



Road traffic noise, air pollution and cardiovascular events in a Swedish cohort[☆]

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ABSTRACT

Urbanization and increasing road traffic cause exposure to both noise and air pollution. While the levels of air pollutants such as nitrogen oxides (NO_x) have decreased in Sweden during the past decades, exposure to traffic noise has increased. The association with cardiovascular morbidity is less well established for noise than for air pollution, and most studies have only studied one of the two highly spatially correlated exposures.

The Swedish Primary Prevention Study cohort consists of men aged 47 to 55 when first examined in 1970–1973. The cohort members were linked to the Swedish patient registry through their personal identity number and followed until first cardiovascular event 1970–2011. The address history during the entire study period was used to assign annual modelled residential exposure to road traffic noise and NO_x. The Cox proportional hazards model with age on the time axis and time-varying exposures were used in the analysis.

The results for 6304 men showed a non-significant increased risk of cardiovascular disease for long-term road traffic noise at the home address, after adjusting for air pollution. The hazard ratios were 1.08 (95% CI 0.90–1.28) for cardiovascular mortality, 1.14 (95% CI 0.96–1.36) for ischemic heart disease incidence and 1.07 (95% CI 0.85–1.36) for stroke incidence, for noise above 60 dB, compared to below 50 dB.

This study found some support for cardiovascular health effects of long-term exposure to road traffic noise above 60 dB, after having accounted for exposure to air pollution.

1. Introduction

Exposure to traffic noise is increasing in Europe, as a result of both urbanization and increasing traffic, and health effects of environmental noise is a large and growing area of concern for public health. Burden of disease estimates indicate that at least one million healthy life years are lost due to traffic-related noise each year in western Europe (WHO, 2011). Noise exposure has been associated with many health effects, among them ischemic heart disease (Vienneau et al., 2015), myocardial infarction (Roswall et al., 2017), psychological distress among persons with poor sleep quality (Sygna et al., 2014), diabetes mellitus (Sorensen et al., 2013) and poorer reading comprehension and attention among school children (Haines et al., 2001; Lercher et al., 2003). A major source of noise as well as air pollution is road traffic. For the association

between exposure to air pollution and cardiovascular morbidity there are consistent findings in a number of studies (WHO, 2013). For residential noise and cardiovascular events, association has been shown in several longitudinal studies (Selander et al., 2009, 2013; Huss et al., 2010; Sorensen et al., 2011, 2012; Gan et al., 2012; Halonen et al., 2015) but there are also non-positive studies (Bodin et al., 2016). A recent systematic review (van Kempen et al., 2018) estimated the evidence for an association with road traffic noise as high for incidence of ischemic heart disease (IHD), but low for stroke. A main remaining source of uncertainty regarding the causality of these associations is the relatively strong spatial correlations between exposure to air pollution and noise, since road traffic is usually the major source of both these exposures. A limited number of longitudinal studies have examined the effect of noise on cardiovascular morbidity taking air pollution into

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List of abbreviations

PPS	The Primary Prevention Study
NOx	nitrogen oxide
CVD	cardio-vascular disease
IHD	ischemic heart disease

AF	atrial fibrillation
L_{den}	level day-evening-night, A-weighted equivalent road traffic noise level with a penalty for traffic in the evening and at night
$L_{Aeq,24h}$	A-weighted 24 h equivalent road traffic noise level

account (Selander et al., 2009; Sorensen et al., 2011; Gan et al., 2012; Halonen et al., 2015; Bodin et al., 2016; Beelen et al., 2009; Raaschou-Nielsen et al., 2012; de Kluizenaar et al., 2013; Sorensen et al., 2014). In some cases, the risk estimates for noise were reduced when air pollution was adjusted for, but in some cases the risk was unchanged. A recent review (Stansfeld, 2015) concluded that it is likely that both noise and air pollution have independent effects, and affect the risk of cardiovascular diseases though partly different mechanisms. Also, the review noted many limitations in the studies, such as limited data on historical addresses, and proposed to model the most traffic-specific air pollutants, such as nitric oxides (NO_x), in future studies.

The aim of this study was to assess the whether road traffic noise is associated with incident cardiovascular events when air pollution, and other cardiovascular risk factors are taken into account. We used data from a cohort of middle-aged Swedish men followed for a study period of almost 40 years, with individual annual residential exposure to air pollution and road traffic noise.

2. Material and methods

2.1. Study population

The Primary Prevention Study cohort (PPS) has been described previously in detail (Wilhelmsen et al., 1972, 1986). Briefly, a random third of all men in the city of Gothenburg born 1915–1925 were enrolled in 1970–1973 ($n = 7,494$, participation rate 75%). Participants filled out questionnaires on background data and potential cardiovascular risk factors (occupation, smoking habits, occupational and leisure time physical activity, diagnosis of diabetes mellitus, antihypertensive medication, psychological stress, and family history of coronary events), and were examined by health care professionals (height, weight, systolic and diastolic blood pressure and cholesterol levels). A follow-up examination was performed in 1974–77. The study was reviewed and approved by the Gothenburg Ethics Committee (refs: T800-8, 107-13, T547-13).

2.2. Covariates

Smoking habits was categorized as: “never-smokers,” “ex-smokers, screening 1,” “smokers quitting between screening 1 and screening 2,” “light smokers” (a consumption of cigars, pipe tobacco, and cigarettes the equivalent of 1–15 cigarettes/day), and “intermediate and heavy smokers” (the equivalent of > 15 cigarettes/day). Occupation, used as marker of individual socioeconomic status, was classified into six classes according to a socioeconomic classification system of Statistics Sweden, as described by Rosengren et al. (1988). The classes were (WHO, 2011): higher civil servants, executives, employed, and self-employed professionals (Vienneau et al., 2015), intermediate, non-manual employees (Roswall et al., 2017), foremen in industrial production and assistant, non-manual employees (Sygna et al., 2014), skilled workers (Sorensen et al., 2013), unskilled and semi-skilled workers, and (Haines et al., 2001) non-professional, self-employed individuals, men with disability pensions, and “unclassifiable.” Physical activity during leisure time was categorized into (WHO, 2011) mainly sedentary activity, such as reading or watching television (Vienneau et al., 2015), moderate activity, such as walking or riding a bike at least 4 h a week (Roswall et al., 2017), regular strenuous physical activity,

such as running or swimming 2–3 h a week, and (Sygna et al., 2014) athletic training or competitive sports several times per week. In our analysis, we combined categories 3 and 4. Psychological stress, reported on a 6-point ordinal scale as described by (Rosengren et al., 2008), was dichotomized into persistent stress (this year or the last five years, yes/no).

A diagnosis of diabetes mellitus at baseline was recorded as “yes/no.” Family history of coronary events or stroke (i.e., reporting event in the subject’s father, mother, or sibling) was dichotomized (yes/no), and heredity for stroke and myocardial infarction were combined into heredity for cardiovascular events. Height and weight was measured and BMI calculated. The mean BMI across the two screening was categorized into quintiles. Systolic and diastolic blood pressure was measured, after 5 min of rest, to the closest 2 mm Hg, and values from screening 1 were used in the analysis. Subjects taking antihypertensive medication in either examination were defined as treated for hypertension. Married and cohabitating were combined into one class and compared with those living alone.

Individual yearly addresses for the study period were retrieved from Statistics Sweden and the National Archives, manually checked, and assigned coordinates. The coordinates were used for assigning exposure (modelled NO_x and road traffic noise, see below).

2.3. Noise exposure

The equivalent sound pressure level due to road traffic on the most exposed façade was estimated using the Nordic method for road traffic noise prediction (Kragh et al., 1996). This method uses information on traffic flow, percentage of heavy vehicles and posted speed limit to calculate a source strength for each road link, and the contributions are summed at each receiver location including the effect of propagation distance, screening by buildings and terrain and acoustic ground effect. The method also takes weather effects such as wind and temperature gradient into account in a simplified manner, mainly for long distances between source and receiver. For dense urban areas many sound rays may reach a receiver via complex pathways when the sound is reflected multiple times in building façades and diffracted around corners or over rooftops, and in order to reduce the calculation time a simplified approach was used for such receiver positions (Ögren and Barregard, 2016).

The calculations were performed using software developed by the authors using GIS data from a number of sources. Building footprints and a digital elevation models were obtained from the Swedish land survey (Lantmäteriet). Information on the placement and height of noise barriers were obtained from the municipality of Gothenburg. The traffic flows were estimated from a comprehensive database of more than 16 000 measurements by the municipality of Gothenburg for the period 1975–2011. A manual check was employed to ensure reasonable estimates of traffic flows for the whole period in special cases such as only a single measurement point available, or drastic changes to the traffic flow pattern due to new links being opened. The method has been described in more detail previously (Ögren and Barregard, 2016).

The standard noise indicator for road traffic noise in Sweden is the A-weighted 24-h equivalent level ($L_{Aeq,24h}$) at the most exposed façade of the dwelling, which was used in this paper. For typical traffic situations the equivalent level can be converted to the EU noise indicator L_{den} (level day evening night) by adding 3 dB (Jonasson, 2005).

2.4. Air pollution exposure

High-resolution dispersion modelling of NO_x (in 50 × 50 m squares) was performed for the period 1990–2011 over the Gothenburg region (93 × 112 km), and has been described in more detail previously (Segersson et al., 2017; Stockfelt et al., 2017). Separate emission inventories were compiled for 1990, 2000, and 2011 using existing local and regional bottom-up emission inventories provided by the municipality, and then supplemented to be consistent for the whole area and time period. Since the year-to-year variations in the most important emission sectors are expected to be small, concentrations for the years in between were interpolated. Year-to-year variations in the local meteorology were considered using a ventilation index for each year, estimated from calculations over the whole time-period in part of the modelling domain. For the period 1975–1990 (modelled for the years 1975, 1983, 1990 and interpolated for the years in-between) we used exposure data from another study, which also used a high-resolution dispersion model, but covering only the city of Gothenburg (Molnár et al., 2015; Stockfelt et al., 2015). The NO_x levels in the model for the earlier time period were slightly lower than for the later model but correlated well ($r^2 = 0.81$). We therefore adjusted the concentrations for the years 1975–1989 to fit the concentrations of the later model.

2.5. Outcomes

Data on cause-specific morbidity and mortality was collected from the national Swedish hospital discharge register and the Swedish national cause-specific death register according to the International Classification of Diseases (ICD), revision 8, 9, or 10. Outcomes were defined as a first registration in any of the two registers of the following

cardiovascular diseases: ischemic heart disease (ICD8, ICD9: 410–414 and ICD10: I20–I25), stroke (ICD8, ICD9: 431–436 and ICD10: I61–I64), atrial fibrillation (ICD8: 427.92, ICD9: 427D and ICD10: I48). We also investigated overall cardiovascular mortality (ICD8, ICD9: 390–459 and ICD10: I00–I99) and natural mortality (ICD8, ICD9: 001–779 and ICD10: A00–R99).

2.6. Statistical methods

The associations between noise and NO_x and the cardiovascular outcomes (natural mortality, cardiovascular mortality, IHD incidence, stroke incidence and atrial fibrillation (AF) incidence) were estimated using Cox proportional hazards models with age as the time axis. Both noise and NO_x were included as annual, time-dependent variables. All participants were followed using their unique Swedish personal identification number from January 1st 1975 until event, death, emigration or the end of the study period at December 31st 2011. Participants were also excluded when exposure information became permanently missing (mainly due to emigration outside the study area). The 5-year average exposure (lag 0–4, arithmetic mean on the dB scale) was used as the main exposure measure, both for noise (dB, L_{Aeq,24h}) and NO_x (µg/m³). Mean values that were based on less than 80% of the intended data (< 4 out of 5 years) were excluded. This exposure measure was entered as time-dependent variables into the regression model. Thus in the analyses, the first year with exposure data was 1978 (mean over the four years 1975–1978). A comparison was made between the 5-year average and a shorter exposure window, namely the average exposure of the current year (lag0). For noise, values below 42 dB were set to 42 dB since many studies indicate that health effects and annoyance from road traffic noise are very low below 45 dB L_{den} (WHO, 2018),

Table 1
Selected characteristics for the PPS cohort. All data are from 1978 (baseline).

		All	Noise ^b (dB) at baseline (1978)			
			L _{Aeq,24h} < 50	50–55	55–60	60–
			L _{den} < 53	53–58	58–63	63–
Persons (n)		6304 ^a	1408	1793	1364	1549
Age 1978 (years)	Mean (min-max)	58.2 (53–63)	58.0 (53–63)	58.3 (53–63)	58.2 (53–63)	58.4 (53–63)
Socioeconomic class by occupation (%)	High rank white collar	11	8	12	11	12
	Mid rank white collar	17	17	18	16	17
	Low rank white collar	19	18	19	19	19
	Skilled manual labor	26	26	26	26	25
	Unskilled manual labor	23	25	20	25	22
	Disability pension & other	5	5	5	4	6
Smoking class (%)	Never-smokers	25	25	28	26	22
	Ex-smokers screening 1	22	21	23	23	21
	Quit before screening 2	10	10	9	9	11
	Light smokers	27	28	26	26	29
	Heavy smokers	16	15	14	16	18
BMI	Mean (p5-p95)	25.4 (20.7–30.7)	25.4 (20.7–30.5)	25.3 (20.7–30.4)	25.5 (20.9–31.1)	25.3 (20.6–30.5)
Antihypertensive medication (%)	Yes	17	17	17	17	16
Leisure-time physical activity (%)	Mainly sedentary	26	27	23	26	27
	Moderate	59	58	60	58	59
	Intermediate and vigorous	15	14	16	16	14
Diabetes (%)	Yes	2.0	1.4	2.4	1.9	2.1
Family history of						
-myocardial infarction (%)	Yes	25	25	24	23	26
-stroke (%)	Yes	29	30	28	28	29
-any cardiovascular event (%)	Yes	45	45	45	44	46
Persistent psycho-logical stress (%)	Yes	15	14	15	17	15
Married/cohab (%)	Yes	85	88	89	85	78
Systolic blood pressure (mmHg)	Mean (p5-p95)	149 (118–190)	149 (116–190)	149 (120–188)	149 (118–190)	149 (118–190)
Diastolic blood pressure (mmHg)	Mean (p5-p95)	95 (76–118)	95 (76–118)	95 (76–118)	95 (76–118)	95 (76–118)
Cholesterol (mmol/L)	Mean (p5-p95)	6.5 (4.8–8.4)	6.5 (4.8–8.3)	6.5 (4.6–8.3)	6.5 (4.9–8.5)	6.5 (4.8–8.5)

^a Data set consisting of individuals with noise and NO_x for at least one year during the study.

^b Not all individuals have noise exposure for the year 1978.

which corresponds to a 24-h equivalent level of 42 dB. A recent comparison showed that the percentage of highly annoyed is lower than 4% for both railway, road traffic and aircraft noise at 45 dB L_{den} (Fredianelli et al., 2019).

Exposures were categorized into four noise categories and NO_x quintiles. Participants older than 85 years were excluded. Two different covariate models were used. Model 1 included variables that were considered to be likely confounders based on a Directed Acyclic Graph DAG model (supplementary figure SF1), namely calendar year, occupation, married/cohabiting. Model 2 included the following variables, based on literature: calendar year, occupation, married/cohabiting, smoking categories, body mass index (BMI, in quintiles), cholesterol levels (continuous), stress (yes/no), heredity for the outcome (at least one parent or a sibling had the disease), diabetes (yes/no), physical activity during leisure time. Both models had age on the time axis. In the regression model, those 6304 individuals were included that had a complete set of covariates. A crude simulation study was performed to illustrate the effect of exposures that are highly correlated. Briefly, the health outcome (event/not event) was generated for each calendar year, as a function of two exposure variables, representing NO_x and noise with different degree of correlation (details in supplementary material). Data analysis was performed using version 9.4 of the SAS software package (SAS Institute, Cary, NC, USA).

3. Results

Characteristics of the PPS cohort are presented in Table 1, and number of events in each exposure category are presented in tables ST1 and ST2.

The mean exposure to noise was 55 dB in the cohort during the study period, and relatively stable over time (Fig. 1). The mean exposure to NO_x decreased during the study period, both in the cohort (from 53 $\mu g/m^3$ in 1978 to 29 in 2010) and in the entire study area (Gothenburg). The mean exposures in Fig. 1 are based on fewer participants in the ends of the study period since about 80% of the cohort died before 2011. Fig. 2 shows the noise and NO_x levels in Gothenburg as a whole, for the years 1990 and 2011, with the noise showing no apparent change and NO_x having a marked decrease.

The results from this study showed that the incidence of IHD, stroke and cardiovascular mortality tended to be higher for those exposed to residential road traffic noise levels above 60 dB ($L_{Aeq,24h}$) in the last five years, compared to those below 50 dB. Associations were generally not significant though, with hazard ratios of 1.14 (0.96–1.36) for IHD incidence, 1.07 (0.85–1.36) for stroke incidence and 1.08 (95% CI 0.90–1.28) for total cardiovascular mortality, adjusted for NO_x and confounders in Model 1 (Table 2). Hazard ratios for the noise category 50–60 dB were not increased compared to those exposed > 50 dB. For natural mortality and atrial fibrillation there was no increase with increasing noise exposure, and for atrial fibrillation the point estimates were below 1. The results for covariate Model 2 were almost identical to Model 1 for all outcomes, in relation to noise.

For a dichotomization of noise at 57 dB ($L_{Aeq,24h}$), the hazard ratios were lower than in Table 2: 1.04 (95% CI 0.91–1.17) for cvd mortality, 1.07 (95% CI 0.94–1.20) for IHD incidence and 1.005 (95% CI 0.85–1.18) for stroke incidence.

For a shorter exposure window, the average exposure of the current year (lag0), associations with IHD, stroke and cardiovascular mortality were similar to those for the 5-year average exposure but generally weaker (ST4). The correlation between current years' exposure and the 5-year average was very high, 0.97.

For exposure to NO_x the risks tended to be lowest in the lowest exposure quintile, but there was no clear dose-response relationship (the risk of stroke and IHD were highest in the second and fifth exposure quintiles), Tables 2 and 3.

An analysis stratified into before and after 1995 (Table ST3) showed that the associations between residential noise exposure and stroke and

cardiovascular mortality tended to be stronger in the earlier part of the study period (before 1995) compared with the later.

When associations were investigated with road traffic noise and NO_x as continuous exposures, there was a clear but non-significant positive tendency for noise and IHD, and weaker tendencies for noise and stroke and cardiovascular mortality. For AF the point estimate for noise was below 1 (ST5). For NO_x exposure there were essentially null associations with IHD and cardiovascular mortality and a non-significant positive tendency for stroke, AF and total natural mortality (ST5). Without adjustment for NO_x , the associations with noise were stronger, though not significant (ST6).

The correlation between noise exposure and NO_x exposure was rather high, Pearson $r = 0.68$, yearly correlations ranging from 0.62 to 0.71. For IHD and cardiovascular mortality the hazard ratio for noise was only marginally affected by not including NO_x in the model though, while for stroke incidence the hazard ratio was higher without adjusting for NO_x (HR = 1.16) compared to after adjustment (HR = 1.07, Table 3 and ST6). This agrees with general theory and was illustrated with a crude simulation study where the health outcome was assumed to be (positively) associated with both noise and air pollution, and these variables were positively correlated. The results showed that if only one exposure variable was included, its estimated effect would be too high (supplementary figures SF3, SF4).

4. Discussion

In this cohort study of long-term effects of road traffic noise and air pollution, we found a non-significant increased risk of cardiovascular disease for road traffic noise over 60 dB $L_{Aeq,24h}$ at the home address, after adjusting for air pollution (NO_x). The hazard ratios were 1.08 (95% CI 0.90–1.28) for cardiovascular mortality, 1.14 (95% CI 0.96–1.36) for IHD incidence and 1.07 (95% CI 0.85–1.36) for stroke incidence, but there was no positive association between noise and atrial fibrillation.

Studies based on a Danish cohort (50–64 years at recruitment in 1993–1997) showed somewhat stronger and more significant associations than the current study, regarding road traffic noise and myocardial infarction (IRR = 1.12 per 10 dB (Sorensen et al., 2012), and stroke (IRR = 1.19 per 10 dB, (Sorensen et al., 2014), after adjustment for air pollution. A Swedish case-control study showed a non-significant association: OR = 1.12 for noise > 50 dB (95% CI 0.95–1.33) (Selander et al., 2009). An analysis of the GLOBE cohort did not find a significant association between road traffic noise and cardiovascular diseases, however (RR = 1.03 per a p5 to p95 increase, (de Kloizenaar et al., 2013). For atrial fibrillation, results from the Danish cohort showed a weak positive association with noise (IRR = 1.04 per 10 dB (95% CI: 0.96–1.11)), after adjustment for NO_x (Monrad et al., 2016). The WHO

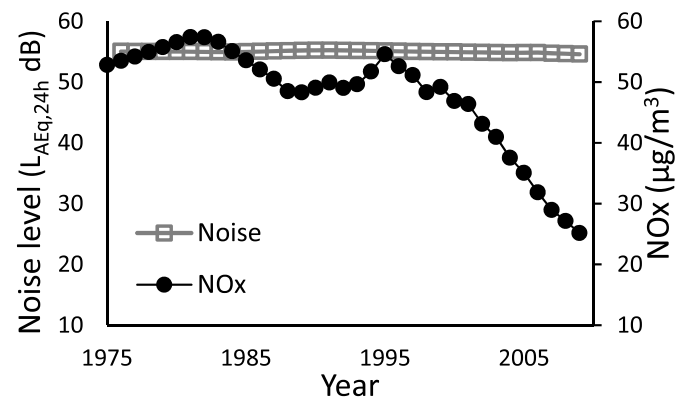


Fig. 1. Time trend for the exposures in the cohort: noise and air pollution (NO_x). Smoothed by 3-point moving average. Only cohort members with both noise and NO_x exposures for the specific year are included.

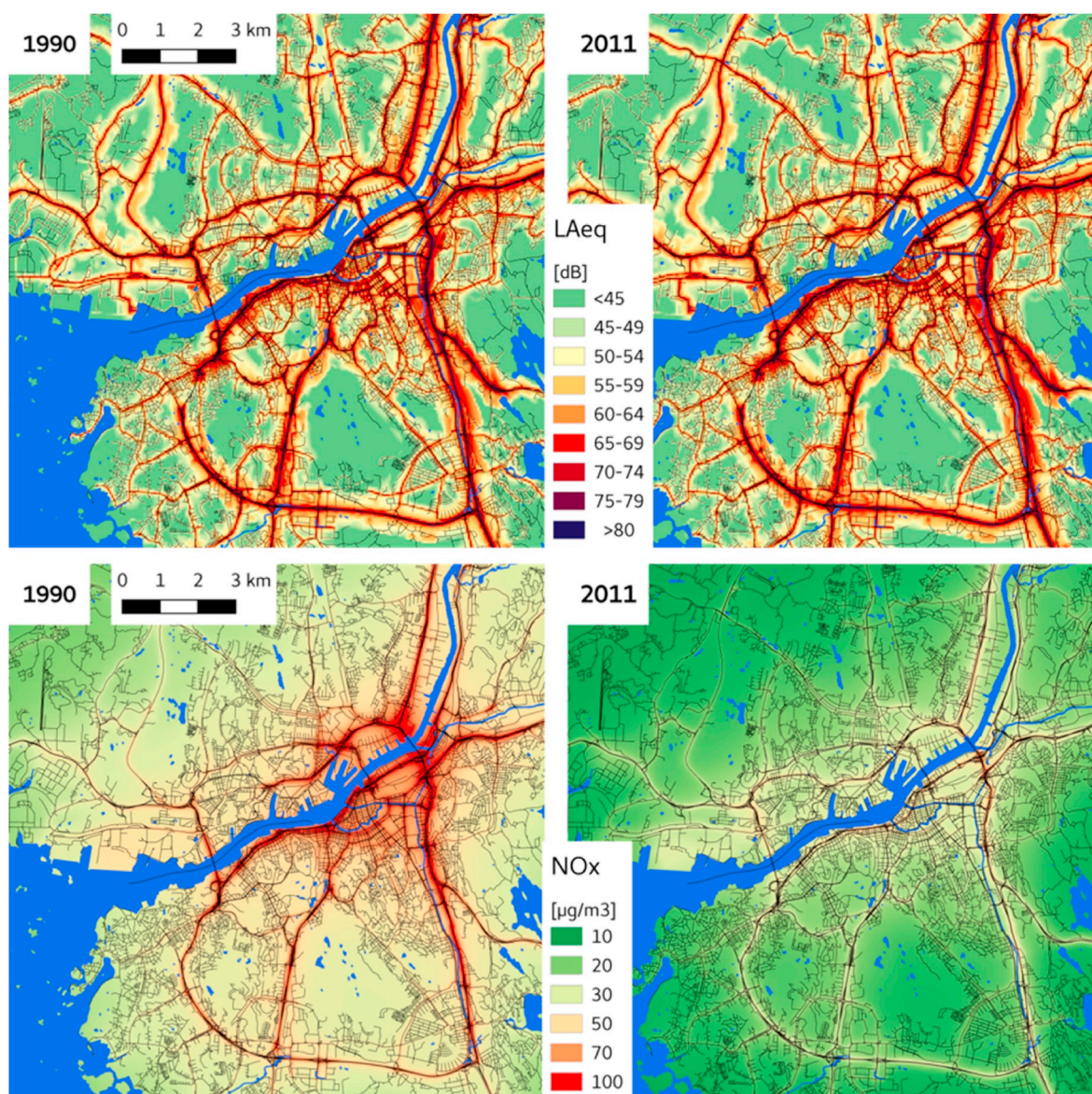


Fig. 2. Noise (top) and NO_x (bottom) levels for the years 1990 and 2011 in the study area Gothenburg, Sweden.

review by [van Kempen et al. \(2018\)](#) combined results from seven longitudinal studies, of which some adjusted for air pollution, and estimated the relative risk of IHD incidence to 1.08 (95% CI: 1.01–1.15) per 10 dB (L_{den}), similar to our results for IHD of HR = 1.06 per 10 dB $L_{Aeq,24h}$ (95% CI 0.97–1.16), after adjustment for air pollution.

The threshold for cardiovascular effects of noise is not yet settled, and may depend on contextual factors such as building insulation. The 2009 WHO Europe guidelines recommended a threshold of 55 dB at night (L_{night}) for protection of cardiovascular risk ([WHO, 2018](#)), and a 2008 review reported no increased risk of myocardial infarction below 57 dB $L_{Aeq,24h}$ (60 dB L_{den}) ([Babisch, 2008](#)). A pooled estimate in a recent meta-analysis indicate a dose-dependent risk increase of IHD starting at 50 dB ([Vienneau et al., 2015](#)), and some have found near linear dose-response relationships also below 50 dB ([Roswall et al., 2017](#); [Sorensen et al., 2012](#); [Sorensen et al., 2014](#)). In this study we found a risk increase for IHD above, but not below, 60 dB. Because of this we also performed an analysis where road traffic noise was dichotomized at 57 dB $L_{Aeq,24h}$, but found weaker hazard ratios than for 60 dB. The statistical power to detect a difference in risk decreases with the exposure contrast, however.

In our study, the Cox regression model included both noise and air

pollution. Traffic is a major source of both road traffic noise and NO_x air pollution, and the correlation in our data was high ($r_{\text{Pearson}} = 0.68$). Generally, including two correlated variables in the model generally leads to larger standard errors and reduced power to detect a true effect. The inclusion of air pollution in the regression model showed similar point estimates of the hazard ratios for cardiovascular mortality (1.07 vs 1.08) and incidence of IHD (1.12 vs 1.14) when air pollution was included. However, for stroke incidence, the hazard ratio was much lower when air pollution was included (1.16 vs 1.07). Stroke incidence was the outcome with the strongest association with air pollution. Because of this we performed a crude simulation study with two correlated exposure variables that both were (positively) associated with the health outcome. In a model that included exposures, the point estimates (of the two HRs) were unbiased, but the standard errors were high. In a model that included only one of the exposure variables (when both variables were associated with the outcome and had a positive correlation with each other), the point estimate of the included exposure variable was too high, but the standard error was low and similar to the situation when the two exposure variables had no correlation with each other. An epidemiological study of cardiovascular health risks of traffic-related noise or air pollution that only includes

Table 2Associations between cardiovascular outcomes and exposure to road traffic noise and NO_x (two-pollutant model, n = 6304).

	Hazard ratio (95% confidence interval in parenthesis)								
	Noise ^a (dB)				NO _x ^a (µg/m ³)				
	< 50	50–55	55–60	60–					
L _{Aeq,24h}	< 53	53–58	58–63	63–	< 36.7	36.7–44.1	44.1–53.3	53.3–64.8	64.8–
Natural mort ^b									
Model 1 ^c	1.00	0.96 (0.87–1.06)	0.92 (0.82–1.03)	1.00 (0.88–1.13)	1.00	1.04 (0.93–1.16)	1.13 (1.01–1.27)	1.02 (0.90–1.16)	1.11 (0.96–1.27)
Model 2 ^d	1.00	1.00 (0.90–1.10)	0.95 (0.85–1.06)	1.00 (0.88–1.13)	1.00	1.00 (0.90–1.12)	1.09 (0.98–1.22)	0.97 (0.86–1.10)	1.06 (0.92–1.22)
CVD mort ^e									
Model 1 ^c	1.00	0.92 (0.80–1.06)	0.93 (0.79–1.09)	1.08 (0.90–1.28)	1.00	1.04 (0.89–1.22)	1.10 (0.94–1.29)	0.98 (0.82–1.17)	1.01 (0.83–1.23)
Model 2 ^d	1.00	0.96 (0.83–1.10)	0.96 (0.82–1.13)	1.08 (0.90–1.28)	1.00	1.00 (0.86–1.18)	1.06 (0.90–1.24)	0.92 (0.78–1.10)	0.96 (0.79–1.17)
IHD inc ^f									
Model 1 ^c	1.00	0.93 (0.80–1.07)	1.00 (0.86–1.17)	1.14 (0.96–1.36)	1.00	1.19 (1.02–1.40)	1.14 (0.97–1.35)	1.09 (0.92–1.29)	1.04 (0.86–1.27)
Model 2 ^d	1.00	0.95 (0.83–1.10)	1.02 (0.88–1.20)	1.14 (0.96–1.35)	1.00	1.17 (0.99–1.37)	1.10 (0.94–1.30)	1.04 (0.87–1.24)	1.01 (0.83–1.23)
Stroke inc ^g									
Model 1 ^c	1.00	0.98 (0.81–1.19)	0.93 (0.75–1.15)	1.08 (0.85–1.36)	1.00	1.17 (0.95–1.44)	1.07 (0.86–1.33)	1.07 (0.85–1.36)	1.24 (0.95–1.60)
Model 2 ^d	1.00	1.001 (0.83–1.21)	0.95 (0.77–1.18)	1.06 (0.84–1.35)	1.00	1.14 (0.93–1.41)	1.06 (0.85–1.31)	1.04 (0.83–1.32)	1.20 (0.93–1.56)
AF ^h									
Model 1 ^c	1.00	0.87 (0.73–1.04)	0.74 (0.60–0.91)	0.86 (0.68–1.07)	1.00	0.95 (0.78–1.16)	1.16 (0.95–1.42)	1.14 (0.92–1.42)	1.13 (0.88–1.46)
Model 2 ^d	1.00	0.89 (0.75–1.06)	0.76 (0.62–0.93)	0.86 (0.69–1.08)	1.00	0.94 (0.77–1.15)	1.15 (0.94–1.40)	1.11 (0.89–1.38)	1.09 (0.84–1.41)

^a For noise, the 5-year average exposure (lag 0–4) is calculated and then categorized. Correspondingly for NO_x.^b Natural (non-accidental) mortality (3182 events, 102 366 person-years).^c Adjusted for calendar year, married/cohabitation, socio economical class, age (on the time axis), apart from noise and NO_x.^d Adjusted for calendar year, married/cohabitation, socio economical class, smoking, BMI, cholesterol, stress, heredity, diabetes, physical activity, age (on the time axis), apart from noise and NO_x.^e Cardiovascular mortality (1569 events, 102 366 person-years).^f Incidence of ischemic heart disease, including deaths (1639 events, 90 650 person-years).^g Incidence of stroke, including deaths (908 events, 97 100 person-years).^h Incidence of atrial fibrillation, including deaths (965 events, 98 183 person-years).

one of the exposures is thus likely to over-estimate the risk of that exposure.

There are several arguments in favor of noise and air pollution

having independent effects on cardiovascular diseases. The review by [Stansfeld \(2015\)](#), based on findings in > 20 epidemiological studies, concluded that the estimated association between traffic noise and

Table 3

Associations between cardio-vascular health outcomes and each exposure (one-pollutant model, n = 6304).

	Hazard ratio (95% confidence interval in parenthesis)				Hazard ratio (95% confidence interval in parenthesis)				
	Noise ^a (dB)				NO _x ^a (µg/m ³)				
	< 50	50–55	55–60	60–					
L _{Aeq,24h}	< 53	53–58	58–63	63–	< 36.7	36.7–44.1	44.1–53.3	53.3–64.8	64.8–
Natural mort ^b									
Model 1 ^c	1.00	0.97 (0.88–1.07)	0.95 (0.85–1.05)	1.04 (0.94–1.15)	1.00	1.03 (0.92–1.15)	1.11 (0.99–1.24)	1.01 (0.90–1.13)	1.12 (0.99–1.25)
Model 2 ^d	1.00	1.00 (0.91–1.11)	0.96 (0.87–1.07)	1.03 (0.93–1.13)	1.00	1.00 (0.89–1.11)	1.08 (0.97–1.20)	0.96 (0.86–1.08)	1.05 (0.94–1.18)
CVD mort ^e									
Model 1 ^c	1.00	0.92 (0.80–1.06)	0.94 (0.81–1.09)	1.07 (0.93–1.23)	1.00	1.04 (0.89–1.21)	1.09 (0.94–1.28)	1.00 (0.85–1.18)	1.09 (0.93–1.28)
Model 2 ^d	1.00	0.96 (0.83–1.10)	0.95 (0.82–1.10)	1.04 (0.90–1.20)	1.00	1.00 (0.86–1.17)	1.06 (0.90–1.23)	0.94 (0.80–1.11)	1.03 (0.87–1.21)
IHD inc ^f									
Model 1 ^c	1.00	0.94 (0.82–1.08)	1.02 (0.88–1.18)	1.12 (0.97–1.29)	1.00	1.20 (1.02–1.40)	1.16 (0.99–1.36)	1.14 (0.97–1.34)	1.17 (1.00–1.38)
Model 2 ^d	1.00	0.96 (0.84–1.10)	1.02 (0.89–1.19)	1.10 (0.96–1.27)	1.00	1.17 (1.00–1.37)	1.12 (0.96–1.32)	1.09 (0.93–1.28)	1.13 (0.96–1.33)
Stroke inc ^g									
Model 1 ^c	1.00	0.99 (0.82–1.20)	0.96 (0.79–1.17)	1.16 (0.97–1.41)	1.00	1.17 (0.95–1.43)	1.06 (0.86–1.31)	1.08 (0.87–1.34)	1.30 (1.06–1.60)
Model 2 ^d	1.00	1.01 (0.84–1.22)	0.97 (0.80–1.19)	1.14 (0.95–1.38)	1.00	1.14 (0.93–1.40)	1.05 (0.85–1.30)	1.05 (0.85–1.30)	1.25 (1.02–1.54)
AF ^h									
Model 1 ^c	1.00	0.90 (0.75–1.07)	0.79 (0.65–0.96)	0.94 (0.78–1.12)	1.00	0.92 (0.76–1.12)	1.08 (0.89–1.31)	1.04 (0.85–1.28)	1.04 (0.84–1.27)
Model 2 ^d	1.00	0.92 (0.77–1.09)	0.80 (0.67–0.97)	0.93 (0.78–1.11)	1.00	0.91 (0.75–1.11)	1.07 (0.89–1.30)	1.02 (0.83–1.24)	1.00 (0.82–1.23)

^a For noise, the 5-year average exposure (lag 0–4) is calculated and then categorized. Correspondingly for NO_x.^b Natural (non-accidental) mortality (3182 events, 102 366 person-years).^c Adjusted for calendar year, married/cohabitation, socio economical class, age (on the time axis), apart from the exposure (noise or NO_x).^d Adjusted for calendar year, married/cohabitation, socio economical class, smoking, BMI, cholesterol, stress, heredity, diabetes, physical activity, age (on the time axis), apart from the exposure (noise or NO_x).^e Cardiovascular mortality (1569 events, 102 366 person-years).^f Incidence of ischemic heart disease, including deaths (1639 events, 90 650 person-years).^g Incidence of stroke, including deaths (908 events, 97 100 person-years).^h Incidence of atrial fibrillation, including deaths (965 events, 98 183 person-years).

cardiovascular outcomes does change only minimally after adjustment for air pollution. Thus, noise and air pollution are likely to have independent effects on the risk of cardiovascular disease. Also an administrative cohort study from Switzerland present results that indicate that the effects of noise and air pollution are additive (Heritier et al., 2019). Another argument for independent effects is that the main biological mechanisms regarding noise exposure and air pollution as risk factors for cardiovascular disease are different: For noise exposure the main mechanism is likely to be psychological stress and/or sleep disturbance. For air pollution, a major hypothesis is low-grade local and systemic inflammation, which is well known to be a cardiovascular risk factor (Brook et al., 2010). Mechanisms may, however, also overlap. Psychological stress may cause increase in blood pressure and sleep disturbances may cause metabolic changes and inflammation (Spiegel et al., 2009; Miller and Cappuccio, 2007).

We have presented results from two different statistical models; Model 1 was based on a DAG and Model 2 on previous knowledge from the literature. Mean income in the residential area 1994 was not included in Model 2 since it had many missing values and it did not change the hazard ratios for noise much. Blood pressure was not included in Model 2 since it was considered a mediator between noise exposure and cardiovascular events. For the associations between noise and cardiovascular outcomes, Model 1 and 2 resulted in similar point estimates and confidence intervals of similar widths. For the associations with NO_x , Model 2 tended to result in lower hazard ratios. One explanation might be that one or several of the explanatory variables could be a mediator. However, the decrease was minor and the variables that decreased the estimate were smoking and physical activity, which are not likely to be mediators on the path from NO_x to cardiovascular disease.

The effect of different noise exposure windows on cardiovascular diseases was investigated, but the differences only minor. The associations with cardiovascular outcomes were similar for 5-year average noise and 1-year average (HR:s 1.14 and 1.12, respectively, for IHD incidence, and 1.07 and 1.04 for stroke, for over 60 dB vs below 50 dB). Previous studies using data from the Danish Diet, Cancer and Health cohort to study exposure time window for myocardial infarction (Roswall et al., 2017; Sorensen et al., 2012) and stroke (Sorensen et al., 2014), found that for myocardial infarction the association with road traffic noise (L_{den}) was similar for the 1-year, 5-year and 10-year average (IRR:s around 1.10 per 10 dB). For stroke the association was slightly stronger for the 1- and 5-year averages (IRR around 1.20 per 10 dB), compared to the 10-year average IRR = 1.16 (95% CI 1.06–1.28).

The trend for noise exposure among the cohort members is different to the overall noise trend in Gothenburg: in the cohort there is practically no change, whereas in Gothenburg as a whole, the noise levels have increased approximately 2 dB between 1975 and 2011 (Ögren and Barregard, 2016). The overall increase in Gothenburg is mostly due to urbanization and the tendency to build new residences in exposed areas. NO_x exposure in the cohort has decreased by over 50% between 1995 and 2011, which is similar to the overall trend in Gothenburg and Sweden (Swedish Environmental Protection Agency, 2019). This decrease is due to several factors, among them the EU road vehicle emission regulation standards, increased use of district heating and the introduction of the NO_x -fee in 1992 for the manufacturing industries, construction and energy industries sectors (Swedish Environmental Protection Agency, 2019).

In a stratified analysis, we compared the periods before and after 1995. There was a stronger association between residential noise exposure and stroke and cardiovascular mortality for the period before 1995. One explanation for this may be the change in indoor noise exposure over the period, not included in our noise calculations since they are calculated outdoors at the most exposed façade of the dwelling. New buildings tend to have better façade insulation and better windows in terms of sound insulation (Rasmussen and Machimbarrena, 2014).

Older buildings might also have received new windows with better sound insulation, both as a consequence of deliberate noise reduction policies, and due to other renovations where windows have been replaced or renovated.

A strength of this study is that individual exposure to road traffic noise and air pollution is available for every year during the study period. Also, the noise calculations are based on the official calculation method for noise prediction in Sweden: the Nordic method. The method states that the standard deviation for the difference between measurements and predictions is 3 dB up to 300 m distance between source and receiver, however for simple cases and short ranges the accuracy is better, typically within 1 dB. The simplifications introduced in our calculations for dense urban areas with multiple sound paths between source and receiver will have some impact on validity. In Ögren and Barregard (2016) a comparison between the simplified method and a full calculation showed an average overestimation of the noise level of 0.5 dB.

Another strength is that the health outcomes are from national Swedish registers, which have a very good coverage and high validity (Hammar et al., 2001). Using the unique personal identity number, Swedish inhabitants can be traced wherever they move within Sweden. Therefore the residential addresses and the cardiovascular outcome data should have a low rate of misclassification. We chose to use NO_x exposure as the air pollution exposure in this study, which can be considered both a strength and a limitation. The cardiovascular health effects of air pollution have been most consistently associated with particle matter, especially fine particles < 2.5 μm ($\text{PM}_{2.5}$). NO_x , however, is a good proxy for traffic-related air pollution (Beckerman et al., 2008; Kwasny et al., 2010; Johansson et al., 2007), and has thus been suggested as a relevant indicator for air pollution in studies of noise exposure (Stansfeld, 2015). We could also model and assign NO_x exposure as far back as 1975, giving us a study period of more than three decades.

The two exposures in this study (noise and air pollution) were modelled at the home address, for every year that the individual was included in the study. To estimate the yearly NO_x levels for each person, different models were used for the early and later part of the study period (1975–1990 and 1990–2011). Both models have been validated against official monitoring stations, and perform well within the prescribed uncertainty limits. The early period used a climatological model while the later period used actual weather for the dispersion model, and was considered more reliable. We thus adjusted the concentrations for the years 1975–1990 to fit the concentrations of the later model (Segerström et al., 2017).

Another limitation of this study is that our cohort consists only of men, but the biological mechanisms for associations between noise and cardiovascular disease are not likely to be sex-specific. Results from a Danish cohort study indicated some effect modification of gender regarding noise and MI, IRR = (1.14, 1.06) for men and women respectively, but the p-value for interaction was 0.37 (Sorensen et al., 2012). There is always the risk that the results can be confounded by unmeasured variables that are associated with both outcome and exposure.

In conclusion, this cohort study found support for cardiovascular health effects of long-term exposure to road traffic noise in Sweden above current guidelines, only marginally affected by co-exposure to air pollution. The number of people exposed to residential road traffic noise above current guidelines is vast, over 1,6 million out of Sweden's 10 million inhabitants above 55 dB $L_{Aeq,24h}$ (Swedish Environmental Protection Agency/SWECO, 2014), and 100 million Europeans above 55 dB L_{den} (EEA, 2018). The evidence of negative health effects of noise exposure has also grown stronger, especially for IHD (van Kempen et al., 2018), and WHO Europe has consequently suggested stricter noise guidelines (WHO, 2018). Swedish authorities have, however, instead recently relaxed noise guidelines allowing for construction of residential buildings at higher noise levels than previously (Förordning

om trafikbuller vid bostadsbyggnader, 2017), which will probably lead to increasing population exposure to traffic-related noise and air pollution. Solid scientific estimates of health effects of road traffic noise in Sweden is thus important for health risk assessments, urban planning, policies and public health in Sweden.

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CRediT authorship contribution statement

Eva M. Andersson: Methodology, Software, Formal analysis, Writing - original draft, Writing - review & editing. **Mikael Ögren:** Methodology, Software, Writing - review & editing. **Peter Molnár:** Methodology, Software, Writing - review & editing. **David Segersson:** Resources, Writing - review & editing. **Annika Rosengren:** Resources, Writing - review & editing. **Leo Stockfelt:** Conceptualization, Supervision, Writing - original draft, Writing - review & editing, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2020.109446>.

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