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Residential proximity to major roadways and risk of incident ischemic stroke in the Northern Manhattan Study

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Abstract

Background and Purpose—The evidence supporting the deleterious cardiovascular health effects of living near a major roadway is growing, although this association is not universal. In primary analyses, we hypothesized that residential proximity to a major roadway would be associated with incident ischemic stroke, and that cardiovascular risk factors would modify that association.

Methods—The Northern Manhattan Study (NOMAS) is an ongoing, population-based cohort study designed to measure cardiovascular risk factors, stroke incidence, and other outcomes in a multiethnic urban population. Recruitment occurred from 1993–2001 and participants are followed-up annually by telephone. Residential addresses at baseline were geocoded and Euclidean distance to nearest major roadway was estimated and categorized as in prior studies. We used Cox proportional hazard models to calculate hazard ratios (HRs) and 95% confidence intervals (95%CIs) for the association of this distance to incidence of stroke and other outcomes, adjusting for sociodemographic and cardiovascular risk factors, year at baseline, and neighborhood socioeconomic status. We assessed whether these associations varied by age, sex, smoking status, diabetes, and hypertension.

Results—During a median follow-up period of 15 years (n=3,287), 11% of participants were diagnosed with ischemic stroke. Participants living <100m from a roadway had a 42% (95%CI 1.01–2.02) higher rate of ischemic stroke versus those living >400m away. This association was more pronounced among non-current smokers (HR 1.54; 95%CI 1.05–2.26) and not evident among smokers (HR 0.69; 95%CI 0.23–2.06). There was no clear pattern of association between

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proximity to major roadways and other cardiovascular events including myocardial infarction, all-cause death, or vascular death.

Conclusions—In this urban multiethnic cohort we found evidence supporting that within-city variation in residential proximity to major roadway is associated with higher risk of ischemic stroke. An individual's smoking history modified this association, with the association remaining only among participants not currently smokers.

Background

Despite recent advances in treatment and prevention, stroke remains the leading cause of serious long-term disability and heart disease is the leading cause of death in the United States.[1–3] There are approximately 795,000 strokes and 735,000 myocardial infarctions (MI) each year.[1–3] While the mortality associated with stroke and MI has decreased, the morbidity associated with these diseases remains high, with a huge cost burden of approximately $17.5 billion per year for direct stroke costs and $11.3 billion for direct MI costs.[1,3] Conventional risk factors such as hypertension, diabetes, sedentary behavior, and smoking do not account for all of the variation in stroke risk.[4–6] Identifying novel modifiable risk factors is therefore of great importance.

The evidence supporting the deleterious effects of residential proximity to a major roadway is growing; however studies looking the effect of living near a major roadway on stroke are limited.[7,8] Therefore, we set out to evaluate the relationship between proximity to roadways and incident ischemic stroke in an urban setting within the context of the multi-ethnic Northern Manhattan Study (NOMAS). We hypothesized that the incidence of stroke events would be greater among individuals living closer to a major roadway.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

NOMAS is an ongoing, prospective, population-based cohort study designed to measure cardiovascular risk factors and outcomes in a stroke-free multi-ethnic urban population in Northern Manhattan. Cohort recruitment occurred from 1993 to 2001 and participants are followed-up annually by telephone. Eligibility included age ≥ 40 years, residency in one of Northern Manhattan's 5 zip codes, living in a home with a telephone, and no history of clinical stroke. Detailed methods of participant recruitment, baseline evaluation, and follow-up have been described previously.[9]

All activities pertaining to NOMAS were approved by the Institutional Review Boards at Columbia University Medical Center and the University of Miami. Written consent was provided by each participant at enrollment.

Residential Proximity to Major Roadway

Participants' residential addresses were collected at baseline examination and geocoded using Geosupport Batch Address Translator Desktop Edition (NYC Department of City

Planning, New York, NY). Participants with primary addresses in New York City were included in the study (99.7%, n=3,287). Eleven individuals were excluded due to insufficient address information.

We used ArcGIS (version 10.3.1, ESRI, Inc., Redlands, CA) to calculate the Euclidean distance from residence to nearest major roadway, defined as US Census Features Class A1 (primary highway with limited access) and A2 roadways (nationally and regionally important highways that do not have limited access), which include most federal and interstate highways and some larger state and county highways. Distance to roadway was modeled as a log-transformed continuous variable (per interquartile range (IQR)) based on prior studies[10,11] and also categorized into <100, 100–<200, 200– <400, and ≥ 400 meters (Figure 1).

Outcome ascertainment

The primary outcome for this analysis was incident ischemic stroke. Secondary outcomes included incident MI, all cause death, and vascular death. All subjects were followed annually via telephone to detect any new neurological or cardiac symptoms, interval hospitalizations, or death. Medical records were reviewed to identify events and verify details of suspected events. Suspected strokes were adjudicated independently by two neurologists. Any disagreements were adjudicated by the principal investigators (R.L.S. and M.E.). Incident MI was defined using criteria adapted from the Cardiac Arrhythmia Suppression Trial and the Lipid Research Clinics Coronary Primary Prevention Trial. The presence of an MI was adjudicated by cardiologists independently after review of all the clinical data. Cause of death was obtained through discussions with the participant's family, review of medical records, and if possible, a copy of the death certificate. Vascular death was defined as a death due to cardiac causes, underlying heart disease or stroke.[12]

Risk Factor Evaluation

At enrollment, participants underwent in-person interviews in their primary language conducted by trained interviewers to assess baseline health status and risk factors using validated data collection instruments, physical, and neurological examinations. Race-ethnicity was collected through self-identification. Cardiovascular risk factors (smoking, alcohol use, hypertension (HTN), diabetes, body mass index (BMI), and high-density lipoprotein levels (HDL)) were assessed using standardized questions and clinical data obtained at the time of exam, as previously described.[13,14] Smoking status was dichotomized into 'non-current smokers', defined as individuals reporting being former or never smokers, and 'current smokers'. Moderate alcohol use was defined as current drinking of >1 drink per month and ≤ 2 drinks per day. Physical activity was defined as engaging in one or more leisure-time activities during the 10 days prior to enrollment. Cardiac disease was defined as having at least one of the following: coronary heart disease, angina, vascular heart disease, bypass surgery or angioplasty, history of atrial fibrillation, heart attack, or medication for any cardiac condition. A summary z-score for neighborhood socioeconomic status (SES) was derived at the census tract level as a neighborhood measure of wealth, education, and occupation (Supplemental Table 1).[15]

Statistical Methods

Distributions of sociodemographic characteristics and cardiovascular risk factors at baseline were calculated as means for continuous variables and proportions for categorical variables. Cox proportional hazard models were used to evaluate the association between residential proximity to roadway and the four outcomes, expressed as hazard ratios (HR) and 95% confidence intervals (95% CI) (Model details provided in the online-only Data Supplement). We present results from unadjusted models (Model 1) and models adjusted for sociodemographic characteristics (age at baseline, sex, race-ethnicity, education, insurance status, year of enrollment, and neighborhood SES; Model 2). Model 3 further adjusted for cardiovascular risk factors ascertained at baseline (smoking, alcohol use, physical activity, HTN, BMI, HDL, diabetes, cardiac disease). To assess effect modification, we tested for multiplicative interaction between risk factors and residential distance to roadway. In sensitivity analyses, we first fitted sub-distribution Cox proportional hazard models with mortality as a competing risk for incident stroke or MI. We then ran a series of sub-analyses removing any participants with history of MI or cardiac disease.

We evaluated possible interaction by age (<70 vs. ≥70 years), sex, smoking status (current smokers vs. non-current smokers), diabetes, and hypertension. Interaction terms of potential effect modifiers and continuous exposures were each included independently in a series of fully adjusted models for each outcome of interest. Interaction terms with a p-value<0.10 were considered potentially statistically significant and models were stratified to look at differences between groups.

All analyses were performed in SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

Characteristics for the cohort at baseline (n= 3,287) are outlined in Table 1. Median age [IQR] at time of enrollment was 69 years [14]. Of the cohort, 37% were men, 53% were Hispanic, 24% were non-Hispanic black, and 21% were non-Hispanic white. On average, participants had lived in Northern Manhattan for 28 years [23]. Participants lived a median distance [IQR; 25^{th} and 75^{th} percentiles] from a major roadway of 248.1 [253.7; 136.1, 389.8] meters, and 17% of the cohort lived less than 100 meters from a major roadway (Figure 1, Supplementary Table 2).

During a median follow-up period of 15 years (range 0.2 – 23.1), 11.0 % of individuals (n=361) were diagnosed with ischemic stroke, and 11.2% (n=368) experienced a MI. Overall, 56.4% (n=1854) of the participants had died by the end of the follow-up period, 24.4% (n=803) due to vascular causes.

Living < 100 meters from a major roadway was associated with a 42% higher rate of incident ischemic stroke (HR: 1.42, 95% CI 1.01, 2.02) when compared to those living > 400m away, in models fully adjusted for sociodemographic and cardiovascular risk factors. A similar pattern was seen with a continuous measure of distance to major roadway; an IQR difference in residential proximity to a major roadway was associated with a 13% higher rate of ischemic stroke (HR: 1.13, 95% CI: 1.02, 1.25) (Table 2; Figure 2). There was no clear

pattern of association between residential proximity to major roadways and MI, all-cause death, or vascular death (Table 2).

We found evidence that the association between proximity to major roadway and ischemic stroke varied among subgroups defined by smoking history (p=0.05). Specifically, the association between proximity to roadway and ischemic stroke was stronger among participants who were non-current smokers versus current smokers living less than 100m from a roadway (HR: 1.54, 95% CI 1.05, 2.26 and HR: 0.69 95% CI 0.23, 2.06, respectively; Figure 2). A similar pattern was observed with the continuous measure of proximity to roadway (data not shown). We observed no statistically significant interactions by age, sex, diabetes, or hypertension.

In sensitivity analyses analyzing mortality as a competing risk, the magnitude of association between proximity to roadway and ischemic stroke and MI remained unchanged, both in overall models and in models stratified by smoking status. In addition, there were no substantial differences in effects when participants with a history of MI or cardiac disease were removed from analyses (Data not shown).

Discussion

In this urban, population-based cohort in Northern Manhattan, we found evidence that residential proximity to a major roadway was associated with a higher risk of incident ischemic stroke. Individuals living closest were particularly at risk; living less than 100 meters away from a major road was associated with a 42% higher risk of ischemic stroke as compared to those living more than 400 meters away. There also appeared to be a positive relationship between those living 100–400 meters from a major roadway and rate of ischemic stroke, although not statistically significant. In addition, we found evidence of interaction by smoking status. Among non-current smokers, the effect of living within 100 meters of a major roadway on incident ischemic stroke was significantly higher than that of individuals who currently smoke. Contrary to our hypothesis, however, we did not observe evidence of an association between proximity to major roadway and the risk of other cardiovascular events such as MI, vascular death, or all cause death.

The evidence supporting the deleterious health effects of living near a major roadway is growing. Individuals living in close proximity to a major roadway have been shown to be at increased risk for stroke,[7,8] CVD,[16,17] hypertension,[18] and post-stroke mortality.[11] Overall, the key exposures believed to be related to living near a major roadway, traffic-related air pollution and noise pollution, have been found to be associated with increased rates of cardio- and cerebrovascular diseases, though results have been inconsistent. Long-term exposure to air pollution has been shown to be associated with increased risk of morbidity and mortality due to CVD,[19] but several studies have reported contrasting results.[20,21] The pattern between long-term exposure and neurological disorders is similar. Higher levels of outdoor air pollution have generally been associated with a higher risk of stroke events,[22] though several studies have reported non-significant associations.[23,24] Traffic-related noise pollution, another byproduct of living near a major roadway, has been associated with many

of the same adverse health effects including CVD,[25–27] stroke,[28,29] and all-cause and cardiovascular mortality.[16,29]

There are several hypothesized mechanisms for how air pollution might affect the brain and cerebral vasculature. A series of experimental animal studies indicate that ambient particles may enter the central nervous system either through the circulatory system or intra-nasally by direct translocation through the olfactory bulb.[30,31] Once inside pollutant particles activate a series of systemic inflammatory pathways leading to vascular inflammation,[32,33] impaired microvascular reactivity,[34] and changes in cerebral hemodynamics.[35]

It has also been suggested that the association between traffic pollution and cerebrovascular disease may be mediated through cardiovascular mechanisms, as there is substantial evidence of an association between long-term exposure to air pollution and several cardiovascular risk factors including diabetes[36–38], total cholesterol and triglycerides[39],and blood pressure.[39–41] In addition, exposure to pollution has been linked to greater carotid atherosclerotic burden.[42,43] In this study, however, adjustment for cardiovascular risk factors strengthened the independent association between residential distance to roadway and ischemic stroke, indicating that in this aging population cardiovascular risk factors were not acting as mediators between the relationship between pollution and ischemic stroke.

Results of the current analysis provide evidence of statistically and clinically significant associations between residential proximity to roadway and incident ischemic stroke, but not MI or mortality. While these cardiovascular diseases share many of the same risk factors, there are some important differences that may be contributing to the results of our study based on their distributions in this cohort.[44] Some risk factors differ in the magnitude of their effect on stroke compared with heart disease; for example, while hypertension and hyperlipidemia are both important risk factors for both conditions, hypertension tends to have a greater effect on stroke while dyslipidemia tends to have a larger effect on cardiac disease. Some risk factors, like atrial fibrillation, are important for stroke but probably do not play a major role for heart disease. Stroke is also more heterogeneous than coronary atherosclerosis; only about 20% of stroke is due to atherosclerosis, while other mechanisms such as embolism and small vessel disease may play important roles. Given the older age of our cohort and the fact that in primary analyses we didn’t exclude people with history of cardiac disease at baseline, some of the cohort may be undergoing treatment for heart disease, hypertension, or dyslipidemia, leading to attenuated estimates of incident cardiovascular disease. In sensitivity analyses where individuals with prior history of MI or cardiac disease were removed, however, we did not see significant differences in effect sizes (data not shown).

Our study had several limitations, first of which is specific to the NOMAS study sample. In an urban study area with a limited geographic extent such as Northern Manhattan, there may have been limited spatial variability in exposure levels. In addition, much of the residential land use is similar throughout the study area with the majority of residents living in multifamily mid-rise apartment buildings, further limiting variability in traffic pollution exposures. However, this is also a strength of the study since this is one of the few studies to focus primarily on intra-urban variation in traffic pollution, potentially eliminating many

confounders that may have existed in prior studies that compared participants living in different urban and/or rural areas. In addition, although we adjusted for individual-level measures of SES in our analyses (race-ethnicity, education, and insurance status), we included a validated census derived SES z-score to adjust further for variations in neighborhood level SES throughout the study area. Another limitation was that our pollution estimates were estimated based on residential location at one time point at baseline during late life. Because of the older age of our participants, and the high percentage of them retired at time of study, we did not have data on lifetime workplace pollution exposures or time spent in locations outside of the home. Given the observational study design, the associations observed in the current study should not be viewed as causal relationships.

On the other hand, there were several strengths to our study. We were able to estimate the influence of individual-level estimates of residential distance to roadways on the cardiovascular health of a stroke-free aging urban population with geographic stability. We utilized the heterogeneous NOMAS population with a well-documented study methodology and ascertainment of clinical risk factors. In addition, all outcomes were identified and adjudicated by trained research associates and neurologists. In addition, this analysis had a larger sample size and a longer prospective follow up period than many prior studies, allowing for long-term ascertainment of cardiovascular events and death.

Conclusions

We found evidence suggesting that within-city variation in residential proximity to a major roadway is associated with higher risk of incident ischemic stroke in an urban, population-based sample of stroke-free participants. Further, an individual's smoking status modified this association, with the association remaining only among non-current smokers. These finding speak to the need for further studies to confirm these findings using measured levels of air pollutants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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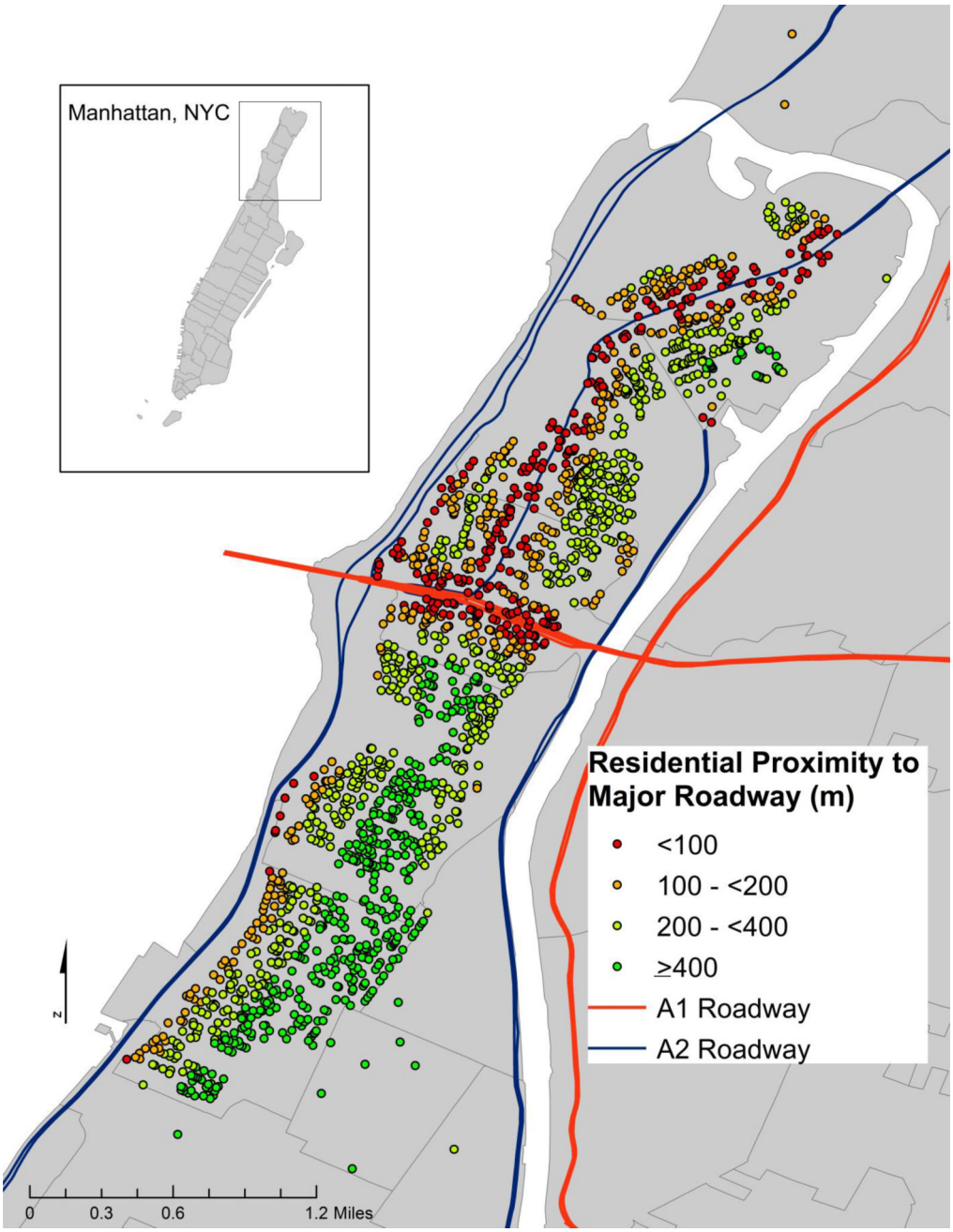

Figure 1.
Distribution of Exposure throughout Northern Manhattan, with US census defined A1 and A2 roadways

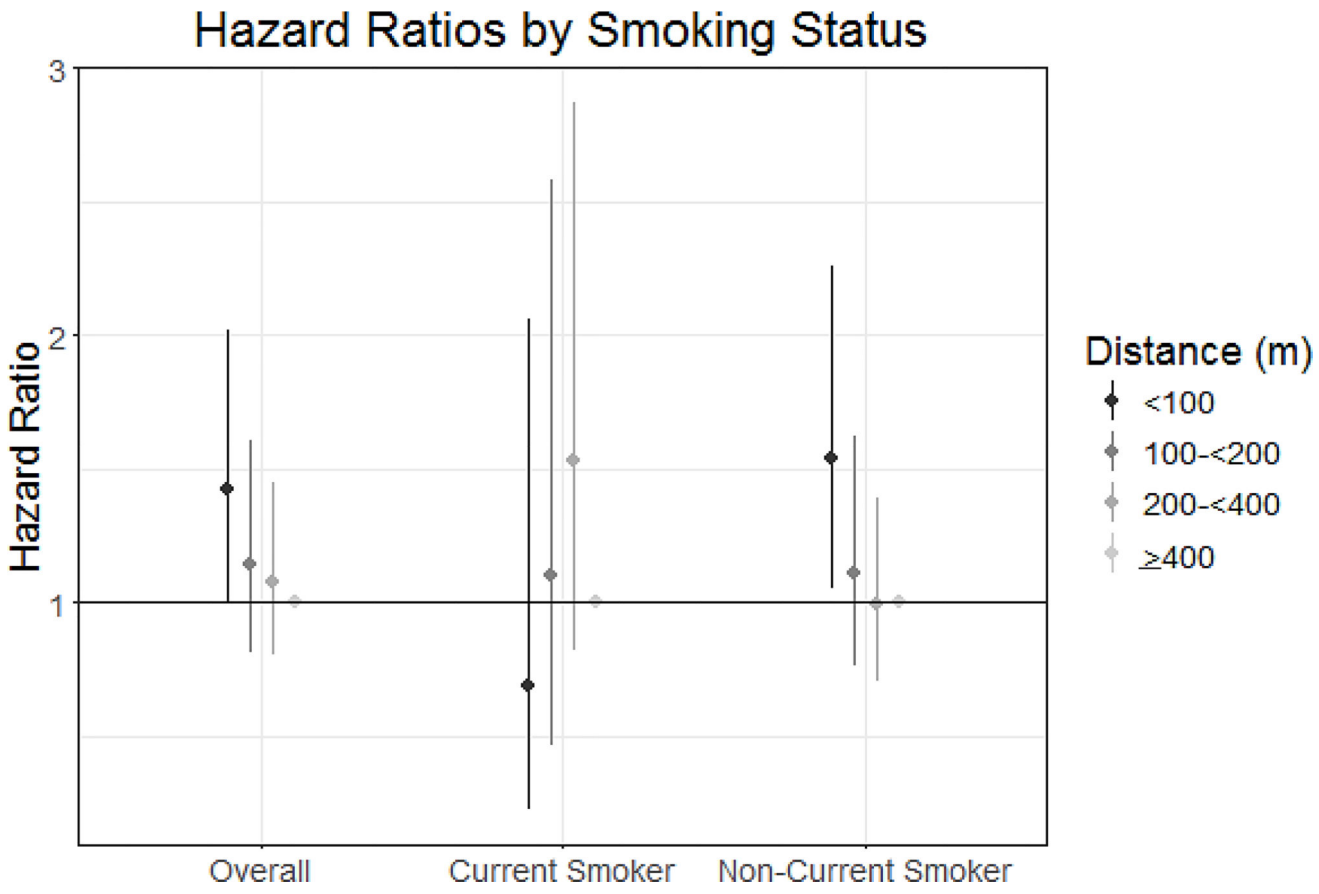

Figure 2.

Hazard ratios and 95% confidence intervals of the association between residential distance to major roadway and incident ischemic stroke, overall and stratified by smoking status. All HRs fully adjusted for sociodemographic and cardiovascular risk factors.

Table 1

Cohort Characteristics (n=3,287)

Sociodemographic Characteristics	Mean [SD] or n (%)
Age at baseline, y	69 [14]
Men	1,222 (37.2)
Race-ethnicity	
White non-Hispanic	688 (20.9)
Black non-Hispanic	797 (24.3)
Hispanic	1,725 (52.5)
Other	77 (2.3)
Completed High School	1,502 (45.7)
Medicaid or Uninsured	1,434 (43.9)
Cardiovascular Risk Factors	
Current Smoker	559 (17)
Any Physical Activity	1,901 (57.8)
Moderate Alcohol Intake *	1,080 (32.9)
Hypertension †	2,420 (73.6)
Diabetes ‡	716 (21.8)
Any Cardiac Disease	789 (24.0)
Mean Body Mass Index §	27.1 [6.2]
Mean High-Density Lipoprotein Cholesterol §	44.0 [19]
Outcomes	
Incident Ischemic Stroke	361 (11.0)
Incident Myocardial Infarction	368 (11.2)
All-cause death	1854 (56.4)
Vascular Death	803 (24.4)

IQR:interquartile range.

* Moderate alcohol use ≤ 2 servings/day,

† Hypertension = systolic blood pressure >140 mm/Hg, diastolic blood pressure recording >90 mm/Hg (average of two measurements), physician diagnosis, self-report,

‡ Diabetes=fasting blood glucose ≥126 mg/dL, self-report, insulin, hypoglycemic use,

§ Standardized

Table 2

Associations between Residential Proximity to Major Roadway and Outcomes

Outcome	Exposure	Model 1*		Model 2†		Model 3‡	
		HR	95% CI	HR	95% CI	HR	95% CI
Ischemic Stroke	<100 m	1.08	0.80, 1.45	1.35	0.96, 1.91	1.42	1.01, 2.02
	100– <200 m	0.92	0.69, 1.24	1.16	0.83, 1.61	1.14	0.81, 1.60
	200– <400 m	1.00	0.77, 1.31	1.10	0.83, 1.48	1.08	0.80, 1.45
	≥400 m	---	---	---	---	---	---
	Log(distance)§	1.04	0.93, 1.15	1.11	1.01, 1.23	1.13	1.02, 1.25
Myocardial Infarction	<100 m	1.15	0.85, 1.56	1.01	0.71, 1.45	1.00	0.69, 1.44
	100– <200 m	1.03	0.77, 1.37	0.89	0.63, 1.27	0.89	0.63, 1.26
	200– <400 m	1.08	0.82, 1.40	1.09	0.81, 1.47	0.98	0.72, 1.33
	≥400 m	---	---	---	---	---	---
	Log(distance)§	1.05	0.95, 1.16	1.00	0.89, 1.12	1.00	0.89, 1.14
All-cause Mortality	<100 m	0.85	0.74, 0.98	0.95	0.81, 1.12	0.95	0.81, 1.13
	100– <200 m	0.92	0.81, 1.04	1.06	0.91, 1.23	1.04	0.90, 1.21
	200– <400 m	0.90	0.80, 1.01	1.07	0.94, 1.21	1.04	0.91, 1.18
	≥400 m	---	---	---	---	---	---
	Log(distance)§	0.95	0.91, 1.00	0.99	0.94, 1.04	1.00	0.95, 1.06
Vascular Mortality	<100 m	0.86	0.70, 1.07	0.92	0.72, 1.17	0.92	0.71, 1.19
	100– <200 m	0.90	0.74, 1.09	0.92	0.78, 1.23	0.94	0.74, 1.19
	200– <400 m	0.90	0.76, 1.08	1.04	0.85, 1.26	1.00	0.82, 1.23
	≥400 m	---	---	---	---	---	---
	Log(distance)§	0.94	0.87, 1.02	0.97	0.90, 1.05	0.98	0.89, 1.07

HR:hazard ratio, CI:Confidence interval. Scaled to interquartile range change

*unadjusted model

†adjusted for age at baseline, sex, race-ethnicity, education, insurance status, year of baseline, neighborhood socioeconomic status

‡adjusted for variables in Model 2 plus smoking, alcohol use, physical activity, body mass index, hypertension, high density lipoprotein levels, diabetes, any cardiac disease