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Residential proximity to major roadways and incident hypertension in post-menopausal women

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Living near major roadways has been associated with increased risk of cardiovascular morbidity and mortality, presumably from exposure to elevated levels of traffic-related air and/or noise pollution. This association may potentially be mediated through increased risk of incident hypertension, but results from prior studies are equivocal. Using Cox proportional hazards models we examined residential proximity to major roadways and incident hypertension among 38,360 participants of the Women's Health Initiative (WHI) Clinical Trial cohorts free of hypertension at enrollment and followed for a median of 7.9 years. Adjusting for participant demographics and lifestyle, trial participation, and markers of individual and neighborhood socioeconomic status, the hazard ratios for incident hypertension were 1.13 (95% CI: 1.00, 1.28), 1.03 (0.95, 1.11), 1.05 (0.99, 1.11), and 1.05 (1.00, 1.10) for participants living ≤ 50, >50–200, >200–400, and >400–1000 m vs >1000 m from the nearest major roadway, respectively ($p_{trend}=0.013$). This association varied substantially by WHI study region with hazard ratios for women living ≤ 50 m from a major roadway of 1.61 (1.18, 2.20) in the West, 1.51 (1.22, 1.87) in the Northeast, 0.89 (0.70, 1.14) in the South, and 0.94 (0.75, 1.19) in the Midwest. In this large, national cohort of post-menopausal women, residential proximity to major roadways was associated with incident hypertension in selected regions of the U.S. If causal, these results suggest residential proximity to major roadways, as a marker for air, noise and other traffic-related pollution, may be a risk factor for hypertension.

1. Introduction

Despite recent medical advances and public health interventions, cardiovascular disease remains the leading cause of morbidity and mortality in the US (Go et al., 2014). Living near major roadways has been associated with higher prevalence of coronary heart disease (Hoffmann et al., 2007, 2006),higher risk of acute myocardial infarction (Tonne et al., 2007), higher risk of death from cardiovascular disease, ischemic heart disease, and stroke (Cesaroni et al., 2013; Hart et al., 2014; Maheswaran and Elliott, 2003), and higher risk of death following stroke and acute myocardial infarction (Rosenbloom et al., 2012; Wilker et al., 2013). Moreover, observational studies suggest that moving away from major roadways is associated with decreased risk of myocardial infarction, coronary heart disease mortality and all-cause

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mortality (Gan et al., 2010; Hart et al., 2013). A growing body of evidence suggests that exposures associated with living near major roadways, including traffic-related air (Cesaroni et al., 2013; Chen et al., 2013; Gan et al., 2011; Raaschou-Nielsen et al., 2012) and noise (Beelen et al., 2009; Gan et al., 2012; Selander et al., 2009) pollution, are likely detrimental to cardiovascular health.

Living near major roadways (with concomitant residential exposure to higher levels of both air and noise pollution) may increase the risk of cardiovascular events through increased incidence of hypertension. A limited number of studies have evaluated this hypothesis and the evidence remains equivocal with most (Fuks et al., 2011, 2014; Kirwa et al., 2014), but not all (Sørensen et al., 2012) prior studies suggesting an association between residential proximity to major roadways and hypertension. Of note, all but one (Kirwa et al., 2014) of these studies have been conducted in Europe and only one (Sørensen et al., 2012) considered incident hypertension rather than prevalent hypertension. The association between long-term exposure to traffic-related air pollutants (e.g.: oxides of nitrogen or NO_2) and hypertension is also unclear with some studies finding a positive association (Chen et al., 2015; Coogan et al., 2012; Dong et al., 2013; Foraster et al., 2014b) and others finding no evidence of an association (Foraster et al., 2014a; Fuks et al., 2014; Sørensen et al., 2012). On the other hand, traffic-related noise has been positively associated with prevalence of hypertension (van Kempen and Babisch, 2012).

Approximately 80% of US residents (and more than half of the world's population) now live in a city and this proportion is expected to grow (Kaiser Family Foundation, 2014). Therefore, understanding the potential health consequences of our physical environment is of increasing public health significance. Accordingly, we assessed the association between residential distance to nearest major roadway and the risk of incident hypertension in the Women's Health Initiative (WHI) Clinical Trial (CT) cohorts, a large, national US prospective study.

2. Methods

2.1. Study population

We obtained data from the WHI CT cohorts, which enrolled 68,132 post-menopausal women between 50 and 79 years of age from 1993 to 1998. We excluded participants with hypertension at baseline (n=29,118), defined as a systolic blood pressure (SBP) $\geq$ 140 mmHg, a diastolic blood pressure (DBP) $\geq$ 90 mmHg, self-reported use of antihypertensive medication at baseline, or use of an antihypertensive medication as determined at baseline via medical inventory. Medications in the following categories were considered antihypertensive agents: angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, calcium channel blockers, diuretics, centrally acting antihypertensive agents, vasodilators, and combinations of these medications (Margolis et al., 2008). We excluded 17 women with missing data on residential distance to roadway and 637 participants with no follow-up data, yielding a final study population of 38,360 eligible women.

2.2. Exposure assessment

We used ArcGIS (ESRI, Redlands, CA, USA) to calculate the distance from each participant's address to the nearest major roadway defined as those with US Census Feature Class Code A1 (primary highways with limited access) and A2 (primary road without limited access), which generally include interstate highways, US highways and some state or county highways. We used road network data from ESRI Data & Maps and from ESRI StreetMap and North American Atlas Products that spanned the study period. We used a Python script in ArcGIS using the *Generate Near Table* function to calculate the Euclidean distance and angle to the nearest major roadway for each participant address.

In a sensitivity analysis we additionally considered residential proximity to nearest A3 roadways (secondary or connecting roads), which are typically smaller and have less traffic compared to A1 and A2 roadways, but can still carry substantial local traffic in urban areas. We additionally considered the total miles of A1 and A2 roadways within 200 m of a geocoded participant's address. Data on traffic volumes or the composition of the local vehicle fleet are not available at the national level.

2.3. Outcome assessment

Blood pressure was measured at WHI clinical centers by trained personnel using standardized procedures after participants had been seated for 5 min (Anderson et al., 2003; Margolis et al., 2008). Two blood pressure measurements were taken in the right arm $\geq$ 30 seconds apart with a conventional mercury sphygmomanometer and an appropriately sized cuff at baseline and at each following approximately annual visit (Anderson et al., 2003; Margolis et al., 2008). We averaged the two measurements from each visit for use in analyses. As in previous studies (Margolis et al., 2012) we defined incident hypertension as a SBP $\geq$ 140 mmHg, a DBP $\geq$ 90 mmHg, or a first self-report of medication prescribed for hypertension.

2.4. Covariate data

Participants provided data on demographics and health behaviors using a self-reported questionnaire at baseline, as described previously (Anderson et al., 2003). Briefly, race/ethnicity was defined as Black/African-American (not of Hispanic origin); Hispanic/Latino; White (not of Hispanic origin); American Indian/Alaskan Native; Asian/Pacific Islander; and Other. Smoking status was categorized as never smoker (smoked < 100 cigarettes in their lifetime); past smoker (smoked $\geq$ 100 cigarettes in lifetime but do not currently smoke); and current smokers (smoked $\geq$ 100 cigarettes and were currently smoking), and alcohol consumption was categorized as nondrinkers (< 12 drinks of any kind in entire life); past drinkers ($\geq$ 12 alcoholic beverages in lifetime but do not currently drink); and current drinkers ($\geq$ 12 alcoholic beverages in lifetime and are currently drinking). Diabetes and high cholesterol at baseline were defined as a self-reported physician's diagnosis (Anderson et al., 2003). Employment status was based on the participant's current job, or if she did not currently have a job, the job she held the longest (Anderson et al., 2003). Information on household income was obtained through self-report.

Body mass index (BMI) was calculated from height (m) and weight (kg) measured at study enrollment using a wall-mounted stadiometer and a balance beam scale, respectively (Anderson et al., 2003). Waist and hip circumference were measured at study enrollment using a standardized measuring tape (Anderson et al., 2003).

We calculated population density defined as the mean population per square meter within a 3-mile buffer zone of a participant's address from 2000 and 2010 Census Tiger/Line files. We used data from the US Census and American Community Survey to calculate an index of neighborhood socioeconomic status (NSES) for each participant based on her address, as previously described (Diez Roux et al., 2001). We calculated z-scores for 4 NSES variables: median household income, percent high school diploma, percent professional occupation, and median value of owner-occupied housing units. We summed each of the z-scores to calculate