Neighborhood Socioeconomic 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 socioeconomic characteristics are associated with cardiovascular disease and possibly diabetes mellitus. However, the joint effect of socioeconomic and PM$_{2.5}$ on these outcomes is uncertain.

Methods: We examined whether clusters of socioeconomic 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.

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.2 Coronary artery disease (CAD) is the most costly type of CVD, costing Americans more than $44 billion as of 2004.3 Myocardial infarction (MI) is an important contributor to overall CVD and CVD mortality.4 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.1,5

The prevalence of CVD and diabetes mellitus are not uniform across the American population. Individual-level socioeconomic 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,
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 health care and nutritious food, psychosocial stress, and environmental factors. Neighborhood disadvantage is associated with metabolic syndrome among black American women. Other studies have found that Asian populations in the United States have higher blood pressure due to neighborhood-level sociodemographic factors, such as poverty and racial segregation. Racial segregation of Census tracts has also been shown to be associated with systolic and diastolic blood pressure. 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. Mirowsky et al. 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. Exposure to fine particulate matter (PM) is associated with CVD outcomes, including hypertension, myocardial infarction (MI), and coronary artery disease (CAD), but the association with diabetes mellitus is less clear. 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, though there was an association between traffic pollution and hypertension.

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. In this study, we examined whether neighborhood-level sociodemographic characteristics modify the effect of annual PM 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 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. 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). 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. Wake, Durham, and Orange counties were selected as they represent the counties 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 concentrations were estimated using a hybrid model developed by Di et al. that trained a neural network to estimate daily PM concentrations at a 1 km 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 monitors. Briefly, the neural network was trained to PM 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. We matched geocoded addresses of CATHGEN participants to the centroid of the nearest 1 km grid cell. We then averaged the PM concentrations of that cell for the 365 days before the index catheterization to create an annual average PM measure for each participant.

**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, and it indicates >75% occlusion of at least one major epicardial coronary vessel. 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/m2) 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 and our selected outcomes. In a previous manuscript by Mirowsky et al., 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. 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

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Diabetes mellitus 30.4% 41.3% 24.3% 28.4% 28.8% 37.6% 28.7%
MI 21.4% 24.8% 22.6% 22.3% 25.7% 20.4% 23.0%
CAD (n = 2,002) 44.7% 34.6% 49.0% 41.2% 51.4% 39.2% 46.1%

Models included the entire regression. Models were adjusted for sex, age, body mass index, hypertension, and diabetes mellitus using multivariable logistic regressions between annual mean PM2.5 and cluster.

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

| Cluster     | (n = 388) | Cluster 2 | (n = 206) | Cluster 3 | (n = 922) | Cluster 4 | (n = 228) | Cluster 5 | (n = 354) | Cluster 6 | (n = 53) | Total (N = 2,192) |
|-------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------------|
| Female      | 41.8%     | 57.3%     | 38.2%     | 37.6%     | 31.6%     | 38.7%     | 39.5%     |           |           |           |           |                 |
| Black race  | 53.1%     | 63.5%     | 15.4%     | 24.5%     | 13.0%     | 10.8%     | 28.9%     |           |           |           |           |                 |
| Current or former smoker | 47.4% | 49.0% | 41.3% | 42.6% | 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/m²) (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)* | 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% |           |           |           |           |                 |

Analytic methods

We estimated overall and cluster-specific odds ratios for the associations between annual average PM2.5 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 regression. Models were adjusted for sex, age, body mass index, hypertension, and diabetes mellitus using multivariable logistic regressions between annual mean PM2.5 and cluster.

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/m²), and greatest proportion of current or former smokers (49.0%). Cluster 5 had the highest prevalence of CAD (51.4%), while cluster 2 had the highest 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 | Public assistance | Black | Other race | Unemployed | Nonmanagerial occupation | Single-parent housing | Vacant |
|---------|-------|---------------------------|-------------------------|---------------------|------------------|------|-----------|-----------|------------------------|----------------------|-------|
| 1       | 88.7  | 23.9                      | 58.2                    | 13.7                | 3.5              | 54.2 | 4.4       | 5.0       | 69.3                   | 25.4                 | 7.0   |
| 2       | 99.9  | 15.0                      | 25.3                    | 34.0                | 9.2              | 71.9 | 7.1       | 15.6      | 79.9                   | 35.6                 | 11.6  |
| 3       | 97.0  | 60.4                      | 75.6                    | 4.4                 | 9.6              | 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   |

Key

Lowest

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*.

| Traffic exposure zone | 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) |
|-----------------------|----------------------|---------------------|---------------------|---------------------|---------------------|-------------------|-------------------|
| Mean (SD)             | Mean (SD)            | Mean (SD)           | Mean (SD)           | Mean (SD)           | Mean (SD)           | Mean (SD)         | Mean (SD)         |
| PM$_{2.5}$ (µg/m$^3$) 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/m$^3$) 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) |

*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/m$^3$) and based on EPA monitors (13.3 µg/m$^3$; Table 3). Cluster 6 had the lowest annual mean PM$_{2.5}$ concentrations from the hybrid model (11.9 µg/m$^3$) and based on EPA monitors (12.6 µg/m$^3$). 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/m$^3$ 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 participants in clusters combined, an increase of 1 µg/m$^3$ annual average PM$_{2.5}$ concentration was associated with a greater 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 association 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...
clusters, with clusters 1 and 2 having the highest proportion of black, impoverished, working in nonmanagerial occupations, 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. 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. 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$_{2.5}$. 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. Indeed, in a recent study, Smith et al 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, as well as the lowest

**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. $^p < 0.05$ OR indicates odds ratio.
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. Correa 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 from 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.$^{13,16,38}$ 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.$^{13}$ 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.$^{13,16,36}$ \textit{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$^{7,20}$ to positive.$^{19}$ Although Park et al$^{17}$ 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,$^{17}$ 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.

\textbf{Limitations}\n
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.
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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