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Neighborhood Sociodemographic Effects on the Associations Between Long-term $PM_{2.5}$ Exposure and Cardiovascular Outcomes and Diabetes Mellitus

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Background: Exposure to $PM_{2.5}$ air pollution and neighborhood-level sociodemographic characteristics are associated with cardiovascular disease and possibly diabetes mellitus. However, the joint effect of sociodemographics and $PM_{2.5}$ on these outcomes is uncertain.
Methods: We examined whether clusters of sociodemographic characteristics modified effects of long-term $PM_{2.5}$ exposure on coronary artery disease (CAD), myocardial infarction (MI), hypertension, and diabetes mellitus. We used medical records data from 2,192 cardiac catheterization patients residing in North Carolina and assigned to one of six previously determined clusters. For each participant, we estimated annual $PM_{2.5}$ exposure at their primary residence using a hybrid model with a 1 km^2 resolution. We used logistic regression models adjusted for age, sex, body mass index, and smoking status to assess cluster-specific associations with $PM_{2.5}$ and to determine if there were interactions between cluster and $PM_{2.5}$ on outcomes.
Results: Compared with cluster 3 (OR = 0.93, 95% CI = 0.82, 1.07; urban, low proportion of black individuals and high socioeconomic status), we observed greater associations between $PM_{2.5}$ and hypertension in clusters 1 (OR = 1.22, 95% CI = 0.99, 1.50, P_{int} 0.03) and 2 (OR = 1.64, 95% CI = 1.16–2.32, P_{int} 0.003), which were urban, high proportion of black individuals, and low socioeconomic status. $PM_{2.5}$ was associated with MI (OR = 1.29, 95% CI = 1.16, 1.42) but not diabetes mellitus, regardless of cluster and was associated with CAD in cluster 3 (OR = 1.15, 95% CI = 1.00, 1.31) and overall (OR = 1.07, 95% CI = 0.98, 1.17).
Conclusion: Areas of relative disadvantage have a stronger association between $PM_{2.5}$ and hypertension compared with areas of relative advantage.

Keywords: Ambient air pollution; Cardiovascular disease; Community, Particulate matter; Socioeconomic status.

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As data used in this study contain personally identifiable information, these data will not be made available. Analytic code may be requested from the corresponding author.

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Cardiovascular disease (CVD) is the leading cause of death in the United States, accounting for 30.8% of all deaths in 2015, and is the most costly health condition with annual direct and indirect costs totaling $329.7 billion between 2013 and 2014.[1] An estimated 92.1 million Americans have at least one form of CVD, including 85.7 million Americans who suffer from hypertension, a risk factor for CVD.[1] Coronary artery disease (CAD) is the most costly type of CVD, costing Americans more than $44 billion as of 2004.[2] Myocardial infarction (MI) is an important contributor to overall CVD and CVD mortality.[1] Diabetes mellitus is a metabolic condition affecting approximately 12.2% of American adults and costing $245 billion in direct and indirect cost; it is a major cause of morbidity and mortality and is also a major risk factor for CVD.[1,3]

The prevalence of CVD and diabetes mellitus are not uniform across the American population. Individual-level sociodemographic characteristics, such as race, income, and education level have been shown to be associated with CVD and diabetes mellitus.[4–6] However, in addition to individual-level disparities,

What this study adds

Previous studies have established associations between $PM_{2.5}$ air pollution and area-level sociodemographic factors on cardiovascular outcomes. This study goes further, in examining differences between the associations of $PM_{2.5}$ on cardiovascular indicators and diabetes mellitus by area-level sociodemographic factors, defined by previously established residential clusters in a high-risk population. We observed that urban residential clusters with lower socioeconomic status and large black populations had stronger associations between $PM_{2.5}$ and hypertension compared with a reference cluster with a higher socioeconomic status and majority white population.

researchers have also observed disparities at the neighborhood or area level. Neighborhood of residence may be associated with factors known to affect health, such as access to healthcare and nutritious food, psychosocial stress, and environmental factors. Neighborhood disadvantage is associated with metabolic syndrome among black American women.[7] Diez Roux et al[8] observed increased incidence of coronary heart disease and higher systolic blood pressure[9] among those who lived in disadvantaged neighborhoods. Racial segregation of Census tracts has also been shown to be associated with systolic and diastolic blood pressure.[10] County of residence has been shown to be associated with life expectancy, with socioeconomic status and race/ethnicity accounting for 60% of county-level variations in life expectancy.[11] Mirowsky et al[12] have reported associations between neighborhood-level sociodemographic factors and diabetes mellitus and hypertension in the Catheterization Genetics (CATHGEN) study, the present study population.

Over the past decades across the United States, improvement in air quality has been associated with a substantial improvement in life expectancy in cities and neighborhoods.[13] Exposure to fine particulate matter ($PM_{2.5}$) is associated with CVD outcomes, including hypertension,[14] myocardial infarction (MI),[15,16] and coronary artery disease (CAD),[16] but the association with diabetes mellitus is less clear.[17–21] Prior studies conducted in the CATHGEN cohort failed to find associations between exposure to traffic pollution, defined by proximity to roadways and traffic, and diabetes mellitus,[21] though there was an association between traffic pollution and hypertension.[22]

Although both ambient air pollution exposure and neighborhood-level sociodemographic indicators contribute to the development of chronic diseases, it is less understood whether neighborhood-level sociodemographic characteristics modify air pollution–related health risks.[23] In this study, we examined whether neighborhood-level sociodemographic characteristics modify the effect of annual $PM_{2.5}$ concentrations on CAD, MI, hypertension, and diabetes mellitus among cardiac catheterization patients enrolled in the CATHGEN study in three North Carolina (NC) counties.

Methods

Study population

The CATHGEN study[24] recruited 9,334 patients who underwent cardiac catheterization at Duke University Medical Center in Durham, NC, between 2001 and 2010. Participants were approached for recruitment to CATHGEN at the time of their cardiac catheterization. Participants underwent a history and physical examination with blood and serum collection at the time of catheterization, and their medical records were integrated into the CATHGEN data repository.[21] All participant data used in this analysis were abstracted from medical records. All CATHGEN participants provided informed consent; CATHGEN procedures were approved by the Duke University Institutional Review Board.

Addresses listed on the medical records for 8,017 (86%) of CATHGEN participants were successfully geocoded by the Children's Environmental Health Initiative (https://cehi.rice.edu).[16,21] We limited this analysis to 2,254 participants with geocoded addresses who resided in Wake, Durham, or Orange counties, NC, and who were previously assigned to a sociodemographic cluster by Mirowsky et al.[12] Wake, Durham, and Orange counties were selected as they represent the county where Duke University Medical Center is located (Durham) plus two populous neighboring counties with high concentrations of CATHGEN participants; 28% of geocoded participants resided in these three counties. We assumed that those who live near Duke University (Wake, Durham, or Orange counties) would be more representative of a typical catheterization patient, both in sociodemographics and in severity of illness, compared with those who live further away. We further excluded 64 participants who did not self-identify as either white or black, bringing our total sample size to 2,192 participants. The CATHGEN study design allowed for repeated visits, arising from multiple catheterizations over the 10-year study period. For the 105 eligible participants with multiple observations, we only included data from the first recorded visit.

Exposure assessment

Daily mean $PM_{2.5}$ concentrations were estimated using a hybrid model developed by Di et al[25] that trained a neural network to estimate daily $PM_{2.5}$ concentrations at a 1 km^2 spatial resolution using the following data: aerosol optical depth, surface reflectance, chemical transport model outputs, meteorology, land-use data, aerosol index data, regional and monthly dummy variables, and $PM_{2.5}$ monitors. Briefly, the neural network was trained to $PM_{2.5}$ monitoring data, using convolutional layers to account for spatial correlations from neighboring cells. Full details of the hybrid model can be found in Di et al.[25] We matched geocoded addresses of CATHGEN participants to the centroid of the nearest 1 km^2 grid cell. We then averaged the $PM_{2.5}$ concentrations of that cell for the 365 days before the index catheterization to create an annual average $PM_{2.5}$ measure for each participant.[25]

Clinical measures

For this study, we examined the following outcomes: CAD, MI, hypertension, and diabetes mellitus. CAD was a binary outcome with individuals having a CAD index >23 determined to be positive for CAD. The CAD index is a measure of coronary occlusion as determined during the cardiac catheterization procedure. CAD index >23 is a common cutpoint used in clinical and epidemiologic studies,[12,16,21,26,27] and it indicates >75% occlusion of at least one major epicardial coronary vessel.[26,27] Of the 2,192 participants in this analysis, 190 (8.7%) were excluded from the CAD analyses because physicians were unable to assess measures of stenosis for all coronary arteries. MI status was determined by either (1) history of MI or thrombolytic therapy for MI as indicated on medical records or (2) referral for catheterization based on recent MI. Data on MI were collected both retrospectively (from medical records) and prospectively (from follow-up exams) relative to the index catheterization; we limited this analysis to MIs that occurred before the index catheterization. The attending physician determined hypertension and diabetes mellitus status. Diabetes mellitus status included individuals with either type 1 or type 2 diabetes mellitus. Potential covariates included: self-reported sex and race, history of smoking (current or former vs. never) as indicated in the medical record, and body mass index (BMI, kg/m^2) calculated from measured height and weight.

Neighborhood clusters

We hypothesized that sociodemographic characteristics of the neighborhoods where CATHGEN participants resided might have modified the association between $PM_{2.5}$ and our selected outcomes. In a previous manuscript by Mirowsky et al,[12] CATHGEN residents of Wake, Durham, and Orange counties, NC were classified into neighborhood clusters based on sociodemographic factors of their block groups of residence. Block groups were chosen as they are the smallest geographic unit (~400 households) for which demographic data are available from the US Census. Mirowsky et al[28] derived six clusters via Ward's hierarchical clustering of the following 11 Census-derived sociodemographic factors at the Census block group level in 2000: urban environment, percent of the population with at least a Bachelor's degree, percent in owner-occupied housing, percent with income below the poverty level, percent of households on public assistance income, percent of population

Table 1

Descriptive characteristics of CATHGEN participants: 2,192 participants in CATHeterization GENetics study, Wake, Durham, and Orange counties, North Carolina, 2001–2010 by cluster[a] and overall

	Cluster 1 (n = 388)	Cluster 2 (n = 206)	Cluster 3 (n = 922)	Cluster 4 (n = 229)	Cluster 5 (n = 354)	Cluster 6 (n = 93)	Total (N = 2,192)
Female	41.8%	57.3%	38.2%	37.6%	31.6%	38.7%	39.5%
Black race	53.1%	83.5%	15.4%	24.5%	13.0%	10.8%	28.9%
Current or former smoker	47.4%	49.0%	41.3%	42.8%	46.3%	40.9%	44.1%
Age (years), mean (SD)	60.3 (12.0)	58.4 (12.0)	62.7 (12.2)	60.9 (12.9)	60.2 (11.6)	61.8 (9.7)	61.3 (12.1)
Body mass index (mean in kg/m^2) (SD)	31.1 (7.9)	32.7 (8.9)	29.5 (6.5)	30.1 (8.0)	30.0 (7.0)	29.5 (6.1)	30.2 (7.3)
CAD (n = 2,002)[b]	44.7%	34.6%	49.0%	41.2%	51.4%	39.2%	46.1%
MI	21.4%	24.8%	22.6%	22.3%	25.7%	20.4%	23.0%
Hypertension	74.2%	82.5%	65.9%	64.6%	65.8%	62.4%	68.7%
Diabetes mellitus	30.4%	41.3%	24.3%	28.4%	28.8%	37.6%	28.7%

[a]Cluster 1—urban, high proportion black and nonmanagerial occupations; cluster 2—urban, high poverty, public assistance, black, single-parent homes, unemployed, and nonmanagerial occupations; cluster 3—urban, high Bachelor's degree, low nonmanagerial occupations, poverty, and unemployed; cluster 4—urban, highest other race, high Bachelor's degree, poverty, and low owner-occupied housing, and nonmanagerial occupation; cluster 5—rural, highest owner-occupied housing and low poverty, black, and unemployed; cluster 6—urban, otherwise similar to cluster 5.
[b]CAD status defined as CAD index >23; 190 participants missing CAD due to incomplete cardiac catheterization.

who identify as black, percent who identify as other race (neither black nor white), percent unemployed, percent in nonmanagerial positions, percent of households with a single parent, and percent vacant housing. Cluster 1 was urban with a high proportion of black individuals and individuals who worked in nonmanagerial occupations. Cluster 2 was urban with a high proportion of individuals with income below the poverty level, public assistance, black individuals, single-parent homes, unemployed, and working in nonmanagerial occupations. Cluster 3 was urban, with a high proportion with at least a Bachelor's degree and a low proportion in nonmanagerial occupations, with income below the poverty level and unemployed; cluster 3 was the reference cluster for interaction analyses. Cluster 4 was urban, had the greatest proportion of individuals of neither black nor white race, high proportion of individuals with at least a Bachelor's degree and with income below poverty level, and a low proportion in owner-occupied housing and nonmanagerial occupation. Cluster 5 was the most rural, with the greatest proportion in owner-occupied housing and low proportion with incomes below the poverty level, black individuals, and unemployed. Cluster 6 was similar to cluster 5 but was more urban. More detailed descriptions of the clusters can be found in Mirowsky et al[12] and Table 2. We matched CATHGEN participants to clusters based on their Census block group of residence and examined cluster-specific associations as well as interactions between annual mean $PM_{2.5}$ and cluster.

Analytic methods

We estimated overall and cluster-specific odds ratios for the associations between annual average $PM_{2.5}$ exposure and CAD, MI, hypertension, and diabetes mellitus using multivariable logistic regression. Models were adjusted for sex, age, body mass index (BMI), race, and history of smoking. Models included the entire sample with a multiplicative interaction term for $PM_{2.5}$ exposure and a dummy variable encoding for neighborhood cluster was added to determine the effect of neighborhood cluster on the association between $PM_{2.5}$ concentration and CAD, MI, hypertension, and diabetes mellitus. In analyses comparing associations between clusters, cluster 3 was chosen as the referent cluster in our analyses, as it was the largest cluster, had the highest socioeconomic status, and to allow comparison with Mirowsky et al's[12] article, which also used cluster 3 as the referent cluster.

Sensitivity analyses

We conducted the following sensitivity analyses. We hypothesized that the associations between $PM_{2.5}$ and cardiovascular outcomes and diabetes mellitus may be due to traffic; we adjusted our results for indicators of traffic exposure, distance to roads (DTR), and traffic exposure zone (TEZ), each in a separate model. DTR was defined as the inverse natural log of distance to A1 or A2 roads (primary highways with or without limited access, respectively).[21] Previous study with the CATHGEN cohort has found approximately linear associations with inverse natural log distance to A1 or A2 roads.[22] TEZ was defined as residence in one of six possible zones of increasing exposure to vehicular traffic, as previously described.[21,29] TEZ 6 had large traffic delays, TEZ 5 had high traffic volumes, TEZ 4 was located near transit authority bus routes, TEZ 3 had high-signal light density, TEZ 2 consisted of all other urban areas, and TEZ 1 constituted of the remainder of the study area. As it is possible for participants to reside in more than one TEZ, they were assigned to the TEZ with the greatest exposure. One participant was excluded from TEZ analysis due to residence within 1 km of the Raleigh-Durham (RDU) International Airport, a major point source of $PM_{2.5}$ in the study area. Because there were small numbers of participants residing in TEZs 5 and 6, we combined them in our analysis and included TEZ as a categorical term. To verify that associations were not purely driven by any artifacts in the air pollution estimation approach, we conducted analyses using data from the US Environmental Protection Agency's network of $PM_{2.5}$ monitors (https://www.epa.gov/outdoor-air-quality-data). We used mean annual $PM_{2.5}$ concentration as recorded at the monitor nearest to participants' home addresses to estimate their exposure to $PM_{2.5}$. We calculated correlations between all continuous exposure metrics: $PM_{2.5}$ from the hybrid model, $PM_{2.5}$ based on EPA monitors, and inverse log DTR; as well as between continuous exposure metrics and TEZ. Additionally, to determine if any neighborhood-level factor was disproportionately influencing the main analyses, we regressed each of the 11 Census variables that determined cluster on cardiovascular outcomes and diabetes mellitus for the total sample and added multiplicative interaction terms for annual $PM_{2.5}$ concentration.

Results

Table 1 compares descriptive characteristics of the 2,192 participants in the six neighborhood clusters. Cluster 3 had the most participants (n = 922) and cluster 6 had the fewest (n = 93). Cluster 2 had the greatest proportion of female participants (57.3%) and both cluster 1 (53.1%) and cluster 2 (83.5%) had a greater proportion of black participants than the other clusters. Participants in cluster 2 had the lowest mean age (58.4 years), greatest mean BMI (32.7 kg/m^2), and greatest proportion of current or former smokers (49.0%). Cluster 5 had the greatest prevalence of CAD (51.4%), while cluster 2 had the greatest prevalence of hypertension (82.5%) and diabetes mellitus (41.3%). MI prevalence

Table 2

Distribution of 11 demographic and socioeconomic variables across six neighborhood clusters, colored by ranking of that variable across clusters

Cluster	Urban	Bachelor's degree or more	Owner-occupied housing	Income below poverty level	Public assistance income	Black	Other race	Unemployment	Non-managerial occupation	Single-parent housing	Vacant Housing	Key
1	88.7	23.9	58.2	13.7	3.5	54.2	4.4	5.0	69.3	25.4	7.0	Lowest
2	99.9	15.0	25.3	34.0	9.2	73.0	7.1	15.6	79.9	35.6	11.6	
3	97.0	60.4	75.6	4.4	0.6	9.6	5.2	2.5	38.9	9.0	4.8	
4	99.4	49.5	31.2	19.9	1.4	20.4	10.5	4.4	56.8	12.7	8.1	
5	9.1	26.7	83.7	6.2	1.8	12.9	2.6	2.7	61.9	12.3	6.7	
6	84.0	30.5	75.8	6.0	1.8	17.0	3.8	3.2	61.1	14.2	6.0	Highest

Blue cells have lowest percentages of those variables; red cells have highest: US Census; Wake, Durham, and Orange and Wake counties, North Carolina; 2000.

Table 3

Descriptive characteristics of air pollution indicators for CATHGEN participants; 2,192 participants in CATHeterization GENetics study, Wake, Durham, and Orange counties, North Carolina, 2001–2010[a]

	Cluster 1 (n = 388) Mean (SD)	Cluster 2 (n = 206) Mean (SD)	Cluster 3 (n = 922) Mean (SD)	Cluster 4 (n = 229) Mean (SD)	Cluster 5 (n = 354) Mean (SD)	Cluster 6 (n = 93) Mean (SD)	Total (N = 2,192) Mean (SD)
$PM_{2.5}$ (μg/m³) from hybrid model	12.9 (1.1)	13.2 (1.0)	12.8 (1.1)	12.8 (1.1)	12.2 (1.2)	11.9 (1.0)	12.7 (1.1)
$PM_{2.5}$ (μg/m³) from EPA monitors	13.1 (1.2)	13.3 (1.1)	13.1 (1.2)	13.0 (1.2)	13.2 (1.2)	12.6 (1.2)	13.1 (1.2)
Distance to A1 or A2 road (m)	764.1 (656.7)	498.2 (423.1)	1,035.7 (830.6)	710.8 (635.1)	2,076.6 (1,559.8)	1,381.3 (1,133.0)	1,083.6 (1,046.6)
Traffic exposure zone							
1 (remaining study area)	13.9%	3.4%	8.0%	11.8%	91.5%	31.2%	23.5%
2 (urban area)	26.8%	3.4%	57.3%	28.0%	6.5%	58.1%	35.6%
3 (high-signal light density)	19.1%	16.0%	16.5%	20.1%	0	7.5%	14.2%
4 (transit routes)	36.1%	74.8%	16.5%	38.9%	2.0%	1.1%	24.8%
5/6 (heavy traffic)	4.1%	2.4%	1.6%	1.3%	0	2.2%	1.9%

[a]Cluster 1—urban, high proportion black, and nonmanagerial occupations; cluster 2—urban, high poverty, public assistance, black, single-parent homes, unemployed, and nonmanagerial occupations; cluster 3—urban, high bachelor's degree, low nonmanagerial occupations, poverty, and unemployed; cluster 4—urban, highest other race, high bachelor's degree, poverty, and low owner-occupied housing, and nonmanagerial occupation; cluster 5—rural, highest owner-occupied housing and low poverty, black, and unemployed; cluster 6—urban, otherwise similar to cluster 5.
EPA indicates Environmental Protection Agency.

did not substantially vary across clusters. Table 2 describes the sociodemographic characteristics of the clusters.

Cluster 2 had the greatest annual mean $PM_{2.5}$ concentration from the hybrid model (13.2 μg/m³) and based on EPA monitors (13.3 μg/m³; Table 3). Cluster 6 had the lowest annual mean $PM_{2.5}$ concentrations from the hybrid model (11.9 μg/m³) and based on EPA monitors (12.6 μg/m³). Participants in cluster 2 lived closest to A1 or A2 roads (mean 498.2 m), and participants in cluster 5 lived furthest (mean 2,076.6 m). Similarly, participants in clusters 1 and 2 resided in the highest TEZs, while those in cluster 5 resided in the lowest.

After adjustment for age, sex, BMI, race, and smoking status, an increase of 1 μg/m³ annual average $PM_{2.5}$ concentration was associated with a greater odds of CAD in cluster 3 (OR = 1.15, 95% CI = 1.00, 1.31) and overall (OR = 1.07, 95% CI = 0.98, 1.17) (Figure and eTable S1; http://links.lww.com/EE/A31). Annual $PM_{2.5}$ concentrations were positively associated with the history of MI in all clusters, although the 95% confidence intervals for clusters 2 and 6 included the null. In an analysis of all clusters combined, an increase of 1 μg/m³ annual $PM_{2.5}$ concentration was associated with an increase in odds of MI (OR = 1.29, 95% CI = 1.16, 1.42); cluster-specific ORs ranged from 1.25 (95% CI = 1.07, 1.46) in cluster 3 to 1.50 (95% CI = 0.81, 2.76) in cluster 6. We did not observe substantial differences in the association between annual average $PM_{2.5}$ concentration and MI across clusters.

Greater annual average $PM_{2.5}$ was associated with greater odds of hypertension in cluster 2 (OR = 1.64, 95% CI = 1.16, 2.32) and cluster 1 (OR = 1.22, 95% CI = 0.99, 1.50) and lower odds of hypertension in clusters 5 (OR = 0.81, 95% CI = 0.66, 1.00) and 6 (OR = 0.63, 95% CI = 0.39, 1.01). Furthermore, the associations between annual $PM_{2.5}$ concentration and hypertension in clusters 1 and 2 were significantly different from that in cluster 3 (OR = 0.93, 95% CI = 0.82, 1.07; *P* for interaction 0.03, 0.003, respectively). We did not observe associations between annual $PM_{2.5}$ concentrations and diabetes mellitus status overall or within clusters.

Sensitivity analyses

In sensitivity analyses, cluster-specific and overall associations between mean annual $PM_{2.5}$ concentrations were not substantially different after adjustment for DTR or TEZ (eTable S1; http://links.lww.com/EE/A31). Cluster-specific and the overall association between mean annual $PM_{2.5}$ concentrations at the nearest EPA air quality monitor and cardiometabolic outcomes were similar to those generated by the hybrid model of $PM_{2.5}$ concentrations (eTable S2; http://links.lww.com/EE/A31). Ambient $PM_{2.5}$ concentrations were highly correlated between the hybrid model and EPA monitors (ρ = 0.87; eTable S3; http://links.lww.com/EE/A31). Annual $PM_{2.5}$ concentrations were only weakly correlated with inverse log distance to A1 or A2 roads. As expected, concentrations of $PM_{2.5}$ increased as TEZ increased, while distance to A1 or A2 roads decreased (eTable S4; http://links.lww.com/EE/A31). As shown in eTable

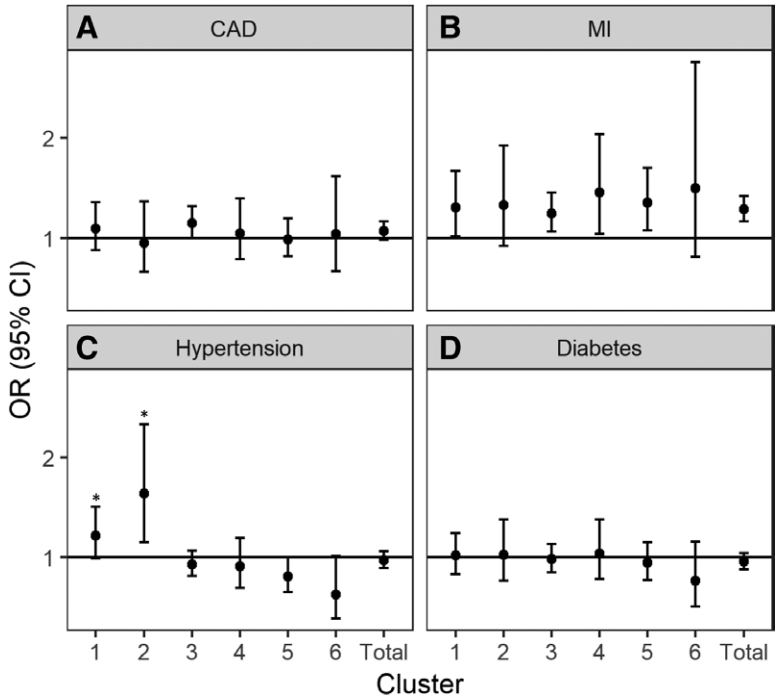

Figure. OR (OR adjusted for age, sex, body mass index, race, and smoking status; and 95% confidence intervals) for the association of annual mean $PM_{2.5}$ concentration and (A) CAD, (B) MI, (C) diabetes mellitus, and (D) hypertension, by cluster (cluster 1—urban, high proportion black, and nonmanagerial occupations; cluster 2—urban, high poverty, public assistance, black, single-parent homes, unemployed, and nonmanagerial occupations; cluster 3—urban, high bachelor's degree, low nonmanagerial occupations, poverty, and unemployed; cluster 4—urban, highest other race, high bachelor's degree, poverty, and low owner-occupied housing, and nonmanagerial occupation; cluster 5—rural, highest owner-occupied housing and low poverty, black, and unemployed; cluster 6—urban, otherwise similar to cluster 5) and overall: 2,192 participants in CATHeterization GENetics study, Wake, Durham, and Orange counties, North Carolina, 2001–2010. $^{*}P_{int} < 0.05$. OR indicates odds ratio.

S5 (http://links.lww.com/EE/A31), most Census-derived variables had null or weak associations with cardiovascular and diabetes mellitus outcomes. The strongest associations were between percent urban and CAD (OR = 0.69, 95% CI = 0.50, 0.96), between percent receiving public assistance income and hypertension (OR = 1.07, 95% CI = 1.03, 1.11) and diabetes mellitus (OR = 1.04, 95% CI = 1.00, 1.07), between percent unemployed and hypertension (OR = 1.04, 95% CI = 1.02, 1.07) and diabetes mellitus (OR = 1.04, 95% CI = 1.02, 1.05). Similar results, albeit of lesser magnitude, were observed between percent income below poverty level, percent black, percent in nonmanagerial occupations, and percent in single-parent housing with hypertension and diabetes mellitus. We observed interactions between $PM_{2.5}$ and the following Census-derived variables in adjusted models for hypertension at the $P < 0.05$ level: Bachelor's degree or more, income below poverty level, black race, nonmanagerial occupation, and single-parent housing.

Discussion

We examined the effect of neighborhood-level sociodemographic factors on the association between $PM_{2.5}$ and CVD and diabetes mellitus in a high-risk population. Our most notable result is that participants residing in clusters 1 and 2, which were urban and had high proportions of individuals who were black, impoverished, working in nonmanagerial positions, unemployed, and living in single-parent homes, had significantly greater associations between $PM_{2.5}$ and hypertension compared with our reference cluster. The reference cluster, 3, was also urban but had low proportions of people who were black, impoverished, working in nonmanagerial occupations, unemployed, and living in single-parent homes. Racial distribution of clusters were based on Census data, and, as expected, reflected the racial distribution of CATHGEN participants across clusters, with clusters 1 and 2 having the highest proportion of participants who were black. Higher prevalence of hypertension among black Americans compared with white Americans has been well documented.[1,30] Racial differences in the associations between $PM_{2.5}$ exposure and hypertension is less well understood. In sensitivity analysis, we observed interaction between percent black population, as well as percent Bachelor's degree or more, percent with income below the poverty level, percent in nonmanagerial occupations, and percent in single-parent housing and $PM_{2.5}$ concentration on hypertension. This indicates that individuals living in neighborhoods with high proportions of black individuals, as well as those with lower socioeconomic indicators, have stronger associations between $PM_{2.5}$ and hypertension compared with those living in more affluent neighborhoods and those with lower proportions of black individuals. Areas with high proportions of black Americans, unemployed people, people who have less than a high school education, and people with incomes below the poverty level are, on average, exposed to relatively high concentrations of $PM_{2.5}$.[31–34] $PM_{2.5}$ exposure was somewhat higher in clusters 1 and 2 compared with other clusters, so greater exposure may be at least partially responsible for these results. Those who live in neighborhoods enriched for black individuals, single-parent homes, and those with relative socioeconomic disadvantage, may suffer from increased psychosocial stress, including perceived discrimination, which may, in turn, influence the development of hypertension.[35,36] Indeed, in a recent study, Smith et al[37] observed increased methylation in genes related to stress and methylation among those who lived in neighborhoods of socioeconomic disadvantage, indicating a biologic mechanism for neighborhood effects on chronic health outcomes.

We observed inverse associations between $PM_{2.5}$ and hypertension in clusters 5 and 6. Cluster 5 was relatively rural compared with our overall study area and clusters 5 and 6 both had low population density, low proportions of poverty, unemployment, and residents who were black,[12] as well as the lowest

$PM_{2.5}$ concentrations. Most studies of $PM_{2.5}$ and cardiometabolic diseases are conducted in urban areas, with greater exposure levels. However, less is known about how $PM_{2.5}$ influences cardiometabolic diseases in rural and suburban areas; it is possible that effects of $PM_{2.5}$ on health may be different in urban and rural areas. Correia et al[13] observed that, in contrast to urban and densely-populated counties, in counties with lower population densities and less than 90% urbanicity, a reduction in $PM_{2.5}$ was associated with decreased life expectancy. Possible reasons for differential effects of $PM_{2.5}$ on health in urban compared with rural areas include different health behaviors and different $PM_{2.5}$ composition in urban compared with rural areas.[13] Additionally, measurement error may be an issue, as $PM_{2.5}$ monitors are located in urban areas, specifically Raleigh and Durham, which are further away from cluster 5 compared with other clusters. Although our satellite-based hybrid exposure model does not solely rely on monitoring data, it still trains on monitor data and may be less accurate in areas further form monitors. In our analyses, only estimates for clusters 1 and 2 were significantly different from those in cluster 3 (the reference cluster). It is possible that significant differences were not detectable given small sample sizes in clusters 5 and 6. Future studies should specifically examine $PM_{2.5}$ associations in rural and suburban areas to determine if this inverse association holds.

When combining all clusters, $PM_{2.5}$ was associated with greater odds of CAD; this effect was greatest in cluster 3, the largest cluster, though there was no significant interaction by cluster. In a larger study including all CATHGEN participants in NC, we observed a positive association between $PM_{2.5}$ exposure and CAD (OR = 1.11, 95% CI = 1.04, 1.19).[16] Our results largely agree with the results of this study, and the association between $PM_{2.5,}$ and CAD in cluster 3 was even stronger than in this previous study. However, the 95% confidence intervals for both the previous NC-wide estimates, current cluster-agnostic estimates, and cluster 3–specific estimates largely overlapped.

We observed associations between $PM_{2.5}$ exposure and MI in all clusters, although 95% confidence intervals included the null in some clusters. These results are consistent with literature that generally shows an association between $PM_{2.5}$ exposure and MI.[15,16,38] Our point estimate, an OR of 1.29, was relatively high compared with past studies, possibly due to the fact that our study population had a high prevalence of MI. In addition, individuals with underlying cardiac disease may be more sensitive to air pollution exposure.[15] Our estimates between $PM_{2.5}$ and MI are somewhat elevated compared those observed in previous studies of all CATHGEN participants in NC, which also noted elevated associations.[16,38] We did not observe substantial differences in odds ratios by cluster, indicating that the associations between $PM_{2.5}$ and MI are independent of our sociodemographically defined clusters for this study area and patient population.

We did not observe associations between $PM_{2.5}$ and diabetes mellitus overall or by cluster. Prior studies on the associations between $PM_{2.5}$ and diabetes mellitus have had mixed results, ranging from null[17,20] to positive.[19] Although Park et al[19] observed an overall positive association between $PM_{2.5}$ and diabetes mellitus prevalence (OR = 1.09, 95% CI = 1.00, 1.17) in the multisite multi-ethnic study of atherosclerosis study, the authors observed a null association at the North Carolina multi-ethnic study of atherosclerosis site,[19] consistent with our findings.

In sensitivity analyses, we observed that our main findings were largely robust to adjustment for traffic indicators, indicating that $PM_{2.5}$ concentrations, and not traffic alone, drive these results. Our results were also robust to an alternative method of assessing $PM_{2.5}$ exposure, and these two measures were highly correlated. $PM_{2.5}$ concentrations were only weakly correlated with distance to road but did increase by traffic exposure zone, as expected. We observed weak interactions between $PM_{2.5}$ and hypertension with the following Census-derived indicators: Bachelor's degree or more, income below poverty level, black race, nonmanagerial occupation, and single-parent housing. It is likely that the combination of these factors, rather than any one individual factor, contributes to the observed association.

Limitations

As we used data from medical records, we did not have access to individual-level data on important demographic and socioeconomic indicators or other important risk factors for CVD and diabetes mellitus, such as nutrition and physical activity. However, we used BMI as a proxy measure. In addition, we did not have gradations of smoking and alcohol consumption, which are important potential confounders. Addition of some covariates to the model (eTable S2; http://links.lww.com/EE/A31) did not substantially change point estimates or 95% CI from crude estimates; it is not clear if addition of more detailed confounding information would substantially change point estimates. Diagnoses were made by physicians in a clinical setting; misclassification is possible, particularly for history of diabetes mellitus and hypertension. This is especially likely if a participant is not a regular user of health services and thus was not previously diagnosed, which is most likely for low-income populations. This would result in an underestimate of hypertension and diabetes mellitus in low-income areas, which had the highest prevalence of both in our study. It is unlikely, but possible, that there is some misclassification of outcome which could bias results toward the null.

Small sample sizes, particularly in clusters 5 and 6, may have hindered our efforts to observe associations. We assessed $PM_{2.5}$ at the primary residence. As individuals do not spend the entirety of their day at their residence, this could lead to exposure misclassification. Additionally, we did not correct for air exchange rates of residences, so we do not have an exact measure of exposure. However, exposures at the primary residence likely capture the majority of exposure time for participants, are the primary means of exposure classification in the field and are potentially relevant for communicating exposure risks—particularly those risks tied to the joint effect of neighborhood and air pollution exposure. We assessed the sensitivity of our associations to our particular air pollution models by using annual average $PM_{2.5}$ as measured at the nearest monitor (mean distance to monitor = 10.8 km). Results from this coarser exposure model were consistent with those from the 1 km^2 resolution hybrid model. This study only included individuals who received a cardiac catheterization, were white or black, and lived in one of three largely urban counties in NC. This limits the generalizability of our study. However, when combining all neighborhood clusters, associations were largely similar to those observed for all of NC. All participants received a cardiac catheterization, thus while this study is not representative of the general population, it likely represents a population with high risk for CVD, more sensitive to the adverse health effects from $PM_{2.5}$ exposure. This study was conducted at a single site, Duke University Medical Center in Durham, NC. This single-site sampling ensures a consistent quality of assessment of clinical variables, in particular the assessment of medical history and imaging of coronary arteries during the cardiac catheterization, which can reduce errors. However, the population is from a relatively small geographic area and is not generalizable to a larger area.

Conclusions

In a high-risk population, we observed elevated associations between $PM_{2.5}$ and hypertension in urban neighborhood clusters defined by high proportions of people who were black, impoverished, unemployed, working in nonmanagerial positions, and living in single-parent homes, as compared with a neighborhood

cluster defined by low proportions of people who were black, impoverished, unemployed, working in nonmanagerial occupations, and living in single-parent homes. Associations with CAD were most prominent in the neighborhood cluster defined by low proportions of people who were black, impoverished, unemployed, working in nonmanagerial occupations, and living in single-parent homes, while associations between annual average $PM_{2.5}$ and MI were relatively consistent across all neighborhoods. We did not observe associations between $PM_{2.5}$ and diabetes mellitus in any cluster. These results indicate that neighborhood residence may be an important contributor to air pollution sensitivity, which partially underlie differences in the prevalence of air pollution associated outcomes such as hypertension and CVD across neighborhoods.

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Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

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