,079 (86.4)
Other	6,520 (13.6)	271 (11.1)	6,249 (13.7)	68 (12.7)	6,452 (13.6)
Smoking status – n (%)					
Never smoked	23,901 (52.4)	1,208 (49.4)	23,901 (52.4)	251 (46.8)	24,858 (52.3)
Past smoker	18.927 (41.5)	1,040 (42.5)	18,927 (41.5)	237 (44.2)	19,730 (41.5)
Current smoker	2,793 (6.1)	198 (8.1)	2,793 (6.1)	48 (9.0)	2,943 (6.2)
BMI (kg/m^2)	27.1 ± 5.7	28.1 ± 6.0	27.0 ± 5.7	27.7 ± 6.5	27.1 ± 5.7
Systolic blood pressure (mmHg)	126.0 ± 17.7	135.8 ± 18.7	125.5 ± 17.5	137.1 ± 19.7	125.9 ± 17.6
Hypertension – n (%)	14,064 (29.3)	1,232 (50.4)	12,832 (28.1)	283 (52.8)	13,781 (29.0)
Hypercholesterolemia – n (%)	5,928 (12.3)	439 (18.0)	5,489 (12.0)	75 (14.0)	5,853 (12.3)
Diabetes – n (%)	1,987 (4.1)	277 (11,3)	1,710 (3.8)	64 (11.9)	1,923 (4.1)
Physical Activity (MET/week)	14.0 ± 14.3	12.0 ± 12.9	14.1 ± 14.3	10.8 ± 11.4	14.0 ± 14.3
Individual SES Variables					
Education – n (%)					
High school or less	9,520 (19.8)	605 (24.7)	8,915 (19.5)	124 (23.1)	9,396 (19.8)
Some college/Associate degree/ trade school	17,156 (35.7)	984 (40.2)	16,172 (35.5)	212 (39.6)	16,944 (35.7)
Bachelor's degree or higher	21,391 (44.5)	857 (35.0)	20,534 (45.0)	200 (37.3)	21,191 (44.6)
Family income – n (%)					
< $20,000	6,565 (13.7)	499 (20.4)	6,066 (13.3)	124 (23.1)	6,441 (13.6)
$20,000 to $34,999	10,882 (22.6)	737 (30.1)	10,145 (22.2)	157 (29.3)	10,725 (22.6)
$35,000 to $49,999	9,921 (20.6)	505 (20.7)	9,416 (20.6)	99 (18.5)	9,822 (20.7)
$50,000 to $74,999	10,132 (21.1)	384 (15.7)	9,748 (21.4)	91 (17.0)	10,041 (21.1)
≥ $75,000	10,567 (22.0)	321 (13.1)	10,246 (22.5)	65 (12.1)	10,502 (22.1)
Occupation – n (%)					47531
Managerial/professional	21,411 (44.5)	914 (37.4)	20,497 (44.9)	198 (36.9)	21,213 (44.6)
Technical/sales/ administrative	14,016 (29.2)	780 (31.9)	13,236 (29.0)	166 (31.0)	13,850 (29.1)
Service/labor	7,828 (16.3)	450 (18.4)	7,378 (16.2)	97 (18.1)	7,731 (16.3)
Homemaker only	4,813 (10.0)	302 (12.4)	4,510 (9.9)	75 (14.0)	4,737 (10.0)
Neighborhood SES Variables					
Median family income ($)	68,556 ± 29,418	65,406 ± 27,652	68,725 ± 29,500	66,523 ± 30,223	68,579 ± 29,408
Percent unemployed	4.6 ± 3.8	4.8 ± 3.8	4.6 ± 3.8	4.9 ± 4.2	4.6 ± 3.8
Percent adults over 25 years with high school degree	86.8 ± 10.6	86.0 ± 10.8	86.8 ± 10.5	86.2 ± 10.8	86.8 ± 10.5
Median value of owner-occupied housing units ($)	196,622 ± 145,391	183,659 ± 134,120	197,317 ± 145,939	194,586 ± 143,597	196,645 ± 145,412
NSES score	76.4 ± 8.4	75.7 ± 8.5	76.4 ± 8.3	75.5 ± 8.8	76.4 ± 8.4

*Data are reported as n (%) or mean ± SD.

Table 2. Number of cardiovascular events and deaths by quintiles of $PM_{2.5}$

	Quintiles of $PM_{2.5}$					
	< 10.5 µg/m^3	**10.6 -11.9 µg/m^3**	**12.0 -13.4 µg/m^3**	**13.5 -15.4 µg/m^3**	**> 15.5 µg/m^3**	**Total**
n	9,614	9,613	9,614	9,613	9,613	48,067
Events*	459 (4.8)	501 (5.2)	462 (4.8)	488 (5.1)	536 (5.6)	2446
Deaths*	84 (0.9)	115 (1.2)	111 (1.2)	103 (1.1)	123 (1.3)	536

*n (%)

Table 3. Predicted annual average fine particulate matter ($PM_{2.5}$) concentration in $\mu g/m^3$, by participant characteristics.

	$PM_{2.5}$ Concentration		
	Mean (SD)	Median	IQR
Overall	12.8 (2.9)	12.5	4.0
Race (%)			
Non-Hispanic White	12.7 (2.8)	12.4	3.9
Other	13.7 (3.0)	14.1	4.3
Smoking status			
Never smoked	12.8 (2.9)	12.5	4.1
Past smoker	12.7 (2.8)	12.5	3.9
Current smoker	13.1 (3.0)	13.0	4.2
Hypertension			
Yes	12.9 (2.9)	12.6	4.1
No	12.7 (2.9)	12.5	4.0
Hypercholesterolemia			
Yes	12.9 (2.9)	12.7	4.1
No	12.8 (2.9)	12.5	4.0
Diabetes			
Yes	13.0 (3.0)	12.9	4.4
No	12.8 (2.9)	12.5	4.0
BMI			
Normal and under (<25.0)	12.7 (2.9)	12.5	3.9
Overweight (25.0-29.9)	12.8 (2.9)	12.5	4.0
Obese (≥30)	12.9 (2.9)	12.6	4.1
Physical Activity (MET per week)			
3.5 or less	13.0 (3.0)	12.7	4.2
3.6 to 10.5	12.9 (2.9)	12.6	4.1
10.6 to 20.2	12.7 (2.8)	12.5	3.9
20.3 or more	12.6 (2.9)	12.3	3.9
Education			
High school or less	12.7 (2.9)	12.5	4.1
Some college/Associate degree/ trade school	12.7 (3.0)	12.4	4.1
Bachelor's degree or higher	12.9 (2.8)	12.7	3.8
Family income			
< $20,000	12.9 (3.0)	12.8	4.4
$20,000 to $34,999	12.7 (2.9)	12.4	4.1
$35,000 to $49,999	12.7 (2.9)	12.4	4.1
$50,000 to $74,999	12.8 (2.8)	12.5	3.9
≥ $75,000	12.9 (2.8)	12.6	3.6
Occupation			
Managerial/professional	12.9 (2.8)	12.6	3.9
Technical/sales/administrative	12.8 (2.9)	12.5	4.0
Service/labor	12.7 (3.0)	12.5	4.2
Homemaker only	12.6 (3.0)	12.4	4.1

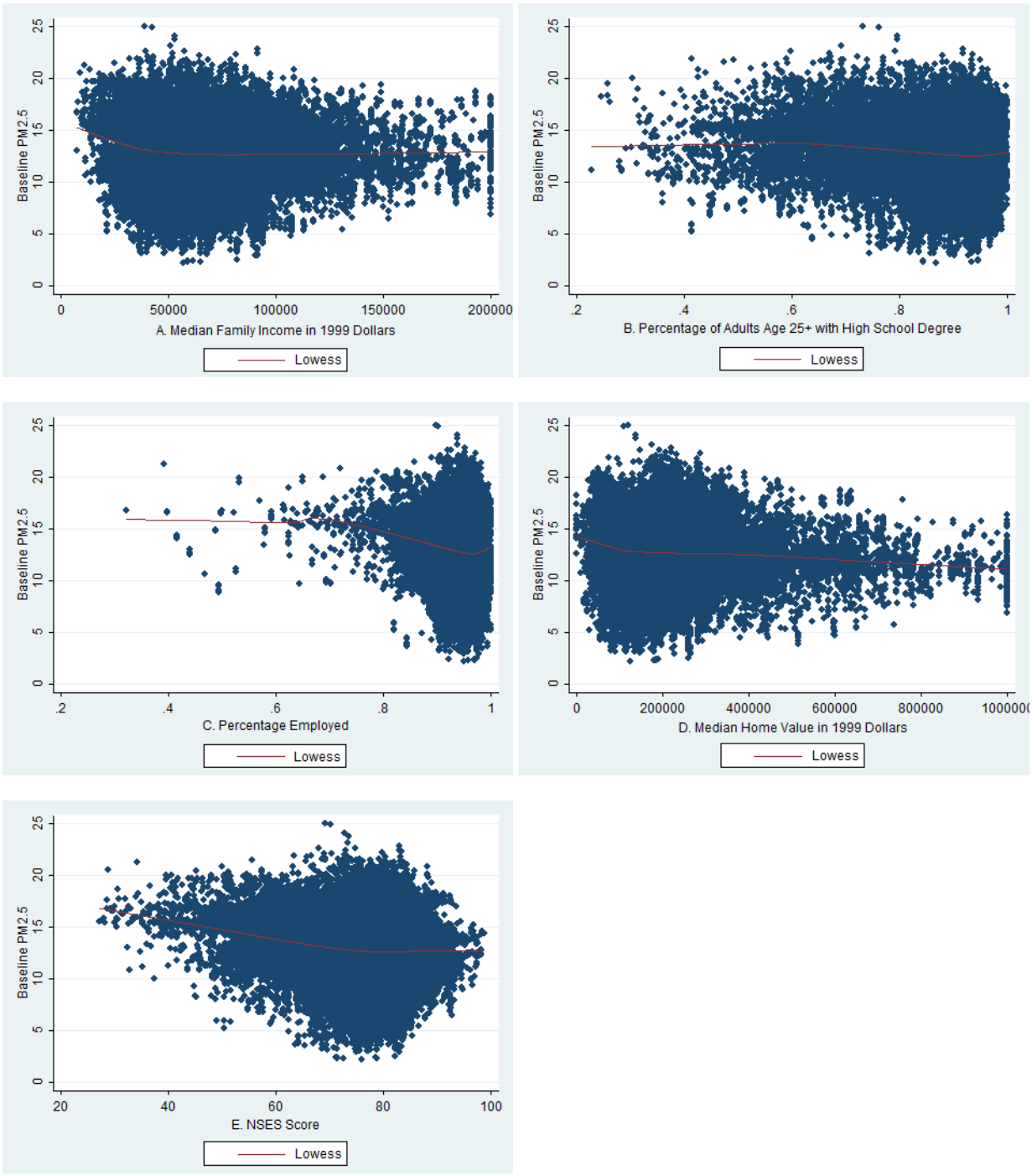

Figure 1. Scatterplots of baseline $PM_{2.5}$ in $\mu g/m^3$ by NSES characteristics with LOWESS curves.

Table 4. Estimated hazard ratios for the time to first cardiovascular event and death associated with 10μg/m^3 higher exposure to fine particulate matter, by different levels of adjustment for individual and neighborhood SES characteristics.

	Cardiovascular Event		**Cardiovascular Death**	
Level of Adjustment	**Age-adjusted Hazard Ratio (95% CI)**	**Fully Adjusted Hazard Ratio (95% CI)***	**Age-adjusted Hazard Ratio (95% CI)**	**Fully Adjusted Hazard Ratio (95% CI)***
$PM_{2.5}$ only	1.25 (1.09 to 1.43)	1.22 (1.06 to 1.40)	1.38 (1.03 to 1.86)	1.31 (0.97 to 1.78)
Individual SES				
Education	1.27 (1.10 to 1.45)	1.23 (1.07 to 1.42)	1.39 (1.03 to 1.87)	1.32 (0.97 to 1.78)
Family income	1.25 (1.09 to 1.43)	1.22 (1.06 to 1.40)	1.38 (1.03 to 1.85)	1.32 (0.97 to 1.78)
Occupation	1.25 (1.09 to 1.44)	1.22 (1.06 to 1.41)	1.39 (1.03 to 1.86)	1.32 (0.97 to 1.78)
Combined[+]	1.26 (1.10 to 1.45)	1.23 (1.07 to 1.42)	1.39 (1.03 to 1.86)	1.32 (0.98 to 1.79)
Neighborhood SES				
Median family income	1.23 (1.07 to 1.41)	1.22 (1.06 to 1.40)	1.37 (1.02 to 1.85)	1.32 (0.97 to 1.80)
Percent unemployed	1.23 (1.07 to 1.42)	1.23 (1.06 to 1.41)	1.34 (0.99 to 1.81)	1.32 (0.97 to 1.79)
Percent adults over 25 years with high school degree	1.20 (1.04 to 1.38)	1.21 (1.05 to 1.39)	1.33 (0.99 to 1.80)	1.32 (0.97 to 1.80)
Median value of owner-occupied housing units	1.21 (1.05 to 1.39)	1.21 (1.05 to 1.38)	1.37 (1.02 to 1.85)	1.33 (0.98 to 1.81)
NSES score	1.20 (1.05 to 1.38)	1.22 (1.06 to 1.40)	1.33 (0.98 to 1.79)	1.33 (0.98 to 1.81)
Combined[‡]	1.20 (1.04 to 1.37)	1.20 (1.04 to 1.38)	1.32 (0.97 to 1.79)	1.31 (0.95 to 1.79)
NSES score adjusted[+]	1.25 (1.09 to 1.43)	1.24 (1.08 to 1.43)	1.35 (1.00 to 1.82)	1.34 (0.99 to 1.82)
Fully Adjusted[§]	1.23 (1.07 to 1.41)	1.22 (1.06 to 1.40)	1.34 (0.98 to 1.82)	1.31 (0.95 to 1.81)

***** Adjusted for age, race/ethnicity, smoking, BMI, diabetes, hypertension, hypercholesterolemia, physical activity, and systolic blood pressure.

[+] Adjusted for the following individual level SES indicators: education, total family income, and occupation.

[‡] Adjusted for the following neighborhood level SES indicators: median family income, percent unemployed, percent adults over 25 years with high school degree, and median value of owner-occupied housing units

[§] Adjusted for all individual and all neighborhood SES indicators except for the NSES score.

Table 5. Estimated hazard ratios for the time to first cardiovascular event and death associated with 10μg/m^3 higher exposure to fine particulate matter, stratified by individual and neighborhood SES.*

	Cardiovascular Event			Cardiovascular Death		
	No. of Events	**Hazard Ratio (95% CI)**	**p+**	**No. of Events**	**Hazard Ratio (95% CI)**	**p+**
Individual SES						
Education			0.46			0.82
High school or less	605	1.05 (0.79 to 1.40)		124	1.55 (0.83 to 2.89)	
Some college/Associate degree/ trade school	984	1.24 (0.97 to 1.51)		212	1.20 (0.64 to 1.77)	
Bachelor's degree or higher	857	1.33 (1.00 to 1.65)		200	1.31 (0.65 to 1.97)	
p for trend			0.24			0.60
Family income			0.19			0.84
< $20,000	499	1.58 (1.17 to 2.14)		124	1.56 (0.85 to 2.87)	
$20,000 to $34,999	737	1.07 (0.80 to 1.34)		157	1.51 (0.67 to 2.35)	
$35,000 to $49,999	505	1.39 (0.96 to 1.81)		99	1.13 (0.34 to 1.93)	
$50,000 to $74,999	384	1.01 (0.65 to 1.38)		91	0.96 (0.24 to 1.67)	
≥ $75,000	321	1.06 (0.64 to 1.49)		65	1.26 (0.14 to 2.4)	
p for trend			0.15			0.36
Occupation at baseline			0.30			0.54
Managerial/professional	914	1.45 (1.15 to 1.84)		198	1.76 (0.99 to 2.76)	
Technical/sales/ administrative	780	1.13 (0.85 to 1.40)		166	1.32 (0.60 to 2.04)	
Service/labor	450	1.06 (0.73 to 1.40)		97	0.89 (0.29 to 1.49)	
Homemaker only	302	1.12 (0.69 to 1.55)		75	1.25 (0.29 to 2.21)	
Neighborhood SES						
Median family income			0.10			0.46
≤ $48,393	694	1.48 (1.15 to 1.90)		159	1.42 (0.84 to 2.40)	
$48,394 to $63,094	630	1.29 (0.94 to 1.63)		124	1.60 (0.58 to 2.61)	
$63,095 to $82,505	594	1.12 (0.80 to 1.44)		128	1.55 (0.64 to 2.47)	
≥ $82,506	528	0.89 (0.60 to 1.18)		125	0.78 (0.19 to 1.36)	
p for trend			0.01			0.27
Percent unemployed			0.30			0.90
≥ 5.6%	571	1.43 (1.05 to 1.81)		129	1.05 (0.47 to 2.31)	
3.7% to 5.5%	606	1.25 (0.93 to 1.58)		120	1.36 (0.50 to 2.21)	
2.5% to 3.6%	599	0.98 (0.69 to 1.27)		122	1.24 (0.49 to 1.99)	
≤ 2.4%	670	1.13 (0.83 to 1.54)		165	1.48 (0.72 to 2.24)	
p for trend			0.12			0.47
Percent adults over 25 years with high school degree			0.01			0.26
≤82.4%	675	1.24 (0.95 to 1.61)		146	1.38 (0.78 to 2.44)	
82.5% to 89.7%	639	1.78 (1.27 to 2.29)		132	2.21 (0.78 to 3.63)	
89.8% to 94.5%	555	0.94 (0.68 to 1.21)		123	1.10 (0.44 to 1.77)	
≥ 94.5%	577	1.03 (0.73 to 1.34)		135	0.89 (0.28 to 1.50)	
p for trend			0.08			0.18
Median value of owner-occupied housing units			0.02			0.52
≤ $104,300 9or less	705	1.60 (1.21 to 2.11)		150	1.93 (1.05 to 3.57)	
$104,901 to $155,200	641	1.37(0.99 to 1.76)		116	1.18 (0.40 to 1.97)	
$155,201 to $235,800	541	1.16 (0.84 to 1.48)		130	1.04 (0.38 to 1.71)	
≥ $235,801	559	0.85 (0.60 to 1.10)		140	1.21 (0.54 to 1.88)	
p for trend			0.001			0.19

Table 5 continued

NSES score‡			0.007			0.05
≤ 72.7	667	1.73 (1.33 to 2.25)		154	1.32 (0.75 to 2.30)	
72.8 to 77.8	642	1.29 (0.96 to 1.63)		143	1.50 (0.61 to 2.40)	
77.9 to 81.8	591	1.00 (0.72 to 1.29)		122	2.22 (1.01 to 3.43)	
≥ 81.8	546	0.91 (0.63 to 1.19)		117	0.60 (0.15 to 1.04)	
p for trend			<0.0001			0.28

* All models are adjusted for age, race/ethnicity, smoking, BMI, diabetes, hypertension, hypercholesterolemia, physical activity, systolic blood pressure, education, family income, occupation, median family income, percentage unemployed, percentage of adults over age 25 with high school degree, and median value of owner-occupied housing units.

+ Effect modification was modeled by adding linear interaction terms. Potential effect modifiers that were measured as continuous variables were grouped into quartiles. There are two p values for the interaction. The p value for the overall interaction is based on models where individual and neighborhood SES variables are included as categorical variables with main effects and linear interaction terms for each indicator variable. The p for trend listed in table results from trend tests where the categories of the potential effect modifier were modeled linearly and continuously with only one main effects term and one interaction term for the potential effect modifier.

‡ The NSES score was adjusted for individual level SES variables but not neighborhood level SES variables.

References

1. Dockery DW, Pope CA 3rd, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. An association between air pollution and mortality in six U.S. cities. N Engl J Med 1993;329(24):1753-9.
2. Pope 3rd C, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Heath Jr CW. Particulate air pollution as a predictor of mortality in a prospective study of US adults. American Journal of Respiratory and Critical Care Medicine 1995;151(3):669.
3. Brook R.D., Rajagopalan S., Pope C.A., Brook J.R., Bhatnagar A., Diez-Roux A.V., Holguin F., Hong Y., Luepker R.V., Mittleman M.A., et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the american heart association. Circulation Circulation 2010;121(21):2331-78.
4. Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. N Engl J Med 2000;343(24):1742-9.
5. Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, Samet JM. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA : The Journal of the American Medical Association 2006;295(10):1127-34.
6. Miller KA, Siscovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, Kaufman JD. Long-term exposure to air pollution and incidence of cardiovascular events in women. N Engl J Med 2007;356(5):447-58.
7. O'Neill MS, Jerrett M, Kawachi I, Levy JI, Cohen AJ, Gouveia N, Wilkinson P, Fletcher T, Cifuentes L, Schwartz J, et al. Health, wealth, and air pollution: Advancing theory and methods. Environ Health Perspect 2003;111(16):1861-70.
8. Jerrett M, Burnett RT, Ma R, Pope CA 3rd, Krewski D, Newbold KB, Thurston G, Shi Y, Finkelstein N, Calle EE, et al. Spatial analysis of air pollution and mortality in los angeles. Epidemiology 2005;16(6):727-36.
9. Particle Epidemiology Reanalysis Project. Reanalysis of the harvard six cities study and the american cancer society study of particulate air pollution and mortality. Health Effects Institute; 2000.
10. Pope CA 3rd, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA : The Journal of the American Medical Association 2002;287(9):1132-41.
11. Brochu P.J., Schwartz J., Herrick R.F., Suh H.H., Yanosky J.D., Paciorek C.J., Chen J.T. Particulate air pollution and socioeconomic position in rural and urban areas of the northeastern united states. Am.J.Public Health American Journal of Public Health 2011;101(SUPPL. 1):S224-30.
12. Chaix B, Gustafsson S, Jerrett M, Kristersson H, Lithman T, Boalt A, Merlo J. Children's exposure to nitrogen dioxide in sweden: Investigating environmental injustice in an egalitarian country. Journal of Epidemiology & Community Health 2006;60(3).
13. Jerrett M. A GIS-environmental justice analysis of particulate air pollution in hamilton, canada. Environ Plann A 2001;33(6):955-73.
14. Roux AVD, Borrell LN, Haan M, Jackson SA, Schultz R. Neighbourhood environments and mortality in an elderly cohort: Results from the cardiovascular health study. J Epidemiol Community Health 2004;58(11):917-23.

15. Sundquist K, Winkleby M, Ahlén H, Johansson S. Neighborhood socioeconomic environment and incidence of coronary heart disease: A follow-up study of 25,319 women and men in sweden. Am J Epidemiol 2004;159(7):655-62.
16. Jerrett M, Burnett R, Brook J, Kanaroglou P, Giovis C, Finkelstein N, Hutchison B. Do socioeconomic characteristics modify the short term association between air pollution and mortality? evidence from a zonal time series in hamilton, canada. J Epidemiol Community Health 2004;58(1):31-40.
17. Næss Ø, Piro FN, Nafstad P, Smith GD, Leyland AH. Air pollution, social deprivation, and mortality: A multilevel cohort study. Epidemiology 2007;18(6):686.
18. Elo IT. Social class differentials in health and mortality: Patterns and explanations in comparative perspective. Annual Review of Sociology 2009;35:553-72.
19. Women's Health Initiative Study Group. Design of the Women's health initiative clinical trial and observational study. Control Clin Trials 1998;19(1):61-109.
20. Langer RD, White E, Lewis CE, Kotchen JM, Hendrix SL, Trevisan M. The women's health initiative observational study: Baseline characteristics of participants and reliability of baseline measures. Ann Epidemiol 2003;13(9 Suppl):S107.
21. Curb JD, Mctiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, Johnson KC, Proulx-Burns L, Pastore L, Criqui M. Outcomes ascertainment and adjudication methods in the women's health initiative. Ann Epidemiol 2003;13(9):122.
22. Soobader M, Cubbin C, Gee GC, Rosenbaum A, Laurenson J. Levels of analysis for the study of environmental health disparities. Environ Res 2006;102(2):172-80.
23. Bird CE, Shih RA, Eibner C, Griffin BA, Slaughter ME, Whitsel EA, Karen M, Escarce J, Jewell A, Mouton C, et al. Neighborhood socioeconomic status and incident coronary heart disease among women. J Gen Intern Med 2009;24(Supplement 1):S127.
24. Goldstein H, editor. Multilevel statistical models. 2nd ed ed. London, New York: Edward Arnold, Wiley; 1995. .
25. Lee EW, Wei L, Amato DA. Cox-type regression analysis for large numbers of small groups of correlated failure time observations. Survival Analysis: State of the Art 1992;211:237-47.
26. Lin D. Cox regression analysis of multivariate failure time data: The marginal approach. Stat Med 1994;13(21):2233-47.
27. Chen LH, Knutsen SF, Shavlik D, Beeson WL, Petersen F, Ghamsary M, Abbey D. The association between fatal coronary heart disease and ambient particulate air pollution: Are females at greater risk? Environ Health Perspect 2005;113(12):1723.
28. Künzli N, Jerrett M, Mack WJ, Beckerman B, LaBree L, Gilliland F, Thomas D, Peters J, Hodis HN. Ambient air pollution and atherosclerosis in los angeles. Environ Health Perspect 2005;113(2):201.
29. Jerrett M, Buzzelli M, Burnett RT, DeLuca PF. Particulate air pollution, social confounders, and mortality in small areas of an industrial city. Soc Sci Med 2005;60(12):2845-63.
30. Fujishiro K, Roux AVD, Landsbergis P, Baron S, Barr RG, Kaufman JD, Polak JF, Stukovsky KH. Associations of occupation, job control and job demands with intima-media thickness: The multi-ethnic study of atherosclerosis (MESA). Occup Environ Med 2011;68(5):319-26.
31. Lutsey PL, Roux AVD, Jacobs Jr DR, Burke GL, Harman J, Shea S, Folsom AR. Associations of acculturation and socioeconomic status with subclinical cardiovascular disease in the multi-ethnic study of atherosclerosis. Journal Information 2008;98(11).

32. Cifuentes L, Vega J, Lave L. Daily mortality by cause and socio-economic status in santiago, chile 1988–1996. Epidemiology 1999;10:S45.
33. Finkelstein MM, Jerrett M, DeLuca P, Finkelstein N, Verma DK, Chapman K, Sears MR. Relation between income, air pollution and mortality: A cohort study. Can Med Assoc J 2003;169(5):397.
34. Forastiere F, Stafoggia M, Tasco C, Picciotto S, Agabiti N, Cesaroni G, Perucci CA. Socioeconomic status, particulate air pollution, and daily mortality: Differential exposure or differential susceptibility. Am J Ind Med 2007;50(3):208-16.
35. Ou CQ, Hedley AJ, Chung RY, Thach TQ, Chau YK, Chan KP, Yang L, Ho SY, Wong CM, Lam TH. Socioeconomic disparities in air pollution-associated mortality. Environ Res 2008;107(2):237-44.
36. Bell ML, Dominici F. Effect modification by community characteristics on the short-term effects of ozone exposure and mortality in 98 US communities. Am J Epidemiol 2008;167(8):986-97.
37. PhD SC, Dales RE, MSc SJ. Respiratory health effects of air pollution gases: Modification by education and income. Archives of Environmental & Occupational Health 2006;61(1):5-10.
38. Bateson TF, Schwartz J. Who is sensitive to the effects of particulate air pollution on mortality?: A case-crossover analysis of effect modifiers. Epidemiology 2004;15(2):143.
39. Dragano N, Hoffmann B, Moebus S, Möhlenkamp S, Stang A, Verde PE, Jöckel KH, Erbel R, Siegrist J. Traffic exposure and subclinical cardiovascular disease: Is the association modified by socioeconomic characteristics of individuals and neighbourhoods? results from a multilevel study in an urban region. Occup Environ Med 2009;66(9):628-35.
40. Cakmak S, Dales RE, Judek S. Do gender, education, and income modify the effect of air pollution gases on cardiac disease? Journal of Occupational and Environmental Medicine 2006;48(1):89.
41. Laurent O, Bard D, Filleul L, Segala C. Effect of socioeconomic status on the relationship between atmosphere pollution and mortality. J Epidemiol Community Health 2007;61:665-675.