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Transportation noise exposure and cardiovascular mortality: 15-years of follow-up in a nationwide prospective cohort in Switzerland

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ABSTRACT

Background: Death from cardiovascular diseases (CVD) has been associated with transportation noise. This nationwide cohort, with state-of-the-art exposure assessment, evaluates these associations by noise source.
Methods: Road traffic, railway and aircraft noise for 2001 and 2011 were linked to 4.1 million adults in the Swiss National Cohort, accounting for address history. Mean noise exposure in 5-year periods was calculated. Time-varying Cox regression models, with age as timescale, were applied to all and cause-specific cardiovascular causes of death. Models included all three noise sources plus $PM_{2.5}$, adjusted for individual and spatial covariates. Nighttime noise events for all sources combined (expressed as intermittency ratio or number of events) were considered in sensitivity analyses. Absolute excess risk was calculated by multiplying deaths/100,000 person-years by the excess risk (hazard ratio-1) within each age/sex group.
Results: During a 15-year follow-up, there were 277,506 CVD and 34,200 myocardial infarction (MI) deaths. Associations (hazard ratio; 95%-CIs) for road traffic, railway and aircraft noise and CVD mortality were 1.029 (1.024–1.034), 1.013 (1.010–1.017), and 1.003 (0.996–1.010) per 10 dB L_{den}, respectively. Associations for MI mortality were a respective 1.043 (1.029–1.058), 1.020 (1.010–1.030) and 1.040 (1.020–1.060) per 10 dB L_{den}. Blood pressure-related, ischemic heart disease, and all stroke mortality were significantly associated with road traffic and railway noise, while ischemic stroke mortality was associated with aircraft noise. Associations were mostly linear, often starting below 40 dB L_{den} for road traffic and railway noise. Higher levels of noise intermittency were also independently associated with each outcome. While the absolute number of deaths attributed to noise increased with age, the hazard ratios declined with age. Relative and absolute risk was higher in males compared to females.
Conclusion: Independent of air pollution, transportation noise exposure is associated with all and cause-specific CVD mortality, with effects starting below current guideline limits.

1. Introduction

Exposure to transportation noise is an important and widespread environmental risk factor, ranking second after air pollution and impacting the health and wellbeing of large numbers of individuals in Europe (Hanninen et al. 2014). In Switzerland, the total external costs of burden due to transportation noise (2.8 billion CHF per year) was found to be somewhat lower than that of traffic related air pollution (4.2 billion CHF) when considering quality of life (Vienneau et al., 2015a, updated for 2018 in ARE, 2021). In a growing number of epidemiological studies, noise from road traffic, railways and aircraft has been shown to be associated with cardiovascular disease (CVD) morbidity and

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mortality amongst other diseases. The WHO Environmental Noise Guidelines Group for Europe rated the evidence for a relationship between ischemic heart disease (IHD) and road traffic to be of high quality, but emphasized that for other noise sources and cardiovascular diseases data from large cohort studies were limited for rating the quality of evidence. Studies published between January 2000 and August 2015 were included, with a reported increased relative risks (RR) for IHD incidence and both road traffic noise (1.08 [95% confidence interval (CI): 1.01–1.15] per 10 dB L_{den}) and aircraft noise (1.09 [1.04 – 1.15] per 10 dB L_{den}) after *meta*-analysis. The RR for mortality were indicative of an association, albeit weaker. No studies on railway noise and IHD incidence were available (van Kamp et al., 2020; van Kempen et al., 2018; WHO, 2018b).

Recent studies showing associations between transportation noise and cardiovascular health not included in the WHO Guidelines include studies from: Germany on various causes of CVD incidence (Seidler et al., 2016a; Seidler et al., 2016b); Toronto on ischemic heart disease and heart failure (Bai et al., 2020) and blood pressure (Shin et al., 2020); Denmark on blood pressure drug prescriptions (Thacher et al., 2020b), and all-cause and CVD mortality (Thacher et al., 2020a); Sweden on CVD mortality (Andersson et al., 2020); and from Switzerland on various causes of CVD mortality using data of the nationwide Swiss National Cohort (SNC) from 2000 to 2008 (Héritier et al., 2017). Nevertheless, the evidence base for quantifying the associations between transportation noise exposure and various CVD outcomes remains thin, in particular for railway noise despite high biological plausibility for a link.

The nationwide SNC offers the opportunity to study the effects of transportation noise from all three of the major sources – road traffic, railway and aircraft – on mortality in Switzerland. Following a recent update, the SNC now provides 15 years of follow-up enhancing the database for ongoing longitudinal research needed to increase the current level of evidence for all transportation noise sources. With address history and high quality noise exposure data available at multiple time points and for various noise metrics such as L_{den}, number of events or intermittency ratio, the ability to reduce exposure misclassification has also been strengthened. Applying a time-varying approach to account for long-term variation in noise exposure, mortality rates and individual covariates is also important, given that various physiological response mechanisms including direct (auditory) sleep disturbances and indirect (non-auditory) stress pathways (Babisch, 2002; Münzel et al., 2021; Munzel et al., 2016) may act on a broad range of induction time periods. Thus the specific aims of this study were to investigate the independent cardiovascular mortality effects of noise from different transportation sources in adults in a nationwide analysis taking account of time trends. To deepen our understanding, we further examined the shape of these exposure–response associations (in mutually adjusted models), and conducted several explorative analyses including potential effect modification by age and sex, adjustment for different air pollutants, and the evaluation of different noise exposure metrics.

2. Methods

2.1. Study population

The Swiss National Cohort (SNC) is a longitudinal research platform, linking the former national decennial census and, since 2010, the annual Registry Based Census and structural surveys with the births, mortality and emigration registries (Bopp et al., 2009; Spoerri et al., 2010). Prior to 2010 the data were probabilistically linked, while since 2010 a deterministic linkage based on personal-identifier is used. Compulsory census participation ensures that practically all residents in Switzerland at the time of the census are represented, i.e. 98.6% in the 04 December 2000 census (Renaud, 2004). The SNC was approved by the Ethics Committees of the Cantons of Zurich and Bern.

The present 15-year analysis was based on SNC data from 01 January 2001 to 31 December 2015. In total, 7.28 million observations were available at baseline. Analysis was based on 4.1 million observations after excluding those: with a mismatch between the probabilistic and deterministic SNC linkage (8.2% of original sample); below 30 years of age (33.4%); missing residential coordinates or designated as living in an institution (4.8%); missing covariates – specifically education and socio-economic position (2.2%); or missing exposure data (0.2%) (Supplement Table S1).

In this closed cohort, the follow-up was divided equally into three periods to support time-varying analysis and evaluate potential time trends by incorporating calendar time (Canchola et al. 2003). These three 5-year periods were also used as virtual sub-cohorts defined as: sub-cohort1 (2001–2005; adults 30+ years old), sub-cohort2 (2006–2010; 35+ years old) and sub-cohort3 (2011–2015; 40+ years old).

The main outcomes under investigation were definitive primary causes of death from all cardiovascular diseases (CVD) (ICD-10: I00-I99), blood pressure-related (BP) (ICD-10: I10-I15), ischemic heart disease (IHD) (ICD-10: I20-I25), myocardial infarction (MI) (ICD-10: I21-I22), heart failure (HF) (ICD-10: I50), all stroke (ICD-10: I60-I64), hemorrhagic stroke (HS) (ICD-10: I60-I62), and ischemic stroke (IS) (ICD-10: I63). All indications of death from these causes, including as the definitive primary cause, concomitant disease, consecutive disease, or initial disease were also investigated.

2.2. Noise exposure data

Noise exposure data was developed in the framework of the SiRENE project (Short and Long Term Effects of Transportation Noise Exposure) (Karipidis et al., 2014; Röösli et al., 2019). It includes a Swiss-wide noise exposure database for 2001 and 2011 for the three major transportation noise sources (road traffic, railway and aircraft). Briefly, road traffic noise emissions and propagation were respectively calculated using sonROAD (Heutschi, 2004) and StL-86 (OFPE, 1987). For railway noise, emissions were calculated using sonRAIL (Thron and Hecht, 2010) and propagation was calculated using SEMIBEL (OFE, 1990). Aircraft noise, calculated with the aircraft noise model FLULA2 (Empa, 2010; Pietrzko and Hofmann, 1988), was included for the three civils airports (Zürich, Geneva and Basel), and a military airfield located in Payerne. For civil airports, aircraft noise exposure was calculated on a yearly basis using air traffic data along with acoustic footprints based on radar data per aircraft type and route. Exposure for the military airport was derived from idealized flight paths, number of flights and approximate operation times.

Exposure was defined as the L_{den} (i.e. weighted logarithmic mean of $L_{eq,day}$, $L_{eq,evening}$ and $L_{eq,night}$ with a respective penalty of 5 dB and 10 dB for evening and night) for each noise source. As an additional noise metric to assess the temporal structure of sound, the intermittency ratio (IR) (Wunderli et al., 2016) was calculated on an hourly basis. IR takes values in the range 0% to 100%, where 0% IR means single events cannot be perceived above background noise and 100% IR means all noise energy is produced by "individual" noise events. As in our previous SNC analysis, IR at night (23:00 to 7:00 h) from all transportation sources combined was used (Héritier et al., 2017). Separately, the number of noise events at night from all transportation sources combined was available; events were defined as vehicle pass-bys that acoustically stand out from the background noise by 3 dB L_{eq}. Noise exposure (L_{den}, dB) at the maximum exposed façade for each dwelling was assigned to participants based on residential geocode and floor of residence. The IR and number of events from the corresponding façade point were also assigned. If information on floor of residence was not available, the noise estimates from the middle floor of the building were substituted (Héritier et al., 2017; Vienneau et al., 2019). L_{den} exposure variables below 35 dB (road traffic noise) or 30 dB (railway and aircraft noise) were censored at the corresponding thresholds, i.e., set to 35 and 30 dB, respectively. This censoring accounts for background noise from diffuse sources in the lowest exposure range (Vienneau et al., 2019).

2.3. Noise exposure assignment

Exposure was assigned at the start of each 5-year period represented by virtual sub-cohorts: 2001 (sub-cohort1), 2006 (sub-cohort2) and 2011 (sub-cohort3). Both the residential geocodes and noise data were available for 2001 and 2011. This temporal alignment allowed direct assignment of exposure to the participant location at sub-cohort1 and 3.

The noise exposure for sub-cohort2 was reconstructed using available information in the census about moving history (moving date and the 2010 census question "living in the same community 5 years before"). The 2001 noise data were assigned to non-movers and to those who moved after 2006. Those who moved before 2006 were assigned the 2011 noise data (16.5%).

2.4. Covariates

Individual-level covariates included sex (female/male), civil status (single, married, widowed, divorced), education level (compulsory education or less, upper secondary level education, tertiary level education), mother tongue (German and Rhaeto-Romansch, French, Italian, other language), nationality (Swiss, non-Swiss) and local index of socioeconomic position (SEP in quartiles; the index is calculated for a small local area of 50 nearest neighbours) (Panczak et al., 2012). Area-level SEP and unemployment rate variables were also computed at community (n = 2896 in 2001, n = 2585 in 2011) and region (n = 26) level to provide broader area context not captured by the local-SEP. All covariates were available at the baseline in 2001. Civil status, nationality, local-SEP, area-SEP and unemployment rate were also recorded in the SNC at 2011, thus updated for sub-cohort3; otherwise the baseline values were retained.

Annual average ambient $PM_{2.5}$ and NO_2 concentrations ($\mu g/m^3$) were available from European 100x100 m hybrid land use regression models for year 2010 (de Hoogh et al., 2018). Though both pollutants were considered separately, $PM_{2.5}$ was selected *a priori* as the more general marker of air pollution (i.e. deriving from both traffic and non-traffic sources) for adjustment in main model.

2.5. Statistical analysis

The multipollutant associations between mortality and transportation noise (all three sources) were analysed using the extended Cox proportional hazards model, stratified by sex, with age as the underlying time scale. The time-varying model accounts for residential history, along with time trends in noise exposure and mortality during follow-up. Participants were followed until emigration, death or end of follow-up, which ever came first. Hazard ratios (HR) and 95% confidence intervals were computed using linear terms, reported per 10 dB increment, for each noise source (L_{den} road, L_{den} rail, L_{den} air). Including all three noise sources in a single model was used given that a proportion of individuals were exposed to multiple sources; it enabled identifying the mutually independent association of any single source (Héritier et al., 2017). The shape of the exposure response was evaluated using natural splines with 3 degrees of freedom.

Different adjustment models were applied: Model 0 included the three noise L_{den} variables, age as time scale, and strata sex and period (i.e. 2001–2005, 2006–2010, or 2011–2015). Model 1 further included the individual-level covariates civil status, education level, mother tongue, nationality and quintiles of local-SEP. Model 2 additionally included the area-SEP and unemployment rate. Model 3, the main model, included additional adjustment for air pollution in quartiles (Model 3 for $PM_{2.5}$, Model 3b for NO_2 as a sensitivity analysis). Finally, Model 4 additionally adjusted for quintiles of noise eventfulness at night from all sources combined – either in Model 4.1 using the intermittency ratio (IR) or Model 4.2 as the number of events. Multicollinearlity between exposure variables was evaluated *post hoc* using variance inflation factor (VIF < 5) (Héritier et al., 2018; Vienneau et al., 2013).

The main analyses were conducted for both sexes and all ages combined, for the full cohort. Stratification was used to separately derive hazard ratios for males and females, three age groups (30–65, 65–80 and over 80 years), and for each of the three virtual sub-cohort periods. Finally, based on the main models the absolute excess risk was calculated from the same population, multiplying the deaths/100,000 person-years (PY) by the excess risk (HR-1) within each age/sex group. Analyses were conducted in Stata 16, while plots and splines were developed in R v4.0.

3. Results

3.1. Study population

A total of 4,136,220 adults, 30 years of age and older and residing in Switzerland on 01 January 2001 met the inclusion criteria. Individuals were followed until 31 December 2015 (56 million person-years with a mean follow-up of 13.4 years). The population included slightly more woman than men (52.2% vs. 47.8%). The majority were Swiss nationals (83.2%), had German or Rhaeto-Romansch as their mother tongue (65.5%), had more than compulsory education (75.3%), and were married (69.9%) (Table 1). During the full follow-up, 277,506 (35.9%)

Table 1
Population characteristics.

Characteristic	2001 (baseline)	2006	2011
Number of participants	4,136,220	3,856,752	3,568,666
Male (%)	47.8	47.3	47.1
Age (%)			
30–64	76.5	79.6	83.4
65–79	18.3	17.2	15.1
80+	5.2	3.3	1.5
Mother tongue (%)			
German and Rhaeto-Romansch	65.5	65.9	66.0
French	19.3	19.3	19.2
Italian	7.4	7.3	7.2
Other	7.8	7.6	7.7
Education (%)			
Compulsory education or less	24.7	23.4	22.0
Upper secondary level	53.0	53.8	54.5
Tertiary level education	22.3	22.8	23.5
Marital status (%) [a]			
Single	13.4	13.6	10.8
Married	69.9	70.8	64.5
Divorced	8.5	8.6	14.2
Widowed	8.2	7.0	10.5
Swiss nationality (%) [a]	83.2	83.7	86.9
Local-SEP (%), mean (SD) [a,b]	63.3 (10.5)	63.4 (10.5)	58.6 (12.3)
Area-SEP community (%), mean (SD) [a]	62.9 (6.7)	62.9 (6.7)	58.2 (8.8)
Area-SEP community-region (%), mean (SD) [a]	0.1 (5.2)	0.1 (5.2)	0.1 (7.1)
Area unemployment community (%), mean (SD) [a]	3.5 (1.4)	3.5 (1.4)	2.5 (1.0)
Area unemployment community-region(%), mean (SD) [a]	0.0 (1.2)	0.0 (1.2)	0.0 (0.9)
Road traffic noise, Lden (dB), mean (SD) [a]	54.3 (8.2)	54.1 (8.1)	54.3 (8.1)
Railway noise Lden (dB), mean (SD) [a]	38.4 (11.0)	38.0 (10.8)	36.6 (9.7)
Aircraft noise Lden (dB), mean (SD) [a]	34.5 (7.7)	34.5 (7.6)	34.5 (6.9)
Total noise Intermittency Ratio (IR) at night (%) [a]	69.7 (20.9)	69.3 (21.0)	67.3 (21.2)
Total noise events at night (count), mean (SD) [a]	171.1 (188.7)	170.0 (190.4)	181.2 (214.2)
$PM_{2.5}$ concentration ($\mu g/m^3$), mean (SD)	15.9 (2.4)	15.9 (2.4)	15.9 (2.4)
NO_2 concentration ($\mu g/m^3$), mean (SD)	23.6 (7.4)	23.6 (7.4)	23.5 (7.3)

a. census/exposure data available at multiple time points, thus updated at 2011.
b. Quartiles of local-socioeconomic position (SEP) used in models.

deaths occurred from all CVD causes of which 39.5%, 14.6% and 11.5% were from IHD, stroke and BP-related diseases (Supplement Table S2).

The mean exposure to transportation noise was similar across sub-cohorts (Table 1). For each noise metric, the Pearson correlations between years were moderate to high, especially between sub-cohort 1 and 2 where, for most individuals, the same 2001 noise model had been used and differences were solely due to moving before 2005. The highest correlations were for aircraft L_{den} (r = 0.83–0.96) followed by railway and road traffic noise (r = 0.67–0.89), then IR and noise events at night (r = 0.56–0.85). The correlation between $PM_{2.5}$ and NO_2 was high (r = 0.70) and both were somewhat correlated with aircraft noise (r = 0.33–0.40). $PM_{2.5}$, the *a priori* selected air pollutant for adjustment in main models, was little correlated to the other noise metrics across all years (r < |0.23|) (Supplement Figure S1). A respective 1.4, 46.1 and 67.6% of values were censored for road traffic, railway and aircraft noise.

3.2. Main findings

In the full cohort, road traffic and railway noise were associated with an increased risk of mortality for all CVD, BP-related, IHD, MI and stroke in each of Models 1 to 3 with increasing confounder adjustment (Table 2). In general, associations slightly strengthened after including area-SEP in Model 2, and remained steady after adjusting for $PM_{2.5}$ in the main Model 3 with HRs of 1.01 to 1.04 per 10 dB for different causes. An increased risk for heart failure (1.019 [1.002–1.036]) and ischemic stroke (1.042 [1.011–1.074]) in relation to road traffic per 10 dB was also found in Model 3 (Table 2). For aircraft noise, most associations in Model 3 were null except for MI (1.040 [1.020–1.060] per 10 dB) and ischemic stroke (1.065 [1.021–1.111] per 10 dB). Also, compared to other noise sources, aircraft noise was more sensitive to adjustment for area-SEP, yielding higher HR in Model 2 than Model 1 (which included the individual-level confounders but not area-SEP).

Including all indications of death (i.e. primary plus concomitant, consecutive, or initial disease) notably increased the number of BP-related and heart failure deaths by 14 and 3.5 times, respectively. Nevertheless, in the fully adjusted models the association between noise and BP-related mortality including all deaths remained similar compared to the main findings, while for heart failure mortality the associations were stronger and significant for all three noise sources (Table S3 vs. Table 2). The additional cases also strengthened the association for ischemic stroke mortality and aircraft noise (Table S3).

3.3. Shape of the exposure response

Natural splines, based on Model 3, indicated no deviation from linear associations for CVD and MI mortality starting from below 40 dB, and often nearer to the censored values (i.e. 35 dB for road traffic, 30 dB for railway noise) (Fig. 1; other outcomes shown in Supplement Figure S2). BP-related mortality followed a similar pattern for road traffic and railway noise. The association for IHD mortality and railway noise also increased linearly from below 40 dB, however the increased risk for road traffic did not begin until noise levels around the guideline limit of 52 dB. Similarly, the slightly increased risk for road traffic and HF mortality was only in the higher exposure range above 50 dB. Overall, the linear association was most consistent across noise sources for MI, which also showed a near linear increased risk for aircraft noise from below 35 dB. For aircraft noise, exposure–response associations were non-linear with the risk increase in the higher noise range above the 45 dB guideline limit (CVD, IHD, HF, stroke), or in the range below (BP-related, ischemic stroke).

3.4. Sensitivity analyses

For all outcomes, adjusting for NO_2 instead of $PM_{2.5}$ (Model 3b vs. Model 3) did not materially change the associations. Also, additionally

Table 2
Hazard Ratios (HR) and 95% confidence intervals (CI) per 10 dB increase in Lden noise for cardiovascular causes of death, full cohort 2001–2015.

Outcome	N cases	Model 1			Model 2			Model 3		
		Road	Rail	Air	Road	Rail	Air	Road	Rail	Air
CVD	277,506	**1.022** (1.017–1.027)	**1.013** (1.009–1.016)	0.980 (0.974–0.985)	**1.029** (1.024–1.034)	**1.014** (1.010–1.017)	1.001 (0.995–1.008)	**1.029** (1.024–1.034)	**1.013** (1.010–1.017)	1.003 (0.996–1.010)
BP-related	31,812	**1.021** (1.007–1.035)	**1.013** (1.003–1.024)	0.975 (0.959–0.991)	**1.037** (1.023–1.052)	**1.017** (1.006–1.028)	**1.020** (1.000–1.041)	**1.035** (1.020–1.049)	**1.016** (1.006–1.027)	1.019 (0.998–1.040)
IHD	109,570	**1.030** (1.022–1.038)	**1.023** (1.017–1.029)	0.991 (0.982–0.999)	**1.035** (1.028–1.043)	**1.022** (1.016–1.028)	0.999 (0.988–1.009)	**1.034** (1.027–1.042)	**1.021** (1.015–1.027)	1.002 (0.991–1.014)
MI	34,200	**1.042** (1.029–1.057)	**1.020** (1.010–1.030)	**1.024** (1.009–1.040)	**1.046** (1.032–1.060)	**1.021** (1.011–1.032)	**1.042** (1.023–1.061)	**1.043** (1.029–1.058)	**1.020** (1.010–1.030)	**1.040** (1.020–1.060)
HF	23,134	0.992 (0.976–1.008)	0.986 (0.974–0.998)	0.942 (0.924–0.961)	1.013 (0.996–1.030)	1.002 (0.990–1.015)	1.011 (0.987–1.034)	**1.019** (1.002–1.036)	1.005 (0.992–1.018)	1.012 (0.988–1.037)
Stroke	40,518	**1.014** (1.002–1.027)	**1.012** (1.003–1.022)	0.996 (0.982–1.010)	**1.016** (1.004–1.029)	**1.011** (1.001–1.020)	1.012 (0.995–1.030)	**1.015** (1.002–1.028)	**1.010** (1.001–1.019)	1.010 (0.992–1.029)
HS	9871	1.021 (0.996–1.047)	1.018 (0.999–1.037)	1.018 (0.990–1.047)	1.014 (0.989–1.040)	**1.019** (1.000–1.038)	1.011 (0.977–1.046)	1.014 (0.989–1.041)	1.019 (0.999–1.038)	1.010 (0.975–1.047)
IS	7052	**1.045** (1.015–1.076)	1.020 (0.997–1.043)	1.033 (0.999–1.068)	**1.045** (1.014–1.077)	1.014 (0.992–1.038)	**1.061** (1.018–1.105)	**1.042** (1.011–1.074)	1.013 (0.990–1.036)	**1.065** (1.021–1.111)

Notes: CVD = all cardiovascular diseases, BP = blood pressure related, IHD = ischemic heart disease, MI = myocardial infarction. HF = heart failure, HS = haemorrhagic stroke, IS = ischemic stroke.
Models were incrementally adjusted: Model 1 included noise exposure (road traffic, railway and aircraft noise; Lden), strata sex and period (i.e. 2001–2005, 2006–2010, or 2011–2015), plus the individual-level covariates civil status, education level, mother tongue, nationality and quintiles of local-SEP; Model 2 additionally included community and regional SEP score and unemployment; the main Model 3 additionally included PM2.5 exposure.

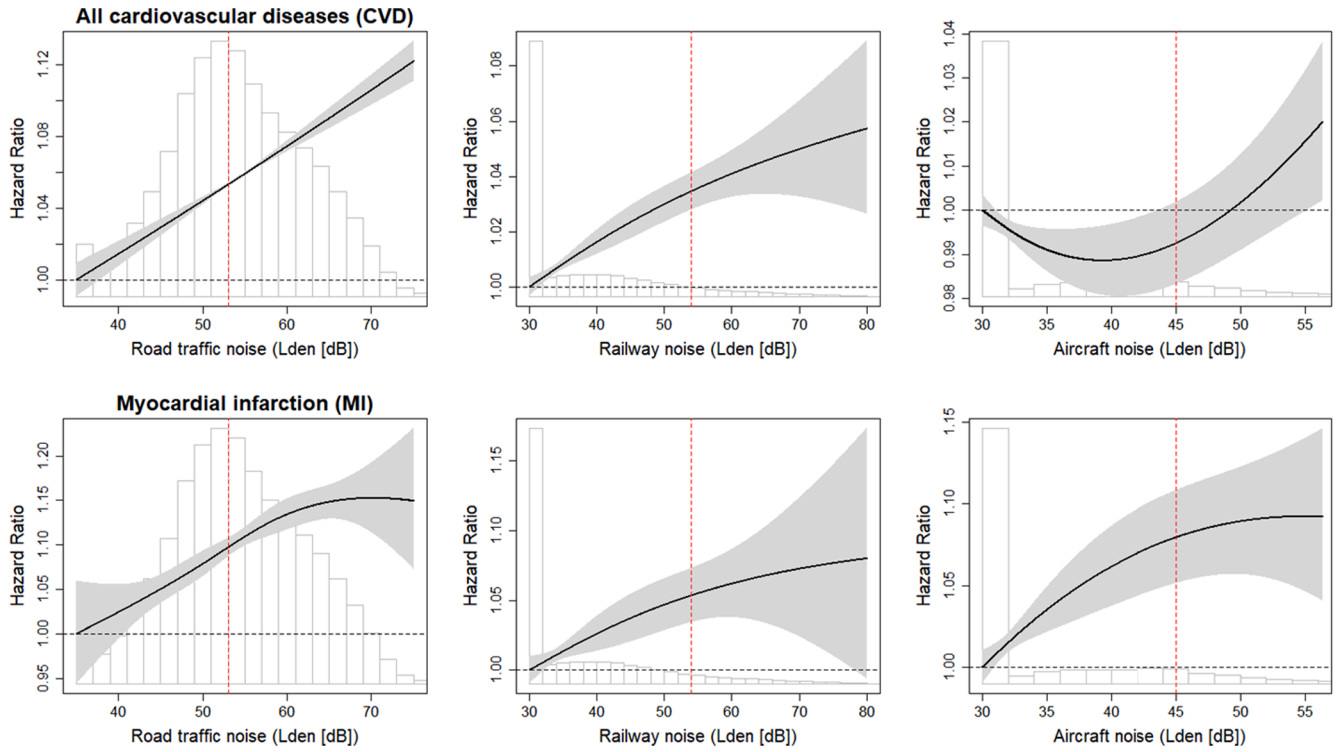

Fig. 1. Natural splines (3 df) for the association between road traffic, railway or aircraft noise and all CVD and MI mortality. Multipollutant models, adjusting for the other two noise sources. Model 3: Included strata sex and period, and adjusted for mother tongue, nationality, civil status, education, local-SEP, area-SEP and unemployment, and $PM_{2.5}$. Vertical red lines show WHO guideline levels based on Lden: road traffic = 53 dB, railway = 54 dB, aircraft = 45 dB. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
Effect modification by sex or age. Relative risk (%) and 95% confidence intervals (CI) per 10 dB increase in Lden road traffic, railway and aircraft noise, full cohort 2001–2015.

Outcome	Source	Sex			Age*			
		Male	Female	p-interaction	30–64	65–79	80+	p-trend
CVD	Road	**1.049 (1.042–1.057)**	**1.011 (1.004–1.018)**	<0.0001	**1.086 (1.073–1.099)**	**1.027 (1.020–1.034)**	**1.008 (1.000–1.016)**	<0.0001
	Rail	**1.018 (1.012–1.023)**	**1.009 (1.004–1.014)**	0.029	**1.024 (1.015–1.033)**	**1.017 (1.011–1.022)**	1.004 (0.998–1.010)	0.0001
	Air	0.999 (0.989–1.009)	1.007 (0.997–1.017)	0.256	**1.018 (1.001–1.035)**	1.004 (0.994–1.014)	0.995 (0.983–1.007)	0.031
BP-related	Road	**1.058 (1.033–1.083)**	**1.022 (1.004–1.040)**	0.022	**1.047 (1.002–1.095)**	**1.035 (1.014–1.056)**	**1.031 (1.008–1.054)**	0.564
	Rail	**1.025 (1.007–1.044)**	1.012 (0.999–1.025)	0.260	**1.036 (1.002–1.071)**	**1.019 (1.004–1.035)**	1.008 (0.992–1.025)	0.133
	Air	1.025 (0.990–1.061)	1.014 (0.988–1.041)	0.647	**1.064 (1.001–1.130)**	1.011 (0.981–1.041)	1.014 (0.981–1.048)	0.329
IHD	Road	**1.052 (1.041–1.062)**	**1.014 (1.003–1.026)**	<0.0001	**1.101 (1.081–1.121)**	**1.028 (1.017–1.040)**	1.009 (0.995–1.022)	<0.0001
	Rail	**1.023 (1.015–1.031)**	**1.019 (1.010–1.027)**	0.500	**1.032 (1.018–1.046)**	**1.026 (1.017–1.034)**	1.008 (0.999–1.018)	0.002
	Air	1.002 (0.987–1.017)	1.002 (0.986–1.019)	0.987	**1.032 (1.007–1.058)**	1.001 (0.985–1.017)	0.985 (0.966–1.004)	0.004
MI	Road	**1.055 (1.036–1.073)**	**1.027 (1.005–1.050)**	0.067	**1.098 (1.070–1.127)**	**1.035 (1.014–1.056)**	1.002 (0.975–1.030)	<0.0001
	Rail	**1.020 (1.007–1.034)**	**1.020 (1.004–1.036)**	0.981	**1.026 (1.006–1.046)**	**1.018 (1.003–1.033)**	1.016 (0.996–1.037)	0.496
	Air	**1.033 (1.007–1.059)**	**1.050 (1.019–1.083)**	0.403	**1.076 (1.038–1.115)**	**1.034 (1.005–1.064)**	1.006 (0.968–1.047)	0.013
HF	Road	**1.062 (1.034–1.090)**	0.992 (0.970–1.013)	<0.0001	1.070 (0.998–1.147)	**1.039 (1.013–1.065)**	0.997 (0.974–1.020)	0.007
	Rail	1.008 (0.988–1.028)	1.003 (0.987–1.019)	0.695	0.988 (0.936–1.043)	1.000 (0.980–1.019)	1.011 (0.993–1.028)	0.300
	Air	0.999 (0.962–1.038)	1.020 (0.988–1.053)	0.423	1.069 (0.976–1.170)	0.985 (0.949–1.023)	1.028 (0.993–1.064)	0.636
Stroke	Road	**1.030 (1.010–1.051)**	1.004 (0.987–1.020)	0.044	**1.057 (1.022–1.093)**	**1.019 (1.001–1.037)**	0.993 (0.972–1.014)	0.002
	Rail	**1.019 (1.004–1.034)**	1.004 (0.991–1.016)	0.127	1.020 (0.994–1.046)	**1.017 (1.003–1.030)**	0.997 (0.982–1.013)	0.063
	Air	1.009 (0.981–1.037)	1.011 (0.987–1.035)	0.907	1.008 (0.962–1.056)	**1.029 (1.003–1.055)**	0.985 (0.955–1.016)	0.189
HS	Road	1.019 (0.980–1.059)	1.011 (0.977–1.046)	0.769	**1.064 (1.015–1.114)**	1.003 (0.968–1.040)	0.966 (0.908–1.028)	0.010
	Rail	1.015 (0.986–1.045)	1.021 (0.995–1.047)	0.766	**1.037 (1.002–1.074)**	1.006 (0.979–1.033)	1.024 (0.980–1.071)	0.497
	Air	0.972 (0.921–1.026)	1.042 (0.994–1.092)	0.058	1.019 (0.956–1.085)	1.024 (0.975–1.075)	0.949 (0.868–1.037)	0.298
IS	Road	1.040 (0.995–1.087)	**1.044 (1.001–1.088)**	0.913	1.049 (0.974–1.129)	**1.050 (1.009–1.093)**	1.020 (0.960–1.083)	0.515
	Rail	1.009 (0.975–1.043)	1.017 (0.986–1.048)	0.735	0.958 (0.902–1.016)	1.029 (0.998–1.060)	1.012 (0.969–1.057)	0.277
	Air	1.058 (0.995–1.125)	**1.071 (1.010–1.136)**	0.777	1.026 (0.927–1.135)	**1.076 (1.017–1.138)**	1.073 (0.986–1.168)	0.544

Notes: CVD = all cardiovascular diseases, BP = blood pressure related, IHD = ischemic heart disease, MI = myocardial infarction. HF = heart failure, HS = haemorrhagic stroke, IS = ischemic stroke.
Sex groups included adults over 30 years old,
Age groups include both sexes.
Model 3 included noise exposure (road traffic, railway and aircraft noise; Lden), strata sex* and period (i.e. 2001–2005, 2006–2010, or 2011–2015), plus the individual-level covariates civil status, education level, mother tongue, nationality and quintiles of local-SEP, community and regional SEP score and unemployment, $PM_{2.5}$ exposure. *only in models including both sexes.

adjusting for eventfulness of noise at night, specified using IR or the number of events, hardly impacted the HRs (Models 4.1 and 4.1 vs. Model 3) (Supplement Figure S3, see Table S4 for hazard ratios). Notably intermittency ratio at night was independently associated with all outcomes in models adjusted for L_{den}, with highest HRs in the third and fourth quartile compared to the first. The number of noise events was less sensitive, with no clear pattern of association. Collinearity with L_{den} was not critical, though slightly stronger for number of events (Model 4.2, VIF $<$ 2.6) than intermittency ratio (Model 4.1 $<$ 1.8) (Supplement Table S5).

For CVD, IHD and stroke the associations with road traffic noise were constant across the three virtual sub-cohorts, whereas the HRs increased for railway noise and decreased for aircraft noise with time. Different patterns were observed for BP-related mortality (i.e. increasing HR for aircraft noise with time) and MI mortality (i.e. middle period in opposite direction compared to the other two periods), although confidence intervals were broadly overlapping for the various periods (Supplement Figure S4).

3.5. Effect modification

The risk of mortality associated with road traffic and railway noise was generally stronger in males vs. females for most outcomes, reaching statistical significance for road traffic noise exposure and CVD, BP-related, IHD, HF and stroke mortality. The pattern was not obvious for aircraft noise. The age stratified analyses showed the associations were often stronger in younger vs. older ages, most consistently for all causes and road traffic noise exposure, though also apparent for CVD, IHD and MI with railway and/or aircraft noise exposure (Table 3, Supplement Figure S5). While these higher relative risks were observed in younger adults, the absolute excess risk was highest in older adults as expected because of higher baseline cardiovascular mortality risk (Table S6, CVD example).

4. Discussion

In this nationwide study, mortality from cardiovascular diseases was associated with source-specific transportation noise. In mutually adjusted models, including $PM_{2.5}$, most outcomes were associated with road traffic, followed by railway noise. A small but consistent mortality risk increase of 1.01 to 1.04 per 10 dB L_{den} road traffic or railway noise was found for all CVD, BP-related, IHD and MI, with splines confirming no deviation from linearity. Exposure-response relationships for these specific exposure-outcome pairs were mainly linear and increased from low noise levels, as much as 20 dB below the recommended values in the WHO (2018b). The exception was IHD mortality and road traffic noise that started at around the 52 dB guideline level, in line with previous *meta*-analyses (van Kempen et al., 2018; Vienneau et al., 2015b). MI mortality stood out as the only outcome associated with all three transportation noise sources after mutual adjustment, with an increased risk between 1.02 and 1.04 per 10 dB L_{den}. Heart failure and stroke were mainly associated with road traffic noise, although all stroke and ischemic stroke mortality were also associated with railway and aircraft noise, respectively. Other associations for aircraft noise were null. Overall, the results were robust to adjustment for eventfulness at night; and higher levels of intermittency were independently associated with each outcome.

In comparison to our findings, the Danish Diet, Cancer, and Health cohort reported higher increased risks of mortality including all-cause, CVD and stroke with HR of 1.08 (1.05–1.11), 1.13 (1.06–1.19) and 1.11(0.99–1.25) per IQR road traffic noise (10.4 dB L_{den}), respectively (Thacher et al., 2020a). These Danish models were adjusted for lifestyle factors not available in the SNC, though such adjustments rather decreased their risk estimates and is thus unlikely to explain the difference. The Danish study did not consider other transportation sources and the population was mainly urban, whereas the SNC covers the whole of Switzerland which may explain our relatively lower risk estimates (Vienneau et al., 2019). In Vancouver, Canada, total community noise was associated with increased risk of coronary heart disease mortality with HRs of 1.13 (1.06–1.21) and 1.09 (1.01–1.18) per 10 dB L_{den}, after adjusting for $PM_{2.5}$ and multiple air pollutants, respectively (Gan et al., 2012).

Other studies have reported null findings for CVD outcomes, or attenuation after air pollution adjustment. In the whole of London, daytime noise was associated with all-cause mortality (1.04 [1.00–1.07]) for small-areas $>$ 60 vs. $<$ 55 dB, but not all CVD, IHD or stroke mortality (Halonen et al., 2015). In the Netherlands, road traffic noise $>$ 65 vs. $\leq$ 50 dB(A) was associated with CVD (1.25 [1.01–1.53]) and heart failure (1.99 [1.05–3.79]) but not IHD or stroke mortality; and after adjusting for air pollution, the CVD and HF risks attenuated to unity (Beelen et al., 2009). A more recent Dutch study (Klompmaker et al., 2020), using the Public Health Monitor survey, found that road traffic and railway noise were not associated with non-accidental or circulatory mortality. Similar to the Danish study, it included detailed lifestyle factors and other environmental exposures. The authors postulate this may either reflect the absence of a true association or be due to methodological issues such as the relatively short 5-year follow-up, confounder adjustment, or population characteristics (Klompmaker et al., 2020). Two smaller studies also focused on mortality in men only, both reporting null associations: the Caerphilly Study, South Wales (n = 2398) on road traffic noise exposure and IHD (Stansfeld et al., 2021); and the Gothenberg, Sweden study (n = 6304) on road traffic noise and non-accidental CVD (Andersson et al., 2020).

Our latest results for Switzerland are in line with the previous SNC study by Héritier et al. (2017), which was based on a shorter follow-up (until 2008) and exposure at baseline only. The associations for MI mortality and each noise source remained very similar. All CVD and IHD mortality were also similar, though now with slightly stronger and more precise estimates due to the longer follow-up. For BP-related mortality, we saw potential signs of effect transfer between road traffic and railway noise. Specifically, Héritier et al. (2017) reported a relatively strong association for BP-related mortality of 1.053 (1.030–1.075) per 10 dB road traffic noise only, whereas we now found smaller increased risk for both road traffic (1.035 [1.020–1.049]) and railway noise (1.016 [1.006–1.027]). Though less pronounced, the risk for heart failure mortality in association with road traffic also persisted (1.019 [1.002–1.036] vs. former 1.051 [1.027–1.074] per 10 dB); however the association for aircraft noise did not (1.012 [0.988–1.037] vs. former 1.056 [1.028–1.085] per 10 dB). On the other hand, the associations between road traffic and aircraft noise with ischemic stroke mortality were confirmed with slightly more precision. Héritier et al. (2017) previously reported no associations for all stroke combined, whereas this latest analysis indicated a small increased risk of death associated both with road traffic (1.015 [1.002–1.028] per 10 dB) and railway noise (1.010 [1.001–1.019] per 10 dB). Note that the increased overall risk of stroke is likely to be driven by ischemic stroke, in line with previous studies (Seidler et al., 2018; Sorensen et al., 2014; Weihofen et al., 2019). These differential outcomes have previously been described for several risk factors, and may relate to differences in the etiology of the subtypes as well as diagnostics (O'Donnell et al., 2010; Weihofen et al., 2019).

The underlying mechanisms by which noise can influence health are grounded in the noise-reaction model (Babisch, 2002). In short, the physiological response evoked with the perception of noise can trigger the release of stress hormones, such as catecholamines, leading to the manifestation of cardiovascular risk factors, including increased blood pressure, inflammation, oxidative stress, vascular dysfunction, diabetes, and ultimately CVD. The adverse effects can also be mediated by sleep disturbance and annoyance (Basner et al., 2014). A multi-exposure epigenome-wide association study (EWAS) in the Swiss SAPALDIA cohort supported this model with mechanistic evidence, showing the enrichment of pathways related to inflammation and immune response

in relation to transportation noise and independent of air pollution (Eze et al., 2020). In the same Swiss cohort, long-term exposure to transportation noise, in particular from railways, was associated with arterial stiffness which is a major determinant of CVD (Foraster et al., 2017). Recent reviews also highlight, for example, that after repeated noise-induced activation of the hypothalamic–pituitaryadrenal axis and the sympathetic nervous system, the elevated catecholamine levels can contribute to atherosclerosis and coronary plaque rupture, in turn influencing the progression of myocardial infarction and stroke (Basner et al., 2014; Recio et al., 2016; WHO, 2018a).

In addition, different specific causes of cardiovascular deaths in association with different noise sources is the consequence of distinct underlying pathophysiological mechanisms as detailed in Münzel et al. (2021). The review concluded that the quality of evidence for associations of various cardiometabolic risk factors with transportation noise has increased since publication of the WHO Environmental Noise Guidelines, although considerable between-study variation remains for investigations on high blood pressure. Further, it is likely that the temporal pattern of noise (e.g. day-night variation and intermittency) and acoustic characteristics may also play a role in the way noise is perceived and can affect health. For instance, we found that higher intermittency increased the risk of all causes of CVD in our analyses.

This analysis is novel and differs from previous analyses in the same cohort in a number of ways. $PM_{2.5}$ rather than NO_2 was selected *a priori* for air pollution adjustment. The sensitivity analysis (Model 3 vs. Model 3b) showed this change had very little influence on the results for exposure-outcome pairs as previously demonstrated for MI (Héritier et al., 2018). Additional area-level SEP variables calculated at community and regional scale have also been included to control for potential differences in risk across the country. For road and railway noise, the sensitivity analysis indicated this had little influence on the results (Model 3 vs. Model 2). For aircraft noise exposure, however, we saw negative confounding (Model 2 vs. Model 1). In Switzerland, a greater proportion (64.8%) of high SEP individuals are exposed to $>$ 55 dB L_{den} aircraft noise than road traffic (45.5%) or railway (39.0%) noise (Héritier et al., 2017). The night-time flight ban and initiatives for sound insulated windows around airports may also explain, at least in part, the overall weak to null associations for aircraft noise exposure in Switzerland. Superimposed aircraft and railway noise in urban areas with airports may also play a role, as seen in a recent case-crossover study around Zürich airport, where associations for acute exposure to aircraft noise and mortality were less pronounced in areas with notable background road or railway noise (Saucy et al., 2021).

Given the longer follow-up, temporal trends were specifically considered in this analysis. As a whole, the population exposure distribution for each noise source remained steady over the 15 year period. For road traffic noise, HRs were also consistent across the three virtual sub-cohorts showing little signs of time trends in mortality risk. Patterns in HRs for railway and especially aircraft noise, however, differed between sub-cohorts depending on outcome. This may mainly reflect random variability for these two sources, where the statistical power was lower compared to the road traffic noise analysis. For aircraft noise the extension of the night-time flight ban at Zürich airport to 23:30–06:00 h in 2010 (Bissegger, 2013), along with increased installation of sound proof windows, may have contributed to the observed decrease of HRs for CVD mortality due to non-differential exposure misclassification. The notable increase in BP mortality in relation to aircraft noise with time thus seems counterintuitive. It may, however, be explained by an increase in the prevalence of BP-related deaths in sub-cohort3 versus the earlier sub-cohorts (Table 2) indicating a different patient mix in an aging cohort possibly more susceptible to noise. In contrast, other causes show a stable or reducing proportion of deaths with time, except ischemic stroke where the aircraft associations by period are all null.

For railway noise the evolution in CVD mortality risk over time is unclear. A hypothetical explanation would be exposure misclassification related to moving. Almost everyone, to some extent, is exposed to road traffic noise; by contrast exposure to railway or aircraft noise is more localized thus individuals may substantially change their exposure situation by moving into or out of areas with these sources. Exposure misclassification due to a poor estimation of the timing of a move is thus expected to be more severe for those experiencing changes in railway or aircraft noise. There is also uncertainty about the relevant induction period and what the most appropriate time-varying exposure would be. Our approach assumes an induction period of acute to 5 year effect, in line with the range studied in previous research (Sørensen et al., 2012; Thacher et al., 2020a). There is no systematic research to judge this assumption. If the induction period would be longer than 5 years, our approach would result in exposure misclassification, most likely to be modest, given the moderate to high correlation of the various noise exposure metrics over time.

4.1. Strengths and limitations

The SNC remains the largest administrative cohort to systematically investigate transportation noise, using comparably high quality, source-specific noise models providing energy-based metrics (L_{den}) and additional acoustic parameters to reflect eventfulness (IR and number of events). Following nearly all adults in Switzerland over 15 years, in a time-varying framework of three virtual sub-cohorts to control for potential time trends in exposure and mortality, is an asset. As far as possible, using information from the census, the relevant spatial and temporal covariates were updated over time. This also provided the framework to handle the gap in the address history between the 2000 and 2010 censuses. Some exposure misclassification, however, is expected and was unavoidable. Approximately 16% of participants were known to have moved in the first few years after the baseline. For these individuals, we assigned the later geocode and noise data (i.e. both for 2011) at the start of the sub-cohort 2 in 2006. While it is crucial to capture the new address, switching to the later noise data early in the follow-up is not necessarily ideal, especially if noise barriers or other infrastructure changes were implemented closer to 2011. This decision likely had little influence on the results as the 2001 and 2011 exposures were very highly correlated at the same location. We argue that the exposure assessment approach appropriately captured the spatial change, which is considered the most important aspect to minimize exposure misclassification. Another limitation of the SNC is the probabilistic linkage between 2001 and 2010. About 8% of the baseline participants could not be linked to the 2010 census, which is a rough indication of the false linkage rate contributing to non-differential outcome and exposure misclassification. These participants were completely omitted from the cohort. As with many large administrative cohorts, the SNC lacks individual data on health lifestyle, such as smoking, alcohol consumption or physical activity. These are known to be important factors for cardiovascular health and act as confounders; although, as shown in several studies (Foraster et al., 2016; Roswall et al. 2017a, 2017b) such lifestyle factors may also be influenced by exposure to transportation noise and thus on the pathway of disease.

5. Conclusion

Transportation noise exposure was associated with CVD mortality in Switzerland. Independent of air pollution, road traffic and railway noise exposure were associated with the majority of CVD causes of death, often with risk increases starting well below the WHO guideline limits. Efforts to reduce or offer protection against excessive transportation noise should remain a priority to reduce the health burden from this leading environmental risk factor. The noted dissimilarity between the relative versus absolute excess risk is also an important consideration for health impact assessment. In particular, use of age-specific relative risks should be considered as the age-related differences in relative risk can substantially influence the calculation of the years of life lost.

Declarations

The SNC was approved by the Ethics Committees of the Canton Bern (No KeK 153/2014, PB_2020-00050).

Authors' contributions

DV, MR study concept and study design; DV, BF data preparation; DV statistical modelling, write and revise manuscript; all data interpretation, review and comment on manuscript.

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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.envint.2021.106974.

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