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Association between Noise and Cardiovascular Disease in a Nationwide U.S. Prospective Cohort Study of Women Followed from 1988 to 2018

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Background: Long-term noise exposure is associated with cardiovascular disease (CVD), including acute cardiovascular events such as myocardial infarction and stroke. However, longitudinal cohort studies in the U.S. of long-term noise and CVD are almost exclusively from Europe and few modeled nighttime noise, when an individual is likely at home or asleep, separately from daytime noise. We aimed to examine the prospective association of outdoor long-term nighttime and daytime noise from anthropogenic sources with incident CVD using a U.S.-based, nationwide cohort of women.

Methods: We linked L_{50} nighttime and L_{50} daytime anthropogenic modeled noise estimates from a U.S. National Parks Service model (L_{50}: sound pressure levels exceeded 50 percent of the time) to geocoded residential addresses of 114,116 participants in the Nurses' Health Study. We used time-varying Cox proportional hazards models to estimate risk of incident CVD, coronary heart disease (CHD), and stroke associated with long-term average (14-y measurement period) noise exposure, adjusted for potential individual- and area-level confounders and CVD risk factors (1988–2018; biennial residential address updates; monthly CVD updates). We assessed effect modification by population density, region, air pollution, vegetation cover, and neighborhood socioeconomic status, and explored mediation by self-reported average nightly sleep duration.

Results: Over 2,548,927 person-years, there were 10,331 incident CVD events. In fully adjusted models, the hazard ratios for each interquartile range increase in L_{50} nighttime noise (3.67 dBA) and L_{50} daytime noise (4.35 dBA), respectively, were 1.04 (95% CI: 1.02, 1.06) and 1.04 (95% CI: 1.02, 1.07). Associations for total energy-equivalent noise level (L_{eq}) measures were stronger than for the anthropogenic statistical L_{50} noise measures. Similar associations were observed for CHD and stroke. Interaction analyses suggested that associations of L_{50} nighttime and L_{50} daytime noise with CVD did not differ by prespecified effect modifiers. We found no evidence that inadequate sleep (<5 h/night) mediated associations of L_{50} nighttime noise and CVD.

Discussion: Outdoor L_{50} anthropogenic nighttime and daytime noise at the residential address was associated with a small increase in CVD risk in a cohort of adult female nurses. https://doi.org/10.1289/EHP12906

Introduction

Noise, or unwanted sound exposure, is the second largest environmental cause of health problems, after air pollution, and has been associated with multiple adverse outcomes, such as annoyance, sleep disturbance, and poor concentration.[1–3] In addition, epidemiological studies have found associations of long-term noise exposure with risk of metabolic and cardiovascular disease (CVD),[4] as well as dementia.[5–7]

Exposure to noise has been linked to short-term changes in circulation, including changes in blood pressure, heart rate, cardiac output, and vasoconstriction.[8–10] These biological changes can occur not only at high sound levels in occupational settings but also during exposure to lower levels of environmental noise in residential settings.[11] During daytime and nighttime exposure, or during waketime and sleeptime exposure, noise activates the central nervous system and triggers a host of changes in various subsystems in the human body identical to a typical stress response.[12] Reactions include activation of the hypothalamic–pituitary–adrenal axis and the sympathetic nervous system, which is triggered by limbic activity in the brain and results in the release of stress hormones (glucocorticoids and catecholamines).[13] Repeated release of stress hormones associated with long-term noise exposure may manifest in aortic calcification and atherosclerosis,[14] insulin-resistance and diabetes,[15] and CVD.[16]

Prospective cohort studies conducted in Europe[17–22] and Canada[23] suggest that higher levels of environmental noise are linked to increased risk of coronary heart disease (CHD) and stroke, although findings are inconsistent, especially for stroke.[24–27] In a 2018 World Health Organization (WHO) review, evidence linking long-term noise exposure with CHD and stroke was graded as high- and moderate-quality, respectively[28]; however, few studies have been conducted on CHD or stroke in the United States, and no study has assessed the prospective association of nighttime anthropogenic noise and CHD and stroke in a nationwide U.S. study. Epidemiological studies indicate that nighttime noise exposure may be more relevant for cardiovascular outcomes than daytime exposure,[28] potentially owing to impacts on sleep.[3] Although many epidemiological studies have weighted noise models to assign a penalty to nighttime noise (e.g., adding a 10-dBA penalty to noise estimates between 2200 and 0700 hours), few studies in

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the U.S. have specifically assessed nighttime noise exposure, which occurs when individuals are most likely to be home and sleeping.

In the United States, anthropogenic noise from multiple sources, including traffic, aircraft, and industry, has been assessed ecologically[29]; however, there remains a deficit of nationwide, individual-level, longitudinal epidemiological evidence on anthropogenic noise and incident CVD, except for two recent Nurses' Health Study (NHS) assessments of aircraft noise around airports,[30,31] which contributed to prior geographically restricted evidence on noise and hypertension, metabolic syndrome, and dementia in the United States.[32–34] Using data from the nationwide, U.S.-based NHS from 1988–2018, we examined the association of anthropogenic nighttime and daytime noise with CVD incidence. We also examined whether the association of noise and CVD differed by population density, region, air pollution level, greenness level, or neighborhood socioeconomic status (nSES), as well as whether associations were mediated by sleep.

Methods

Population

The NHS is a prospective cohort study designed to assess risk factors for chronic disease among women. In 1976, 121,701 female registered nurses who were 30–55 years of age and from 11 states (California, Connecticut, Indiana, Iowa, Kentucky, Massachusetts, Michigan, Missouri, New York, North Carolina, Ohio, Pennsylvania, South Carolina, and Texas) returned an initial health-related questionnaire and have since been followed with biennial questionnaires on demographic and physical characteristics, lifestyle, and health status. Response rates at each questionnaire cycle have consistently been ≥90%.[31,35] NHS residential addresses have been geocoded (i.e., assigned latitude and longitude) and updated at each move of address. NHS participants currently reside in all states in the contiguous United States and the District of Columbia (Figure 1). This analysis was conducted among all women who were alive and had no prior CVD in 1988 and had at least one residential address geocoded in the contiguous United States for exposure assessment between 1988 and 2018. This study was approved by the institutional review board of Brigham and Women's Hospital, Boston, Massachusetts.

Outcome

On the baseline and all subsequent biennial follow-up questionnaires, participants were asked to report all occurrences of clinician-diagnosed CVD (CHD or stroke) and participants (or next of kin for fatal cases) provided consent to review medical records pertaining to their diagnosis. Methods to confirm incident CVD in the NHS have been published in detail elsewhere.[36–38] In brief, incident CVD was determined as the first occurrence of either nonfatal myocardial infarction (MI) or fatal CHD categorized according to the *International Statistical Classification of Diseases, Ninth Revision* (ICD-9[39] code 410) or nonfatal or fatal stroke (ICD-9 codes 430–437). Cases of nonfatal CVD were confirmed through medical record review or through interview or a letter confirming hospitalization for the nonfatal MI or stroke. Cases of fatal CHD or fatal stroke were confirmed through hospital record review, autopsy, report of the underlying cause on the death certificate, a history of CHD or stroke and CHD or stroke was the most plausible cause of death, or supporting information provided by a family member. Stroke subcauses were classified according to the criteria of the National Survey of Stroke as due to ischemia (embolic or thrombotic; ICD-9 codes 430–432), hemorrhage (subarachnoid hemorrhage or intracerebral hemorrhage; ICD-9 codes 433–434 and 436), or other, unspecified/unknown cause.

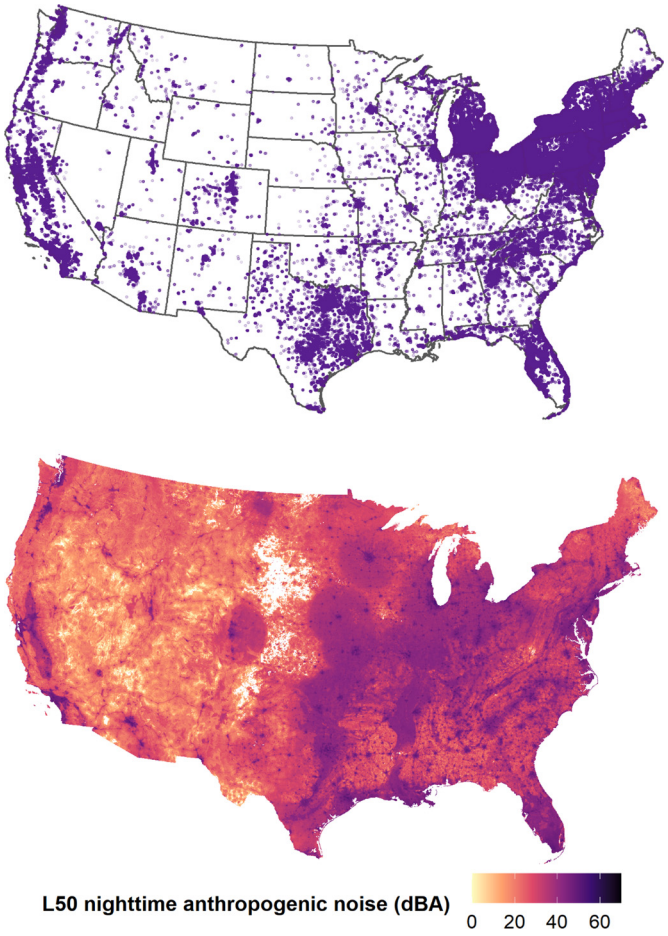

Figure 1. Location of Nurses' Health Study addresses (n participants = 114,116) from 1988–2018 (above) and map of anthropogenic nighttime L_{50} sound (dBA) in 2000–2014 (below). Note: L_{50}, noise level exceeded 50% of the time.

Exposure

National Park Service (NPS) researchers created a geospatial noise model to predict outdoor sound levels for the contiguous United States (Figure 1).[40] The model used acoustic data from 1.5 million h of long-term measurements from 159 urban and 333 rural monitoring sites located across the contiguous United States during 2000–2014.[40] Urban monitoring sites were within a 25-km radius of airports or within 14 small and large urban areas across the United States (San Antonio, Texas; Austin, Texas; Vicksburg, Mississippi; Los Angeles, California; Riverside, California; Kill Devil Hills, North Carolina; San Francisco, California; Washington, District of Columbia; Denver, Colorado; Bridgeport, Connecticut; New York, New York; Boston, Massachusetts; Milwaukee, Wisconsin; and Seattle, Washington).[40] The model regressed monitored sound levels with spatial data sets of environmental factors, such as topography, climate, hydrology, population density, and anthropogenic activity. Using a random forest approach (a tree-based machine learning algorithm), the ensemble of spatial data sets that best predicted measured sound levels were retained, and their relative contribution to sound levels at monitoring sites was used to estimate sound levels in locations where monitoring stations were not present (land-use regression). Anthropogenic factors were highly ranked predictors of

anthropogenic noise, for example, light-at-night and transportation infrastructure access were the first and third ranked variables of the 45 variables included in the noise level exceeded 50% of the time (L_{50}) anthropogenic noise model.[40] Noise estimates were validated using leave-one-out cross-validation. Cross-validated residuals relative to those from the null model indicated that the root mean squared error ranged from 4.5 to 4.9 dB; the median absolute deviation, from 2.3 to 2.4 dB, and the percentage of variance explained, from 80% to 84% across the noise metrics. The resulting model enabled the mapping of sound levels at a 270 m × 270 m resolution across the contiguous United States over a 14-y period (long-term average). We appended NPS noise estimates to each NHS residential address throughout the follow-up period (updated each time a participant moved address), based on the 270-m grid cell that the address was contained within. We carried backward and forward the temporally invariant noise estimates from 2000–2014 to 1988–2018 addresses (mean participant follow-up time: 22.3 y). Environmental sound levels vary diurnally and were summarized by NPS researchers using a variety of statistics across multiple timescales and frequency ranges. Given the posited mechanism of nighttime noise to increase physiologic stress,[32] coupled with the increased likelihood that participants were occupying their residence during nighttime hours, we used the anthropogenic nighttime (1900–0700 hours) A-weighted L_{50} sound pressure level metric as our primary noise exposure. The L_{50} is an exceedance metric that corresponds to the sound pressure level exceeded 50% of the time. A-weighting is an adjustment in decibels (dBA) that reflects how the human ear perceives sound across the frequency spectrum. Although many noise measures are available from the NPS model, we focused on anthropogenic L_{50} nighttime (1900–0700 hours) and, for completeness, anthropogenic L_{50} daytime (0700–1900 hours) sound pressure levels in dBA, which were used in a prior U.S. study.[29]

Energy-equivalent noise levels (L_{eq}) are commonly reported in epidemiological studies of transportation noise.[28] NPS researchers calculated total (i.e., anthropogenic plus natural source) A-weighted energy-equivalent noise over 24 h ($L_{eq(24)}$), A-weighted energy-equivalent noise over the 8-h night period from 2300 hours to 0700 hours (L_{night}), and A-weighted energy-equivalent noise over day–evening–night periods (24-h total) with a penalty of 10 dBA for night noise (2300–0700 hours) and a penalty of 5 dBA for evening noise (1900–2300 hours) (L_{den}).[40] In addition to the L_{50} statistical noise metrics, we appended these total (i.e., anthropogenic plus natural source) L_{eq} noise metrics to each NHS residential address for comparison with epidemiological studies that used L_{eq} noise estimates, with the caveat that the NPS L_{eq} estimates are not generated from traffic-specific sources but, rather, were estimated via land-use regression using total (i.e., anthropogenic plus natural) sound.

Statistical Analysis

Person-months of follow-up were accrued from the return date of the 1988 questionnaire until either the participant became a case or died or the end of the follow-up period (31 May 2018). We fit time-varying Cox proportional hazards regression models to calculate the hazard ratio (HR) and 95% confidence interval (95% CI) for developing CVD (CHD or stroke; monthly follow-up) associated with exposure to long-term average (14-y measurement period) L_{50} anthropogenic nighttime and daytime noise. Note, the time-invariant, long-term average noise estimates (14-y average: 2000–2014) were carried backward and forward to cover the NHS CVD follow-up period (1988–2018); therefore, residential noise estimates changed over time only if a participant moved residential address location (NHS addresses were updated biennially throughout the follow-up). In addition, we assessed the associations of CVD with energy-based noise metrics [long-term average (14-y measurement period) $L_{eq(24)}$, L_{night}, L_{den}], from both anthropogenic and natural sources, given that energy-based (L_{eq}) noise metrics are more commonly reported in epidemiological studies of transportation noise.[28] We used restricted cubic splines to determine the linearity of exposure–response associations with a likelihood ratio test comparing the linear model to the model with linear and cubic spline terms. There were no deviations from linearity observed; therefore, herein we present continuous exposure–response results, modeled per interquartile range (IQR). There were no violations of the proportional hazards assumption, which we tested by including the interaction terms of noise exposure and age.

Models included strata for age at follow-up and time period (month), and we examined the following covariates, determined *a priori* as potential confounders because they are CVD risk factors and may be correlated with noise (all variables are time-varying unless otherwise indicated): race [White (southern European/Mediterranean/Scandinavian/other Caucasian)/non-White (African American/Hispanic/Asian/Native American/other)], smoking (current/past/never), pack-years smoked (continuous), family history of MI (yes/no), menopausal status (premenopausal/postmenopausal/dubious or missing), postmenopausal hormone use (premenopausal/never/current/former/missing), diet based on the Alternate Healthy Eating Index estimated from food frequency questionnaires[41] (continuous), alcohol consumption (in grams per day: 0/0.1–4.9/5.0–14.9/ ≥15/missing), weight status [normal and underweight (body mass index, i.e., BMI in kilograms per meter squared) <24.9/overweight (BMI 25–29.9)/obese (BMI >30)], and night shift work before 1989 (never/1–14 y of shift work/15–29 y of shift work/ ≥30 y of shift work; time invariant). Some individual race/ethnicities are underpowered in the NHS, so we grouped them together as non-White and used this variable as a proxy for unmeasured consequences of racism; time invariant.

To account for individual-level SES, we included information on self-reported parental occupation for the participant's mother (housewife/other; time invariant) and father (professional or manager/other; time invariant), whether the participant had a registered nursing degree (yes/no; time invariant), marital status (married/other), and husband's highest educational attainment (<high school/high school graduate/ > high school/missing or not married; time invariant). We accounted for area-level SES by using an nSES index that we developed specifically to differentiate neighborhood deprivation among NHS participants.[42] We obtained the U.S. Census tract-level variables for the temporally closest census from the Neighborhood Change Database (NCDB), which provides U.S. Census data from 1970, 1980, 1990, 2000, and 2010 with normalized boundaries over time.[43] To create the nSES score, we *z*-standardized and summed the following nine variables: median household income, median home value, percentage with a college degree, percentage non-Hispanic White, percentage non-Hispanic Black, percentage of foreign-born residents, percentage of families receiving interest or dividends, percentage of occupied housing units, and percentage unemployed (with higher score indicating less deprived).[42] We assigned Census Region (Northeast/Midwest/West/South) and, for sensitivity, Census Division (Divisions 1–9) of the United States. U.S. Census Divisions nest under Census Regions in the hierarchy of census geographies (Northeast: New England/Middle Atlantic; Midwest: East North Central/West North Central; South: South Atlantic/East South Central/West South Central; West: Mountain/Pacific).

Fine particulate matter air pollution [particulate matter ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$)] estimates were predicted monthly at each participants' geocoded address; the air pollution exposure model has been detailed elsewhere.[44] For

interaction analyses only, we classified census tract-level population density as $<1{,}000$ people/mi^2 (386.1 people/km^2) or $\geq 1{,}000$ people/mi^2 (386.1 people/km^2) and we assigned vegetation cover (greenness) in a 270-m buffer around each participant's residential address, which was derived using Google Earth Engine from 30 m × 30 m Landsat Normalized Difference Vegetation Index (NDVI) data; the exposure assessment method has been detailed elsewhere.[45] Participant observations missing air pollution were excluded from analyses. The missing indicator method was used to account for missing categorical covariates.

To assess whether the association between noise exposure and CVD risk differed across susceptible subpopulations, we examined prespecified effect modification by population density ($<1{,}000$ people/mi^2/ $\geq 1{,}000$ people/mi^2), Region (Northeast/Midwest/West/South), air pollution quintile, greenness quintile, or nSES score quintile. Behaviors, health care access, and/or CVD risk may vary by urbanicity and region in the United States and could modify the associations of noise with CVD incidence. Furthermore, environmental coexposures could modify associations of noise and CVD.[46] For example, exposure to high air pollution exposure or neighborhood deprivation could interact with noise exposure to increase risk of CVD; alternatively, coexposure to greenness could directly buffer noise levels at the residential addresses to lower CVD risk or could indirectly lower risk of CVD through other benefits to cardiovascular health.[47] To evaluate whether the association between continuous noise and CVD risk varied across levels of each potential modifier, we fit models that included a multiplicative interaction term between noise and the effect modifier. We reported stratum-specific HRs and 95% CIs and used likelihood ratio tests to determine statistical significance of departure from the null of no effect modification across levels of the modifier.

In sensitivity analyses, we restricted analyses to 2000–2018 to assess the impact of carrying back the time-invariant noise estimates to 1988 (prior to noise sampling). We also assessed the impact of additionally adjusting for comorbidities (ever reported diabetes, elevated cholesterol, and/or high blood pressure), statin use, aspirin use, and physical activity [<3 metabolic equivalent hours (MET h) per week/3 to <9 MET h per week/9 to <18 MET h per week/ ≥18 MET h per week] in fully adjusted models because we believe these variables potentially lie along the causal pathway between noise and CVD. We adjusted for Census Division rather than Census Region in the fully adjusted model to assess for potential spatial autocorrelation. We removed area-level covariates (nSES, Region, and/or air pollution) from the otherwise fully adjusted model to compare the fully adjusted model to a model adjusted for individual-level covariates only. In addition, we assessed associations of noise exposure categorized into quintiles (Qs) and CVD risk to compare noise exposure at the lowest levels to potentially more etiologically relevant, louder levels. We also assessed fatal CVD, CHD, and stroke events, censoring only when a fatal event occurred, for comparison with studies of noise and CVD mortality.

We assessed mediation of the relationship between noise exposure and CVD by sleep duration, which was self-reported by NHS participants on 1986, 2000, 2002, 2008, 2012, and 2014 questionnaires. We defined inadequate sleep duration as ≤5 h/night, as in other NHS studies of sleep and CHD.[48] We calculated the mediation proportion and its 95% CI by comparing the noise effect estimate from a model that included the exposure, a potential intermediate mediator variable, and covariates with the noise effect estimate obtained from a partial model that did not include the intermediate mediation variable. The mediation proportion relates to the increased CVD risk explained by higher exposure to noise that can be attributed to inadequate sleep. We calculated CIs for the mediation proportion using the data duplication method.[49] We assumed no unmeasured exposure–outcome confounding, no unmeasured mediator–outcome confounding, no unmeasured exposure–mediator confounding, and no mediator–outcome confounder affected by exposure. We included richly characterized confounders in our mediation analyses, and therefore, we believe our assumptions are reasonable. Analyses were conducted in SAS (version 9.4; SAS Institute, Inc.). Graphics and maps were produced using R (version 4.2.2; R Development Core Team).

Results

We observed 10,331 total CVD cases over 2,548,927 person-years of follow-up among the 114,116 eligible cohort members from 1988–2018. In cause-specific analyses, we observed 5,321 CHD cases and 5,010 stroke cases, of which 1,929 were ischemic and 553 were hemorrhagic stroke and 2,528 were unspecified. The mean age over the follow-up period was 67.6 y (Table 1). Participants were predominantly White and lived in the Northeastern United States. Those living in areas with higher levels of nighttime noise lived in areas with higher population density, higher levels of air pollution, and were less likely to be White. Nighttime and daytime noise were correlated with each other (0.73) and weakly correlated with other environmental variables (Figure S1).

The associations between nighttime noise and CVD, CHD, and stroke (total or subtype-specific) risks are shown in Table 2. Each IQR increase in L_{50} nighttime noise (3.67 dBA) was associated with an HR of 1.04 (95% CI: 1.02, 1.06) in fully adjusted models for CVD. Overall nighttime noise and CVD results were driven primarily by CHD [HR = 1.05 (95% CI: 1.02, 1.09)], as opposed to stroke [HR = 1.02 (95% CI: 0.99, 1.06)]. Ischemic stroke and hemorrhagic stroke findings were not statistically significant, although there was a suggestive positive association of nighttime noise with hemorrhagic stroke [HR = 1.08 (95% CI: 0.98, 1.19)]. Similar patterns were observed in the analyses of L_{50} daytime noise. In addition, findings from analyses using L_{eq} total noise levels (from both anthropogenic and natural sources; Table 3) were consistent with our findings on L_{50} anthropogenic noise, although CVD associations were slightly stronger per IQR increase [e.g., $L_{eq(24)}$ total 24-h noise HR = 1.06 (95% CI: 1.03, 1.08), IQR 3.86 dBA; L_{night} total nighttime noise HR = 1.06 (95% CI: 1.04, 1.09), IQR 4.00 dBA; L_{den} total day–evening–night weighted noise HR = 1.07 (95% CI: 1.04, 1.09), IQR 3.90 dBA].

Interaction analyses showed that associations of stroke with nighttime noise varied by population density (Figure S2 and Table S1). We observed positive associations for stroke among those living in census tracts with $<1{,}000$ people/mi^2 and null association of nighttime noise with stroke among those living in census tracts with $\geq 1{,}000$ people/mi^2 ($p_{interaction} = 0.03$). Nighttime and daytime noise associations with CVD outcomes did not differ by all other prespecified effect modifiers (Figure S3 and Table S2).

In sensitivity analyses, associations for nighttime and daytime noise with CVD were slightly smaller in prespecified analyses restricted to the 2000–2018 follow-up period (Tables S3 and S4). We found no appreciable difference in associations when time-varying statin use or aspirin use was added to fully adjusted models (Table S5 and Table S6). The impact of adjustment for physical activity in fully adjusted models, which may be considered a mediator of the association between noise exposure and cardiometabolic diseases,[50,51] resulted in no change in associations. In addition, adjusting models for population density resulted in slightly stronger associations of nighttime [HR = 1.06 (95% CI: 1.03, 1.09)] and daytime [HR = 1.07 (95% CI: 1.03, 1.10)] anthropogenic noise with CHD; however, we chose not to adjust for population density in our main fully adjusted model because it was a predictor used in

Table 1. Age-adjusted Nurses' Health Study participant characteristics [mean ± SD or %] by quintiles of nighttime anthropogenic L_{50} in dBA from 1988 to 2018 ($n = 114{,}116$; averaged over 2,548,927 person-years).

		Quintile				
Characteristic	Total	1	2	3	4	5
Person-years[a]	2,548,927	517,094	510,964	511,952	508,106	500,810
L_{50} anthropogenic nighttime noise (dBA)	43.0 (3.5)	37.9 (3.5)	41.9 (0.6)	43.3 (0.4)	44.7 (0.5)	47.1 (1.3)
L_{50} anthropogenic daytime noise (dBA)	46.1 (4.2)	40.8 (4.7)	45.2 (2.4)	47.1 (2.1)	48.2 (2.1)	49.3 (2.5)
$L_{eq(24)}$ anthropogenic and natural 24-h noise (dBA)	52.4 (3.3)	48.7 (3.2)	51.6 (2.0)	53.1 (2.2)	53.9 (2.3)	54.9 (2.4)
L_{night} anthropogenic and natural nighttime noise (dBA)	49.8 (3.3)	45.9 (3.1)	48.9 (1.9)	50.4 (2.1)	51.3 (2.2)	52.4 (2.4)
L_{den} anthropogenic and natural weighted day–evening–night noise (dBA)	56.9 (3.2)	53.2 (3.1)	56.1 (1.9)	57.6 (2.1)	58.4 (2.2)	59.6 (2.3)
Age (y)[a]	67.6 (10.6)	67.0 (10.7)	67.3 (10.6)	67.5 (10.6)	67.9 (10.5)	68.1 (10.5)
Race (%)						
White	94	96	96	94	93	90
Non-White	6	4	4	6	7	10
Alternative Healthy Eating Index	51.6 (10.2)	51.6 (10.2)	51.3 (10.1)	51.6 (10.2)	52.0 (10.2)	51.8 (10.1)
Alcohol categories [g/d (%)]						
0	29	30	29	28	27	29
0.1–4.9	19	19	19	19	19	18
5.0–14.9	12	12	12	13	12	11
≥15	8	8	8	8	8	7
Missing	32	30	31	32	33	35
BMI categories (%)						
Normal/underweight	41	41	41	42	42	39
Overweight	29	30	30	29	28	29
Obese	19	19	19	18	18	19
Missing	11	10	10	11	12	13
Smoking status (%)						
Never smoker	45	45	45	44	45	46
Past smoker	43	43	43	43	43	41
Current smoker	10	9	10	10	9	10
Missing	3	2	2	2	3	3
Pack-years of smoking	11.7 (18.6)	11.7 (18.5)	11.8 (18.5)	12.1 (18.9)	11.6 (18.7)	11.3 (18.6)
Participant's highest education (%)						
Nursing (RN) degree	74	76	75	74	73	72
No RN degree	26	24	25	26	27	28
Marital status (%)						
Married	63	66	65	64	62	60
Never married or divorced or widowed	37	34	35	36	38	40
Husband's highest education (%)						
<High school	4	4	4	3	3	4
High school grad	26	29	28	25	23	25
>High school education	37	35	36	38	39	35
Not married	34	31	32	33	35	37
Mother's occupation (%)						
Housewife	64	63	64	64	64	64
Out-of-home	36	37	36	36	36	36
Father occupation (%)						
Professional or manager	26	25	25	26	27	25
Not professional or manager	74	75	75	74	73	75
Family history of MI (%)	26	26	27	26	26	25
Menopausal status (%)						
Premenopausal or missing	44	46	44	44	43	43
Postmenopausal	56	54	56	56	57	57
Postmenopausal hormone use (%)						
Premenopausal	8	8	8	8	8	8
Never	21	22	21	21	20	19
Current	22	21	21	22	23	23
Former	33	34	34	34	33	32
Missing	16	15	16	16	17	18
Night shift work (%)						
Never	31	32	30	31	30	30
1–14 y	39	39	40	39	39	37
15–29 y	4	4	4	4	4	4
≥30 y	1	1	1	1	1	1
Missing	25	24	25	25	26	28
Sleep duration [h/night (%)]						
≥5	94	94	94	94	94	93
<5	6	6	6	6	6	7
Cancer during follow-up (%)						
No	93	93	93	93	92	93
Yes	7	7	7	7	8	7
Population density ≥1,000/mi^2 (%)	65	39	57	70	79	81

Table 1. (*Continued.*)

Characteristic	Total	Quintile 1	2	3	4	5
Region (%)						
Northeast	45	58	55	46	37	31
Midwest	16	11	18	17	14	20
South	17	13	13	18	21	18
West	13	9	6	10	18	20
Missing	9	9	8	9	10	10
12-month average $PM_{2.5}$ ($\mu g/m^3$)	12.6 (4.6)	11.0 (4.1)	12.3 (4.3)	13.0 (4.5)	13.2 (4.7)	13.7 (5.0)
nSES (time-varying) quintile (%)[b]						
Q1	20	31	24	17	14	16
Q2	21	20	23	20	18	22
Q3	23	21	22	23	22	24
Q4	13	11	12	13	15	15
Q5	23	17	19	26	31	22

Note: BMI, body mass index; L_{50}, noise level exceeded 50% of the time; L_{den}, A-weighted energy-equivalent noise over day–evening–night periods (24-h total) with a penalty of 10 dBA for night noise (2300–0700 hours) and a penalty of 5 dBA for evening noise (1900–2300 hours); $L_{eq(24)}$, A-weighted energy-equivalent noise over 24 h; L_{night}, A-weighted energy-equivalent noise over the 8-h night period from 2300 hours to 0700 hours; MI, myocardial infarction; nSES, neighborhood socioeconomic status; $PM_{2.5}$, particulate matter $\leq$2.5 μm in aerodynamic diameter; Q, quintile; RN, registered nurse; SD, standard deviation.
[a]Value is not age-adjusted.
[b]Time-varying quintiles for nSES were calculated at every (monthly) time interval during follow-up and therefore do not sum to 100%.

the NPS noise exposure model. Adjusting for Census Division rather than Census Region in fully adjusted models did not substantially alter associations. Models adjusted for individual-level covariates [i.e., without adjustment for area-level covariates (nSES, region, air pollution)], showed weaker associations with nighttime and daytime noise. Mediation analyses showed no evidence that the association of nighttime noise and CVD risk was mediated by inadequate sleep duration (statistically nonsignificant), defined as self-reported $\leq$5 h of sleep per night (Table S7).

In categorical analyses (Table S8), the risk of incident CVD was higher in the loudest quintiles (Q4 and Q5) of L_{50} nighttime and L_{50} daytime anthropogenic noise compared with the lowest quintile (Q1). Associations of fatal CVD with noise were attenuated toward the null compared with our main analyses, which included nonfatal CVD cases. However, a suggestive association of incident fatal stroke with L_{50} nighttime noise [HR = 1.02 (95 CI: 0.97, 1.07), IQR 3.67 dBA] was observed (Table S9).

Discussion

In this nationwide prospective analysis of female nurses, we observed small positive associations of nighttime and daytime noise exposure with total CVD [L_{50} anthropogenic nighttime noise HR = 1.04 (95% CI: 1.02, 1.06), IQR: 3.67 dBA; L_{50} anthropogenic daytime noise HR = 1.04 (95% CI: 1.02, 1.07), IQR: 4.35 dBA] that were robust to adjustment for important CVD risk factors. Associations with total incident CVD were generally consistent across multiple noise metrics, including L_{eq} noise estimates [e.g., L_{night} total (anthropogenic plus natural) nighttime noise HR = 1.06 (95% CI: 1.04, 1.09), IQR: 4.00 dBA]. Associations were slightly stronger for CHD than CVD (CHD and stroke, combined). Associations of noise with CVD did not substantially differ by prespecified effect modifiers. We did not observe evidence that the relationship between noise and CVD risk was mediated by self-reported inadequate sleep duration.

Our findings were generally consistent with previous analyses of environmental noise exposure and CVD. In 2018, the WHO stated that high- and moderate-quality evidence was available to conclude that road traffic noise increased the risk of CHD and stroke, respectively.[28,70] Since the publication of the WHO report, evidence on noise and stroke has shown mixed findings, and a 2021 publication called for further assessment of noise and stroke subtypes—specifically ischemic stroke—using richly contextualized, individual-level longitudinal studies.[4] In agreement with other cohort studies, our study found increased risk of CHD (nonfatal MI or fatal CHD) associated with noise, but relatively smaller associations for stroke or stroke subtypes.[26,27,52–54] Similarly, a nationwide cohort study of the entire Danish population found positive associations of traffic noise with CHD [L_{den} traffic-noise adjusted-HR = 1.04 (95% CI: 1.03, 1.05), per 10-dBA increment]. In addition, positive associations of traffic noise, but not railway noise, with stroke were found in a pooled analysis of nine Scandinavian cohorts [L_{den} traffic-noise adjusted-HR = 1.06 (95% CI: 1.03, 1.08), per 10-dBA

Table 2. Hazard ratios (HRs) and 95% confidence intervals (CIs) per interquartile range increase (IQR) of anthropogenic L_{50} nighttime or anthropogenic L_{50} daytime sound pressure (dBA) and cardiovascular disease (CVD) incidence in the Nurses' Health Study from 1988 to 2018 (n = 114,116; person-years = 2,548,927).

	L_{50} nighttime noise		L_{50} daytime noise	
	Age and calendar year adjusted	Fully adjusted[a]	Age and calendar year adjusted	Fully adjusted[a]
CVD (n = 10,331)	1.01 (0.99, 1.03)	1.04 (1.02, 1.06)	1.01 (0.99, 1.03)	1.04 (1.02, 1.07)
CHD (n = 5,321)	1.02 (1.00, 1.05)	1.05 (1.02, 1.09)	1.02 (0.99, 1.05)	1.06 (1.02, 1.09)
Stroke (n = 5,010)	1.00 (0.97, 1.02)	1.02 (0.99, 1.06)	1.00 (0.97, 1.03)	1.03 (1.00, 1.06)
Ischemic stroke (n = 1,929)	0.96 (0.92, 1.01)	1.00 (0.96, 1.05)	0.98 (0.93, 1.02)	1.04 (0.99, 1.09)
Hemorrhagic stroke (n = 553)	1.07 (0.98, 1.18)	1.08 (0.98, 1.19)	1.08 (0.99, 1.18)	1.10 (0.99, 1.21)

Note: Total CVD (CHD or stroke), CHD, stroke, and stroke subtypes (ischemic and hemorrhagic stroke) are shown. IQR for anthropogenic L_{50} nighttime sound: 3.67 dBA; IQR for anthropogenic L_{50} daytime sound: 4.35 dBA. BMI, body mass index; CHD, coronary heart disease; L_{50}, noise level exceeded 50% of the time; MI, myocardial infarction; nSES, neighborhood socioeconomic status; $PM_{2.5}$, particulate matter $\leq$2.5 μm in aerodynamic diameter; RN, registered nurse.
[a]HRs are adjusted for age and calendar year, race, smoking status, pack-years smoked, family history of MI, menopausal status, postmenopausal hormone use, diet, alcohol consumption, BMI, night shift work, parental occupation, educational attainment (RN degree), marital status, husband's highest education, nSES score quintile, region, and air pollution ($PM_{2.5}$).

Table 3. Hazard ratios (HRs) and 95% confidence intervals (CIs) per interquartile range increase (IQR) of energy-equivalent noise estimates (L_{eq}; in dBA) averaged over 24-h ($L_{eq(24)}$), nighttime (L_{night}), or 24-h day–evening–night periods with an additional 10-dBA penalty added to the nighttime period and an additional 5-dBA penalty added to the evening period (L_{den}), and cardiovascular disease (CVD) incidence in the Nurses' Health Study from 1988 to 2018 ($n = 114{,}116$; person-years = 2,548,927).

	$L_{eq(24)}$ total 24-h noise		L_{night} total nighttime noise		L_{den} total 24-h weighted noise	
	Age and calendar year adjusted	Fully adjusted[a]	Age and calendar year adjusted	Fully adjusted[a]	Age and calendar year adjusted	Fully adjusted[a]
CVD ($n = 10{,}331$)	1.02 (0.99, 1.04)	1.06 (1.03, 1.08)	1.02 (1.00, 1.05)	1.06 (1.04, 1.09)	1.03 (1.00, 1.05)	1.07 (1.04, 1.09)
CHD ($n = 5{,}321$)	1.04 (1.01, 1.08)	1.08 (1.04, 1.12)	1.05 (1.02, 1.09)	1.09 (1.05, 1.13)	1.06 (1.02, 1.09)	1.09 (1.05, 1.13)
Stroke ($n = 5{,}010$)	0.99 (0.95, 1.02)	1.03 (1.00, 1.07)	0.99 (0.96, 1.03)	1.04 (1.00, 1.08)	1.00 (0.97, 1.03)	1.04 (1.00, 1.08)
Ischemic stroke ($n = 1{,}929$)	0.97 (0.92, 1.02)	1.05 (0.99, 1.11)	0.97 (0.91, 1.02)	1.04 (0.98, 1.10)	0.97 (0.92, 1.02)	1.04 (0.98, 1.10)
Hemorrhagic stroke ($n = 553$)	1.02 (0.92, 1.13)	1.03 (0.93, 1.15)	1.03 (0.93, 1.14)	1.04 (0.93, 1.17)	1.03 (0.93, 1.13)	1.04 (0.93, 1.16)

Note: Total CVD (CHD or stroke), CHD, stroke, and stroke subtypes (ischemic and hemorrhagic stroke) are shown. IQR for $L_{eq(24)}$: 3.86 dBA; IQR for L_{night}: 4.00 dBA; IQR for L_{den} 3.90 dBA. BMI, body mass index; CHD, coronary heart disease; MI, myocardial infarction; nSES, neighborhood socioeconomic status; $PM_{2.5}$, particulate matter ≤2.5 μm in aerodynamic diameter; RN, registered nurse.

[a]HRs are adjusted for age and calendar year, race, smoking status, pack-years smoked, family history of MI, menopausal status, postmenopausal hormone use, diet, alcohol consumption, BMI, night shift work, parental occupation, educational attainment (RN degree), marital status, husband's highest education, nSES score quintile, region, and air pollution ($PM_{2.5}$).

increment], but several other cohort studies found no evidence for the association of traffic noise with stroke or stroke subtypes after the models were adjusted for air pollution.[26,54] In fully adjusted models that included adjustment for $PM_{2.5}$, we generally found positive associations with stroke and stroke subtypes. Finally, in contrast to other cohort studies that explored associations of stroke subtypes with noise,[21,26,53–55] we found suggestions of stronger associations for hemorrhagic stroke compared with ischemic stroke in anthropogenic noise models, although hemorrhagic stroke CIs were wide in our study.

An analysis of 2009 Medicare data on adults ≥65 years of age living around airports in the United States linked to Federal Aviation Administration aircraft noise contour data found that a 10-dBA higher aircraft noise exposure at the ZIP code level was associated with a higher cardiovascular hospital admission rate [3.5% (95% CI: 0.2%, 7.0%), per 10-dBA increment], after controlling for age, sex, race, ZIP code-level SES and demographics, ZIP code-level air pollution ($PM_{2.5}$ and ozone), and roadway density.[56] In addition, NHS cohort studies examined the relationship of airport noise and hypertension,[31] an important risk factor for CHD and stroke, and airport noise and CHD and stroke,[30] and found limited evidence of positive associations; however, the NHS residential addresses had low levels of exposure to airport noise. These findings added to prior high-quality, but geographically restricted, U.S. evidence on positive associations of noise with hypertension, metabolic syndrome, and dementia.[6,7,32–34] Our study is the first to provide nationwide, longitudinal, individual-level evidence of associations of anthropogenic noise (from multiple sources, including traffic, aircraft, and industry) with total CVD (CHD and stroke), CHD, and stroke in the United States.

There is no reason to believe that the biological pathways mediating the effects of noise on human health differ in U.S. citizens compared with those from other countries; however, U.S.-based evidence is crucial to guide U.S. legislation. Although associations of CVD with anthropogenic noise in our study were small, a 4% increased risk per IQR increase could be an important long-term risk factor for CVD because such a large percentage of the population is exposed to anthropogenic noise.[29] In addition, higher anthropogenic noise levels are concentrated in U.S. Census blocks with higher proportions of non-White, Hispanic, and/or low-SES residents,[29] which could potentially also contribute to racial/ethnic and/or socioeconomic health disparities. In addition, this 4% increase is likely an underestimate owing to potential nondifferential exposure measurement error. More refined noise exposure models with higher spatial resolution, especially in urban areas (i.e., with greater exposure contrast among addresses in the loudest areas), may result in stronger associations with CVD outcomes. Indeed, a Swiss cohort study showed that reducing exposure measurement error by modeling traffic noise using high spatiotemporal resolution inputs compared with lower resolution inputs resulted in stronger associations with MI.[57] U.S. noise models could be improved by using sound propagation models that incorporate reflection, diffraction, and absorption by sound barriers (e.g., buildings).[19,22,58] Development of a historic U.S. source-specific (e.g., traffic) noise model with high spatial resolution data inputs (e.g., vehicle flows) will be important in future analyses for accurately estimating the health effects of transportation noise and providing policy-relevant epidemiological evidence.

This study has limitations. First, the nationwide noise model approximated outdoor noise exposure at a 270 m × 270 m resolution, which may not accurately capture noise variability over fine spatial scales, particularly in urban environments that have high variability in emissions, reflection, diffraction, and absorption.[57] Although our predictions of outdoor noise contained measurement error, the noise model performed well in cross-validation ($R^2 \geq 0.8$),[40,59] although leave-one-out cross-validation can be inflated compared with other validation approaches given that only one monitor is dropped at a time. In addition, although information on changes in residential address were incorporated over the follow-up period, the noise model surface did not vary over time. Owing to using long-term average noise predictions (2000–2014), we back-extrapolated the time-invariant exposure to biennially updated addresses between 1988 and 1999, which could result in exposure misclassification. However, in sensitivity analyses we found similar associations with slightly larger CIs when using 2000 as a baseline, potentially arising from substantial participant exclusions due to prior CVD occurring before 2000. In addition, noise control engineers conducted repeat measurement campaigns in 10 U.S. cities between 1974, 1998, 2008, and 2009 and found that sound levels remained similar,[60] indicating that sound levels in U.S. cities were stable over the study period, supporting our decision to back-extrapolate long-term noise. Another limitation is that we could not measure factors that might alter individual noise exposure, such as housing quality or noise in the indoor environment. In addition, our noise model did not differentiate between specific sources of sound, including road traffic, trains, aircraft, and industrial land uses. Therefore, there was likely unsystematic, nondifferential error in measuring true exposure to noise that could bias our observed associations toward the null; however, if systematic, differential measurement error occurred, this may have biased associations in either direction.

With any study of neighborhood factors and health, there is the possibility that participants may self-select into certain

neighborhoods they deem healthier than others. Therefore, healthier individuals may have chosen to move to neighborhoods with lower levels of noise, which may explain our findings. However, adjustment for multiple CVD risk factors along with our prospective analysis of incident CVD would decrease the potential for this type of bias, and a study has demonstrated residential self-selection is not a major concern in the NHS.[61] We did not find evidence of effect mediation by short sleep duration; however, humans react to environmental sounds while asleep,[3,62] and irrespective of sleep impairment and cognitive perception of noise,[63] nighttime noise has been shown in experimental studies to induce both endothelial dysfunction and prothrombotic inflammatory changes to the plasma proteome in healthy individuals.[64,65] Therefore, self-reported short sleep duration may not adequately capture the breadth of potential effects of nighttime noise on CVD risk. Because all participants were female nurses at enrollment, the generalizability of our findings to males and individuals in lower SES, nonworking groups is also potentially limited. Finally, although we adjusted for numerous risk factors for CVD, we cannot rule out the possibility that other factors that are correlated with noise might explain the observed association between noise exposure and CVD risk.

This analysis has several strengths. First, this nationwide, 30-y prospective analysis included residence-level metrics of exposure to nighttime and daytime noise with medical record-confirmed or participant/medical professional-corroborated CVD end points. Second, our analyses incorporated time-varying individual-level information on important CVD risk factors, including smoking, family history of MI, diet, menopausal status, postmenopausal hormone use, BMI, and night shift work, as well as area-level data on nSES, region, and air pollution. Because of the breadth of information available in the NHS cohort, we were able to conduct interaction analyses and to examine the potential mediation of the noise and CVD relationship by short sleep duration. Finally, this nationwide study covered a broad geographic region with a considerable range of noise levels and included participants residing in high- and low-population density areas of the United States, which increases the generalizability of findings. In the future, it will be crucial to add to the epidemiological evidence using U.S. transportation noise estimates modeled and validated around major roads, such as those modeled by the U.S. Department of Transportation from 2016,[66] as well as using historical traffic noise estimates modeled for both major and minor (residential) road locations to reduce potential bias in estimates of long-term noise associations with CVD due to exposure measurement error. Validating a historic, nationwide traffic-noise model will require extensive sound measurement in diverse geographical locations across the United States.[40,67–69]

This prospective study, conducted over 30 y of follow-up with objective measures of anthropogenic nighttime and daytime noise across the entire United States, provides evidence that nighttime and daytime noise is modestly associated with CVD (CHD and stroke) incidence and that nighttime and daytime noise is more strongly associated with incident CHD than incident stroke, after accounting for individual- and area-level risk factors for CVD.

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Access to Channing Division of Network Medicine Cohorts, which include the Nurses' Health Study, requires the proposal and approval of the specific research project and is not directly sharable. Details on obtaining access are available at https://nurseshealthstudy.org/researchers.

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