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$PM_{2.5}$ and Diabetes and Hypertension Incidence in the Black Women's Health Study

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Abstract

Background—Clinical studies have shown that exposure to fine particulate matter ($PM_{2.5}$) can increase insulin resistance and blood pressure. The epidemiologic evidence for an association of $PM_{2.5}$ exposure with the incidence of type 2 diabetes or hypertension is inconsistent.

Methods and Results—We used Cox proportional hazards models to calculate hazard ratios (HRs) and 95% confidence intervals (CI) for incident type 2 diabetes and hypertension associated with exposure to $PM_{2.5}$ in a large cohort of African American women living in 56 metropolitan areas across the U.S., using data from the Black Women's Health Study. Pollutant levels were estimated at all residential locations over follow-up with a hybrid model incorporating land use

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regression and Bayesian Maximum Entropy techniques. During 1995 to 2011, 4387 cases of diabetes and 9570 cases of hypertension occurred. In models controlling for age, questionnaire cycle, and metro area there were positive associations with diabetes (HR = 1.13, 95% CI 1.04–1.24) and hypertension (HR = 1.06, 95% CI 1.00–1.12) per interquartile range of $PM_{2.5}$ (2.9 μg/m^3). Multivariable HRs, however, were 0.99 (95% CI 0.90–1.09) for diabetes and 0.99 (95% CI 0.93–1.06) for hypertension. HRs were increased in some subgroups, e.g, 1.36 (95% CI 0.91–2.04) for diabetes among women with body mass index<25 kg/m^2.

Conclusions—Our results provide little support for an association of $PM_{2.5}$ with hypertension incidence. Results from the overall cohort do not support an association of air pollution with diabetes incidence, but there was a suggestive increase in lean women.

Introduction

Numerous epidemiological studies have shown associations between exposure to air pollutants, including particulate matter and the traffic-related nitrogen oxides, and acute health effects including cardiovascular mortality and morbidity. [1] Recent evidence suggests that these pollutants may also contribute to the genesis of diabetes [2–6] and hypertension.[7] Possible mechanisms include the production of oxidative stress leading to systemic inflammation and the triggering of autonomic nervous system imbalance.[8] An association of air pollution with diabetes and hypertension would be of great public health importance given the ubiquity of exposure and the high prevalence of the conditions. Globally, high blood pressure is the leading physiological risk factor for mortality, accounting for 9.4 million deaths in 2010; high fasting plasma glucose, the third leading risk factor, accounted for 3.4 million deaths. [9] Associations would be of importance for African American women, among whom incidence rates of diabetes and hypertension are especially high.[10] In addition, due to the legacy of residential segregation and environmental injustice, African Americans tend to live in areas of higher air pollution than do white Americans. [11]

The purpose of the present analysis was to assess the association of $PM_{2.5}$ with type 2 diabetes and hypertension incidence among participants in the Black Women's Health Study (BWHS), a large prospective cohort study of African American women. We have previously published data on the association of $PM_{2.5}$ with these outcomes in BWHS participants living in Los Angeles, based on follow-up from 1995 to 2005.[6] In those analyses, diabetes and hypertension incidence were positively associated with levels of $PM_{2.5}$ and nitrogen oxides.

Methods

Study population

The BWHS was established in 1995, when 59,000 black women aged 21 through 69 years of age were recruited mainly from subscribers to Essence magazine, a general readership magazine targeted to black women.[12] The baseline questionnaire elicited information on demographic and lifestyle factors, reproductive history, and medical conditions. The cohort is followed biennially with mailed and Web-based health questionnaires. All questionnaires are available for viewing at http://www.bu.edu/bwhs/for-researchers/sample-bwhs-questionnaires/.

Follow-up of the original cohort is 80% through eight questionnaire cycles. The study protocol was approved by the Institutional Review Board of Boston University School of Medicine. Participants indicate consent by completing and returning the questionnaires.

The present analysis includes data from the baseline questionnaire (1995) and eight subsequent follow-up cycles (1997–2011). The base population included 45,231 women who lived in any of 56 metropolitan areas in the United States and had complete information on body mass index (BMI) at baseline. Women excluded because they did not live in the 56 metro areas (n=11,914) did not differ from the included women in terms of mean age, BMI, or prevalence of diabetes or hypertension. For the *diabetes analytic cohort*, follow-up started at 30 years of age to exclude potential cases of type 1 diabetes. From the base population, we excluded 2228 women with prevalent diabetes, leaving a total of 43,003 women. For the *hypertension analytic cohort,* from the base population we excluded 10,744 women with prevalent hypertension and 716 women who had not had their blood pressure checked within 3 years before baseline, leaving a total of 33,771 women.

Diagnosis of Incident Diabetes and Hypertension

We defined an incident case of type 2 diabetes as self-report of doctor-diagnosed diabetes at age 30 or older during follow-up through 2011. In a validation study, among 227 participants who met this criterion and whose physicians provided data from their medical records, the diagnosis of type 2 diabetes was confirmed in 96%.[13]

We defined an incident case of hypertension as self-report of doctor-diagnosed hypertension during follow-up through 2011 together with concurrent use of a diuretic, or report of use of an anti-hypertensive medication with or without a diagnosis of hypertension. We assessed the accuracy of self-report among 139 participants who met the case criteria for whom we were able to obtain medical records or physician checklists; hypertension was confirmed in 99%, with all systolic pressures being 140 mm Hg or higher and diastolic pressures being 90 mm Hg or higher. [14]

Ascertainment of Covariates

Self-reported height was reported at baseline and weight was updated on all follow-up questionnaires. In a validation study conducted among 115 participants, the Spearman correlation coefficients between self-reported and technician-measured weight and height were 0.97 and 0.93, respectively.[15] Smoking history, alcohol consumption, and hours per week spent in vigorous exercise were obtained at baseline and updated on follow-up questionnaires. In 1995 and 2001, dietary data was obtained with a 68-item modification of the short form Block-National Cancer Institute food frequency questionnaire.[16] We used factor analysis of 35 food groups to identify two dietary patterns, one characterized by high intake of vegetables and fruit and the other by high intake of meat and fried food.[17] Regression coefficients from the factor analysis were used to weight the intake of the food groups for calculation of the two diet pattern scores. Information was also obtained on household income (2003), educational attainment (1995, 2003), and parental history of diabetes (1999).

Residential addresses to which questionnaires were mailed from 1995 to 2009 were geocoded and linked to US Census data at the block group level, subdivisions of census tracts that generally average approximately 1500 people.[18] We used factor analysis to create a neighborhood socioeconomic status (SES) score that included seven census variables (median household income; median housing value; percent of households receiving interest, dividend or net rental income; percent of adults aged ≥25 years that completed college; percent of families with children headed by a single female; percent of population living below the poverty line; and percent African American). Factor loadings for the variables are shown in eTable 1. Regression coefficients from the factor analysis were used to weight the variables for a combined neighborhood score, with higher scores indicating higher neighborhood SES.

Estimation of $PM_{2.5}$

We used a hybrid modeling approach to estimate ambient $PM_{2.5}$ at all residential addresses to which questionnaires were mailed biennially from 1995 through 2009, described in detail elsewhere.[19] Briefly, we used a two-stage modeling strategy that incorporated a land use regression (LUR) approach and a Bayesian Maximum Entropy (BME) approach. We developed the models with $PM_{2.5}$ measurements from the U.S. Environmental Protection Agency's Air Quality System U.S.-wide network of 1464 monitoring locations. The final data set comprised 104,172 monthly $PM_{2.5}$ measures from January 1999 through December 2008.

We first used LUR to construct a deterministic model that used measured $PM_{2.5}$ as the dependent variable and various measures of traffic, land use, and population as fixed predictors. We applied BME methods to the set of monthly spatio-temporal residuals from the LUR model. Validation of the final LUR-BME model in the cross-validation dataset showed strong agreement between observed and predicted $PM_{2.5}$ levels with no evidence of bias; the cross-validation R^2 was 0.79. Additional details of the modeling approach and cross-validation performance are given in the eAppendix (eFigures 1–3).

Statistical Methods

We used Cox proportional hazard models stratified by age in 1-year intervals, 2-year questionnaire cycle, and metro area (n=56) to estimate hazard ratio (HR) and 95% confidence intervals (CI) for the incidence of diabetes and hypertension per interquartile range (IQR) (2.9 $\mu g/m^3$) increase in $PM_{2.5}$. Person-time was calculated from the start of follow-up in 1995 until the occurrence of incident hypertension or diabetes, loss to follow-up, death, or end of follow-up, whichever happened first. Penalized splines were examined to evaluate the linearity of $PM_{2.5}$, but did not improve the fit compared with the linear model. We tested the proportional hazards assumption using Schoenfeld residuals and by assessing interactions between $PM_{2.5}$ and linear and log-transformed time. Participants could move among the 56 metro areas, but were censored when they moved outside of the 56 areas. For each participant, exposure to ambient $PM_{2.5}$ was modeled as the overall mean of monthly estimates from 1999–2008 (years for which $PM_{2.5}$ estimates were available) at all addresses at which she had lived during follow-up, weighted by time spent at each address.

We conducted analysis using several models. All models adjusted for age, questionnaire cycle, and metro area by including them in the strata statement. The basic model included only those variables. In a second model we added BMI alone (weight in kg/height^2 in m) (<25, 25–29, 30–34, 35–39, ≥40), and in a third model we added neighborhood SES alone (continuous). In the fully adjusted model, we added all covariates that by themselves changed the coefficient for $PM_{2.5}$ by at least 10% (i.e., BMI, neighborhood SES, years of education (<=12, 13–15, 16, ≥17), hours/week vigorous exercise (none, <5, ≥5), and the two diet pattern scores (quintiles)). We also show a model adjusted for all covariates that met the10% criteria with the exception of neighborhood SES and BMI. Covariates that met the 10% criteria were the same for hypertension and diabetes. All variables were time-varying. If a value was missing for any questionnaire cycle, the prior value was brought forward.

We conducted analyses stratified by neighborhood SES, BMI, age, education, presence of hypertension (diabetes analysis), presence of diabetes (hypertension analysis), vigorous exercise, smoking status, and meat/fried foods score. Deviations from multiplicative joint effects were assessed by the likelihood ratio test comparing models with and without interaction terms.

The main exposure metric accounted for spatial, but not temporal, variation in $PM_{2.5}$. In a sensitivity analysis, we accounted for time-trends in $PM_{2.5}$ by modeling exposure as the average of monthly values before diagnosis, weighted by time spent at each address. Follow-up for this analysis was from 1999–2011.

Neighborhood SES and $PM_{2.5}$ levels were inversely correlated, so control for neighborhood SES might over-control for $PM_{2.5}$ levels. Thus we calculated HRs within three categories of metro areas based on the magnitude of the Spearman correlation coefficient for SES and $PM_{2.5}$: $r < 0.20$, $0.20 \leq r < 0.40$, and $r \geq 0.40$. We expected the least confounding by neighborhood SES in areas with the lowest correlation.

Results

The 56 metro areas included in the study are shown in the map (Figure 1). At baseline, $PM_{2.5}$ levels at participant residences ranged from 3.1 μg/m^3 to 24.2 μg/m^3, with a mean of 13.9 μg/m^3 (SD=2.3). The 25th and 75th percentiles were 12.4 μg/m^3 and 15.3 μg/m^3, respectively. Mean $PM_{2.5}$ levels decreased from 15.6 μg/m^3 in 1999 to 11.5 μg/m^3 in 2008 (eFigure 4). $PM_{2.5}$ levels in each of 56 metropolitan areas is shown in eTable 2.

Table 1 shows participant characteristics at baseline for the diabetes and hypertension analytic cohorts. Women in both cohorts were in their late 30's, approximately one-third had a household income of <$50,000, almost half were college graduates, and the majority were non-drinkers and non-smokers. Approximately a quarter of the women were obese, and 13–15% reported 5 or more hours of vigorous exercise per week.

Over 16 years of follow-up, 4387 cases of incident diabetes and 9570 cases of incident hypertension occurred. The HR from the basic model for diabetes incidence per IQR increase (2.9 μg/m^3) in $PM_{2.5}$ was 1.13 (95% CI 1.04–1.24) (table 2). Control for BMI alone reduced the HR to 1.05 (95% CI 0.96–1.15), while control for neighborhood SES alone

reduced the HR to 1.01 (95% CI 0.92–1.10). The fully adjusted HR was 0.99 (95% CI 0.90–1.09). For hypertension, the basic HR was 1.06 (95% CI 1.00–1.12). When BMI was added, the HR was 1.03 (95% CI 0.97–1.10). When neighborhood SES was added, the HR was 0.99 (95% CI 0.93–1.05), and it did not change upon addition of all covariates. When education, vigorous exercise, and diet, but not BMI and neighborhood SES, were added to the basic model, the HR was 1.09 (95% CI 0.99–1.19) for diabetes and 1.03 (0.97–1.10) for hypertension.

When we confined follow-up to years for which $PM_{2.5}$ levels were estimated (1999–2011), results were similar (data not shown). When we used the exposure metric that accounted for time trends in $PM_{2.5}$ levels, the results were also similar. For example, the basic HR for diabetes was 1.08 (95% CI 0.97–1.19) and the fully adjusted HR was 0.94 (95% CI 0.85–1.04); the corresponding HRs for hypertension were 1.06 (95% CI 0.99–1.14) and 1.00 (95% CI 0.93–1.07).

Fully adjusted HRs for diabetes and hypertension within strata of covariates are shown in table 3. The HRs for diabetes were increased among women with BMI<25 (1.36, 95% CI 0.91–2.04) and among women aged ≤40 (1.19, 95% CI 0.94–1.51). The HR for hypertension was highest among women reporting ≥5 hours/week of vigorous exercise (1.27, 95% CI, 0.95–1.71).

Table 4 shows HRs for diabetes in three groups of metro areas classified by the magnitude of the correlation of neighborhood SES and $PM_{2.5}$. Neighborhood SES scores, and the correlation coefficients for $PM_{2.5}$ level and neighborhood SES score, for each metropolitan area are shown in eTable 2. The largest HR for diabetes occurred in the lowest correlation category, where the basic HR was 1.16 (95% CI 1.02–1.32); it fell by 4% upon addition of neighborhood SES alone (HR=1.11, 95% CI 0.98–1.26). Addition of other covariates did not change the SES-adjusted HR. In the two higher categories of correlation, basic HRs for diabetes fell to below 1.0 upon addition of neighborhood SES, and did not change materially in the fully adjusted model. HRs for hypertension from all models were near 1.0 in the lowest correlation category. In the two higher correlation categories, increases in the basic HRs disappeared upon control for neighborhood SES.

We previously assessed $PM_{2.5}$ and incidence of diabetes and hypertension in BWHS participants living in Los Angeles.[6] $PM_{2.5}$ levels at the zip code level were interpolated with a kriging model using data from 23 monitoring stations from the year 2000.[20] With follow-up from 1995–2005, the HR per 10 μg/m^3 increase in $PM_{2.5,}$ adjusted for age, education, income, smoking, alcohol consumption, vigorous exercise, BMI, and neighborhood SES was 1.63 (95% CI 0.78–3.44) for diabetes (183 cases) and 1.48 (95% CI 0.95–2.31) for hypertension (531 cases). In the present analysis, with exposure estimates from the LUR-BME model and with additional follow-up through 2011, the fully adjusted HRs per 2.9 μg/m^3 increase in $PM_{2.5}$ were 1.12 (0.92, 1.36) for diabetes (292 cases) and 0.96 (0.85, 1.08) for hypertension (704 cases).

Discussion

There was little evidence of an association of $PM_{2.5}$ with hypertension in this population of black women. $PM_{2.5}$ was not associated with increased diabetes incidence in the overall cohort, but there were increases in lean women and in younger women, both low risk groups. In addition, there was a slight increase in diabetes incidence in metro areas where the confounding by neighborhood SES was minimal.

Because neighborhood SES and air pollution are correlated in the U.S., control for neighborhood SES might in part control for $PM_{2.5}$ level. The minimal confounding of the HR for diabetes by neighborhood SES in the cities where SES and $PM_{2.5}$ were minimally correlated, and the greater level of confounding where the correlations were higher, indicate that it may be difficult to disentangle the effect of neighborhood SES from $PM_{2.5}$ in areas where they are highly correlated.

Some animal data and epidemiologic studies in children suggest that PM may contribute to weight gain.[21] If PM contributed to weight gain in adults, then BMI would be a step in a causal chain linking PM exposure to diabetes and hypertension incidence. In the present study, in models adjusted only for confounders other than the two variables that theoretically could introduce over-control for exposure (BMI and neighborhood SES), the HR for diabetes was higher (1.09) than in the fully adjusted model, though compatible with 1.0.

HRs for diabetes were increased among women with BMI<25, and to a lesser extent, among younger women. Obesity is a powerful risk factor for diabetes.[22] An effect of $PM_{2.5}$ might be more apparent in lower risk groups, including in leaner and in younger women. In contrast, the incidence of hypertension did not vary materially by age or BMI, although it was increased among women at the highest level of vigorous exercise. Variations in the HRs across the strata could have occurred by chance.

To date, the association of $PM_{2.5}$ with diabetes incidence has been assessed in four other cohorts.[2–4,23] In a small study (187 cases) set in Germany's highly polluted Ruhr area,[2] the crude HR for PM_{10} estimated from monitoring stations was 1.64 (95% CI 1.20–2.25) per 10 $\mu g/m^3$ increase, and it was reduced to 1.16 (95% CI 0.81–1.65) upon adjustment for individual-level covariates. A positive association of $PM_{2.5}$ and diabetes incidence was observed in a study of 62,000 residents (6310 cases) of Ontario, Canada.[4] $PM_{2.5}$ levels were estimated at subjects' baseline addresses using satellite observations and atmospheric chemistry models. The HR per 10 μg/m3 increase in $PM_{2.5}$ was 1.08 (95% CI 0.99–1.17), adjusted for sex, age, year, and region. Upon addition of individual- and neighborhood-level covariates, the HR was 1.11 (95% CI 1.02–1.21). The HR was highest among women (HR=1.17, 95% CI 1.03–1.32) and among people with BMI<25 (HR=1.20, 95% CI 1.00–1.45), consistent with findings in the present study. The inverse association of pollutant levels with neighborhood SES observed in the US is not as apparent in Canada,[24] so the Canadian HR of 1.11 is most comparable to the HR of 1.11 that we observed in cities where $PM_{2.5}$ and SES were minimally correlated.

In the Nurse's Health Study (NHS) and the Health Professionals Follow-Up Study (HPFU),[3] $PM_{2.5}$ levels were estimated with a model incorporating land use and meteorological

predictors at all residences over follow-up. In the NHS (3784 cases), the HR for diabetes per IQR (4.0 μg/m^3) from a model adjusted only for age, state, year, and season was 1.07 (95% CI 1.01–1.13); it was reduced to 1.02 (95% CI 0.94–1.09) upon addition of individual covariates. In the HPFU cohort (688 cases), the basic HR was 1.05 (95% CI 0.91–1.22) and the fully adjusted HR was 1.07 (95% CI 0.92–1.24). In contrast to the present findings, the addition of neighborhood SES did not change the fully adjusted estimates in either cohort, and there was no effect modification by BMI.

In the Multi-Ethnic Study of Atherosclerosis (MESA), $PM_{2.5}$ was estimated using a model based on measurements at participants' homes and at EPA monitors that incorporated land use and traffic data.[23] Of 5,135 participants, 622 developed diabetes. The HR, adjusted for individual covariates, neighborhood SES, and study site was 1.10 (95% CI 0.85, 1.41) among women and it was 1.00 (95% CI 0.75, 1.32) among men.

Although several studies have found positive associations between long-term PM exposure and continuous measures of blood pressure,[25–28] few studies have prospectively assessed $PM_{2.5}$ and hypertension incidence.[7,29,30] In the Ontario-based cohort described above,[7] the HR for incident hypertension (869 cases) per 10 unit increase in $PM_{2.5}$ was 1.13 (95% CI 1.05–1.22), adjusted for individual and neighborhood level factors, and it was 1.52 (95% CI 1.09–2.14) among people with pre-existing diabetes. In a large Danish study, there was little evidence of an association of nitrogen oxides with hypertension incidence, while measured blood pressure at baseline was inversely associated with pollutant levels.[30] In the Sister Study of 43,629 women living throughout the U.S.,[29] $PM_{2.5}$ was not predictive of incident hypertension despite the fact that long-term exposures were positively associated with chronic elevations in blood pressure. The explanations posited by the investigators to explain the discrepancy are plausible.[29] First, there is more power to detect changes in a continuous outcome like measured blood pressure, than in a binary outcome like hypertension incidence. Furthermore, while blood pressure can be accurately, homogeneously, and repetitively ascertained (allowing for the identification of small and continuous changes), the identification of incident hypertension is less accurate due to numerous potential variations across study sites (e.g., clinician practice variations). Moreover, smaller but clinically-important blood pressure elevations can occur without an individual crossing the threshold to overt hypertension, which may require greater increases and generally only impacts those poised to become hypertensive, with baseline levels already close to abnormal. This explanation also applies to diabetes: small adverse changes in insulin sensitivity may occur due to $PM_{2.5}$ exposures, despite patients not transitioning into overt diabetes mellitus.

In our previous analysis of BWHS participants who lived in Los Angeles, we found $PM_{2.5}$ levels associated with increased risks of diabetes and hypertension. In contrast, in the present report, the HRs for both outcomes were closer to the null. The discrepancy could be due to the greater number of cases in the present analysis (60% more diabetes cases and 33% more hypertension cases), additional follow-up time, differences in the exposure estimation method, and slightly differing boundaries of the LA metro area.

The hypothesis that $PM_{2.5}$ could increase the risk of diabetes and hypertension is mechanistically plausible.[28,31] Numerous studies demonstrate that the inhalation of

particulate air pollutants over both the short [32,33] and long-term[27,34] is capable of raising blood pressure by a clinically-meaningful degree. Several pro-hypertensive biological pathways have been elucidated in human and animal experiments including PM-induced sympathetic nervous system activation, endothelial dysfunction, and vasoconstriction, along with chronic vascular oxidative stress, inflammation and remodeling.[28,35–37] Similarly, mounting evidence also suggests that exposure to particulate air pollutants could heighten the potential for metabolic disorders including insulin resistance[38] and overt diabetes mellitus.[31] Animal studies demonstrate that $PM_{2.5}$ is capable of instigating several metabolic perturbations including adipocyte and per-vascular fat inflammation, altered adipocytokine expression, and autonomic imbalance, along with hepatic steatosis and endoplasmic reticulum stress that together potentiate the risk for insulin resistance and diabetes.[31] Finally, recent animal mechanistic studies have confirmed the pro-hypertensive and diabetogenic actions of longer-term $PM_{2.5}$ exposures and have further uncovered a role for hypothalamic inflammation in the etiology of both conditions.[39]

Strengths of the study include the prospective study design, the ability to control for a wide range of confounding factors, and the large sample size. With regard to the outcomes under study, validation studies in the BWHS have demonstrated a high degree of accuracy of self-report of these conditions.[13,14] The diabetes analytic cohort was limited to women age 30 and over which increased the likelihood that the cases were type 2 diabetes. Virtually all participants had health insurance and access to regular care, which diminishes the possibility of bias from undiagnosed conditions.

The exposure model used to estimate $PM_{2.5}$ levels was very strong. Estimates were based on an extensive network of ground-based monitors and used the highest quality geographic information available to inform the estimates. Cross validation results indicated that the model was highly predictive of ground level concentrations. Because the model relied on government monitoring sites, whose locations may underrepresent near-source environments such as roadways, it is possible that the model over-smoothed the data in areas of high spatial contrast in $PM_{2.5}$ levels (e.g., near roadway or industrial areas). Thus levels of $PM_{2.5}$ may be underestimated in some areas of high exposure, which would likely bias the results toward the null.

In the main exposure metric, we applied the overall mean of air pollution estimates from 1999 through 2008 at a particular address to that address over the entire follow-up period, on the assumption that the spatial pattern of $PM_{2.5}$ was relatively stable over follow-up. This assumption was supported by the fact that metropolitan areas with the highest and lowest $PM_{2.5}$ levels in 1999 retained their relative rankings through 2008, and that the majority of variation in total $PM_{2.5}$ values was spatial (87% of variance), not temporal (13% of variance). Temporal changes could have been of importance, however, so we assessed an exposure metric that reflected temporal trends in $PM_{2.5}$. The results were similar to results using the overall mean.

A limitation is that $PM_{2.5}$ levels were estimated only at each woman's residential location. Time-activity studies show that Americans spend on average 67% of their time at home.[40] We did not have exposure measures based on personal monitoring devices, nor did we have

information on indoor air quality. However, most studies of long-term exposure to air pollution have relied on ambient outdoor measurements modeled at the home location, including those that have documented associations of air pollution with increased mortality and cardiovascular outcomes.[41]

In conclusion, our results provide little support for an association of $PM_{2.5}$ with hypertension incidence. Results from the overall cohort do not support an association of air pollution with diabetes incidence, but there were suggestions of increases in lean women and in young women. Our data also suggest that in some situations control for neighborhood SES may mask associations of outcomes with $PM_{2.5}$.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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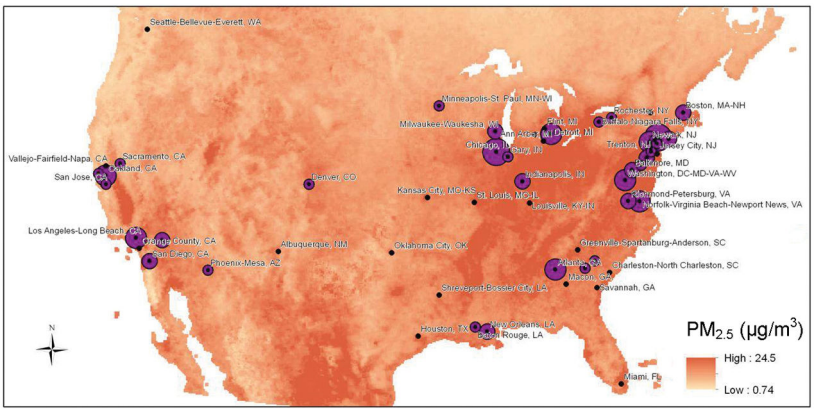

Figure 1.

Map of 56 metro areas included in the analysis. Circles indicate relative numbers of BWHS participants.

Table 1

Characteristics of the diabetes and hypertension analytic cohorts in 1995, BWHS

Characteristics	Diabetes(n=43,003)	Hypertension (n=33,771)
Age (mean ±SD)	38.7 ± 10.6	36.8 ± 9.7
BMI (mean ±SD)	27.7 ± 6.5	27.0 ± 6.1
Income < $50,000 (%)	32	31
College graduate (%)	46	48
Obese (%)	28	24
Vigorous physical activity ≥5 hours/week (%)	13	15
Never drinker (%)	56	58
Never smoker (%)	64	66

Table 2

Hazard ratios for diabetes and hypertension per IQR $PM_{2.5}$ (2.9 μg/m^3) from five models[a], BWHS 1995–2011

Model	HR (95% CI)	
	Diabetes (4387 cases/453,221 person-years)	Hypertension (9570 cases/348,154 person-years)
Basic model	1.13 (1.04–1.24)	1.06 (1.00–1.12)
Basic model + BMI	1.05 (0.96–1.15)	1.03 (0.97–1.10)
Basic model + neighborhood SES	1.01 (0.92–1.10)	0.99 (0.93–1.05)
Basic model + BMI, neighborhood SES, education, vigorous exercise, diet pattern	0.99 (0.90–1.09)	0.99 (0.93–1.06)
Basic model + education, vigorous exercise, and diet	1.09 (0.99–1.19)	1.03 (0.97–1.10)

Table 3

Stratified hazard ratios[a] for diabetes and hypertension per IQR (2.9 μg/m^3) of $PM_{2.5}$, BWHS 1995–2011

	DIABETES		HYPERTENSION	
	Cases/PYs	**HR (95% CI)**	**Cases/PYs**	**HR (95% CI)**
Neighborhood SES				
Quintile 1	1081/85569	0.96 (0.73, 1.26)	2013/66181	0.81 (0.66, 0.99)
Quintile 2	934/86213	0.98 (0.77, 1.25)	1888/66531	0.99 (0.84, 1.17)
Quintile 3	879/88921	1.16 (0.92, 1.47)	1927/68180	1.07 (0.92, 1.25)
Quintile 4	833/95834	0.82 (0.66, 1.03)	1980/73782	0.96 (0.83, 1.12)
Quintile 5	660/96683	0.91 (0.70, 1.18)	1762/73480	1.04 (0.90, 1.21)
Interaction p-value:		p=0.92		p=0.08
BMI				
<25	298/135021	1.36 (0.91, 2.04)	1654/127103	0.87 (0.75, 1.02)
25–29	1184/154702	0.95 (0.79, 1.13)	3321/117230	0.94 (0.85, 1.05)
≥30	2905/163498	1.04 (0.92, 1.18)	4595/103820	1.07 (0.96, 1.18)
Interaction p-value:		p=0.85		p=0.09
Age				
<40	655/133509	1.19 (0.94, 1.51)	1853/153497	0.99 (0.86, 1.13)
40–54	2200/224159	0.98 (0.86, 1.11)	5418/153645	1.02 (0.95, 1.11)
≥55	1532/95553	1.02 (0.89, 1.18)	2299/41011	0.89 (0.80, 1.00)
Interaction p-value:		p=0.31		p=0.91
Education				
≤HS	980/71966	1.12 (0.87, 1.44)	1552/48230	0.88 (0.72, 1.08)
Some college	1476/142585	0.99 (0.84, 1.18)	3105/112957	1.07 (0.95, 1.19)
College graduate	1926/238024	0.95 (0.82, 1.10)	4902/186414	0.94 (0.86, 1.03)
Interaction p-value:		p=0.62		p=0.26
Presence of hypertension				
No	1932/310669	1.02 (0.88, 1.18)	-	-
Yes	2455/142551	0.92 (0.81, 1.05)	-	-
Interaction p-value:		p=0.03		
Presence of diabetes				
No	-	-	8544/334552	0.99 (0.92, 1.05)
Yes	-	-	1026/13602	0.85 (0.62, 1.16)
Interaction p-value:				p=0.67
Vigorous exercise				
<5 hrs/week	4157/407886	0.99 (0.90, 1.09)	8886/307402	0.98 (0.92, 1.05)
≥5 hrs/week	187/41596	0.81 (0.47, 1.39)	634/37992	1.27 (0.95, 1.71)
Interaction p-value:		p=0.29		p=0.08
Smoking				
Never	2344/281409	0.96 (0.85, 1.10)	5558/232588	0.97 (0.89, 1.06)
Past or current	2037/170892	1.01 (0.87, 1.17)	3996/114985	1.03 (0.93, 1.15)

	DIABETES		HYPERTENSION	
	Cases/PYs	**HR (95% CI)**	**Cases/PYs**	**HR (95% CI)**
Interaction p-value:		p=0.53		p=0.55
Meat/fried food diet pattern score				
Quintile 1	700/87221	1.02 (0.77, 1.34)	1679/67257	1.11 (0.92, 1.32)
Quintile 2	755/85892	0.99 (0.76, 1.29)	1738/66267	0.96 (0.80, 1.14)
Quintile 3	814/86307	0.97 (0.75, 1.26)	1766/66443	1.06 (0.89, 1.25)
Quintile 4	866/86104	0.88 (0.70, 1.11)	1926/65958	0.84 (0.72, 0.99)
Quintile 5	965/84832	1.01 (0.80, 1.28)	2024/64417	1.04 (0.89, 1.23)
Interaction p-value:		p=0.90		p=0.93

Table 4

Hazard ratios for diabetes and hypertension per IQR of $PM_{2.5}$ (2.9 μg/m^3) from three models[a] stratified by magnitude of the Spearman correlation coefficient between neighborhood SES and $PM_{2.5}$, BWHS, 1995–2011

	r<0.20	0.20≤r<0.40	r≥0.40
	HR (95% CI)	HR (95% CI)	HR (95% CI)
DIABETES			
Cases/person-years	1,386/152,331	2,269/235,719	732/65,170
Basic model	1.16 (1.02, 1.32)	1.10 (0.96, 1.27)	1.12 (0.85, 1.48)
Basic model + neighborhood SES	1.11 (0.98, 1.26)	0.94 (0.81, 1.08)	0.84 (0.61, 1.15)
Basic model + neighborhood SES, BMI, education, vigorous exercise, diet patterns	1.11 (0.97, 1.27)	0.89 (0.77, 1.04)	0.88 (0.64, 1.23)
HYPERTENSION			
Cases/person-years	3,755/150,256	4,473/153,214	1,342/44,684
Basic model	1.00 (0.92, 1.08)	1.13 (1.02, 1.24)	1.16 (0.94, 1.43)
Basic model + neighborhood SES	0.97 (0.90, 1.06)	1.03 (0.93, 1.14)	0.92 (0.73, 1.17)
Basic model + neighborhood SES, BMI, education, vigorous exercise, diet patterns	0.98 (0.91, 1.07)	1.02 (0.92, 1.13)	0.94 (0.74, 1.19)