Residential Proximity to Major Roadways and Prevalent Hypertension Among Postmenopausal Women: Results From the Women's Health Initiative San Diego Cohort

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***Background*—**Living near major roadways has been linked with increased risk of cardiovascular events and worse prognosis. Residential proximity to major roadways may also be associated with increased risk of hypertension, but few studies have evaluated this hypothesis.

***Methods and Results*—**We examined the cross-sectional association between residential proximity to major roadways and prevalent hypertension among 5401 postmenopausal women enrolled into the San Diego cohort of the Women's Health Initiative. We used modified Poisson regression with robust error variance to estimate the association between prevalence of hypertension and residential distance to nearest major roadway, adjusting for participant demographics, medical history, indicators of individual and neighborhood socioeconomic status, and for local supermarket/grocery and fast food/convenience store density. The adjusted prevalence ratios for hypertension were 1.22 (95% CI: 1.07, 1.39), 1.13 (1.00, 1.27), and 1.05 (0.99, 1.12) for women living ≤100, >100 to 200, and >200 to 1000 versus >1000 m from a major roadway (*P* for trend=0.006). In a model treating the natural log of distance to major roadway as a continuous variable, a shift in distance from 1000 to 100 m from a major roadway was associated with a 9% (3%, 16%) higher prevalence of hypertension.

***Conclusions*—**In this cohort of postmenopausal women, residential proximity to major roadways was positively associated with the prevalence of hypertension. If causal, these results suggest that living close to major roadways may be an important novel risk factor for hypertension. **(*J Am Heart Assoc*. 2014;3:e000727 doi: 10.1161/JAHA.113.000727)**

Key Words: environment • hypertension • traffic pollution • women

A growing body of evidence suggests that living near major roadways may be detrimental to cardiovascular health. Specifically, residential proximity to major roadways has been associated with increased prevalence of coronary heart disease,[1] increased risk of acute myocardial infarction,[2] increased risk of stroke mortality,[3] increased risk of death following stroke[4] and acute myocardial infarction,[5] increased evidence of coronary atherosclerosis,[6] increased left ventricular mass index,[7] narrower retinal arteriolar diameter,[8] and reduced renal function.[9]

The specific agent or agents responsible for these associations are not completely known. Proximity to roadways with high traffic volumes has been associated with increased levels of several traffic-related air pollutants,[10,11] as well as increased traffic noise.[12,13] Ambient fine particulate matter ($PM_{2.5}$) has been convincingly associated with cardiovascular morbidity and mortality, with air pollution from traffic playing a key role.[14] Transportation noise has also been associated with cardiovascular morbidity and mortality even after adjusting for local air pollution levels.[15–17] Individuals living closest to major roadways also generally have lower individual and/or neighborhood socioeconomic status,[18,19] highlighting the importance of addressing potential confounding by socioeconomic factors.

Hypertension is a major risk factor for premature cardiovascular disease and may be a potential causal intermediate between residential proximity to major roadways and decreased cardiovascular health. Indeed, a number of studies suggest that long-term exposure to traffic-related air pollutants

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and noise may each be associated with higher blood pressure and/or higher risk of hypertension,[20–28] although the results for air pollution have not been entirely consistent.[29–31] However, few studies have specifically evaluated whether living close to major roadways is associated with hypertension, with some,[23,31] but not all[29] prior studies suggesting an association.

This question is important because the majority of the world's population now lives in a city (≈80% in the United States), and this proportion continues to grow. Thus, understanding the potential health consequences of our physical environment is of increasing public health significance. Accordingly, we evaluated the cross-sectional association between residential proximity to a major roadway and prevalent hypertension among postmenopausal women enrolled in the San Diego cohort of the Women's Health Initiative (WHI), adjusting for a number of potential confounders.

Methods

Study Design and Study Participants

We used baseline data from the San Diego cohort of the WHI study to quantify the cross-sectional association between residential proximity to the nearest major roadway and the prevalence of hypertension. The WHI is a national, prospective study of postmenopausal women, consisting of a randomized Clinical Trial (CT) component and an Observational Study (OS) component.[32] Between 1993 and 1998, the CT enrolled 68 133 postmenopausal women aged 50 to 79 into trials testing hormone therapy, dietary modification, and calcium/vitamin D supplementation strategies for disease prevention. Concurrently, the OS recruited a cohort of 93 676 women to study the relationship between lifestyle, health, risk factors, and specific disease outcomes. A total of 5626 women from San Diego County were enrolled into either the CT (n=2060) or OS (n=3341) components of the WHI. The study was approved by the institutional review boards at each participating institution, and all participants provided written informed consent.

Assessment of Exposure and Outcome

Blood pressure measurements were performed at the WHI clinical site by trained personnel using standardized procedures, as previously described.[33] We used the average of 2 blood pressure measurements taken 30 seconds apart following a 5-minute rest during the respondent's last screening visit.

We defined hypertension as previously described in WHI.[34] Briefly, at enrollment, participants were asked whether they had been diagnosed with high blood pressure or hypertension by a physician and whether they were taking medications for hypertension. Medication inventories were conducted at enrollment, and the product or generic name of the medications on the label was entered into the study database and matched to the corresponding item in a pharmacy database (Master Drug Data Base; Medi-Span, Wolters Kluwer Health, Indianapolis, IN). Consistent with prior studies in WHI,[34] we considered participants to have prevalent hypertension if they met any of the following criteria at enrollment: a systolic blood pressure (SBP) ≥140 mm Hg, a diastolic blood pressure (DBP) ≥90 mm Hg, a self-reported history of physician-diagnosed hypertension, or self-reported use of medication for the treatment of hypertension. At enrollment in the WHI, 94% of women with self-reported hypertension treatment had an antihypertensive agent in the baseline drug inventory.[34]

We geocoded residential addresses using ArcGIS 9.3 (ESRI, Redlands, CA) and calculated the Euclidean distance to the nearest major roadway, defined as freeways, freeway ramps, or prime arterial roads. We could not geocode the residential addresses of 225 (4.0%) of the 5626 participants due to post office box addresses (n=125), addresses outside San Diego County (n=93), or missing addresses (n=2). Therefore, this analysis included 5401 participants for whom data on residential distance to nearest major roadway were available.

Upon enrollment, participants provided comprehensive self-reported information on demographics, lifestyle, diet, and medical history through standardized questionnaires. Body weight, height, and waist and hip circumference were measured at the WHI clinical site, as previously described.[33] Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Physical activity was measured by asking respondents about their weekly frequency, intensity, and duration of exercise and walks longer than 10 minutes. Metabolic equivalent values were then allocated as previously described,[35] and total physical activity was calculated as a sum of metabolic equivalent/hours per week.

To determine neighborhood socioeconomic and food environment features, we used street-network buffers drawn in various distances from each participant's home address. To establish a buffer area of distance *x* miles, lines were drawn from a given address to *x* miles away along all possible street routes and the buffers are formed using the detailed street-network buffer option of the Network Analyst Extension in ArcGIS. This approach attempts to accurately describe an area within reasonable reach from a given location and has been described in built environment literature as "behaviorally relevant."[36] We estimated median household income (area-apportioned from the 2000 US Census) and percent of population that is nonwhite within half mile, 1-mile, and 3-mile buffers around each residence as proxies for neighborhood socioeconomic characteristics. We also estimated the density of supermarkets, grocery stores, fast food, and convenience stores per 10 000 population (apportioned from the 2000 US

Census) within half-mile, 1-mile, and 3-mile buffers around each residence. Food outlets were identified from a commercial database (InfoUSA, Omaha, NE) for the year 2000, which included outlet name, address, latitude and longitude, number of employees, annual sales volume, North American Industry Classification System code, and Standard Industrial Classification (SIC) codes. To obtain a more comprehensive listing of food outlets, a locally compiled business list for San Diego called *Inside Prospects* was merged with the InfoUSA database. Food premises were then classified as grocery stores, supermarkets, or limited-service (eg, fast food outlets and convenience stores) outlets based on North American Industry Classification System and Standard Industrial Classification codes and company names, as in prior studies.[37]

Statistical Analysis

We used a modified Poisson procedure with robust error variance to assess the cross-sectional association between residential distance to nearest major roadway and the prevalence of hypertension, adjusting for potential confounders. The modified Poisson model provides a direct estimate of the prevalence ratio (and 95% CI) whereas, in this context, standard logistic regression would instead provide an estimate of the prevalence odds ratio.[38] We modeled residential distance to nearest major roadway in 4 categories: ≤100, >100 to 200, >200 to 1000, and >1000 m. In a first model, we adjusted for potential confounding by age (natural cubic spline with 3 *df*), study component (OS versus CT), ethnicity (white non-Hispanic, Hispanic, or other), smoking status (current, former, or never), education (<high school, high school, some college, college graduate, or professional degree), household income (<\$35 000, \$35 000 to <\$50 000, \$50 000 to <\$100 000, and ≥\$100 000), and median household income and percent of residents who are nonwhite in a 1-mile buffer. In a subsequent model, we additionally adjusted for the following variables that could plausibly be considered either confounders or causal intermediates: total cholesterol (linear continuous), BMI and waist–hip ratio (each with natural cubic spline with 3 *df*), history of diabetes, and physical activity (tertiles). In a third model, we further adjusted for potential confounding by the density of supermarkets, grocery, and limited-service stores per 10 000 inhabitants. We tested for trends across exposure categories by assigning each exposure category the natural log of the median distance within that category and including the term as a continuous variable in the regression model. The resultant *P* value represents the linear component of trend on the natural log scale. We used multiple imputation by chained equations[39] to create 20 data sets with missing covariates imputed. All variables were missing in <1% of participants, except for household income, which was missing in 4.1% of participants, and smoking status, which was missing in 1.0% of participants. Each of the imputed data sets was obtained by cycling through each imputation with 50 iterations.

We performed a number of sensitivity analyses to assess the robustness of our results. First, to evaluate the sensitivity of our results to the choice of exposure categories, we instead considered the following categories of residential distance to nearest major roadway: ≤50, >50 to 200, >200 to 400, and >400 m. Second, we considered the natural log of residential distance to nearest roadway as a continuous variable. Third, to further assess the functional form of this association, we modeled the natural log of distance to roadway using a natural cubic spline with 3 *df*. Fourth, we restricted analyses to participants living <4000 m from a major roadway. Fifth, we considered supermarket, grocery, and limited-service outlet density within half-mile and 3-mile network buffers instead of the 1-mile buffer used in the main analysis.

In an additional set of analyses, we used linear regression to estimate the association between residential distance to major roadways and either SBP and DBP using 5 different modeling approaches: (1) all participants, no adjustment for antihypertensive treatment; (2) all participants, adjusted for antihypertensive treatment; (3) restricted to participants without self-reported antihypertensive medication; (4) restricted to participants with self-reported antihypertensive medication; and (5) a censored regression approach that attempts to predict untreated SBP or DBP for participants using antihypertensive medications.[31,40] In all models we again adjusted for potential confounding by age, study component, ethnicity, smoking status, total cholesterol, BMI and waist–hip ratio, history of diabetes, physical activity, education, household income and percent nonwhite residents within a 1-mile buffer, and density of supermarkets, grocery, and limited-service stores per 10 000 inhabitants.

We assessed whether the association between residential distance to nearest major roadway and prevalent hypertension varied by race, age, education level, history of diabetes, study component, and household income by including interaction terms in the fully adjusted models.

In exploratory post-hoc analyses, we used Cox proportional hazards models to estimate the association between residential distance to nearest major roadway and incident hypertension, defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg. Of the 5401 participants, 3132 were free of hypertension at baseline, 979 of whom had at least 1 blood pressure measurement after enrollment. Due to the limited sample size, we considered only 3 categories of residential distance to roadway (≤200, >200 to 1000, and >1000 m). As in the main analysis, in a first model we adjusted for age, race, smoking, education, family income, marital status, alcohol consumption, percent of population nonwhite, and average household income in 1-mile buffer. In subsequent models we additionally adjusted for BMI, waist–hip ratio, diabetes, physical activity, cholesterol and separately, additionally adjusted for density of supermarkets, grocery stores, convenience stores, and limited-service outlets.

Analyses were performed in Revolution R Enterprise version 6.2 (Revolution Analytics, Palo Alto, CA). A 2-sided *P*-value of 0.05 was considered statistically significant.

Results

At enrollment, the mean age of participants was 64.7 (SD=7.7) years, and the prevalence of hypertension was 42% (Table 1). A majority of participants were white non-Hispanic (75%), had at least some college education (69%), and had an annual household income of less than \$50 000 (64%). Approximately half of participants (51%) were current

Table 1. Characteristics of 5401 Women Enrolled in the San Diego Cohort of the Women's Health Initiative (WHI) Between 1993 and 1998

Characteristic	Overall (N=5401)	Residential Distance to Nearest Major Roadway			
		≤100 m (n=226)	>100 to 200 m (n=338)	>200 to 1000 m (n=2518)	>1000 m (n=2319)
Age (y), mean (SD)	64.7 (7.7)	65.0 (8.2)	64.2 (7.7)	64.6 (7.7)	64.9 (7.6)
Ethnicity, %					
White non-Hispanic	75.4	68.9	69.3	73.8	78.6
Hispanic	15.9	23.6	22.6	17.5	12.5
African American	3.8	2.7	3.0	3.7	4.1
Other	4.9	4.9	5.1	5.0	4.8
Highest level of education, %					
Less than high school	11.2	19.2	16.8	12.5	8.2
High school or vocational training	20.5	18.8	21.9	20.0	21.0
Some college or associate's degree	32.6	32.1	30.0	32.8	32.8
College graduate or some graduate school	21.7	21.0	20.7	21.0	22.7
Professional degree	14.0	8.9	10.5	13.7	15.2
Household income (\$/year), %					
<\$35 000	45.3	61.8	58.7	46.3	40.7
\$35 000 to <\$50 000	19.1	12.9	15.2	19.8	19.5
\$50 000 to <\$100 000	27.7	22.1	22.0	26.1	30.7
≥\$100 000	7.9	3.2	4.0	7.7	9.0
Smoking status, %					
Never smoker	49.1	45.9	49.4	49.4	49.1
Former smoker	43.9	45.9	44.1	43.7	43.9
Current smoker	7.0	8.2	6.5	6.9	7.1
Body mass index (BMI), %					
Underweight (BMI <18.5)	1.1	1.8	1.2	0.8	1.3
Normal weight (BMI 18.5 to 24.9)	35.7	30.4	31.7	35.9	36.7
Overweight (BMI 25 to 29.9)	36.1	37.9	35.5	35.4	36.7
Obese (BMI 30 and above)	27.0	29.9	31.7	27.9	25.2
Systolic blood pressure, mean (SD)	126.4 (15.8)	127.8 (17.5)	128.3 (15.8)	126.8 (15.8)	125.7 (15.6)
Diastolic blood pressure, mean (SD)	75.9 (8.9)	76.3 (8.9)	77.0 (9.5)	75.9 (8.9)	75.6 (8.9)
Diabetes, %	6.0	5.3	8.3	6.0	5.8
History of hypertension*, %	42.0	51.8	46.2	42.4	40.0
Study component†, clinical trial, %	38.1	37.2	35.5	38.6	38.1

*Hypertension defined as either mean baseline systolic blood pressure ≥140 or mean baseline diastolic blood pressure ≥90 or self-reported history of use of antihypertensive medications.
†Whether enrolled in the WHI clinical trials or the observational study.

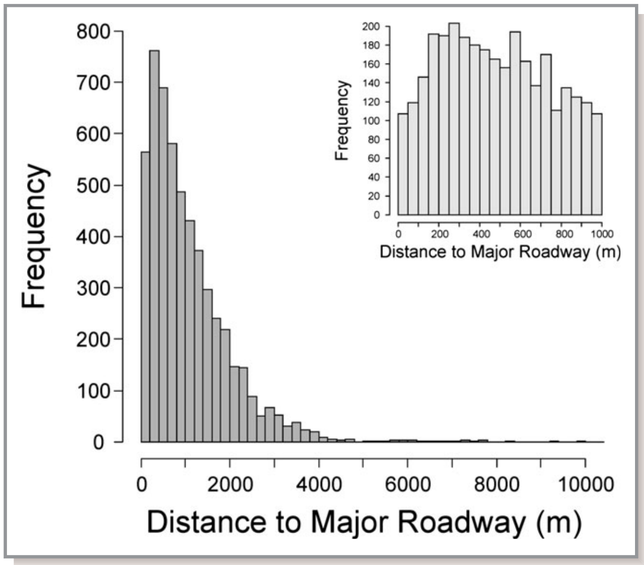

Figure 1. Distribution of residential distance to nearest major roadway among 5401 participants of the Women's Health Initiative San Diego cohort. The inset shows the distribution of distances among participants living within 1000 m from the nearest major roadway.

or former smokers. The mean SBP and DBP at enrollment were 126.4 (SD=15.8) and 75.9 (SD=8.9) mm Hg, respectively. The median residential distance to nearest major roadway was 836.8 m (25th—75th percentiles: 408.8—1510.7 m), with 4.2% of participants residing within 100 m of a major roadway (Figure 1).

Prevalence of hypertension increased monotonically across categories of decreasing distance to nearest major roadway, adjusting for age, race, smoking, study component, education, household income, marital status, alcohol consumption, and 2 markers of neighborhood socioeconomic status (Table 2). Specifically, participants living within 100 m of a major roadway were 23% (95% CI: 8, 40) more likely to have prevalent hypertension compared to participants living >1000 m from a major roadway. Further adjustment for potential causal intermediates (BMI, waist–hip ratio, diabetes, physical activity, and total cholesterol) or the local food environment (density of grocery stores, supermarkets, and limited-service outlets) did not materially change the results.

In a sensitivity analysis, we considered the natural log of distance to major roadway as a continuous variable and found that living 100 m versus 1000 m from a major roadway was associated with a 9% (95% CI: 3, 16) higher prevalence of hypertension. We used natural cubic splines to further explore the functional form of the association between residential distance to roadway and hypertension prevalence and found no evidence to suggest departure from a linear association on the log scale (Figure 2).

Results were not materially different in additional sensitivity analyses excluding participants living >4000 m from a major roadway (data not shown) or when we used an alternative categorization scheme for distance to major roadway (Table 3). Adjusting for indicators of neighborhood socioeconomic status and food outlet densities within half-mile or 3-mile buffers rather than 1-mile buffers also yielded very similar findings (Table 4).

We did not find evidence to suggest that the association between distance to major roadway and prevalence of hypertension varied by participant age or history of diabetes. However, the association was statistically significantly stronger among participants who were white (P_h=0.016), had higher household income (P=0.013), had higher educational attainment (P_h=0.006), and participants enrolled in the OS component of the WHI San Diego cohort (P_h=0.022) (Table 5).

We additionally considered the cross-sectional association between residential distance to major roadway and SBP and DBP measured at study entry. SBP tended to be higher among participants living closer to major roadways—with the P-value from the test for linear trend ranging from 0.010 to 0.18—but the association was not entirely monotonic (Table 6). There was little evidence suggesting an association between distance to major roadway and DBP (Table 7).

Table 2. Prevalence Ratio and 95% CI of Hypertension Associated With Residential Distance to Nearest Major Roadway Among 5401 Postmenopausal Women Enrolled in the WHI San Diego Cohort

	Distance to Nearest Major Roadway					
Model *	≤100 m	>100 to 200 m	>200 to 1000 m	>1000 m	P_{trend}	Continuous †
1	1.23 (1.08, 1.40)	1.11 (0.98, 1.25)	1.05 (0.98, 1.12)	1.0	0.014	1.09 (1.02, 1.15)
2	1.21 (1.06, 1.37)	1.09 (0.97, 1.23)	1.04 (0.98, 1.11)	1.0	0.022	1.08 (1.02, 1.14)
3	1.22 (1.07, 1.39)	1.13 (1.00, 1.27)	1.05 (0.99, 1.12)	1.0	0.009	1.09 (1.03, 1.16)

BMI indicates body mass index; WHI, Women's Health Initiative.

*Model 1: Adjusted for age, race, smoking, study component, education, household income, marital status, alcohol consumption, percent of population nonwhite, and average household income in 1-mile buffer. Model 2: Additionally adjusted for BMI, waist–hip ratio, diabetes, physical activity, total cholesterol. Model 3: Additionally adjusted for density of supermarkets, grocery stores, convenience stores, and limited-service outlets.

†Natural log of distance to major roadway modeled as a linear continuous variable and expressed as comparing someone living 100 m vs 1000 m from a major roadway.

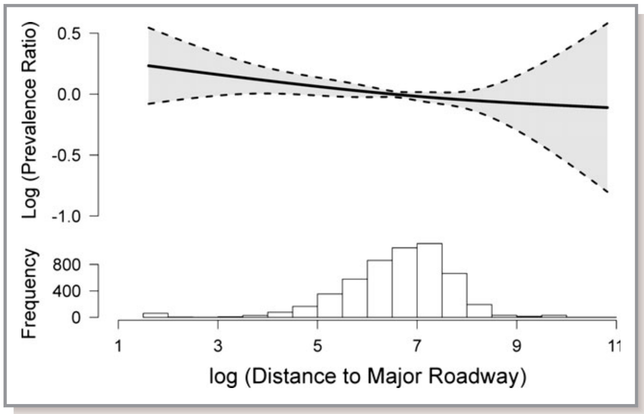

Figure 2. Spline representation of the association between the natural log of residential distance to nearest major roadway and prevalence of hypertension. The shaded region indicates 95% CIs. The histogram in the lower panel of the figure shows the frequency distribution of residential distances to nearest major roadways.

In exploratory post-hoc analyses we used Cox proportional hazards models to estimate the association between residential distance to nearest major roadway and incident hypertension among 979 participants free of hypertension at baseline and with at least 1 follow-up blood pressure measurement. During a median follow-up time of 3 years, 511 of the 979 (52.2%) participants developed incident hypertension; 43 of those participants lived within 200 m of a major roadway. There was little evidence in support of an association, but the confidence intervals were wide due to the small sample size (Table 8).

Discussion

Few studies have evaluated the potential role of living close to major roadways as a risk factor for hypertension, and prior results have been inconsistent. In this cross-sectional analysis of 5401 participants enrolled in the WHI San Diego Cohort, we found that residential proximity to a major roadway was associated with the prevalence of hypertension as assessed at enrollment. This association was observed even after adjusting for a number of potential confounders including the local food environment and was robust to a number of sensitivity analyses. We also found results suggestive of an association between living close to a major roadway and elevated SBP, but not DBP, assessed at enrollment.

Table 3. Prevalence Ratio and 95% CI for the Cross-Sectional Association Between Residential Distance to Nearest Major Roadway and Prevalence of Hypertension Among 5401 Postmenopausal Women Enrolled in the WHI San Diego Cohort Using Alternative Categorization of Distance to Major Roadway

Model *	Distance to Nearest Major Roadway				P_{trend}	Continuous†
	≤0 to 50 m	>50 to 200 m	>200 to 400 m	>400 m		
1	1.36 (1.16, 1.60)	1.04 (0.95, 1.14)	1.08 (0.97, 1.20)	1.0	0.010	1.09 (1.02, 1.15)
2	1.31 (1.12, 1.53)	1.04 (0.95, 1.14)	1.07 (0.96, 1.19)	1.0	0.019	1.08 (1.02, 1.14)
3	1.31 (1.12, 1.53)	1.05 (0.96, 1.14)	1.10 (0.99, 1.22)	1.0	0.007	1.09 (1.03, 1.16)

BMI indicates body mass index; WHI, Women's Health Initiative.
*Model 1: Adjusted for age, race, smoking, study component, individual socioeconomic variables (education, household income), marital status, alcohol consumption, percent of population nonwhite, and average household income in 1-mile buffer. Model 2: Additionally adjusted for BMI, waist–hip ratio, diabetes, physical activity, and total cholesterol. Model 3: Additionally adjusted for density of supermarkets, grocery stores, convenience stores, and limited-service outlets.
†Natural log of distance to major roadway modeled as a linear continuous variable and expressed as comparing someone living 100 m vs 1000 m from a major roadway.

Table 4. Prevalence Ratio and 95% CI for the Cross-Sectional Association Between Residential Distance to Nearest Major Roadway and Prevalence of Hypertension Among 5401 Postmenopausal Women Enrolled in the WHI San Diego Cohort When Modeling Markers of Neighborhood Socioeconomic Status and Food Environments Within Half-Mile and 3-Mile Network Buffers Instead of 1-Mile Buffers*

Buffer Size	Distance to Nearest Major Roadway				P_{trend}
	≤100 m	>100 to 200 m	>200 to 1000 m	>1000 m	
0.5 mile	1.22 (1.07, 1.39)	1.12 (0.99, 1.27)	1.05 (0.98, 1.12)	1.0	0.011
3 mile	1.23 (1.08, 1.40)	1.13 (1.00, 1.27)	1.05 (0.98, 1.12)	1.0	0.009

WHI indicates Women's Health Initiative.
*From models adjusted for age, race, smoking, study component, education, household income, marital status, alcohol consumption, median household income and percent of population nonwhite in 0.5-mile or 3-mile buffer, body mass index, waist–hip ratio, diabetes, physical activity, total cholesterol, and food environment.

Table 5. Prevalence Ratios and 95% CIs of Hypertension Comparing Participants Living 100 m Versus 1000 m From the Nearest Major Roadway, Stratified by Participant Characteristics

Characteristic	Number of Participants	Prevalence Ratio (95% CI)*	$P_{homogeneity}$
Age, y			0.81
≤65	2947	1.10 (1.00, 1.21)	
>65	2452	1.08 (0.93, 1.27)	
Ethnicity			0.016
White	4059	1.13 (1.06, 1.21)	
Other	1325	0.95 (0.81, 1.11)	
Household income ($/y)			0.013
≤50 000	3435	1.05 (0.98, 1.12)	
>50 000	1966	1.24 (1.07, 1.45)	
Education level†			0.006
Less than college degree	3446	1.03 (0.96, 1.11)	
College degree or more	1913	1.23 (1.07, 1.42)	
History of diabetes			0.77
Yes	325	1.13 (0.86, 1.49)	
No	5063	1.09 (1.02, 1.15)	
WHI component			0.022
Clinical Trial	2060	1.00 (0.91, 1.10)	
Observational Study	3341	1.15 (0.98, 1.34)	

BMI indicates body mass index; WHI, Women's Health Initiative.
*Prevalence ratios expressed comparing someone living 100 m vs 1000 m from the nearest major roadway. Estimated from a model treating the natural log of distance to roadway as a continuous variable and adjusted for age, race, smoking, study component, education, household income, marital status, alcohol consumption, percent of population nonwhite and average household income in 1-mile buffer, BMI, waist–hip ratio, diabetes, physical activity, cholesterol, and the local food environment.
†Less than college education includes some college or associate's degree, high school or vocational training, or any education less than high school. College degree or more includes college graduate or some graduate school or professional degree attainment.

Our results regarding hypertension are in agreement with a prior study by Fuks et al,[23] which found that among 4291 participants of the Heinz Nixdorf Recall Study in Germany, living ≤50 m versus >200 m from a roadway with high volumes of heavy-duty traffic, there was an association with an odds ratio for prevalent hypertension of 1.51 (95% CI: 0.98, 2.34), which did not quite reach statistical significance. On the other hand, among 57 053 participants in the Danish Diet, Cancer and Health cohort study, Sorensen et al[29] found that self-reported prevalent hypertension was not associated with living near a major roadway nor with an estimate of cumulative traffic density within 200 m, although they did find that living within 50 m of a major roadway was marginally associated with incident hypertension. In a pooled analysis of 15 European cohorts with >100 000 participants, Fuks et al[31] found that cumulative traffic density within 100 m of the home was not statistically significantly associated with the risk of prevalent hypertension. Differences in assessment of the exposure or outcome, study populations, local topography or land-use characteristics, housing characteristics, and characteristics of the local vehicle fleet may explain, at least partly, the heterogeneous results across studies.

Our findings in support of an association between residential proximity to major roadways and SBP, but not DBP, are also consistent with some prior studies. In the pooled analysis of 15 European cohorts, Fuks et al[31] found that cumulative traffic density within 100 m of the home was associated with a small increase in SBP and DBP among participants not being treated for hypertension. In a cohort of 1017 older Puerto Rican adults living in the Boston area, Rioux et al[41] found that living <100 m versus ≥100 m from a major roadway was associated with a 2.2 mm Hg (95% CI: 0.13 to 4.3) higher pulse pressure, but results for SBP and DBP were not presented. Additional indirect evidence is provided by Van Hee et al,[7] who found that participants in the Multi-Ethnic Study of Atherosclerosis living within 50 m versus >150 m from a major roadway had a significantly higher left ventricular mass index of the same magnitude as a 5.6 mm Hg increase in long-term systolic blood pressure.

As noted already, proximity to major roadways is associated with higher levels of both traffic-related air pollutants and noise, each of which may be associated with risk of hypertension. The mechanisms by which traffic-related air pollution may increase the risk of hypertension are incompletely understood. A large body of literature indicates that short-term exposure to traffic-related air pollution is associated with increased cardiac sympathetic nervous system activity, vascular resistance, and blood pressure.[42–49] However, whether traffic-related air pollutants can lead to the long-term shifts in the renal pressure natriuresis mechanisms presumed to underlie chronic hypertension remains unknown.[50] The cardiovascular effects of exposure to noise are also poorly understood, but thought to involve a combination of autonomic nervous and endocrine system activation, psychological responses (eg, annoyance), and sleep disturbances.[28] It is plausible that our results reflect the combined effects of living close to both traffic-related noise and air pollution, but future studies that assess both these exposures simultaneously are needed.

Prior studies suggest that residential proximity to major roadways is associated with increased risk of cardiovascular morbidity and mortality.[1–9] If causal, our findings raise the possibility that these associations may be mediated, at least in part, through an increased risk of hypertension. If so, prevention or treatment for hypertension may represent a

Table 6. Cross-Sectional Association (and 95% CI) Between Categories of Residential Distance to Nearest Major Roadway and Systolic Blood Pressure (mm Hg) Among Postmenopausal Women Enrolled in the WHI San Diego Cohort*

Model	n	Distance to Nearest Major Roadway				P_{trend}
		≤100 m	>100 to 200 m	>200 to 1000 m	>1000 m	
All participants, no adjustment for hypertension treatment	5401	0.70 (−1.36, 2.75)	2.06 (0.32, 3.81)	0.91 (0.06, 1.77)	0.0	0.012
All participants, adjusted for self-reported hypertension treatment	5401	−0.12 (−2.09, 1.84)	1.63 (−0.04, 3.30)	0.93 (0.12, 1.75)	0.0	0.027
Restricted to participants with no self-reported hypertension treatment	3827	−1.09 (−3.44, 1.26)	0.92 (−1.01, 2.85)	0.84 (−0.07, 1.76)	0.0	0.18
Restricted to participants with self-reported hypertension treatment	1574	1.64 (−1.94, 5.22)	2.73 (−0.56, 6.02)	0.93 (−0.77, 2.64)	0.0	0.11
Censored regression model	5227	1.68 (−1.13, 4.48)	2.74 (0.40, 5.09)	0.93 (−0.21, 2.07)	0.0	0.010

WHI indicates Women's Health Initiative.
*All models are adjusted for age, race, smoking, study component, education, household income, marital status, alcohol consumption, median household income and percent of population nonwhite in 1-mile buffer, body mass index, waist–hip ratio, diabetes, physical activity, total cholesterol, and food environment.

Table 7. Cross-Sectional Association (and 95% CI) Between Categories of Residential Distance to Nearest Major Roadway and Diastolic Blood Pressure (mm Hg) Among Postmenopausal Women Enrolled in the WHI San Diego Cohort*

Model	n	Distance to Nearest Major Roadway				P_{trend}
		≤100 m	>100 to 200 m	>200 to 1000 m	>1000 m	
All participants, no adjustment for hypertension treatment	5401	0.17 (−1.02, 1.37)	0.88 (−0.14, 1.90)	0.05 (−0.45, 0.55)	0.0	0.41
All participants, adjusted for self-reported hypertension treatment	5401	−0.21 (−1.37, 0.96)	0.68 (−0.31, 1.67)	0.06 (−0.42, 0.55)	0.0	0.60
Restricted to participants with no self-reported hypertension treatment	3827	0.44 (−0.98, 1.87)	−0.21 (−1.38, 0.96)	0.13 (−0.42, 0.69)	0.0	0.68
Restricted to participants with self-reported hypertension treatment	1574	−1.12 (−3.14, 0.91)	2.17 (0.31, 4.03)	−0.16 (−1.13, 0.80)	0.0	0.85
Censored regression model	5226	1.23 (−0.30, 2.76)	1.17 (−0.21, 2.55)	0.01 (−0.63, 0.65)	0.0	0.13

WHI indicates Women's Health Initiative.
*All models are adjusted for age, race, smoking, study component, education, household income, marital status, alcohol consumption, median household income and percent of population nonwhite in 1-mile buffer, body mass index, waist–hip ratio, diabetes, physical activity, total cholesterol, and food environment.

Table 8. Hazard Ratios and 95% CIs of Incident Hypertension Associated With Residential Distance to Nearest Major Roadway Among 979 Participants Enrolled in the WHI San Diego Cohort and Free of Hypertension at Baseline

Model*	Distance to Nearest Major Roadway (m)			P_{trend}	Continuous†
	≤200 (n=86)	>200 to 1000 (n=483)	>1000 (n=410)		
1	1.09 (0.78, 1.53)	1.13 (0.93, 1.37)	1.0	0.25	1.06 (0.86, 1.29)
2	0.98 (0.67, 1.42)	1.07 (0.86, 1.32)	1.0	0.69	0.98 (0.78, 1.23)
3	0.96 (0.66, 1.42)	1.07 (0.86, 1.32)	1.0	0.71	0.98 (0.78, 1.22)

WHI indicates Women's Health Initiative.
*Model 1: Adjusted for age, race, smoking, education, family income, marital status, alcohol consumption, percent of population nonwhite and average household income in 1-mile buffer. Model 2: Additionally adjusted for body mass index, waist–hip ratio, diabetes, physical activity, cholesterol. Model 3: Additionally adjusted for density of supermarkets, grocery stores, convenience stores, and limited-service outlets.
†Natural log of distance to major roadway modeled as a linear continuous variable and expressed as comparing someone living 100 m vs 1000 m from a major roadway.

feasible strategy to reduce the public health burden of these effects. Studies are currently under way to formally test these hypotheses in cohorts with high-quality data on both incident cardiovascular events and incident hypertension.

A prior study within the context of the CT component of the WHI found that the density of grocery stores and supermarkets around participants' residences was cross-sectionally associated with both blood pressure and BMI,[37] potentially indicating that the local food environment may contribute to the development of hypertension. Interestingly, our results were robust to adjustment for the local food environment, suggesting that the local food environment was not an important confounder or mediator of the association between residential proximity to major roadways and prevalent hypertension. Moreover, our results were nearly identical whether or not we adjusted for potential intermediates between residential proximity to major roadways and hypertension, such as physical activity, BMI, and prevalent diabetes, suggesting that these factors were likely not important mediators of the observed associations.

Counter to our expectations, we found that the association between residential proximity to major roadways and prevalent hypertension was more pronounced among whites, those with at least a college degree, and participants recruited for the OS component of the WHI. At the same time, we did not find appreciable heterogeneity by age or diabetes history, again contrary to our expectations based on the broader literature on air pollution and health. Future studies across multiple geographic areas are needed to clarify whether these observations represent causal relationships or chance observations.

In exploratory, post-hoc analyses, we did not find evidence of a statistically significant association between residential proximity to major roadways at enrollment and risk of incident hypertension. In our basic model, not adjusting for potential causal intermediates (BMI, waist–hip ratio, diabetes, physical activity, and cholesterol), the hazard ratios for incident hypertension were elevated, but not statistically significant. These results were attenuated and close to the null after adjustment for these potential intermediates. However, the sample size for this analysis was inadequate and the confidence intervals around our point estimates were wide. Thus, based on these exploratory analyses, it is unclear whether residential proximity to major roadways might have different associations with prevalent versus incident hypertension. While a well-done longitudinal analysis of incident hypertension would be ideal, the San Diego cohort of the WHI is too small for this purpose.

Our study has other limitations worthy of discussion. First, because this is a cross-sectional analysis of prevalent hypertension, we cannot exclude the possibility that participants with hypertension are more likely to choose to live closer to major roadways. However, our results were robust to adjustment for a number of cardiovascular risk factors and individual and neighborhood-level indicators of socioeconomic status, limiting the potential for reverse causation. Nonetheless, adequately powered prospective studies of incident hypertension are needed to completely exclude this possibility. Second, we do not have data on residential history of participants, nor on the amount of time participants spent away from home. These sources of exposure misclassification may have biased our results either towards or away from the null hypothesis of no association. However, the utility of exposure measures based on current home address is supported by national surveys showing that Americans spend an average of 68% of their time at home,[51] and that this age group is expected to have limited residential mobility. Third, major roadways may carry a combination of truck (diesel) and car (predominantly gasoline in the United States) traffic, with potentially different effects on cardiovascular health. However, we were not able to assess this possibility. Fourth, living closer to a major roadway is associated with higher exposure to both air and noise pollution.[10–13] As noted above, we did not have data on either air or noise pollution in the study area, and therefore cannot evaluate whether the observed associations are due to air pollution, noise, or other stressors related to living close to a major roadway. Fifth, although we controlled for a number of markers of both individual and neighborhood socioeconomic status, we cannot exclude the possibility of residual confounding by economic factors. Sixth, our study was limited to postmenopausal women living in the San Diego area, potentially limiting the generalizability of these findings to other geographic areas, younger individuals, or men. In particular, our results are not necessarily generalizable to other cities with very different vehicle fleets, fuels, or topography.

On the other hand, our study has important strengths, including a well-characterized cohort, large sample size, and the ability to adjust for multiple potential individual and neighborhood confounders including the food environment.

Hypertension affects ≈78 million or a third of US adults and ≈1 billion adults worldwide.[52] Hypertension has been consistently associated with increased risk of adverse cardiovascular events, independent of other risk factors. Thus, identifying novel risk factors and potential targets for interventions that may reduce the risk of hypertension is an important public health goal. Our results suggest that among postmenopausal women, residential proximity to major roadways may be an important novel risk factor for hypertension. When comparing women living 1000 m versus 100 m from a major roadway, we observed an increase in prevalence of hypertension corresponding approximately to a 2-year increase in age in this cohort. If causal, these results suggest that regulatory efforts to reduce traffic emissions (noise and/

or air pollution) may reduce the public health burden of hypertension. Given the increasing proportion of the world's population living in urban environments and chronically exposed to potentially high levels of traffic-related air and noise pollution, as well as the high global rates of hypertension, additional studies are needed to confirm or refute these results.

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Disclosures

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References

1. Hoffmann B, Moebus S, Stang A, Beck EM, Dragano N, Mohlenkamp S, Schmermund A, Memmesheimer M, Mann K, Erbel R, Jockel KH. Residence close to high traffic and prevalence of coronary heart disease. *Eur Heart J*. 2006;27:2696–2702.
2. Tonne C, Melly S, Mittleman M, Coull B, Goldberg R, Schwartz J. A case-control analysis of exposure to traffic and acute myocardial infarction. *Environ Health Perspect*. 2007;115:53–57.
3. Maheswaran R, Elliott P. Stroke mortality associated with living near main roads in England and Wales: a geographical study. *Stroke*. 2003;34:2776–2780.
4. Wilker EH, Mostofsky E, Lue SH, Gold D, Schwartz J, Wellenius GA, Mittleman MA. Residential proximity to high-traffic roadways and poststroke mortality. *J Stroke Cerebrovasc Dis*. 2013;22:e366–e372.
5. Rosenbloom JI, Wilker EH, Mukamal KJ, Schwartz J, Mittleman MA. Residential proximity to major roadway and 10-year all-cause mortality after myocardial infarction. *Circulation*. 2012;125:2197–2203.
6. Hoffmann B, Moebus S, Mohlenkamp S, Stang A, Lehmann N, Dragano N, Schmermund A, Memmesheimer M, Mann K, Erbel R, Jockel KH. Residential exposure to traffic is associated with coronary atherosclerosis. *Circulation*. 2007;116:489–496.
7. Van Hee VC, Adar SD, Szpiro AA, Barr RG, Bluemke DA, Diez Roux AV, Gill EA, Sheppard L, Kaufman JD. Exposure to traffic and left ventricular mass and function: the multi-ethnic study of atherosclerosis. *Am J Respir Crit Care Med*. 2009;179:827–834.
8. Adar SD, Klein R, Klein BE, Szpiro AA, Cotch MF, Wong TY, O'Neill MS, Shrager S, Barr RG, Siscovick DS, Daviglus ML, Sampson PD, Kaufman JD. Air pollution and the microvasculature: a cross-sectional assessment of in vivo retinal images in the population-based multi-ethnic study of atherosclerosis (MESA). *PLoS Med*. 2010;7:e1000372.
9. Lue SH, Wellenius GA, Wilker EH, Mostofsky E, Mittleman MA. Residential proximity to major roadways and renal function. *J Epidemiol Community Health*. 2013;67:629–634.
10. Zhu Y, Hinds WC, Kim S, Sioutas C. Concentration and size distribution of ultrafine particles near a major highway. *J Air Waste Manag Assoc*. 2002;52:1032–1042.
11. Reponen T, Grinshpun SA, Trakumas S, Martuzevicius D, Wang ZM, LeMasters G, Lockey JE, Biswas P. Concentration gradient patterns of aerosol particles near interstate highways in the greater Cincinnati airshed. *J Environ Monit*. 2003;5:557–562.
12. Hothersall DC, Chandlerwilde SN. Prediction of the attenuation of road traffic noise with distance. *J Sound Vib*. 1987;115:459–472.
13. Lee EY, Jerrett M, Ross Z, Coogan PF, Seto EY. Assessment of traffic-related noise in three cities in the United States. *Environ Res*. 2014;132C:182–189.
14. Brook RD, Rajagopalan S, Pope CA III, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A, Siscovick D, Smith SC Jr, Whitsel L, Kaufman JD. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation*. 2010;121:2331–2378.
15. Selander J, Nilsson ME, Bluhm G, Rosenlund M, Lindqvist M, Nise G, Pershagen G. Long-term exposure to road traffic noise and myocardial infarction. *Epidemiology*. 2009;20:272–279.
16. Gan WQ, Davies HW, Koehoorn M, Brauer M. Association of long-term exposure to community noise and traffic-related air pollution with coronary heart disease mortality. *Am J Epidemiol*. 2012;175:898–906.
17. Tetreault LF, Perron S, Smargiassi A. Cardiovascular health, traffic-related air pollution and noise: Are associations mutually confounded? A systematic review. *Int J Public Health*. 2013;58:649–666
18. Hajat A, Diez-Roux AV, Adar SD, Auchincloss AH, Lovasi GS, O'Neill MS, Sheppard L, Kaufman JD. Air pollution and individual and neighborhood socioeconomic status: evidence from the multi-ethnic study of atherosclerosis (MESA). *Environ Health Perspect*. 2013;121:1325–1333.
19. Krieger N, Waterman PD, Gryparis A, Coull BA. Black carbon exposure more strongly associated with census tract poverty compared to household income among US black, white, and Latino working class adults in Boston, MA (2003–2010). *Environ Pollut*. 2014;190:36–42.
20. Chen H, Burnett RT, Kwong JC, Villeneuve PJ, Goldberg MS, Brook RD, van Donkelaar A, Jerrett M, Martin RV, Kopp A, Brook JR, Copes R. Spatial association between ambient fine particulate matter and incident hypertension. *Circulation*. 2014;129:562–569.
21. Foraster M, Basagana X, Aguilera I, Rivera M, Agis D, Bouso L, Deltell A, Marrugat J, Ramos R, Sunyer J, Vila J, Elosua R, Kunzli N. Association of long-term exposure to traffic-related air pollution with blood pressure and hypertension in an adult population-based cohort in Spain (the REGICOR study). *Environ Health Perspect*. 2014;122:404–411.
22. Chuang KJ, Yan YH, Chiu SY, Cheng TJ. Long-term air pollution exposure and risk factors for cardiovascular diseases among the elderly in Taiwan. *Occup Environ Med*. 2011;68:64–68.
23. Fuks K, Moebus S, Hertel S, Viehmann A, Nonnemacher M, Dragano N, Mohlenkamp S, Jakobs H, Kessler C, Erbel R, Hoffmann B; Heinz Nixdorf Recall Study Investigative G. Long-term urban particulate air pollution, traffic noise, and arterial blood pressure. *Environ Health Perspect*. 2011;119:1706–1711.
24. Sorensen M, Hvidberg M, Hoffmann B, Andersen ZJ, Nordsborg RB, Lillelund KG, Jakobsen J, Tjonneland A, Overvad K, Raaschou-Nielsen O. Exposure to road traffic and railway noise and associations with blood pressure and self-reported hypertension: a cohort study. *Environ Health*. 2011;10:92.
25. Coogan PF, White LF, Jerrett M, Brook RD, Su JG, Seto E, Burnett R, Palmer JR, Rosenberg L. Air pollution and incidence of hypertension and diabetes mellitus in black women living in Los Angeles. *Circulation*. 2012;125:767–772.
26. Schwartz J, Alexeeff SE, Mordukhovich I, Gryparis A, Vokonas P, Suh H, Coull BA. Association between long-term exposure to traffic particles and blood pressure in the Veterans Administration Normative Aging Study. *Occup Environ Med*. 2012;69:422–427.
27. Dong GH, Qian ZM, Xaverius PK, Trevathan E, Maalouf S, Parker J, Yang L, Liu MM, Wang D, Ren WH, Ma W, Wang J, Zelicoff A, Fu Q, Simckes M. Association between long-term air pollution and increased blood pressure and hypertension in China. *Hypertension*. 2013;61:578–584.
28. van Kempen E, Babisch W. The quantitative relationship between road traffic noise and hypertension: a meta-analysis. *J Hypertens*. 2012;30:1075–1086.
29. Sorensen M, Hoffmann B, Hvidberg M, Ketzel M, Jensen SS, Andersen ZJ, Tjonneland A, Overvad K, Raaschou-Nielsen O. Long-term exposure to traffic-related air pollution associated with blood pressure and self-reported hypertension in a Danish cohort. *Environ Health Perspect*. 2012;120:418–424.

30. Babisch W, Wolf K, Petz M, Heinrich J, Cyrys J, Peters A. Associations between traffic noise, particulate air pollution, hypertension, and isolated systolic hypertension in adults: the KORA study. *Environ Health Perspect*. 2014;122:492–498.

31. Fuks KB, Weinmayr G, Foraster M, Dratva J, Hampel R, Houthuijs D, Oftedal B, Oudin A, Panasevich S, Penell J, Sommar JN, Sorensen M, Tiittanen P, Wolf K, Xun WW, Aguilera I, Basagana X, Beelen R, Bots ML, Brunekreef B, Bueno-de-Mesquita HB, Caracciolo B, Cirach M, de Faire U, de Nazelle A, Eeftens M, Elosua R, Erbel R, Forsberg B, Fratiglioni L, Gaspoz JM, Hilding A, Jula A, Korek M, Kramer U, Kunzli N, Lanki T, Leander K, Magnusson PK, Marrugat J, Nieuwenhuijsen MJ, Ostenson CG, Pedersen NL, Pershagen G, Phuleria HC, Probst-Hensch NM, Raaschou-Nielsen O, Schaffner E, Schikowski T, Schindler C, Schwarze PE, Sogaard AJ, Sugiri D, Swart WJ, Tsai MY, Turunen AW, Vineis P, Peters A, Hoffmann B. Arterial blood pressure and long-term exposure to traffic-related air pollution: an analysis in the European Study of Cohorts for Air Pollution Effects (ESCAPE). *Environ Health Perspect*. 2014;122:896–905.

32. Rossouw JE, Anderson GL, Oberman A. The Women's Health Initiative baseline summary—foreword. *Ann Epidemiol*. 2003;13:S1–S4.

33. Anderson GL, Manson J, Wallace R, Lund B, Hall D, Davis S, Shumaker S, Wang CY, Stein E, Prentice RL. Implementation of the Women's Health Initiative study design. *Ann Epidemiol*. 2003;13:S5–S17.

34. Margolis KL, Martin LW, Ray RM, Kerby TJ, Allison MA, Curb JD, Kotchen TA, Liu S, Wassertheil-Smoller S, Manson JE; Women's Health Initiative Investigators. A prospective study of serum 25-hydroxyvitamin D levels, blood pressure, and incident hypertension in postmenopausal women. *Am J Epidemiol*. 2012;175:22–32.

35. Meyer AM, Evenson KR, Morimoto L, Siscovick D, White E. Test-retest reliability of the Women's Health Initiative physical activity questionnaire. *Med Sci Sports Exerc*. 2009;41:530–538.

36. Feng J, Glass TA, Curriero FC, Stewart WF, Schwartz BS. The built environment and obesity: a systematic review of the epidemiologic evidence. *Health Place*. 2010;16:175–190.

37. Dubowitz T, Ghosh-Dastidar M, Eibner C, Slaughter ME, Fernandes M, Whitsel EA, Bird CE, Jewell A, Margolis KL, Li W, Michael YL, Shih RA, Manson JE, Escarce JJ. The Women's Health Initiative: the food environment, neighborhood socioeconomic status, BMI, and blood pressure. *Obesity (Silver Spring)*. 2012;20:862–871.

38. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159:702–706.

39. Su Y, Gelman A, Hill J, Yajima M. Multiple imputation with diagnostics (mi) in R: opening windows into the black box. *J Stat Softw*. 2011;45:1–31.

40. Tobin MD, Sheehan NA, Scurrah KJ, Burton PR. Adjusting for treatment effects in studies of quantitative traits: antihypertensive therapy and systolic blood pressure. *Stat Med*. 2005;24:2911–2935.

41. Rioux CL, Tucker KL, Mwamburi M, Gute DM, Cohen SA, Brugge D. Residential traffic exposure, pulse pressure, and C-reactive protein: consistency and contrast among exposure characterization methods. *Environ Health Perspect*. 2010;118:803–811.

42. Briet M, Collin C, Laurent S, Tan A, Azizi M, Agharazii M, Jeunemaitre X, Alhenc-Gelas F, Boutouyrie P. Endothelial function and chronic exposure to air pollution in normal male subjects. *Hypertension*. 2007;50:970–976.

43. Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F. Inhalation of fine particulate air pollution and ozone causes acute arterial vasoconstriction in healthy adults. *Circulation*. 2002;105:1534–1536.

44. O'Neill MS, Veves A, Zanobetti A, Sarnat JA, Gold DR, Economides PA, Horton ES, Schwartz J. Diabetes enhances vulnerability to particulate air pollution-associated impairment in vascular reactivity and endothelial function. *Circulation*. 2005;111:2913–2920.

45. Auchincloss AH, Roux AV, Dvonch JT, Brown PL, Barr RG, Daviglus ML, Goff DC, Kaufman JD, O'Neill MS. Associations between recent exposure to ambient fine particulate matter and blood pressure in the multi-ethnic study of atherosclerosis (MESA). *Environ Health Perspect*. 2008;116:486–491.

46. Schneider A, Neas L, Herbst MC, Case M, Williams RW, Cascio W, Hinderliter A, Holguin F, Buse JB, Dungan K, Styner M, Peters A, Devlin RB. Endothelial dysfunction: associations with exposure to ambient fine particles in diabetic individuals. *Environ Health Perspect*. 2008;116:1666–1674.

47. Wellenius GA, Boyle LD, Wilker EH, Sorond FA, Coull BA, Koutrakis P, Mittleman MA, Lipsitz LA. Ambient fine particulate matter alters cerebral hemodynamics in the elderly. *Stroke*. 2013;44:1532–1536.

48. Brook RD, Urch B, Dvonch JT, Bard RL, Speck M, Keeler G, Morishita M, Marsik FJ, Kamal AS, Kaciroti N, Harkema J, Corey P, Silverman F, Gold DR, Wellenius G, Mittleman MA, Rajagopalan S, Brook JR. Insights into the mechanisms and mediators of the effects of air pollution exposure on blood pressure and vascular function in healthy humans. *Hypertension*. 2009;54:659–667.

49. Wellenius GA, Wilhelm-Benartzi CS, Wilker EH, Coull BA, Suh HH, Koutrakis P, Lipsitz LA. Ambient particulate matter and the response to orthostatic challenge in the elderly: the maintenance of balance, independent living, intellect, and zest in the elderly (MOBILIZE) of Boston study. *Hypertension*. 2012;59:558–563.

50. Brook RD, Rajagopalan S. Particulate matter, air pollution, and blood pressure. *J Am Soc Hypertens*. 2009;3:332–350.

51. Klepeis NE, Nelson WC, Ott WR, Robinson JP, Tsang AM, Switzer P, Behar JV, Hern SC, Engelmann WH. The national human activity pattern survey (NHAPS): a resource for assessing exposure to environmental pollutants. *J Expo Anal Environ Epidemiol*. 2001;11:231–252.

52. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Magid D, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER, Moy CS, Mussolino ME, Nichol G, Paynter NP, Schreiner PJ, Sorlie PD, Stein J, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6–e245.