ORIGINAL RESEARCH

Association Between Road Traffic Noise and Incidence of Diabetes Mellitus and Hypertension in Toronto, Canada: A Population-Based Cohort Study

Saeha Shin, MPH;* Li Bai, PhD;* Tor H. Oiamo, PhD; Richard T. Burnett, PhD; Scott Weichenthal, PhD; Michael Jerrett, PhD; Jeffrey C. Kwong, MD, MSc; Mark S. Goldberg, PhD; Ray Copes, MD, MSc; Alexander Kopp, MSc; Hong Chen, PhD

***Background*—**Exposure to road traffic noise has been linked to cardiometabolic complications, such as elevated blood pressure and glucose dysregulation. However, epidemiologic evidence linking road traffic noise to diabetes mellitus and hypertension remains scarce. We examined associations between road traffic noise and the incidence of diabetes mellitus and hypertension in Toronto, Canada.

***Methods and Results*—**Using the Ontario Population Health and Environment Cohort, we conducted a retrospective, population-based cohort study of long-term residents of Toronto, aged 35 to 100 years, who were registered for provincial publicly funded health insurance, and were without a history of hypertension (n=701 174) or diabetes mellitus (n=914 607). Road traffic noise exposure levels were assessed by the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day and the equivalent continuous A-weighted sound pressure level for the night (11 PM–7AM). Noise exposures were assigned to subjects according to their annual residential postal codes during the 15-year follow-up. We used random-effect Cox proportional hazards models adjusting for personal and area-level characteristics. From 2001 to 2015, each interquartile range increase in the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day (10.0 dBA) was associated with an 8% increase in incident diabetes mellitus (95% CI, 1.07–1.09) and a 2% increase in hypertension (95% CI, 1.01–1.03). We obtained similar estimates with the equivalent continuous A-weighted sound pressure level for the night (11 PM–7AM). These results were robust to all sensitivity analyses conducted, including further adjusting for traffic-related air pollutants (ultrafine particles and nitrogen dioxide). For both hypertension and diabetes mellitus, we observed stronger associations with the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day among women and younger adults (aged <60 years).

***Conclusions*—**Long-term exposure to road traffic noise was associated with an increased incidence of diabetes mellitus and hypertension in Toronto. **(*J Am Heart Assoc*. 2020;9:e013021. DOI: 10.1161/JAHA.119.013021.)**

Key Words: diabetes mellitus • hypertension • incidence • road traffic noise

Cardiometabolic diseases are highly prevalent conditions that pose a significant challenge to many countries.[1,2] Globally, an estimated 8% of the adult population has developed diabetes mellitus, and >25% of adults are living with hypertension.[1,2] Patients with these 2 conditions are at a high risk of developing adverse cardiovascular events, such as stroke and myocardial infarction, and the concomitant presence of diabetes mellitus and hypertension confers an

From the Public Health Ontario, Toronto, Ontario, Canada (S.S., J.C.K., R.C., H.C.); ICES, Toronto, Ontario, Canada (L.B., J.C.K., A.K., H.C.); Department of Geography and Environmental Studies, Ryerson University, Toronto, Ontario, Canada (T.H.O.); Environmental Health Science and Research Bureau, Population Studies Division (R.T.B., H.C.), and Air Health Science Division (S.C.), Health Canada, Ottawa, Ontario, Canada; Department of Epidemiology, Biostatistics, and Occupational Health and Gerald Bronfman Department of Oncology (S.C.), and Department of Medicine (M.S.G.), McGill University, Montreal, Québec, Canada; Department of Environmental Health Sciences, Fielding School of Public Health, University of California, Los Angeles, CA (M.J.); Dalla Lana School of Public Health (J.C.K., R.C., H.C.), and Department of Family and Community Medicine (J.C.K.), University of Toronto, Toronto, Ontario, Canada; and Centre for Outcomes Research and Evaluation, Research Institute of the McGill University Health Centre, Montreal, Québec, Canada (M.S.G.).

Accompanying Tables S1 through S8 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013021

*Ms Shin and Dr Bai contributed equally to this work.

Correspondence to: Hong Chen, PhD, Environmental Health Science and Research Bureau, Health Canada, 101 Tunney's Pasture Driveway, A.L. 0201A, Ottawa, Ontario, Canada K1A 0K9. E-mail: hong.chen@canada.ca

Received April 23, 2019; accepted January 10, 2020.

Clinical Perspective

What Is New?

- In this population-based retrospective cohort study, we explored the association between long-term exposure to road traffic noise with cardiometabolic diseases, including diabetes mellitus and hypertension, in Toronto, Ontario, Canada.
- The results demonstrated that every 10-dBA increase of long-term exposure to road traffic noise was associated with an 8% increased risk of incident diabetes mellitus and a 2% increased risk of incident hypertension among individuals, aged 35 to 100 years, who resided in Toronto.
- We found independent associations for road traffic noise with diabetes mellitus and hypertension from air pollution (nitrogen dioxide and ultrafine particles).

What Are the Clinical Implications?

- As the burden of environmental risk factors and cardiometabolic diseases increases in North America, understanding such relationship can have important public health implications.
- Given these findings, long-term exposure to road traffic noise may be an important risk factor for cardiometabolic diseases.

even greater risk.[3,4] To mitigate the burden of cardiometabolic diseases and related complications, the identification of modifiable risk factors related to lifestyle and environment has emerged as an important public health priority. Previous accumulated evidence from mechanistic studies suggested an elevated risk of cardiometabolic disease associated with road traffic noise, which is a pervasive source of environmental stress.[5] Exposure to noise provokes a stress response and reduces sleep quality, which can activate the autonomic nervous and the endocrine systems, and increase levels of circulating stress hormones, blood pressure, heart rate, and glucose dysregulation.[6,7] These noise-induced pathophysiological changes may be contributing to the development of diabetes mellitus and hypertension.[8–11]

Despite the biological plausibility of persistent exposure to noise affecting cardiometabolic diseases, epidemiologic studies linking long-term effects of road traffic noise to diabetes mellitus and hypertension remain scarce, especially in North America. Most epidemiologic studies of road traffic noise were conducted in Europe, where architectural and urban design settings, such as the proximity between buildings and roads, often differ from conditions found in North America.[12] Few studies have examined the associations between past exposure to road traffic noise and the incidence of diabetes mellitus. In 1 Canadian and 2 European cohorts, road traffic noise was associated with increased incidence of diabetes mellitus.[13–15] In contrast, the effects of long-term exposure to road traffic noise on the incidence of hypertension were inconsistent in prior studies. The ESCAPE (European Study of Cohorts for Air Pollution Effects) reported a positive association with self-reported hypertension,[16] whereas other studies did not find evidence of an association.[17–19]

With the global shift toward urbanization, traffic-related noise pollution appears to be a widespread public health issue for cities, where residents may be exposed to levels exceeding the recommended World Health Organization guidelines.[12,20] Thus, we conducted a large population-based cohort study in Toronto, Canada, the fourth largest city in North America, to investigate whether past exposure to road traffic noise is associated with increased incidence of diabetes mellitus and hypertension.

Methods

The health administrative data used in this study are held securely in coded form at ICES. Data sharing agreements and privacy regulations in Ontario prohibit ICES from making the data publicly available, and access may be granted to those who meet prespecified criteria for confidential access (www.ices.on.ca/DAS).

Study Design and Participants

This study used the population-based, retrospective Ontario Population Health and Environment Cohort, described in detail previously.[21] Briefly, the Ontario Population Health and Environment Cohort comprises long-term residents of Ontario, aged ≥35 years on April 1, 1996, who were registered for provincial publicly funded health insurance. Those who were not born in Canada were excluded using the Immigration, Refugee and Citizenship Canada (IRCC) Permanent Resident Database. The health insurance program of Ontario provides universal access to both hospital and physician services. We created this cohort by linking health administrative and environmental databases using unique encoded identifiers at ICES.[21] The use of data in this study was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board.

We restricted our study population to individuals who were residents of Toronto for ≥5 years, were aged between 35 and 100 years, and were free from hypertension or diabetes mellitus at baseline (January 1, 2001). All individuals were followed up until the year of diabetes mellitus or hypertension diagnosis, death, relocation outside of Toronto, or the end of follow-up (December 31, 2015).

Assignment of Road Traffic Noise

Our estimates of traffic noise levels were obtained from a noise propagation model, described elsewhere.[22] Briefly, the noise model was developed using SoundPLAN noise modeling software (Backnang, Germany). In SoundPLAN, traffic noise emissions were estimated using the US Federal Highway Administration Traffic Noise Model (TNM2.5), which implements the attenuation standards for road surface reflectance and ground absorption.[22] This model has been used often in other North American cities, such as New York City.[23] Sound pressure propagation was modeled according to the International Organization for Standardization calculation method (9613-2), taking into account physical effects, such as vehicle type, geometrical spreading, and reflection from surfaces. International Organization for Standardization 9613-2 is a widely used technique in noise mapping to predict long-term average A-weighted sound pressure levels (dBA) with an accuracy of 3 dBA for distances up to 1 km.[24] Various geospatial inputs were prepared with ArcGIS 10.4 software (ESRI, Redlands, CA), including a digital elevation model from the Ontario Ministry of Natural Resources to evaluate topographic effects on road network elevation changes and associated impacts on noise emissions, building mass data to account for façade reflection of noise, and the center line network and associated traffic volume data based on a suite of past traffic counts from Toronto.[22]

The integrated model was validated with 193 noise measurements from a monitoring study completed between August and October 2016 throughout Toronto. The noise monitoring was conducted for a week using a Noise Sentry RT sound level meter data logger that was selected from a combination of population densities, land uses (ie, residential, open space, employment, and industrial/commercial), and sites of particular interest (eg, schools, long-term care facilities, and hospitals) because of concerns surrounding noise exposures.[22] The traffic noise model used in the current study explains 59% and 60% of variance for the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day ($L_{Aeq,24\ h}$) and the equivalent continuous A-weighted sound pressure level for the night (11 PM–7AM), respectively, in observed noise levels.[22]

Using the estimates derived from the traffic noise model, we assigned each subject a 3-year moving average of $L_{Aeq,24\ h}$ and $L_{Aeq,night}$ at his/her annual residential postal code for every year of follow-up. For instance, an individual's exposure in 2001 was estimated as the mean exposure over the years 1998 to 2000. This moving average approach accounted for the variability in exposures caused by residential mobility patterns.

Ascertainment of Outcomes

We identified incident cases of diabetes mellitus and hypertension using the Ontario Diabetes Dataset and the Ontario Hypertension Dataset, respectively. These data sets were created from health administrative databases and algorithms previously validated against patient's charts in Ontario, using the Ontario's physician fee codes and the *International Classification of Diseases, Ninth Revision* (*ICD-9*), and the *International Classification of Diseases, Tenth Revision* (*ICD-10*).[25–27] An incident case of diabetes mellitus was defined as an individual with 2 physician claims with a diabetes mellitus diagnostic code (*ICD-9* code 250 and *ICD-10* codes E10-E14), 1 physician claim with a diabetes mellitus–related fee code (Q040, K029, K030, K045, and K046), or 1 hospitalization with a diabetes mellitus diagnostic code within 2 years.[26] This validated algorithm has a high sensitivity (86%) and specificity (97%).[26] Similarly, we identified an incident case of hypertension based on ≥1 hospitalization with a hypertension diagnosis or one physician claim followed by another physician claim or hospitalization with a hypertension diagnosis within 2 years (*ICD-9* codes 401-405 and *ICD-10* codes I10-I15).[27] This validated algorithm has a sensitivity of 72% and a specificity of 95%.[27]

Covariates

We considered several covariates available from the administrative databases, including age at baseline and sex. We also included 4 time-varying neighborhood-level contextual variables, derived on the closest census years (ie, 1996, 2001, and 2006 Canadian censuses). At the census tract level (small and relatively homogeneous geographic units consisting of a population of 2500–8000), variables included the following: (1) proportion of residents aged ≥15 years with less than a high school education; (2) unemployment rate for residents aged ≥15 years; (3) proportion of recent immigrants; and (4) community-specific income quintile, which is based on household income (accounting for household size).[28] Furthermore, we selected several preexisting comorbidities, previously related to individual-level lifestyle and risk factors of cardiovascular outcomes,[29–33] including stroke, diabetes mellitus (in the analysis where hypertension was the outcome of interest), hypertension (in the analysis where diabetes mellitus was the outcome of interest), chronic obstructive pulmonary disease, asthma, and cancer (Table S1).

Given that long-term noise exposure shares many sources with ambient air pollution,[34] we also obtained estimates of ultrafine particles (UFPs; or particles with aerodynamic diameter of ≤0.1 μm) and nitrogen dioxide (NO_2), both of which were derived from land-use regression models for Toronto.[35,36] For residential exposure to UFPs, the land-use regression model was developed from mobile monitoring data in Toronto, conducted over 2 weeks in September 2010 and 1 week in March 2011.[35,37] Real-time ambient UFP levels at 1-

second resolution were monitored using 3 vehicles equipped with roof-top monitoring devices (TSI model 3007) and sampled on 405 road segments across Toronto.[37] Briefly, this UFP model was constructed using variables related to the distance to highways, major roadways, the central business district, the international airport, bus routes, as well as several land-use variables for park land, open space, on-street trees, and length of bus routes (R^2=0.67).[37] Similarly, we obtained mean annual estimates of NO_2 from a land-use regression model, constructed by combining NO_2 measurements with a range of predictors, including the lengths of expressways and major roads, industrial land use, density of dwellings, 24-hour traffic counts, and being downwind of an expressway (R^2=0.69).[36] The samples were collected over 2-week periods in September 2002 and May 2004 using duplicate 2-sided Ogawa passive diffusion samplers at 95 fixed-site monitors in Toronto.[36] These land-use regression models for UFP and NO_2 have been used in previous studies to examine the associations of traffic-related air pollution with chronic disease.[38–40] Similar to the noise exposures, we estimated UFP and NO_2 exposures using a 3-year moving window for each year of follow-up.

Statistical Analysis

We used spatial random-effects Cox proportional hazards models, with random effects represented by baseline neighborhoods in Toronto (a total of 140), to estimate the associations between $L_{Aeq,24\ h}$ or $L_{Aeq,night}$ and the incidence of diabetes mellitus and hypertension. Similar to previous studies, we considered neighborhood-level random effects to account for the spatial patterns of health where subjects in the same neighborhoods would be expected to be more similar than those in more distant neighborhoods.[39,40] We incrementally adjusted our models for a series of covariates. First, we stratified by age and sex to account for the possible differences in health status in the baseline characteristics of the individuals. We then added 4 time-varying neighborhood-level contextual variables. The latter model was considered as the fully adjusted main model. In addition to considering noise estimates as a continuous variable, we also modeled noise estimates as categorical variables in 5-dBA increments. Similar to previous studies,[41–44] we considered ≤55 dBA for $L_{Aeq,24\ h}$ and ≤45 dBA for $L_{Aeq,night}$ as the reference category based on the World Health Organization guidelines for road traffic noise (53 dBA day-evening-night noise level over a whole day with a penalty of 10 dBA for night-time noise and 5 dBA for evening noise and 45 dBA for $L_{Aeq,night}$) and the Ontario Ministry of Environment and Climate Change recommendations (55 dB for daytime and 50 dB for nighttime).[45,46] In addition, we also considered quantiles of long-term exposure to road traffic noise.

Several sensitivity analyses were conducted by further adjusting for additional covariates to the fully adjusted main model. First, we additionally adjusted for traffic-related air pollutants, UFPs, and NO_2. Second, we further adjusted for selected preexisting comorbidities. Third, we indirectly adjusted for the potential influence of 2 unavailable behavioral-level risk factors (smoking and obesity). Briefly, we used a previously validated method to mathematically adjust the hazard ratios (HRs) for smoking and obesity while simultaneously controlling for the variables that were included in our models (eg, area-level socioeconomic status variables).[47] The details of this method have been reported previously,[47] and the method has been implemented in previous Ontario Population Health and Environment Cohort studies[48,49] and other cohorts.[50,51]. This method requires spatial associations between observed and unobserved variables (ie, smoking and obesity) from an auxiliary data set. To do this, we used data from the 2001, 2003, 2005 and 2007 cycles of the Canadian Community Health Survey.[47,52] We also obtained the associations between the 2 risk factors and outcomes using the survey cohorts (Table S2). Last, we repeated the analyses by considering 2- and 5-year moving averages of noise exposure estimates.

We conducted subgroup analyses to investigate potential effect modification between $L_{Aeq,24\ h}$ and cardiometabolic disorders by age (<60, 60–74, and ≥75 years), sex, income quintile, and preexisting comorbidities (hypertension or diabetes mellitus, depending on the outcome). In addition, we conducted a subgroup analysis to estimate the association between long-term exposure to road traffic noise and incidence of diabetes mellitus and hypertension among individuals with hearing loss (Table S3). We also examined the potential effect modification by quintiles of UFPs and NO_2. Given the high correlation between 2 exposure metrics for road traffic noise, we only reported the findings from $L_{Aeq,24\ h}$.

We present the HRs from categorical predictors and linear associations, which were expressed per interquartile range (IQR) increase (ie, HR_{IQR}) and 95% CIs for $L_{Aeq,24\ h}$ and $L_{Aeq,night}$ to facilitate comparisons among the different exposure metrics in this study.

Results

Baseline Characteristics

Of the 914 607 subjects in the diabetes mellitus cohort, 53.7% were women, and the mean age at baseline was 55.3 years, whereas of the 701 174 subjects in the hypertension cohort, 52.0% were women, and the mean age at baseline was 51.9 years (Table 1). During the 15-year follow-up, we identified 159 442 incident cases of diabetes mellitus (17.4% of the

Table 1. Baseline Characteristics of the Study Cohorts by Outcome in Toronto, Canada, in 2001

Characteristic	Diabetes Mellitus Cohort (n=914 607)	Hypertension Cohort (n=701 174)
Incident cases during follow-up, n (%)	159 442 (17.4)	262 488 (37.4)
Individual-level risk factors		
Age, mean (SD), y	55.3 (14.4)	51.9 (13.0)
Sex, n (%)		
Men	423 463 (46.3)	336 564 (48.0)
Women	491 144 (53.7)	364 610 (52.0)
Comorbid conditions, n (%)		
Hypertension	254 261 (27.8)	. . .
Diabetes mellitus	. . .	40 668 (5.8)
Stroke	12 804 (1.4)	3506 (0.5)
Chronic obstructive pulmonary disease	82 315 (9.0)	50 485 (7.2)
Asthma	25 609 (2.8)	17 529 (2.5)
Cancer	51 218 (5.6)	29 449 (4.2)
Area-level risk factors*		
Less than high school education, %	24.5	24.2
Unemployment, %	6.7	6.7
Recent immigrants, %	9.8	9.8
Average household income, 1000 CAD	63.9	63.3

CAD indicates Canadian dollars.
*Area-level risk factors are derived from Canadian censuses at the census-tract level. Information on unemployment and less than high school education was derived for individuals who are aged ≥15 years.

diabetes mellitus cohort) and 262 488 incident cases of hypertension (37.4% of the hypertension cohort) (Table S4).

At baseline, the mean levels of the 3-year moving averages of $L_{Aeq,24\ h}$ and $L_{Aeq,night}$ were ≈56 and ≈50 dBA, respectively, for both diabetes mellitus and hypertension cohorts (Table S5). The IQRs for both $L_{Aeq,24\ h}$ and $L_{Aeq,night}$ in the diabetes mellitus and hypertension cohorts were 10.0 dBA. The mean exposure to NO_2 at baseline was ≈29.3 parts per billion for both cohorts, whereas the mean exposure to UFPs was 28 200 and 28 430 counts/cm^3 for diabetes mellitus and hypertension cohorts, respectively. We found moderate correlations between models of road traffic noise and air pollution exposures (r=0.19–0.35, depending on the pollutant) (Table S6).

Association Between Noise Exposure and Outcomes

In linear analysis, we found that exposure to $L_{Aeq,24\ h}$ was associated with an increased incidence of both diabetes mellitus (HR_{IQR}=1.08; 95% CI, 1.08–1.09) and hypertension (HR_{IQR}=1.02; 95% CI, 1.02–1.03) (Table 2). Similar HR_{IQR} values were observed with $L_{Aeq,night}$ (HR_{IQR}=1.08 for diabetes mellitus, and HR_{IQR}=1.02 for hypertension) (Table 2). The associations between exposures to $L_{Aeq,24\ h}$ and $L_{Aeq,night}$ and incident diabetes mellitus were not sensitive to additional adjustments for comorbidities and traffic-related air pollution (HR_{IQR}=1.07; 95% CI, 1.06–1.08). Similarly, we found positive associations (HR_{IQR}=1.02) between hypertension and $L_{Aeq,24\ h}$ and $L_{Aeq,night}$, after adjusting for comorbidities and UFPs and NO_2. Furthermore, indirectly adjusting for smoking and obesity had little influence on the estimated HRs for both incident diabetes mellitus and hypertension (Table 2).

In the fully adjusted model using categorical predictors, we found that individuals exposed to higher levels of $L_{Aeq,24\ h}$ generally had stronger associations with incident diabetes mellitus than those in low levels (ie, HR=1.08 for 55–60 dBA, HR=1.07 for 60–65 dBA, and HR=1.12 for >65 dBA compared with those with exposures below the guideline level of ≤55 dBA) (Table 2). Similarly, higher levels of $L_{Aeq,night}$ were associated with increased incidence of diabetes mellitus (ie, HR=1.06 for 45–50 dBA, HR=1.12 for 50–55 dBA, and HR=1.15 for >55 dBA compared with the reference at ≤45 dBA). There was an increasing dose-response relationship between road traffic noise and diabetes mellitus when we

Table 2. HRs and 95% CIs for the Associations Between Long-Term Exposure to Road Traffic Noise and Incidence of Diabetes Mellitus and Hypertension

Exposure	Model*	HR (95% CI)	
		Diabetes Mellitus	Hypertension
$L_{Aeq,24\ h}$	Stratified by age and sex	1.08 (1.08–1.09)	1.02 (1.02–1.03)
	+ Neighborhood-level SES†	1.08 (1.07–1.08)	1.02 (1.01–1.03)
	Additional adjustments‡		
	+ UFPs and NO_2	1.07 (1.06–1.08)	1.02 (1.01–1.03)
	+ Comorbidities§	1.07 (1.06–1.08)	1.02 (1.01–1.02)
	+ Smoking and BMI	1.07 (1.04–1.11)	1.01 (1.00–1.03)
	Time windows of exposure		
	2-y Moving average	1.08 (1.07–1.09)	1.02 (1.02–1.03)
	5-y Moving average	1.07 (1.06–1.08)	1.02 (1.01–1.02)
$L_{Aeq,night}$	Stratified by age and sex	1.08 (1.08–1.09)	1.02 (1.02–1.03)
	+ Neighborhood-level SES†	1.08 (1.07–1.09)	1.02 (1.01–1.03)
	Additional adjustments‡		
	+ UFPs and NO_2	1.07 (1.06–1.08)	1.02 (1.01–1.03)
	+ Comorbidities§	1.07 (1.06–1.08)	1.02 (1.01–1.02)
	+ Smoking and BMI	1.07 (1.04–1.11)	1.01 (1.00–1.03)
	Time windows of exposure		
	2-y Moving average	1.08 (1.07–1.09)	1.02 (1.01–1.02)
	5-y Moving average	1.07 (1.06–1.08)	1.01 (1.00–1.03)

HRs and 95% CIs are for an interquartile range increase in noise exposures (10 dB). BMI indicates body mass index; HR, hazard ratio; $L_{Aeq,24\ h}$, the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day; $L_{Aeq,night}$, the equivalent continuous A-weighted sound pressure level for the night (11 PM–7AM); NO_2, nitrogen dioxide; SES, socioeconomic status; UFP, ultrafine particle.

*Mixed-effect Cox proportional hazards models with neighborhoods (n=140) at baseline as the random effects.

†Fully adjusted model, adjusting for age, sex, and 4 SES variables derived from Canadian censuses at the census-tract area level: proportions of residents (aged ≥15 years) who were unemployed, proportions of residents (aged ≥15 years) who had not completed high school, proportions of residents who were recent immigrants, and community-specific income quintile.

‡Sensitivity analyses using the fully adjusted model above and additionally adjusting for the listed covariates.

§Comorbidities include stroke, chronic obstructive pulmonary disease, asthma, and cancer. For diabetes mellitus, we also adjusted for hypertension; for hypertension, we also adjusted for diabetes mellitus.

considered noise as a categorical variable and in quantiles (Table 3 and Table S7, respectively). With the hypertension cohort, evidence for a heightened risk of hypertension in association with noise levels exceeding the Ontario Ministry of Environment and Climate Change guidelines for noise (55 dB for 24 hours and 50 dB for nighttime) (eg, $L_{Aeq,24\ h}$: HR=1.04; and $L_{Aeq,night}$: HR=1.05) remained, but the linear trend of the dose-response relationship was less clear. We found a similar pattern of associations with quartiles of $L_{Aeq,24\ h}$ and $L_{Aeq,night}$ and incident diabetes mellitus and hypertension (Table S7). With incident diabetes mellitus, we found increasingly stronger associations in higher quartiles of $L_{Aeq,24\ h}$ and $L_{Aeq,night}$, whereas with incident hypertension, we found a supralinear relationship where the degree of change in association from the lowest quartile was generally consistent between higher quartiles. For example, in the fully adjusted model, individuals in the lowest quartile of $L_{Aeq,24\ h}$ were associated HRs of 1.06 (95% CI, 1.03–1.10), 1.07 (95% CI, 1.04–1.11), and 1.05 (95% CI, 1.01–1.10) in individuals in the second, third, and fourth quartiles, respectively.

In the subgroup analysis of incident diabetes mellitus and $L_{Aeq,24\ h}$ by sex (Figure 1 and Table S8), women exhibited a higher risk of developing diabetes mellitus in association with $L_{Aeq,24\ h}$ (HR_{IQR}=1.10; 95% CI, 1.09–1.11) than men (HR_{IQR}=1.06; 95% CI, 1.04–1.07) ($P_{interaction}$<0.001). We also found that the associations of $L_{Aeq,24\ h}$ with diabetes mellitus varied by age, with younger individuals exhibiting a stronger association than older adults (aged <60 years: HR_{IQR}=1.10 [95% CI, 1.09–1.11] versus aged ≥75 years: HR_{IQR}=1.06 [95% CI, 1.04–1.08]; $P_{interaction}$<0.001). For hypertension, we observed similar patterns in subgroup analysis by sex and age (Figure 2). Individuals with higher household income exhibited a higher risk of diabetes mellitus (eg, HR_{IQR}=1.11 [95% CI, 1.09–1.13] in the highest income quintile versus HR_{IQR}=1.03 [95% CI, 1.02–1.05] in the lowest income quintile) and hypertension (eg, HR_{IQR}=1.03 [95% CI, 1.02–1.05] in the

Table 3. HRs and 95% CIs for the Associations of Incident Hypertension and Diabetes Mellitus With Long-Term Exposure to Road Traffic Noise Using Exposure Categories

Exposure	Model*	HR (95% CI)	
		Diabetes Mellitus	Hypertension
$L_{Aeq,24\ h}$, dBA	≤55 (Reference)	1.00	1.00
	55–60	1.08 (1.06–1.09)	1.04 (1.03–1.06)
	60–65	1.07 (1.01–1.13)	1.03 (1.02–1.04)
	>65	1.12 (1.10–1.13)	1.02 (1.01–1.03)
$L_{Aeq,night}$, dBA	≤45 (Reference)	1.00	1.00
	45–50	1.06 (1.04–1.07)	1.05 (1.04–1.06)
	50–55	1.12 (1.10–1.14)	1.08 (1.06–1.09)
	>55	1.15 (1.14–1.17)	1.05 (1.03–1.06)

HR indicates hazard ratio; $L_{Aeq,24\ h}$, the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day; $L_{Aeq,night}$, the equivalent continuous A-weighted sound pressure level for the night (11 PM–7 AM).
*Mixed-effect Cox proportional hazards models with neighborhoods (n=140) at baseline as the random effects, using the fully adjusted models, stratified by age and sex, and adjusted for 4 socioeconomic variables derived from Canadian census at the dissemination-area level: proportions of residents aged ≥15 years who had not completed high school, proportions of residents who were recent immigrants, unemployment rate for residents aged ≥15 years, and community-specific income quintile.

highest income quintile versus HR_{IQR}=1.00 [95% CI, 0.99–1.01] in the lowest income quintile) in association with $L_{Aeq,24\ h}$. There were indications of a stronger association with $L_{Aeq,24\ h}$ among individuals living in areas with low levels of traffic-related air pollution (eg, for diabetes mellitus, HR_{IQR}=1.10 [95% CI, 1.08–1.12] in the lowest UFP quintile versus HR_{IQR}=1.04 [95% CI, 1.02–1.06] in the highest UFP quintile). Similarly, we found stronger associations for diabetes mellitus in the lowest NO_2 quintile (HR_{IQR}=1.12; 95% CI, 1.10–1.14) compared with the highest NO_2 quintile (HR_{IQR}=1.02; 95% CI, 1.01–1.04). We observed a similar pattern of associations, albeit smaller in magnitude, for hypertension in subgroups of traffic-related air pollution levels.

Discussion

In this large population-based cohort study, we found that increased exposures to road traffic noise was associated with higher incidence of both diabetes mellitus and hypertension in Toronto, the fourth largest city in North America. These associations were robust in various sensitivity analyses, including adjustment for UFPs and NO_2, thus suggesting the effect of traffic noise on the development of these 2 conditions is independent of traffic-related air pollution. The association with diabetes mellitus tended to be stronger among women, younger individuals, people living in higher-income neighborhoods, and those who had preexisting hypertension. We found that the associations also varied by levels of UFPs and NO_2 for both diabetes mellitus and hypertension. A similar pattern was observed in the association of hypertension with road traffic noise.

To date, only a handful of studies have examined the association between long-term exposure to traffic-related noise and diabetes mellitus. The estimated associations across those previous studies are broadly consistent with our findings. A recent cohort study conducted in British Columbia, Canada, reported a positive association between residential transportation noise and diabetes mellitus (odds ratio=1.08; 95% CI, 1.05–1.10 per IQR increase of 6.8 dB).[15] A Danish cohort study reported that a 10-dB increase in residential exposure to traffic noise was associated with an 8% (95% CI, 1.02–1.14) higher risk of incident diabetes mellitus, and the association remained positive even after adjusting for residential nitrogen oxides.[14] However, Eze et al did not find a statistically significant association between diabetes mellitus incidence and per 10-dB increase in traffic noise (relative risk, 1.17; 95% CI, 0.88–1.53).[13]

On the other hand, several studies linking long-term exposure to noise and incidence of hypertension were conducted in Europe, with inconsistent findings. Some of these studies indicated weak or insignificant associations between traffic noise, blood pressure, and hypertension.[17,53–55] Similar to our findings of a positive association when further controlling for NO_2 and UPFs, 3 European studies also reported positive associations between traffic noise and hypertension, which were robust to adjustment for NO_2.[17,55,56] In the ESCAPE, traffic noise was associated with self-reported hypertension incidence, but these associations were attenuated after adjustment for particulate matter with an aerodynamic diameter of <2.5 $\mu g/m^3$.[16] The inconsistencies in these findings may be attributed to the adjustments of different pollutants, differences in local characteristics, such as the architectural and urban designs between Europe and North America, and characteristics of the traffic noise sources.[57]

When considering possible effect modification by the levels of traffic-related air pollution, we found that the associations between road traffic noise and cardiometabolic disorders tended to be stronger among individuals living in areas with lower concentrations of UFPs and NO_2. Similar to our findings, the Danish cohort study reported that individuals living in areas with lower levels of nitrogen oxides tended to exhibit a stronger association between noise and incident diabetes mellitus.[14] For example, individuals with residential exposure to nitrogen oxides of <14.1 $\mu g/m^3$ were at an 11% increased risk (95% CI, 0.97–1.26) compared with the 2% increased risk (95% CI, 0.91–1.14) for those with nitrogen oxides exposure of >25.1 $\mu g/m^3$.[14] These results may be explained partly by the fact that the average levels of road traffic noise were

higher in areas with high levels of air pollution, and the synergistic interaction between the environmental factors could make individuals more desensitized to a noise-induced stress response and less susceptible to the adverse impact of noise exposure. However, given the small variability in the mean levels of exposure to noise when stratified by the quintile levels of air pollution, further studies are needed to investigate the potential interaction between noise and air pollution exposures.

In addition, among the selected subgroups we considered, individuals who were younger (aged <60 years) were at an increased risk of diabetes mellitus and hypertension from exposure to road traffic noise. The differences could be caused by age-related hearing loss, as typically it is more difficult for relatively older individuals to detect noise, and the varying degrees of stress people of different age groups experience from noise.[58] In addition, our observation that noise exposure was more strongly associated with cardiometabolic disease among individuals who are women and younger, separately, suggests that menopause might play a modifying role. Some epidemiologic studies have shown that age-related hearing decline begins around the age of 50 to 60 years in women,[59,60] which coincides with the menopausal transition in most women. These studies implicated a biological plausibility that menopause might be linked to auditory deterioration and consequent reduced sensitivity to the adverse effects of noise through the proposed mechanisms by which noise induces stress related to annoyance and sleep disturbance. It is also possible that the difference in association by age and sex in our study might be explained by the depletion of susceptible individuals in the older age groups in the closed cohort design or other physiological reasons, including the reduced responsiveness to autonomic nervous system stimuli, which occurs among older individuals, different genetic signatures, which could correlate with different life span lengths, and ages of onset of major age-related diseases, such as cardiovascular disease.[61–63] Furthermore, we found an increased risk of cardiometabolic disorders from road traffic noise exposures for individuals with a higher income. A possible explanation for the stronger association among higher-income populations is that such individuals tend to be in better health and have lower levels of basic needs, such that they might be more susceptible to a noise-induced stress response.[64,65] However, given that

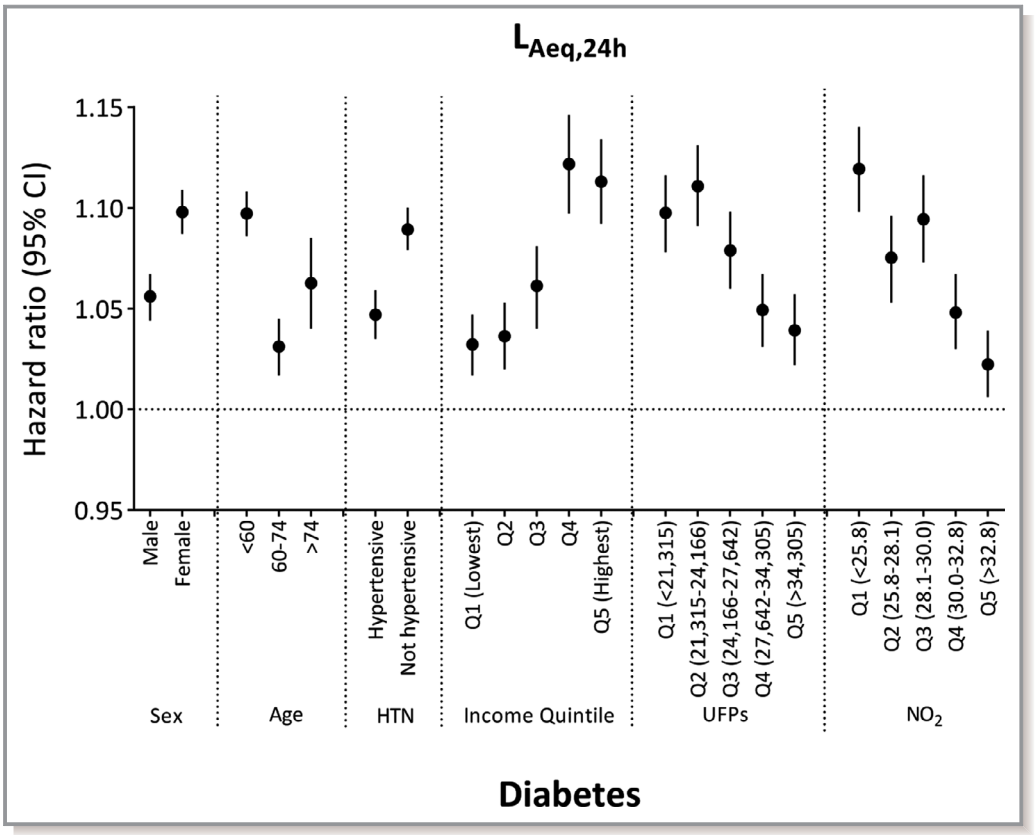

Figure 1. Subgroup analysis for incident diabetes mellitus with long-term exposure to road traffic noise by selected individual- and area-level characteristics. HTN indicates hypertension; $L_{Aeq,24\ h}$, the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day; NO_2, nitrogen dioxide (parts per billion); Q, quintile; UFP, ultrafine particle (counts/cm^3).

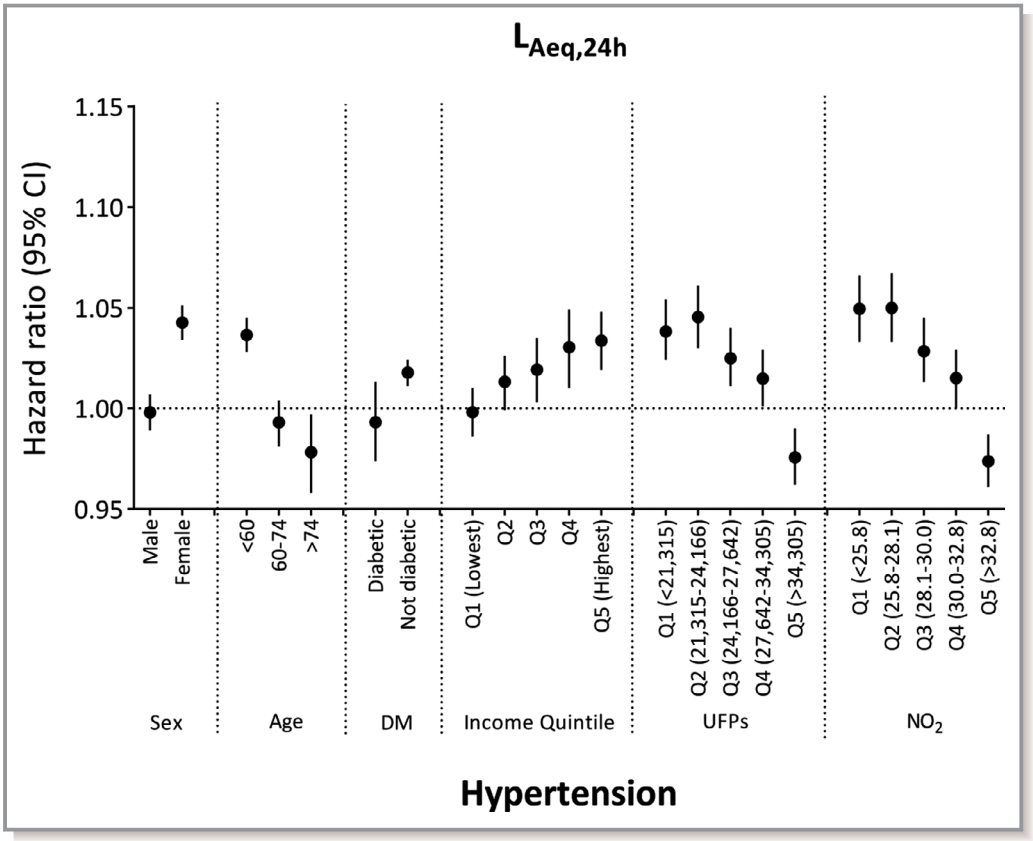

Figure 2. Subgroup analysis for incident hypertension with long-term exposure to road traffic noise stratified by selected individual- and area-level characteristics and levels of ultrafine particles (UFPs; counts/cm^3) and nitrogen dioxide (NO_2; parts per billion). DM indicates diabetes mellitus; $L_{Aeq,24\ h}$, the equivalent continuous A-weighted sound pressure level (dBA) for the 24-hour day; Q, quintile.

environmental risks may be jointly and independently associated with adverse cardiometabolic effects, further exploration of exposures to road traffic noise and the social gradient in cardiometabolic health is needed to better understand the unequal health effects between socioeconomic groups.

The association of road traffic noise with incidence of diabetes mellitus and hypertension is in line with existing experimental evidence demonstrating the adverse cardiometabolic effects of noise. The proposed mechanisms suggest that traffic noise may lead to the development of diabetes mellitus and hypertension through multiple stress responses.[5] Noise may induce a typical stress response, with the activation of the sympathetic autonomic nervous system, followed by increased blood pressure, heart rate, and vasoconstriction.[66] Also, stress responses to long-term activation of the hypothalamic-pituitary-adrenal axis may result in metabolic impairment, insulin resistance, and increased levels of stress hormones, including cortisol.[6,7] Moreover, exposure to noise during the night has been associated with sleep disturbances, which might affect metabolic, endocrine, and immune functions, as sleep is known to have a strong regulatory influence on the immune system.[6,7] Disturbances in sleep have also been associated with inflammation, endothelial dysfunctions, and oxidative stress, all of which contribute to an increased risk of cardiometabolic disease.[8–11] In addition to such possible mechanisms through which long-term exposure to noise can affect the cardiometabolic system on the basis of repeated exacerbations of cardiometabolic risk factors potentially leading to long-term progression of cardiometabolic disease, growing evidence has noted associations between short-term exposures to noise and acute physiological changes, including increases in blood pressure, heart rate, cardiac output, and blood lipids.[67] Thus, further research to explicate the differences between short-term and long-term effects of road traffic noise on cardiometabolic events is warranted, which will further elucidate the pathological mechanism of cardiometabolic disease.

Some limitations of our study merit mention. Because of data limitations, the precise impact of the soundscape and the temporal variability of traffic data, particularly the annual average daily traffic data, could not be characterized. As a result, the levels of noise exposures during the 15-year follow-up were highly correlated and attributed to residential mobility

patterns, which may have contributed to exposure misclassification. However, noise propagation models have been developed to provide increasingly accurate and reliable predictions of long-term noise estimates, and such misclassification represents nondifferential error across our study population, biasing the risk estimates toward the null. We also lacked information on individual characteristics, such as hearing ability, time spent at home, sleep quantity and quality, bedroom location, and occupational and indoor exposures. Given that our area-based exposure assessment was likely subject to nondifferential misclassification, this could have attenuated our associations. In addition, by using health administrative databases, we were only able to obtain physician-diagnosed incident cases of diabetes mellitus and hypertension. Similarly, we were only able to identify physician-diagnosed cases of hearing loss in our sensitivity analysis, and thus were unable to account for the potential influence of subclinical hearing loss on the associations of noise and diabetes mellitus and hypertension. However, both measurement errors are expected to be independent of exposure to noise, which may have led to an underestimation of the associations. In addition, given that age is upstream of hearing loss and has minimal measurement misclassification, our analytical approach in which we stratified our Cox proportional hazards models by age at baseline may have reduced the potential influence of hearing loss (if any) on the associations between road traffic noise exposure and incidence of diabetes mellitus and hypertension. More important, we lacked information on individual-level lifestyle and behavioral risk factors related to cardiometabolic disease, such as smoking and obesity. To address the concern of residual confounding, we conducted various sensitivity analyses by further adjusting for selected comorbidities that are likely to be associated with behavioral factors, as well as by indirectly adjusting for body mass index and smoking. We found that our associations remained generally consistent. Despite these efforts, we were unable to completely rule out the possibility of residual confounding by unmeasured individual-level confounders.

This study has notable strengths. To our knowledge, this is the largest epidemiological study to date in North America that examined the long-term impact of exposure to road traffic noise on incidence of diabetes mellitus and hypertension. Given universal access to health care in Canada, the potential for selection bias was minimized. In addition, we adjusted for traffic-related air pollution, including NO_2, and for the first time UFPs, which were moderately correlated with traffic noise. We found that exposure to traffic noise was significantly associated with an increased risk for diabetes mellitus and hypertension, despite adjustment for these 2 air pollutants, suggesting an independent effect of traffic noise on these outcomes. Furthermore, we used random-effects Cox models with a frailty term for 140 neighborhoods in Toronto, which allowed us to control for unmeasured factors affecting health that are common to subjects within a spatial cluster but may vary between adjacent clusters, including immigration, ethnic composition, opportunities for physical activity, and access to healthy and unhealthy food.

Conclusions

Exposure to traffic noise was associated with increased incidence of hypertension and diabetes mellitus in Toronto, Canada.

Sources of Funding

This study was supported by the Canadian Institutes of Health Research (CIHR; MOP-133463). This study was also supported by Public Health Ontario (PHO) and ICES, which are funded by annual grants from the Ontario Ministry of Health and Long-Term Care (MOHLTC). Parts of this material are based on data and information compiled and provided by the Canadian Institute for Health Information (CIHI). However, the analyses, conclusions, opinions, and statements expressed herein are not necessarily those of CIHI, PHO, ICES, and MOHLTC. Parts of this report are based on Ontario Registrar General information on deaths, the original source of which is ServiceOntario. The views expressed therein are those of the author and do not necessarily reflect those of the Ontario Office of the Registrar General (ORG) or Ministry of Government Services. We would like to thank Toronto Public Health and the city of Toronto for financial support toward development and validation of environmental noise data. Jeff Kwong is supported by a Clinician Scientist Award from the Department of Family and Community Medicine, University of Toronto.

Disclosures

None.

References

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365:217–223.
2. World Health Organization. Global Report on Diabetes 1. Diabetes Mellitus - Epidemiology. 2016;21–33.
3. American Diabetes Association. 8: Cardiovascular disease and risk management. *Diabetes Care*. 2016;39(Suppl. 1):S60–S71.
4. Hu G, Sarti C, Jousilahti P, Peltonen M, Qiao Q, Antikainen R, Tuomilehto J. The impact of history of hypertension and type 2 diabetes at baseline on the incidence of stroke and stroke mortality. *Stroke*. 2005;36:2538–2543.
5. World Health Organization (WHO). Burden of disease from environmental noise: Quantification of healthy life years lost in Europe. *World Health*. 2011; 1–105.

6. Recio A, Linares C, Banegas JR, Díaz J. Road traffic noise effects on cardiovascular, respiratory, and metabolic health: an integrative model of biological mechanisms. *Environ Res*. 2016;146:359–370.
7. Münzel T, Sørensen M, Gori T, Schmidt FP, Rao X, Brook FR, Chen LC, Brook RD, Rajagopalan S. Environmental stressors and cardio-metabolic disease: part II-mechanistic insights. *Eur Heart J*. 2017;38:557–564.
8. Foraster M, Eze IC, Schaffner E, Vienneau D, Héritier H, Endes S, Rudzik F, Thiesse L, Pieren R, Schindler C, Schmidt-Trucksäss A, Brink M, Cajochen C, Wunderli JM, Röösli M, Probst-Hensch N. Exposure to road, railway, and aircraft noise and arterial stiffness in the SAPALDIA study: annual average noise levels and temporal noise characteristics. *Environ Health Perspect*. 2017;125:097004.
9. Basner M, Müller U, Elmenhorst E-M. Single and combined effects of air, road, and rail traffic noise on sleep and recuperation. *Sleep*. 2011;34:11–23.
10. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. *Diabetes Care*. 2010;33:414–420.
11. Schmidt FP, Basner M, Kröger G, Weck S, Schnorbus B, Muttray A, Sariyar M, Binder H, Gori T, Warnholtz A, Münzel T. Effect of nighttime aircraft noise exposure on endothelial function and stress hormone release in healthy adults. *Eur Heart J*. 2013;34:3508–3514a.
12. van Kempen E, Casas M, Pershagen G, Foraster M. WHO environmental noise guidelines for the European region: a systematic review on environmental noise and cardiovascular and metabolic effects: a summary. *Int J Environ Res Public Health*. 2018;15:379.
13. Eze IC, Foraster M, Schaffner E, Vienneau D, Héritier H, Rudzik F, Thiesse L, Pieren R, Imboden M, von Eckardstein A, Schindler C, Brink M, Cajochen C, Wunderli JM, Röösli M, Probst-Hensch N. Long-term exposure to transportation noise and air pollution in relation to incident diabetes in the SAPALDIA study. *Int J Epidemiol*. 2017;46:1115–1125.
14. Sørensen M, Andersen ZJ, Nordsborg RB, Becker T, TjØnneland A, Overvad K, Raaschou-Nielsen O. Long-term exposure to road traffic noise and incident diabetes: a cohort study. *Environ Health Perspect*. 2013;121:217–222.
15. Clark C, Sbihi H, Tamburic L, Brauer M, Frank LD, Davies HW. Association of long-term exposure to transportation noise and traffic-related air pollution with the incidence of diabetes: a prospective cohort study. *Environ Health Perspect*. 2017;125:087025.
16. Fuks KB, Weinmayr G, Basagaña X, Gruzieva O, Hampel R, Oftedal B, Sørensen M, Wolf K, Aamodt G, Aasvang GM, Aguilera I, Becker T, Beelen R, Brunekreef B, Caracciolo B, Cyrys J, Elosua R, Eriksen KT, Foraster M, Fratiglioni L, Hilding A, Houthuijs D, Korek M, Künzli N, Marrugat J, Nieuwenhuijsen M, Östenson CG, Penell J, Pershagen G, Raaschou-Nielsen O, Swart WJR, Peters A, Hoffmann B. Long-term exposure to ambient air pollution and traffic noise and incident hypertension in seven cohorts of the European study of cohorts for air pollution effects (ESCAPE). *Eur Heart J*. 2017;38:983–990.
17. Sørensen M, Hvidberg M, Hoffmann B, Andersen ZJ, Nordsborg RB, Lillelund KG, Jakobsen J, Tjønneland 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 Heal A Glob Access Sci Source*. 2011;10:92.
18. Zeeb H, Hegewald J, Schubert M, Wagner M, Dröge P, Swart E, Seidler A. Traffic noise and hypertension: results from a large case-control study. *Environ Res*. 2017;157:110–117.
19. Carey IM, Anderson HR, Atkinson RW, Beevers S, Cook DG, Dajnak D, Gulliver J, Kelly FJ. Traffic pollution and the incidence of cardiorespiratory outcomes in an adult cohort in London. *Occup Environ Med*. 2016;73:849–856.
20. Drudge C, Johnson J, MacIntyre E, Li Y, Copes R, Ing S, Johnson S, Varughese S, Chen H. Exploring nighttime road traffic noise: a comprehensive predictive surface for Toronto, Canada. *J Occup Environ Hyg*. 2018;15:389–398.
21. Chen H, Kwong JC, Copes R, Villeneuve PJ, Goldberg MS, Weichenthal S, Van Donkelaar A, Jerrett M, Martin RV, Brook JR, Kopp A, Burnett RT. Cohort profile: the ONtario Population Health and Environment Cohort (ONPHEC). *Int J Epidemiol*. 2017;46:405–405j.
22. Oiamo T, Davies H, Rainham D, Rinner C, Drew K, Sabaliauskas K, Macfarlane R. A combined emission and receptor-based approach to modelling environmental noise in urban environments. *Environ Pollut*. 2018;242:1387–1394.
23. Lee EY, Jerrett M, Ross Z, Coogan PF, Seto EYW. Assessment of traffic-related noise in three cities in the United States. *Environ Res*. 2014;132:182–189.
24. 9613-2 ISO. Acoustics: Attenuation of Sound During Propagation Outdoors—Part 2. Geneva, Switzerland: International Organisation for Standardisation; 1996.
25. Hinds A, Lix LM, Smith M, Quan H, Sanmartin C. Quality of administrative health databases in Canada: a scoping review. *Can J Public Health*. 2016;107:e56–e61.
26. Lipscombe LL, Hux JE. Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995–2005: a population-based study. *Lancet*. 2007;369:750–756.
27. Tu K, Campbell NR, Chen Z-L, Cauch-Dudek KJ, McAlister FA. Accuracy of administrative databases in identifying patients with hypertension. *Open Med*. 2007;1:e18–e26.
28. Statistics Canada. User guide for the survey of household spending. 2011. Available at: http://www.statcan.gc.ca/pub/62f0026m/2013001/part-partie1-eng.htm. Accessed January 8, 2018.
29. Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, Rinfret S, Schiffrin EL, Eisenberg MJ. The metabolic syndrome and cardiovascular risk: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2010;56:1113–1132.
30. Shah AD, Langenberg C, Rapsomaniki E, Denaxas S, Pujades-Rodriguez M, Gale CP, Deanfield J, Smeeth L, Timmis A, Hemingway H. Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1·9 million people. *Lancet Diabetes Endocrinol*. 2015;3:105–113.
31. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. *Arch Intern Med*. 2001;161:996–1002.
32. Sidney S, Sorel M, Quesenberry CP, DeLuise C, Lanes S, Eisner MD. COPD and incident cardiovascular disease hospitalizations and mortality: Kaiser Permanente Medical Care Program. *Chest*. 2005;128:2068–2075.
33. Iribarren C, Tolstykh IV, Miller MK, Sobel E, Eisner MD. Adult asthma and risk of coronary heart disease, cerebrovascular disease, and heart failure: a prospective study of 2 matched cohorts. *Am J Epidemiol*. 2012;176:1014–1024.
34. Davies HW, Vlaanderen JJ, Henderson SB, Brauer M. Correlation between co-exposures to noise and air pollution from traffic sources. *Occup Environ Med*. 2009;66:347–350.
35. Weichenthal S, Van Ryswyk K, Goldstein A, Shekarrizfard M, Hatzopoulou M. Characterizing the spatial distribution of ambient ultrafine particles in Toronto, Canada: a land use regression model. *Environ Pollut*. 2016;208:241–248.
36. Jerrett M, Arain MA, Kanaroglou P, Beckerman B, Crouse D, Gilbert NL, Brook JR, Finkelstein N, Finkelstein MM. Modeling the intraurban variability of ambient traffic pollution in Toronto, Canada. *J Toxicol Environ Health A*. 2007;70:200–212.
37. Weichenthal S, Van Ryswyk K, Kulka R, Sun L, Wallace L, Joseph L. In-vehicle exposures to particulate air pollution in Canadian metropolitan areas: the urban transportation exposure study. *Environ Sci Technol*. 2015;49:597–605.
38. Bai L, Weichenthal S, Kwong J, Burnett R, Hatzopoulou M, Jerrett M, van Donkelaar A, Martin R, Van Ryswyk K, Lu H, Kopp A, Chen H. Associations of long-term exposure to ultrafine particles and nitrogen dioxide with increased incidence of congestive heart failure and acute myocardial infarction. *Am J Epidemiol*. 2019;188:151–159.
39. Bai L, Chen H, Hatzopoulou M, Jerrett M, Kwong JC, Burnett RT, van Donkelaar A, Copes R, Martin RV, van Ryswyk K, Lu H, Kopp A, Weichenthal S. Exposure to ambient ultrafine particles and nitrogen dioxide and incident hypertension and diabetes. *Epidemiology*. 2018;29:323–332.
40. Weichenthal S, Bai L, Hatzopoulou M, Van Ryswyk K, Kwong JC, Jerrett M, Van Donkelaar A, Martin R V., Burnett RT, Lu H, Chen H. Long-term exposure to ambient ultrafine particles and respiratory disease incidence in in Toronto, Canada: a cohort study. *Environ Health*. 2017;16:64.
41. Vienneau D, Schindler C, Perez L, Probst-Hensch N, Röösli M. The relationship between transportation noise exposure and ischemic heart disease: a meta-analysis. *Environ Res*. 2015;138:372–380.
42. Babisch W. Updated exposure-response relationship between road traffic noise and coronary heart diseases: a meta-analysis. *Noise Health*. 2014;16:1–9.
43. Cantley LF, Galusha D, Cullen MR, Dixon-Ernst C, Rabinowitz M, Neitzel RL. Association between ambient noise exposure, hearing acuity, and risk of acute occupational injury. *Scand J Work Environ Heal*. 2015;41:75–83.
44. Yang WT, Wang VS, Te Chang L, Chuang KJ, Chuang HC, Liu CS, Bao BY, Chang TY. Road traffic noise, air pollutants, and the prevalence of cardiovascular disease in Taichung, Taiwan. *Int J Environ Res Public Health*. 2018;15:1707.
45. Toronto Public Health. How loud is too loud? Health impacts of environmental noise in Toronto. Technical Report. 2017. Available at: https://www.toronto.ca/legdocs/mmis/2017/hl/bgrd/backgroundfile-104525.pdf. Accessed January 8, 2018.
46. World Health Organization (WHO). Environmental Noise Guidelines for the European Region. Basel, Switzerland: World Health Organization (WHO); 2018:1-160.
47. Shin HH, Cakmak S, Brion O, Villeneuve P, Turner MC, Goldberg MS, Jerrett M, Chen H, Crouse D, Peters P, Pope CA, Burnett RT. Indirect adjustment for multiple missing variables applicable to environmental epidemiology. *Environ Res*. 2014;134:482–487.

48. Chen H, Kwong JC, Copes R, Tu K, Villeneuve PJ, van Donkelaar A, Hystad P, Martin RV, Murray BJ, Jessiman B, Wilton AS, Kopp A, Burnett RT. Living near major roads and the incidence of dementia, Parkinson's disease, and multiple sclerosis: a population-based cohort study. *Lancet*. 2017;389:718–726.
49. Shin S, Burnett RT, Kwong JC, Hystad P, van Donkelaar A, Brook JR, Copes R, Tu K, Goldberg MS, Villeneuve PJ, Martin RV, Murray BJ, Wilton AS, Kopp A, Chen H. Effects of ambient air pollution on incident Parkinson's disease in Ontario, 2001 to 2013: a population-based cohort study. *Int J Epidemiol*. 2018;47:2038–2048.
50. Crouse DL, Peters PA, Hystad P, Brook JR, van Donkelaar A, Martin RV, Villeneuve PJ, Jerrett M, Goldberg MS, Arden Pope C, Brauer M, Brook RD, Robichaud A, Menard R, Burnett RT. Ambient PM2.5, O3, and NO2 exposures and associations with mortality over 16 years of follow-up in the Canadian census health and environment cohort (CanCHEC). *Environ Health Perspect*. 2015;123:1180–1186.
51. Weichenthal S, Crouse DL, Pinault L, Godri-Pollitt K, Lavigne E, Evans G, van Donkelaar A, Martin RV, Burnett RT. Oxidative burden of fine particulate air pollution and risk of cause-specific mortality in the Canadian Census Health and Environment Cohort (CanCHEC). *Environ Res*. 2016;146:92–99.
52. Statistics Canada. Canadian Community Health Survey—annual component. Available at: http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&Id=3359. Accessed January 8, 2018.
53. de Kluizenaar Y, Gansevoort RT, Miedema HM, de Jong PE. Hypertension and road traffic noise exposure. *J Occup Environ Med*. 2007;49:484–492.
54. Barregard L, Bonde E, Ohrström E. Risk of hypertension from exposure to road traffic noise in a population-based sample. *Occup Env Med*. 2009;66:410–415.
55. Dratva J, Phuleria HC, Foraster M, Gaspoz JM, Keidel D, Künzli N, Sally Liu LJ, Pons M, Zemp E, Gerbase MW, Schindler C. Transportation noise and blood pressure in a population-based sample of adults. *Environ Health Perspect*. 2012;120:50–55.
56. Foraster M, Künzli N, Aguilera I, Rivera M, Agis D, Vila J, Bouso L, Deltell A, Marrugat J, Ramos R, Sunyer J, Elosua R, Basagaña X. High blood pressure and long-term exposure to indoor noise and air pollution from road traffic. *Environ Health Perspect*. 2014;122:1193–1200.
57. Ragettli MS, Goudreau S, Plante C, Perron S, Fournier M, Smargiassi A. Annoyance from road traffic, trains, airplanes and from total environmental noise levels. *Int J Environ Res Public Health*. 2016;13:90.
58. Van Gerven PWM, Vos H, Van Boxtel MPJ, Janssen SA, Miedema HME. Annoyance from environmental noise across the lifespan. *J Acoust Soc Am*. 2009;126:187–194.
59. Davis A. *Hearing in Adults*. London, UK: Whurr Publishers Ltd; 1995.
60. Pearson JD, Morrell CH, Gordon-Salant S, Brant LJ, Metter EJ, Klein LL, Fozard JL. Gender differences in a longitudinal study of age-associated hearing loss. *J Acoust Soc Am*. 1995;97:1196–1205.
61. Esler MD, Thompson JM, Kaye DM, Turner AG, Jennings GL, Cox HS, Lambert GW, Seals DR. Effects of aging on the responsiveness of the human cardiac sympathetic nerves to stressors. *Circulation*. 1995;91:351–358.
62. Cohen L, Curhan GC, Forman JP. Influence of age on the association between lifestyle factors and risk of hypertension. *J Am Soc Hypertens*. 2012;6:284–290.
63. Sebastiani P, Solovieff N, DeWan AT, Walsh KM, Puca A, Hartley SW, Melista E, Andersen S, Dworkis DA, Wilk JB, Myers RH, Steinberg MH, Montano M, Baldwin CT, Hoh J, Perls TT. Genetic signatures of exceptional longevity in humans. *PLoS One*. 2012;7:e29848.
64. Cohen S, Doyle WJ, Baum A, Status S, Associated I, Stress W, Cohen S, Doyle WJ, Baum A, Status S, Associated I, Stress W. Socioeconomic status is associated with stress hormones. *Psychosom Med*. 2006;68:414–420.
65. Cohen S, Janicki-Deverts D. Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, 2006, and 2009. *J Appl Soc Psychol*. 2012;42:1320–1334.
66. Münzel T, Schmidt FP, Steven S, Herzog J, Daiber A, Sørensen M. Environmental noise and the cardiovascular system. *J Am Coll Cardiol*. 2018;71:688–697.
67. Münzel T, Gori T, Babisch W, Basner M. Cardiovascular effects of environmental noise exposure. *Eur Heart J*. 2014;35:829–836.

SUPPLEMENTAL MATERIAL

Table S1. Diagnostic codes for comorbidities at baseline in 2001

Comorbidity	Case definition	ICD-9/ ICD-O-3 Codes
Stroke	≥1 hospitalization	Ischemic: 434, 436 Hemorrhagic: 430, 431
Chronic obstructive pulmonary disease*	≥1 hospitalization or day surgery summary, or ≥1 physician claim	491, 492, 496
Asthma*	≥1 hospitalization, or ≥2 physician claims within a 2-year period	493
All cancer (other than non-melanoma skin cancer)*	≥1 hospitalization or day surgery summary, or a pathology report, or a record of referral to one of Cancer Care Ontario's nine specialized institutions treating cancer patients in Ontario	140-208

ICD-9, *International Classification of Diseases*, ninth revisions; ICD-O-3, International Classification of Diseases for Oncology, third edition.
*Selected health outcomes were obtained from validated ICES-derived cohorts, including Chronic Obstructive Pulmonary Disease (COPD) for chronic obstructive pulmonary disease cases, Ontario asthma dataset (ASTHMA) for asthma cases, and Ontario Cancer Registry (OCR) for cancer cases.

Table S2. Linear associations of smoking and body mass index (BMI) with noise measures, adjusted for neighborhood-level covariates and an indicator of neighborhoods from the Canadian Community Health Survey

Missing risk factors	$L_{Aeq,24h}$			$L_{Aeq,night}$		
	Delta	95% CI		Delta	95% CI	
Smoking Status						
Never smoker (reference)	-	-	-	-	-	-
Current smoker	0.00294	0.00057	0.00530	0.00236	0.00013	0.00459
Former smoker	0.00074	-0.00028	0.00176	0.00067	-0.00028	0.00162
BMI (kg/m^2)						
<25.0 (reference)	-	-	-	-	-	-
25.0-29.9	-0.00535	-0.02262	0.01191	-0.00380	-0.01973	0.01213
≥ 30	0.00392	-0.02041	0.02825	0.00354	-0.01889	0.02598

$L_{Aeq,24h}$, the long-term average A-weighted sound pressure level for the 24-hour day; $L_{Aeq,Night}$, the long-term average A-weighted sound pressure level for the night (2300-0700 hours); CI, confidence interval; BMI, body mass index.

Table S3. Hazard ratios (HR) and 95% confidence intervals (CI) for the associations of incident diabetes and hypertension with interquartile range increase of long-term exposure to road traffic noise (10 dBA) in individuals with hearing loss.

	Diabetes	Hypertension
Noise Type	**HR (95% CI)**	**HR (95% CI)**
$L_{Aeq,24h}$ (dBA)	1.08 (1.06-1.11)	1.02 (1.00-1.04)
$L_{Aeq,Night}$ (dBA)	1.08 (1.06-1.11)	1.02 (1.00-1.03)

Table S4. Descriptions of loss to follow-up in our cohorts by outcome from 2001 to 2015.

	Diabetes (n=914,607)	**Hypertension (n=701,174)**
Reason for loss to follow-up, n (%)		
Developed outcome	159,442 (17.4)	262,488 (37.4)
Died	140,569 (15.4)	50,408 (7.2)
Moved outside of Toronto	21,900 (2.4)	11,172 (1.6)
Reached the end of follow-up	592,696 (64.8)	377,106 (53.8)

Table S5. Baseline characteristics of estimated long-term average exposures by outcome in the City of Toronto, 2001.

	Road Traffic Noise		Air Pollutants	
	$L_{Aeq,24h}$ (dBA)	**$L_{Aeq,night}$ (dBA)**	**UFPs (counts/cm^3)**	**NO_2 (ppb)**
Diabetes				
Mean	56.3	50.0	28,380	29.3
Median	54.0	48.0	25,930	29.0
Maximum	85.3	82.0	109,800	65.8
Minimum	15.0	7.0	3,795	4.2
IQR	10.0	10.0	10,230	5.6
Hypertension				
Mean	56.2	49.9	28,200	29.3
Median	54.0	48.0	25,800	29.0
Maximum	85.3	82.0	109,800	65.8
Minimum	15.0	7.0	3,795	4.2
IQR	10.0	10.0	9,970	5.6

$L_{Aeq,24h}$, the long-term average A-weighted sound pressure level for the 24-hour day; $L_{Aeq,Night}$, the long-term average A-weighted sound pressure level for the night (2300-0700 hours); UFP, ultrafine particles; and NO_2, nitrogen dioxide; IQR, interquartile range

Table S6. Pearson correlation coefficients between long-term averages exposures to noise and air pollution.

Exposure[*]	**$L_{Aeq,24h}$**	**$L_{Aeq,night}$**	**NO_2**	**UFP**
$L_{Aeq,24h}$	1.00	0.99	0.34	0.19
$L_{Aeq,night}$	-	1.00	0.35	0.21
NO_2	-	-	1.00	0.30
UFP	-	-	-	1.00

$L_{Aeq,24h}$, the long-term average A-weighted sound pressure level for the 24-hour day; $L_{Aeq,Night}$, the long-term average A-weighted sound pressure level for the night (2300-0700 hours); UFP, ultrafine particles; and NO_2, nitrogen dioxide.
[*]All Pearson correlation coefficients between noise and air pollutants had a p-value of <0.001.

Table S7. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between quartiles of long-term exposure to road traffic noise and incidence of diabetes and hypertension.

			Diabetes	Hypertension
Noise Type	**Model**	**Exposure Level**	**HR (95% CI)**	**HR (95% CI)**
$L_{Aeq,24h}$ (dBA)	Stratified by age and sex	Q1 (ref)	-	-
		Q2	1.06 (1.04-1.08)	1.06 (1.03-1.10)
		Q3	1.14 (1.12-1.15)	1.07 (1.04-1.11)
		Q4	1.17 (1.15-1.19)	1.06 (1.01-1.10)
	+ Neighborhood-level SES†	Q1 (ref)	-	-
		Q2	1.06 (1.04-1.07)	1.06 (1.03-1.10)
		Q3	1.12 (1.11-1.14)	1.07 (1.04-1.11)
		Q4	1.16 (1.13-1.18)	1.05 (1.01-1.10)
	+ UFP and NO_2	Q1 (ref)	-	-
		Q2	1.05 (1.04-1.07)	1.06 (1.03-1.10)
		Q3	1.11 (1.09-1.13)	1.07 (1.04-1.11)
		Q4	1.14 (1.12-1.16)	1.04 (1.00-1.09)
$L_{Aeq,Night}$ (dBA)	Stratified by age and sex	Q1 (ref)	-	-
		Q2	1.06 (1.04-1.08)	1.06 (1.02-1.09)
		Q3	1.13 (1.12-1.15)	1.08 (1.04-1.11)
		Q4	1.17 (1.15-1.20)	1.05 (1.01-1.10)
	+ Neighborhood-level SES†	Q1 (ref)	-	-
		Q2	1.06 (1.04-1.07)	1.06 (1.02-1.10)
		Q3	1.12 (1.10-1.14)	1.07 (1.04-1.11)
		Q4	1.16 (1.14-1.18)	1.05 (1.01-1.10)
	+ UFP and NO_2	Q1 (ref)	-	-
		Q2	1.05 (1.04-1.07)	1.06 (1.02-1.10)
		Q3	1.11 (1.09-1.13)	1.07 (1.03-1.11)
		Q4	1.14 (1.12-1.17)	1.04 (0.99-1.09)

$L_{Aeq,24h}$, the long-term average A-weighted sound pressure level for the 24-hour average; HR, hazard ratio; CI, confidence interval; SES, socioeconomic status; UFP, ultrafine particles; and NO_2, nitrogen dioxide.

Table S8. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the subgroup analysis by selected characteristics for $L_{Aeq,24h}$.

Characteristic	Group	$L_{Aeq,24h}$ (SD)	Diabetes	Hypertension
			HR (95% CI)	HR (95% CI)
Sex	Male		1.06 (1.04-1.07)	1.00 (0.99-1.01)
	Female		1.10 (1.09-1.11)	1.04 (1.03-1.05)
	$P_{heterogeneity}$		<0.001	0.001
Age	<60		1.10 (1.09-1.11)	1.04 (1.03-1.05)
	60-74		1.03 (1.02-1.04)	0.99 (0.98-1.00)
	≥75		1.06 (1.04-1.08)	0.98 (0.96-1.00)
	$P_{heterogeneity}$		<0.001	<0.001
Comorbidities	Hypertensive		1.05 (1.04-1.06)	—
	Not hypertensive		1.09 (1.08-1.10)	—
	$P_{heterogeneity}$		<0.001	—
	Diabetic		—	0.99 (0.97-1.01)
	Not diabetic		—	1.02 (1.01-1.02)
	$P_{heterogeneity}$		—	0.019
Income Quintile	Q1	58.8 (7.5)	1.03 (1.02-1.05)	1.00 (0.99-1.01)
	Q2	56.2 (7.1)	1.04 (1.02-1.05)	1.01 (1.00-1.03)
	Q3	55.5 (6.4)	1.06 (1.04-1.08)	1.02 (1.00-1.04)
	Q4	55.2 (6.4)	1.12 (1.10-1.15)	1.03 (1.01-1.05)
	Q5	54.7 (6.8)	1.11 (1.09-1.13)	1.03 (1.02-1.05)
	$P_{heterogeneity}$		<0.001	0.001
UFP	Q1 (<21,315)	55.1 (6.7)	1.10 (1.08-1.12)	1.04 (1.02-1.05)
	Q2 (21,315-24,166)	54.9 (6.6)	1.11 (1.09-1.13)	1.05 (1.03-1.06)
	Q3 (24,166-27,642)	56.1 (6.9)	1.08 (1.06-1.10)	1.03 (1.01-1.04)
	Q4 (27,642-34,305)	56.8 (7.5)	1.05 (1.03-1.07)	1.02 (1.00-1.03)
	Q5 (≥34,305)	58.2 (7.0)	1.04 (1.02-1.06)	0.98 (0.96-0.99)
	$P_{heterogeneity}$		<0.001	<0.001
NO_2	Q1 (<25.8)	54.3 (5.5)	1.12 (1.10-1.14)	1.05 (1.03-1.07)
	Q2 (25.8-28.1)	54.6 (5.8)	1.08 (1.05-1.10)	1.05 (1.03-1.07)

Q3 (28.1-30.0)	54.7 (6.4)	1.09 (1.07-1.12)	1.03 (1.01-1.05)
Q4 (30.0-32.8)	56.8 (7.5)	1.05 (1.03-1.07)	1.02 (1.00-1.03)
Q5 (≥32.8)	60.5 (7.8)	1.02 (1.01-1.04)	0.97 (0.96-0.99)
$P_{heterogeneity}$		<0.001	<0.001

$L_{Aeq,24h}$, the long-term average A-weighted sound pressure level for the 24-hour average; HR, hazard ratio; CI, confidence interval; SD, standard deviation; UFP, ultrafine particles; and NO_2, nitrogen dioxide.