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Exposure to Road Traffic Noise and Incidence of Acute Myocardial Infarction and Congestive Heart Failure: A Population-Based Cohort Study in Toronto, Canada

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Background: Epidemiological evidence for the association between traffic-related noise and the incidence of major cardiovascular events such as acute myocardial infarction (AMI) and congestive heart failure (CHF) is inconclusive, especially in North America.

Objectives: We evaluated the associations between long-term exposure to road traffic noise and the incidence of AMI and CHF.

Methods: Our study population comprised ∼1 million people 30–100 years of age who lived in Toronto, Canada, from 2001 to 2015 and were free of AMI (referred to as the AMI cohort) or CHF (the CHF cohort) at baseline. Outcomes were ascertained from health administrative databases using validated algorithms. Annual average noise levels were estimated as the A-weighted equivalent sound pressure level over the 24-h period (LAeq24) and during nighttime (LAeqNight), respectively, using propagation modeling, and assigned to participants' annual six-digit postal code addresses during follow-up. We calculated hazard ratios (HRs) and 95% confidence intervals (CIs) for incident AMI and CHF in relation to LAeq24 and LAeqNight using random-effects Cox proportional hazards models adjusting for individual- and census tract–level covariates, including traffic-related air pollutants [e.g., ultrafine particles (UFPs) and nitrogen dioxide].

Results: During follow-up, there were 37,441 AMI incident cases and 95,138 CHF incident cases. Each interquartile range change in LAeq24 was associated with an increased risk of incident AMI (HR = 1.07; 95% CI: 1.06, 1.08) and CHF (HR = 1.07; 95% CI: 1.06, 1.09). Similarly, LAeqNight was associated with incident AMI (HR = 1.07; 95% CI: 1.05, 1.08) and CHF (HR = 1.06; 95% CI: 1.05, 1.07). These results were robust to various sensitivity analyses and remained elevated after controlling for long-term exposure to UFPs and nitrogen dioxide. We found near-linear relationships between noise and the incidence of AMI and CHF with no evidence of threshold values.

Conclusion: In this large cohort study in Toronto, Canada, chronic exposure to road traffic noise was associated with elevated risks for AMI and CHF incidence. https://doi.org/10.1289/EHP5809

Introduction

Exposure to road traffic noise has been linked to cardiovascular risk factors, including arterial hypertension (Foraster et al. 2014; Münzel et al. 2014, 2017). Traffic-related noise has been hypothesized to increase the level of stress hormones, vascular oxidative stress, and blood pressure, which may subsequently lead to endothelial dysfunction, autonomic imbalance, and metabolic abnormalities, ultimately increasing the risk of developing cardiovascular disease (Guzik and Channon 2017; Münzel et al. 2018). Some experimental studies also found that long-term exposure to traffic noise may contribute to the progression of atherosclerosis and increased risk for acute cardiovascular events (Guzik and Channon 2017; Münzel et al. 2018). However, epidemiological evidence for the associations between road traffic noise and the incidence of major cardiovascular events such as acute myocardial infarction (AMI) and congestive heart failure (CHF) is still inconclusive. Furthermore, it is not clear which populations may be most susceptible to the potential adverse impacts of road traffic noise on the development of AMI and CHF.

A number of previous studies have found a positive association between chronic exposure to road traffic noise and the incidence of AMI (Babisch et al. 2005; Babisch 2014; Roswall et al. 2017; Selander et al. 2009; Seidler et al. 2016a; van Kempen et al. 2018; Vienneau et al. 2015). A recent World Health Organization (WHO) meta-analysis reported a relative risk (RR) of 1.08 [95% confidence interval (CI): 1.01, 1.15] per 10 decibels (dB) (L_{DEN}) for the association between road traffic noise and the incidence of AMI (van Kempen et al. 2018). However, most of these previous studies were performed in Europe, with none of them being conducted in North America. In addition, among these previous studies, few considered adjusting for the potential effect of traffic-related air pollution [e.g., nitrogen dioxide (NO_2) and fine particulate matter with aerodynamic diameter $\leq$2.5 μm ($PM_{2.5}$)] (Roswall et al. 2017; Selander et al. 2009; Sørensen et al. 2012). Evidence is scarce about the association between road traffic noise and CHF incidence, with only two studies published to date (Seidler et al. 2016b; Sørensen et al. 2017). These two studies were conducted in European cities and found that exposure to road traffic noise was positively associated with CHF incidence (Seidler et al. 2016b; Sørensen et al. 2017). The potential impact of noise from road traffic in North America on CHF is unknown.

The aim of this study was to evaluate associations between long-term exposure to road traffic noise and incident AMI and CHF in Toronto, Canada, the fourth largest city in North America. To account for potential confounding by traffic-related

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air pollution, we also included NO_2 and ultrafine particles (UFPs; $\leq$0.1 μm in diameter). Additionally, we characterized the shape of the concentration–response (CR) relationships between road traffic noise and these two conditions (Nasari et al. 2016).

Methods

Study Population

The study was based on the Ontario Population Health and Environment Cohort (ONPHEC), which has been described in detail previously (Chen et al. 2017). Briefly, this large, retrospective cohort comprised virtually the entire population of long-term residents of the province of Ontario, Canada, who were 35 years of age or older in 1996 ($\sim$4.9 million). Those who were not born in Canada were excluded using the Immigration, Refugee and Citizenship Canada (IRCC) Permanent Resident Database (Government of Canada 2020). All subjects were registered with Ontario's provincial health insurance plan on 1 April 1996. In Ontario, hospital, laboratory, and physician services are funded by the provincial government through a single-payer universal healthcare system that covers virtually all residents (Chen et al. 2017).

We restricted our study cohort to individuals who were residents of the City of Toronto for 5 or more years, were 30 to 100 years of age, and did not have a previous diagnosis of AMI or CHF at baseline (1 January 2001). Toronto is the capital of Ontario, with a population of 2,731,571 in 2016 and a land area of 630.2 km^2. Follow-up ended when participants died, moved out of Toronto, or reached the end of follow-up (31 December 2015).

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.

Exposure Assessment

To derive residential exposure to road traffic noise, we used a noise propagation model developed by Oiamo and colleagues (Oiamo et al. 2018). In Oiamo et al. (2018), two modeling methods were used: a propagation model estimating the noise exposure from road traffic specifically and a combined propagation and land-use regression modeling that captured total environment noise. In this present study, we only used estimates of road traffic noise derived from the propagation model based on a 10×10 m resolution. Briefly, this model was prepared in SoundPLAN (SoundPLAN GmBH) using U.S. Federal Highway Administration Traffic Noise Model® version 2.5 (TNM2.5) emission, attenuation, and reflectance standards (Oiamo et al. 2018; Square 2004). Noise propagation was modeled based on the International Organization for Standardization calculation method (ISO 9613-2). Geospatial inputs for the noise model include *a*) 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, *b*) building massing data from the City of Toronto to account for facade reflection of noise (City of Toronto 2016), and *c*) hourly road traffic histograms for different vehicle classes (heavy, medium, and light) and road types (both major and minor roads) to distribute annual average daily traffic (AADT) volumes obtained from the City of Toronto. The calculation included a 2-km search radius, and reflections were set to the first order. Validating the final traffic noise surface against observed levels showed that the proportion of variance explained ranged from 55% for daytime noise to 61% for nighttime noise (Oiamo et al. 2018).

We extracted the noise estimates of A-weighted equivalent sound pressure level over the 24-h period (LAeq24) and during nighttime (LAeqNight) from the geographic coordinates of the postal codes on a traffic noise grid map. A sensitivity analysis to assess potential exposure misclassification was based on calculating traffic noise grid estimates at building facades only instead of the average of all grid values within postal code polygons. We also censored postal code noise estimates for the sensitivity analysis at 45 A-weighted dB (dBA) for the 24-h period and 40 dBA for the nighttime period based on minimum background noise levels observed during the monitoring campaign. We assigned the traffic noise estimates of LAeq24 and LAeqNight to each subject's annual six-character residential postal code for each year during follow-up between 2001 and 2015. In urban areas in Canada, a single six-digit residential postal code can correspond to a block face (one side of a city street between consecutive intersections), a community mailbox, or an apartment/business building. There are a total of 54,949 postal codes in Toronto, with an average size of 0.011 km^2 for each postal code. The spatial structure of the noise exposure was not assessed in a time-dependent manner, and variation in exposure for each subject was attributed solely to residential mobility. There are insufficient historical traffic data to describe long-term spatiotemporal patterns of traffic noise, but these are assumed to be relatively stable over the study time period in Toronto. Therefore, we calculated 3-y moving averages of these estimates beginning in 1998. For example, a subject's moving window of exposure for 2001 was estimated as the mean of the exposures assigned to that subject's postal codes over the 3 y from 1998 to 2000.

Outcome and Covariates

We ascertained incident physician-diagnosed cases of AMI and CHF during the study period (2001–2015) through data linkage to the Ontario Myocardial Infarction Database (Austin et al. 2002) and the Ontario Congestive Heart Failure Database (Schultz et al. 2013), respectively. Once included in these two databases, individuals remain in them until death or termination of Ontario health insurance.

The AMI database (Austin et al. 2002) was created based on hospital discharge abstracts from the Canadian Institute for Health Information Discharge Abstract Database (DAD) (Canadian Institute for Health Information 2020a). AMI was clinically diagnosed based on European Society of Cardiology/American College of Cardiology (ESC/ACC) clinical criteria: electrocardiographic (ECG) changes, typical symptoms (i.e., chest discomfort), and enzyme elevation (Alpert et al. 2000). Incidence of AMI was defined as any individual having at least one hospital admission for AMI and not having an admission for AMI in all previous years (Austin et al. 2002). The CHF database (Schultz et al. 2013) was created using data from DAD, physician service claims from the Ontario Health Insurance Plan database (Ontario Ministry of Health and Long-Term Care 2020), and the National Ambulatory Care Reporting System (Canadian Institute for Health Information 2020b). Any individual having one hospital admission with a CHF diagnosis or a physician claim with a CHF diagnosis followed within 1 y by either a second record with a CHF diagnosis from any source was considered an incident case of CHF. The diagnosis date of CHF was defined as either the first admission date or the first service date (whichever happened first). *International Classification of Diseases, Ninth Edition* (ICD-9) (Centers for Disease Control and Prevention 2015) and *International Classification of Diseases, Tenth Edition* (ICD-10) (WHO 2016) diagnosis codes for AMI and CHF are listed in Table S1. To ensure that only the first-ever cases of AMI and CHF were captured, we excluded patients who had a previous history of AMI or CHF prior to the baseline in 2001. Previous validation studies have demonstrated the accuracy of these methods to ascertain AMI (sensitivity, 89%; specificity, 93%) and CHF (sensitivity, 85%; specificity, 97%) (Austin et al. 2002; Schultz et al. 2013).

For covariates, we considered age (continuous) and sex at baseline, and derived four time-varying census tract–level variables using 1996, 2001, and 2006 Canadian census tract data: *a*) the proportion of recent immigrants, *b*) the proportion of the population ≥15 years of age who had not completed high school, *c*) unemployment rate, and *d*) mean household income. The 1996, 2001, and 2006 data were assigned to years 1996–2000, 2001–2005, and 2006–2015, respectively. In addition, we ascertained several preexisting comorbidities [i.e., diabetes, hypertension, stroke, asthma, chronic obstructive pulmonary disease (COPD), and cancer]. People with preexisting diabetes, hypertension, asthma, or COPD were identified using validated databases of all residents diagnosed with these conditions in Ontario, which are established based on the hospital discharge abstracts and physician service claim data (ICD-9 and ICD-10 diagnosis codes are listed in Table S1). For comorbid stroke, we determined prior history of hospital admissions for stroke using hospital discharge abstracts. We ascertained prior history of cancer (i.e., malignant, *in situ*, benign, and uncertain neoplasms) using the Ontario Cancer Registry (Cancer Care Ontario 2020). Because we had historical information on prior diseases since 1991, the presence of the diagnosis of a specific disease between 1991 and 2001 was defined as the presence of that comorbidity. The selection of these comorbidities was done *a priori* based on a review of existing literature and availability of data. These conditions have been related to lifestyle behaviors such as smoking habits, diet, or obesity (Au et al. 2009; Poirier et al. 2006). All data sets were linked using unique encoded identifiers and analyzed at ICES.

To further assess whether road traffic noise is associated with incident AMI and CHF, independent of traffic-related air pollution, we also considered ambient UFPs and NO_2, two common traffic-related pollutants. Details about the estimates of UFPs and NO_2 have been described previously (Jerrett et al. 2007; Weichenthal et al. 2015, 2016). Briefly, to derive residential exposure to UFPs, we used a land-use regression model that was developed using mobile monitoring data collected in Toronto (Weichenthal et al. 2015, 2016). The model included variables related to traffic intensity, land use, and distances to major roadways and explained 67% of the spatial variation in mean UFP levels. Residential exposure to NO_2 was also estimated using a land-use regression model derived from a dense measurement campaign of ground-level concentrations of NO_2 conducted in Toronto. The R^2 value of the final regression model was 70% (Jerrett et al. 2007). The estimates of UFPs and NO_2 have been applied previously to examine the associations of traffic-related air pollution with various health outcomes (Bai et al. 2018, 2019; Weichenthal et al. 2017). We assigned annual estimates of UFPs and NO_2 to the centroid of each subject's annual residential postal code for each year during follow-up and calculated 3-y moving averages of these estimates.

Statistical Analysis

Random-effects Cox proportional hazards models were used to estimate the associations between the two measures of road traffic noise (i.e., LAeq24h and LAeqNight) and incidence of AMI and CHF. Random effects were represented by Toronto's 140 neighborhoods defined based on census tract boundaries. Each neighborhood is comprised of 2–5 census tracts, with a minimum population of 7,000–10,000. Studies suggest that the lack of statistical control for spatial variables may bias estimates of environment–health associations and underestimate standard errors (Ma et al. 2003; Pankratz et al. 2005). More details on the geographic levels of variables in this study are in Table S2.

We conducted separate analyses for AMI and CHF. The models were first stratified by age and sex (basic models) and were further adjusted for the four time-varying census tract–level variables (fully adjusted models). The 3-y moving averages of LAeq24h or LAeqNight were included in the models as time-varying variables. We reported hazard ratios (HRs) and 95% CIs for each interquartile range (IQR) increase of LAeq24h and LAeqNight. As well, we estimated the associations between the noise estimates (in categories) and AMI and CHF. Consistent with previous studies, we used the cutoffs of ≤55, 56–60, 61–65, and >65 dBA for LAeq24h and ≤45, 46–50, 51–55, and >55 dBA for LAeqNight (Babisch 2014; Vienneau et al. 2015).

We performed several sensitivity analyses by *a*) further controlling for traffic-related air pollutants (i.e., UFPs and NO_2); *b*) further controlling for selected comorbidities [the presence of each comorbidity was included in the models as a dichotomous variable (yes or no)]; *c*) considering different time windows of exposure (i.e., 2- and 5-y moving averages); *d*) restricting the study population to those who lived in areas with average LAeq24 ≤45 dBA and LAeqNight ≤40 dBA, respectively; *e*) restricting the study population to those who were living in downtown Toronto with relatively smaller sizes (i.e., typically an apartment/ business building); *f*) using traffic noise grid estimates at building facades; and *g*) controlling for neighborhoods as a categorical variable in standard Cox models, given that the unavailable individual-level risk factors (e.g., income and education levels) may cluster at a fine spatial scale (Meng et al. 2015).

In addition, we indirectly adjusted for potential confounding by smoking and obesity using a method developed by Shin et al. (2014). Briefly, this method adjusts observed hazard ratios for a series of risk factors that are unavailable in the data set at hand while simultaneously controlling for the risk factors included in the survival model (e.g., census tract–level covariates in this study). The method requires estimates of the linear associations between the variables included in the survival models and the variables indirectly adjusted for (i.e., smoking and obesity). To derive these associations, we used data from the 2001, 2003, 2005, and 2007 cycles of the Canadian Community Health Survey in Ontario (Statistics Canada 2019a). This method has been used in serval large cohort studies of environmental health based on health administrative data (Bai et al. 2019; Weichenthal et al. 2017).

To understand whether certain subpopulations may be more susceptible to the effect of noise, random-effects multivariate meta-regression models were used to test potential effect modification by age groups, sex, selected comorbidities, and income levels in stratified analyses. Additional stratified analyses were also conducted to assess whether associations between exposure to noise and incidence of AMI and CHF might vary according to UFPs and NO_2 levels by quintiles. Effect modification was considered statistically significant if the effect modifier's *p*-values (i.e., meta-regression model *p*-values) were <0.05.

Lastly, we examined the shapes of the associations of incidence of CHF and AMI with LAeq24h. While several previous studies examined the shape of the association between environmental risk factors and health outcomes using natural, restricted, or smoothing splines (Kim et al. 2017; Liu et al. 2014), these previous approaches often yielded the shapes unsuitable for health impact assessment (i.e., not being monotonically increasing, displaying an extreme amount of curvature, or concealing the threshold–type association) (Nasari et al. 2016). We used a newly developed class of CR models [shape-constrained health impact function (SCHIF)] (Nasari et al. 2016). Briefly, this method not only captures various shapes of the relationships between environmental factors and health outcomes (including linear, log linear, threshold, and variations on sigmoidal shapes) but also yields shapes suitable for health impact assessment. This was achieved

Table 1. Baseline characteristics of the study population, by outcome.

	AMI cohort ($n = 1{,}005{,}214$)	CHF cohort ($n = 986{,}295$)
Number of incident cases	37,441	95,138
Individual risk factors		
Age [y (SD)]	56.1 (14.5)	55.6 (14.2)
Men (%)	46.5	46.8
Comorbid conditions (%)		
Hypertension	30.7	29.8
Diabetes	10.2	9.7
CHF	3.0	0.0
AMI	0.0	1.1
CHD	3.6	3.7
Stroke	1.7	1.4
COPD	9.5	8.9
Asthma	2.9	2.8
Cancer	5.9	5.7
Census tract–level risk factors[a]		
Percentage of the population ≥15 years of age with less than a high school education (SD)	24.8 (11.7)	24.7 (11.6)
Percentage of the population ≥15 years of age without employment (SD)	6.8 (2.5)	6.8 (2.5)
Percentage of recent immigrants (SD)	9.9 (7.1)	9.9 (7.1)
Average household income with all ages [$1,000 CAN (SD)]	63.2 (28.4)	63.3 (28.4)

Note: AMI, acute myocardial infarction; CHD, coronary heart disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; SD, standard deviation.
[a]From Canadian Census 1996, at the census tract level (Statistics Canada 2019b).

by using the product of either a linear or log-linear function of exposure concentration multiplied by a logistic weighting function, yielding a large number of flexible risk functions that can be fit to survival models. Uncertainty in the risk functions is quantified using simulation methods. In this study, an ensemble model was derived by a weighted average of all the shapes of associations examined, with weights defined by the likelihood function values. The SCHIF has been increasingly used in large cohort studies to determine the shape of the CR relationships between various health outcomes and environmental factors such as air pollution and urban greenness (Burnett et al. 2018; Crouse et al. 2017).

Results

At baseline, our two study cohorts consisted of 1,005,214 and 986,295 eligible participants free of AMI and CHF, respectively (Table 1). The mean ages of both cohorts at baseline were ~56 y. During the follow-up, we identified 37,441 incident cases of AMI and 95,138 incident cases of CHF. The 3-y moving averages of LAeq24 and LAeqNight were 56.3 dBA and 50.0 dBA, respectively (Table 2). The Pearson correlation coefficients between LAeq24 and UFPs and NO_2 were 0.18 and 0.33, respectively. Similarly, the correlations between LAeqNight and UFPs and NO_2 at baseline were 0.21 and 0.35, respectively. Exposure to UFPs was moderately correlated with exposure to NO_2 ($r = 0.30$).

Table 2. Distribution of the 3-y moving averages of road traffic noise measures (LAeq24 and LAeqNight) and concentrations of ultrafine particles (UFPs) and nitrogen dioxide (NO_2) at baseline in 2001.

			UFPs (count/cm^3)		
	LAeq24 (dBA)[a]	LAeqNight (dBA)[a]	AMI cohort	CHF cohort	NO_2 (ppb)
Mean	56.3	50.0	28,434.3	28,422.7	29.4
SD	7.1	7.0	9,122.3	9,125.3	5.2
Median	54.0	48.0	25,990.7	25,968.6	29.1
Maximum	85.3	82.0	109,750.0	109,750.0	65.8
Minimum	15.0	7.0	3,795.0	3,795.0	4.2
IQR	10.7	10.0	10,267.4	10,250.8	5.7

Note: dBA, A-weighted decibels; IQR, interquartile range; SD, standard deviation.
[a]Noise levels were measured as equivalent A-weighted decibels for 24-h average (LAeq24) and 8-h nighttime average (LAeqNight).

In the basic models adjusting for only age and sex, we found each IQR increase in LAeq24 and LAeqNight to be associated with 7%–8% increases in the risk of incident AMI and CHF (Table 3). These associations were unchanged when further adjusting for census tract–level covariates. In these fully adjusted models, each IQR increase in LAeq24 was associated with a 7% increased risk for both incident AMI (95% CI: 6, 8) and CHF (95% CI: 6, 9). Similarly, each IQR increase in LAeqNight was associated with a 7% (95% CI: 5, 8) increased incidence of AMI and a 6% (95% CI: 5, 7) increased CHF incidence.

The estimated associations of incident AMI and CHF increased monotonically across the levels of LAeq24 and LAeqNight (Table 3). For example, compared with the lowest level of LAeq24 (≤55 dBA), the HRs for incident AMI in the levels of 56–60 dBA, 61–65 dBA, and >65 dBA were 1.07 (95% CI: 1.03, 1.10), 1.10 (95% CI: 1.06, 1.13), and 1.12 (95% CI: 1.08, 1.15), respectively.

Our estimated risks were robust to the sensitivity analyses in which we considered different exposure estimates (i.e., 2- and 5-y moving averages) and further adjusted for traffic-related air pollution (i.e., UFPs and NO_2) (Table 4). Further controlling for selected comorbidities and indirectly adjusting for smoking and obesity slightly attenuated the estimated associations (Table 4). We also found that the estimated risks remained positive in the sensitivity analyses after restricting to those with average LAeq24 ≤45 dBA and LAeqNight ≤40 dBA, but these estimates were statistically insignificant, which might be partially due to the small sample sizes (Table S3). The estimated risks did not change after restricting the study population to those who were living in downtown Toronto (Table S4). In addition, we observed that the estimated associations between noise and AMI/CHF remained pronounced when we used the noise measures accounting for the building facades (Table S5 and Table S6). The estimated risks based on standard Cox models with neighborhoods controlled as a categorical variable were similar to those using random-effect Cox models (Table S7).

In the stratified analyses, we found that the associations of road traffic noise (LAeq24) with incident AMI and CHF tended to be modified by age (Table 5). For example, there was a stronger association of LAeq24 with incident CHF in subjects <60 years of age (HR = 1.18; 95% CI: 1.16, 1.21) compared to those 60–74 years of age (HR = 1.07; 95% CI: 1.05, 1.09) and ≥75 years of age (HR = 1.01; 95% CI: 0.99, 1.02) ($p < 0.001$). We also found those who were diagnosed with asthma prior to baseline might be at higher risk of developing AMI in relation to noise compared to those without asthma diagnosis ($p = 0.202$). In addition, we also observed that the relationship between exposure to noise and incidence of CHF was weaker when exposures to UFPs and NO_2 were elevated.

Our analyses of the CR relationships showed the relationships between LAeq24 and the incidence of AMI and CHF were nearly linear (Figure 1). We did not observe any apparent thresholds from these two CR shapes.

Discussion

In this large population-based cohort study, we found that long-term exposure to noise from road traffic (modeled as LAeq24 and LAeqNight) was associated with elevated risk of incident AMI and CHF. Importantly, these associations were independent of exposures to UFPs and NO_2. Furthermore, the estimated associations of incident AMI and CHF increased monotonically across the levels of noise. We also observed some evidence of effect modification by age, preexisting asthma, and levels of UFPs and NO_2.

Table 3. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations of incidence of acute myocardial infarction (AMI) and congestive heart failure (CHF) with exposure to road traffic noise (LAeq24 and LAeqNight) using interquartile range (IQR) increases and quartiles of exposures.

	Incident AMI			Incident CHF		
Model[a]	HR	95% CI		HR	95% CI	
LAeq24 (10.7 dBA per IQR)						
Stratified by age and sex	1.08	1.06	1.09	1.07	1.06	1.08
Further adjusted for census tract–level covariates[b]	1.07	1.06	1.09	1.07	1.06	1.08
LAeq24 (by categories) (dBA)[c]						
≤55	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
56–60	1.07	1.03	1.10	1.07	1.05	1.09
61–65	1.10	1.06	1.13	1.11	1.09	1.04
>65	1.12	1.08	1.15	1.11	1.09	1.13
LAeqNight (10.0 dBA per IQR)						
Stratified by age and sex	1.07	1.06	1.09	1.07	1.06	1.08
Further adjusted for census tract–level covariates[b]	1.07	1.05	1.08	1.06	1.05	1.07
LAeqNight (by categories) (dBA)[c]						
≤45	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
46–50	1.05	1.02	1.08	1.04	1.02	1.06
51–55	1.10	1.06	1.14	1.10	1.08	1.13
>55	1.14	1.11	1.18	1.13	1.11	1.15

Note: dBA, A-weighted decibels; LAeqNight, A-weighted decibels for nighttime (8-h average); LAeq24, A-weighted decibels for 24-h average; Ref., the reference level.
[a]Random-effects Cox proportional hazards models adjusting for neighborhoods ($n = 140$).
[b]Further adjusted for census tract–level recent immigrants, unemployment rate, education, and annual household income.
[c]Hazard ratios by categories were estimated in the models stratified by age and sex and adjusted for census tract–level variables.

Our findings support the hypothesis that exposure to environmental noise may facilitate the development of cardiovascular events. A growing number of experimental studies exploring the pathophysiological mechanisms have shown that exposure to traffic-related noise is associated with annoyance, stress, sleep disturbance, and impaired cognitive performance, which may lead to chronic stress reactions (Münzel et al. 2014, 2018). It has been also proposed that chronic stress reactions may induce vascular dysfunction, mainly through induction of oxidative stress and subsequent activation of prothrombotic pathways and vascular inflammation (Babisch 2003; Münzel et al. 2018). In addition to endothelial dysfunction, other physiological changes, including elevated blood pressure, dyslipidemia, changes in blood glucose levels, and altered heart rate variability, could contribute to the development or progression of atherosclerosis and cardiovascular events (Münzel et al. 2014, 2017, 2018). A recent study found that noise-exposed animals had significant changes of several important genes [e.g., endothelial nitric oxide synthase (*eNOS*), heme oxygenase 1 (*HO-1*), peroxisome proliferator-activated receptor gamma co-activator 1-alpha (*PGC*-1α), and nicotinamide-adenine dinucleotide phosphate oxidase 1 (*NOX-1*)] partly responsible for the regulation of vascular function, vascular remodeling, and cell death (Guzik and Channon 2017).

The majority of previous studies of traffic noise and incident AMI failed to reach statistical significance, partly due to small sample sizes. In our study, we found that there was a 7% increase in the risk of incident AMI in relation to both LAeq24 (HR = 1.07; 95% CI: 1.06, 1.09 per 10.7 dBA) and LAeqNight (HR = 1.07; 95% CI: 1.06, 1.08 per 10.0 dBA), adjusted for potentially confounding variables at the individual and neighborhood levels. These findings are in line with a recent systematic review synthesizing 10 studies with case–control and cohort designs reporting an RR for the incidence of ischemic heart disease of 1.06 (95% CI: 1.03, 1.09) per 10-dBA increase in traffic noise exposure (L_{DEN}) above 50 dBA (Vienneau et al. 2015). As well, our estimated risks are similar to a recent WHO meta-analysis based on the results of seven European longitudinal studies, which showed an RR for the risk of ischemic heart disease of 1.08 (95% CI: 1.01, 1.15) per 10-dB (L_{DEN}) increase in exposure to road traffic noise (van Kempen et al. 2018). Although there is

Table 4. Sensitivity analyses for the associations of incidence of acute myocardial infarction (AMI) and congestive heart failure (CHF) with every interquartile range (IQR) increase in exposure to road traffic noise (LAeq24 and LAeqNight).

	Incident AMI			Incident CHF		
Model[a]	HR	95% CI		HR	95% CI	
LAeq24 (10.7 dBA per IQR)						
Used different exposure estimates						
2-y moving average	1.08	1.06	1.09	1.07	1.06	1.08
5-y moving average	1.06	1.05	1.08	1.05	1.04	1.06
Adjusted for ultrafine particles and NO_2	1.06	1.04	1.08	1.07	1.06	1.08
Adjusted for comorbidities[b]	1.05	1.04	1.07	1.05	1.04	1.06
Indirectly adjusted for smoking and BMI	1.06	1.02	1.10	1.04	1.00	1.09
LAeqNight (10.0 dBA per IQR)						
Used different exposure estimates						
2-y moving average	1.07	1.06	1.09	1.07	1.06	1.08
5-y moving average	1.06	1.04	1.08	1.05	1.04	1.06
Adjusted for ultrafine particles and NO_2	1.05	1.03	1.07	1.07	1.06	1.08
Adjusted for comorbidities[b]	1.05	1.03	1.07	1.05	1.04	1.06
Indirectly adjusted for smoking and BMI	1.06	1.02	1.09	1.04	1.00	1.08

Note: BMI, body mass index; dBA, A-weighted decibels; LAeqNight, A-weighted decibels for 8-h average; LAeq24, A-weighted decibels for 24-h average; NO_2, nitrogen dioxide.
[a]Random-effects Cox proportional hazards models adjusting for neighborhoods ($n = 140$). All sensitivity analyses were conducted based on the models stratified by age and sex and adjusted for census tract–level variables.
[b]Comorbidities included diabetes, hypertension, stroke, asthma, chronic obstructive pulmonary disease, and cancer.

Table 5. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations of incidence of acute myocardial infarction (AMI) and congestive heart failure (CHF) with every interquartile range (IQR) increase in exposure to road traffic noise (LAeq24) by selected characteristics.

	Incident AMI				Incident CHF			
	HR	95% CI		*p*-Value	HR	95% CI		*p*-Value
Age (y)								
<60	1.14	1.11	1.18	—	1.18	1.16	1.21	—
60–74	1.07	1.04	1.10	—	1.07	1.05	1.09	—
≥75	1.01	0.98	1.04	0.00	1.01	0.99	1.02	0.00
Sex								
Men	1.07	1.05	1.09	—	1.06	1.04	1.07	—
Women	1.08	1.06	1.11	0.59	1.07	1.06	1.09	0.38
Comorbid AMI								
Yes	—	—	—	—	1.03	1.01	1.05	—
No	—	—	—	—	1.06	1.05	1.08	0.04
Comorbid CHF								
Yes	1.05	1.00	1.10	—	—	—	—	—
No	1.07	1.05	1.09	0.47	—	—	—	—
Comorbid hypertension								
Yes	1.06	1.04	1.09	—	1.05	1.03	1.06	—
No	1.08	1.05	1.11	0.36	1.09	1.07	1.11	0.00
Comorbid diabetes								
Yes	1.07	1.04	1.10	—	1.03	1.01	1.05	—
No	1.06	1.04	1.08	0.59	1.06	1.05	1.08	0.04
Comorbid asthma								
Yes	1.13	1.01	1.22	—	1.07	1.01	1.12	—
No	1.07	1.05	1.09	0.20	1.07	1.06	1.08	1.00
Neighborhood income quintile								
Q1	1.05	1.02	1.09	—	1.03	1.01	1.05	—
Q2	1.06	1.02	1.09	—	1.03	1.01	1.05	—
Q3	1.06	1.02	1.10	—	1.06	1.03	1.08	—
Q4	1.04	0.99	1.09	—	1.06	1.03	1.09	—
Q5	1.06	1.02	1.10	0.96	1.08	1.06	1.10	0.00
UFP level (count/cm^3)								
Q1 (<21,315)	1.05	1.02	1.09	—	1.09	1.07	1.12	—
Q2 (21,315–24,166)	1.07	1.03	1.11	—	1.10	1.07	1.12	—
Q3 (24,167–27,642)	1.10	1.06	1.14	—	1.07	1.05	1.09	—
Q4 (27,643–34,305)	1.04	1.00	1.07	—	1.02	1.00	1.04	—
Q5 (≥34,306)	1.04	1.01	1.08	0.14	1.02	1.00	1.05	0.00
NO_2 level (ppb)								
Q1 (<25.8)	1.08	1.04	1.13	—	1.11	1.08	1.14	—
Q2 (25.8–28.1)	1.07	1.02	1.11	—	1.10	1.07	1.13	—
Q3 (28.2–30.0)	1.07	1.03	1.11	—	1.07	1.04	1.09	—
Q4 (30.1–32.8)	1.04	1.00	1.08	—	1.02	1.00	1.05	—
Q5 (≥32.9)	1.05	1.01	1.08	0.65	1.00	0.98	1.02	0.00

Note: Hazard ratios and 95% CI were estimated in random-effects Cox proportional hazards models that were stratified by age and sex and adjusted for census tract–level variables (i.e., the proportion of recent immigrants, the proportion of population ≥15 years of age who had not completed high school, unemployment rate, and mean household income). Random-effects multivariate meta-regression models were used to test potential effect modification by selected characteristics and levels of ultrafine particles (UFPs) and nitrogen dioxide (NO_2). Effect modification was considered statistically significant if the effect modifier's *p*-value was less than 0.05. —, no data.

growing evidence regarding the association between traffic noise and AMI, little is known about the shape of the CR relationship in the existing literature (Babisch 2014; Vienneau et al. 2015). In this study, the use of a newly developed class of CR models (SCHIF) enabled us to reasonably characterize the shape of the CR associations. We found a near-linear relationship between LAeq24 and AMI incidence with no evidence of threshold values, which implies an absence of a safe level of noise.

Compared to AMI incidence, there is much less evidence regarding the association between road traffic noise and CHF incidence, with only two studies published so far (Seidler et al. 2016b; Sørensen et al. 2017). Both of these previous studies found that long-term exposure to traffic-related noise was positively associated with incident CHF: the Danish Diet, Cancer and Health cohort study reported a 14% (95% CI: 8, 21) elevated risk in association with each 10-dBA increase in road traffic noise (LAeq24) (Seidler et al. 2016b), and a case–control study conducted in Germany observed a risk increase of 2.4% (95% CI: 1.6, 3.2) per 10-dBA increase in noise from road traffic (L_{DEN}) (Sørensen et al. 2017). Consistently, we found a positive association between exposure to road traffic noise and the development of CHF (HR = 1.07 per 10.7 increase in LAeq24; 95% CI: 1.06, 1.08). Similar to AMI incidence, we also observed a nearly linear relationship between LAeq24 and CHF incidence with no evidence of thresholds. No previous studies have been conducted to investigate the shape of the CR relationship between road traffic noise and incident CHF.

Our stratified analyses showed that age might modify the association between road traffic noise and incidence of AMI and CHF with higher risk among young individuals compared with the elderly. This pattern was also seen in our previous study, which showed an increasing risk for incidence of AMI and CHF in relation to exposure to traffic-related air pollution among younger adults in Toronto (Bai et al. 2018). This might be explained by the reduced responsiveness to autonomic nervous system stimuli that occurs among older individuals, different genetic signatures that could correlate with different life span lengths, and ages of onset of major age-related diseases such as cardiovascular disease (Cohen et al. 2012; Esler et al. 1995; Sebastiani et al. 2012). This may be also related to a higher prevalence of deafness and hearing loss among the elderly (WHO

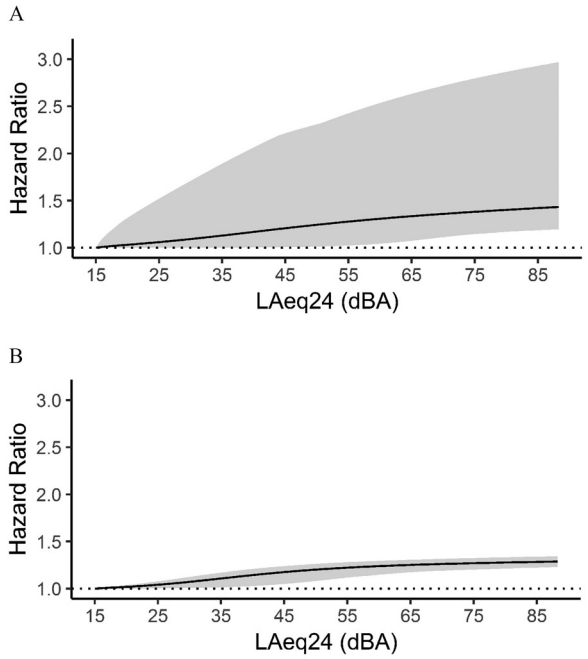

Figure 1. The concentration–response relationships between exposure to road traffic noise (LAeq24) and (A) incidence of acute myocardial infarction and (B) congestive heart failure using the shape-constrained health impact function. The concentration–response models were stratified by age and sex and adjusted for census tract–level variables (i.e., the proportion of recent immigrants, the proportion of population ≥15 years of age who had not completed high school, unemployment rate, and mean household income).

2019). Furthermore, we found that those who were diagnosed with adult-onset asthma tended to be at a greater risk of developing AMI in relation to exposure to road traffic noise compared with those not having asthma prior to baseline, which may be attributable to the fact that patients with asthma could contribute to the development of coronary heart disease due to its inflammatory nature (Iribarren et al. 2012). The absence of previous studies examining the effect modification of comorbid asthma for the association between noise and AMI makes our finding novel, which requires replication in future studies.

Additionally, we observed that people living in high-income areas exhibited a higher risk of incidence of CHF in association with noise than those living in low-income areas. This finding is supported by several recent studies conducted in the United States and Europe, which found that the noise level from road traffic was higher in affluent neighborhoods, which is in part due to the desire of individuals to live near transportation networks (Casey et al. 2017; Havard et al. 2011; Cesaroni et al. 2010). Indeed, we also observed high average noise levels near busy public transportation facilities in Toronto (Drew et al. 2017).

Interestingly, we found that the associations between noise and CHF tended to be stronger among people living in areas with low levels of traffic-related air pollution (both UFPs and NO_2). This might be explained by the fact that traffic-related noise and air pollution are affected differently by multiple road traffic factors such as speed, traffic load, and road conditions. For example, previous studies suggest that in areas where the volume of traffic is high and the speed is low, noise levels may be lower, but air pollution emissions could be dramatically higher; on the other hand, in areas where traffic is moving well, noise levels may be higher, but emissions may be lower (Münzel et al. 2017; Samuel 2006).

The main strength of the present study is our ability to characterize the associations of exposure to road traffic noise with the incidence of AMI and CHF in two large cohorts over 15 y of follow-up. To derive residential exposure to road traffic noise, we used a propagation model, which enabled us to predict fine-resolution noise exposures in Toronto (Oiamo et al. 2018). We also accounted for each subject's residential mobility by assigning noise exposures to the annual residential postal code of each subject. Furthermore, our study is the first to examine the noise–health association with adjustment for the effect of exposure to both UFPs and NO_2. Most previous noise studies controlling for traffic-related pollution relied on exposure to NO_2 only; however, NO_2 could not capture the role of UFPs, which, in urban areas, are primarily emitted by diesel vehicles. Exposure to UFPs in our study was measured based on a land-use regression model explaining the majority of the spatial variation in ambient UFPs in Toronto (Weichenthal et al. 2015, 2016). Our study also benefited from the use of province-wide registries and algorithms with high sensitivity and specificity, which substantially reduced outcome misclassification in identifying incident AMI and CHF. In addition, we were able to reasonably characterize the shape of the CR associations of noise with incident CHF and AMI using the SCHIF (Nasari et al. 2016).

Our study also has some limitations. First, we were unable to obtain detailed street addresses for the study subjects due to data confidentiality, and thus, we were unable to assign exposures to their residential addresses. Previous studies have shown that the finer scale introduced less measurement error, and subsequent bias and use of noise maps to represent residential exposure may underestimate noise-induced health effects (Eriksson et al. 2013; Vienneau et al. 2019). Since a single postal code in Toronto (with an average size of $\sim 0.011\,km^2$) only corresponds to a block face, a community mailbox, or an apartment/business building, we assume the variations of exposure within a postal code could be small. However, we acknowledged that it is possible that some geographic coordinates of the postal codes on the traffic noise grid might be inside the building polygons, which may lead to misclassification within some postal codes. We therefore further derived the noise data based on averaged noise levels at the loudest facades of all buildings within postal code polygons. We found that the estimated risks generally remain unchanged when using the noise measures accounting for the building facades. In addition, in a sensitivity analysis that we restricted the study population to those living in downtown Toronto where postal codes have even smaller sizes, we found that our estimated risk is virtually insensitive to this adjustment.

As well, we lacked information on personal exposure to noise, which may be affected by hearing impairment/loss, indoor exposures, bedroom location, ventilation, exposures at work, and personal activity patterns. However, given that our spatially derived exposure assessment was likely subject to nondifferential misclassification, this could have attenuated our effect estimates. A previous study found that the association between road traffic noise and incident AMI was stronger when several of the above factors were considered (Selander et al. 2009).

Another limitation is that our exposures only capture noise emissions from road traffic but not rail and air traffic. Although the monitoring and modeling process took these noise sources into account, their precise impacts on the soundscape could not be inferred. Our exposure data is also limited by the lack of information on sound barriers and noise walls, which may lead to some of the major roadways noise levels being overestimated.

Furthermore, our facade noise levels were calculated by attributing the closest grid center value to the facade instead of using receivers placed directly on the building facade. There may be some minor bias in using the closest grid values instead of facade values, depending on the grid cell size (e.g., extra reflection

off the building facade). However, the bias might be negligible due to the high resolution (10 m × 10 m) used in our study.

In addition, as our study was based on the use of administrative data, we lacked information on important personal risk factors for cardiovascular disease such as smoking and obesity. However, previous studies found that adjusting for these individual risk factor variables had little impact on the relationship between road traffic noise and coronary heart diseases (Babisch 2014; Vienneau et al. 2015). In addition, in an effort to assess their potential influence on our estimated associations, we indirectly adjusted for smoking and BMI using ancillary data sources (the Canadian Community Health Survey) and observed similar estimated associations after this indirect adjustment. Furthermore, we controlled for several selected respiratory and cardiovascular comorbidities in an attempt to reduce the potential influence of individual-level confounders because individual-level confounders such as income may affect the risks of CHF/AMI through affecting the selected comorbidities (C2→M→Y) (Figure S1). However, we recognize that these comorbidities could act as mediators in the causal chain between noise and CHF/AMI and may attenuate our effect estimates. Lastly, to further account for individual risk factors that may cluster at a fine spatial scale (Meng et al. 2015), we conducted a sensitivity analysis by including a categorical variable of neighborhoods in standard Cox models and found that the estimated risks were similar to those using random-effect Cox models.

In conclusion, our study showed positive associations between long-term residential exposure to road traffic noise and the incidence of AMI and CHF in Toronto, Canada, with nearly linear exposure–response relationships.

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