

Transportation noise exposure and cardiovascular mortality: a nationwide cohort study from Switzerland.

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Abstract

Background: Most studies published to date consider single noise sources and the reported noise metrics are not informative about the peaking characteristics of the source under investigation. Our study focuses on the association between cardiovascular mortality in Switzerland and the three major transportation noise sources – road, railway and aircraft traffic– along with a novel noise metric termed intermittency ratio (IR), expressing the percentage contribution of individual noise events to the total noise energy from all sources above background levels.

Methods: We generated Swiss-wide exposure models for road, railway and aircraft noise for 2001. Noise from the most exposed façade was linked to geocodes at the residential floor height for each of the 4.41 million adult (>30y) Swiss National Cohort (SNC) participants. For the follow-up period 2000 to 2008, we investigated the association between all noise exposure variables ($L_{den}(\text{Road})$, $L_{den}(\text{Rail})$, $L_{den}(\text{Air})$, and IR at night) and various cardiovascular primary causes of death by multipollutant Cox regression models adjusted for potential confounders including NO_2 .

Results: The most consistent associations were seen for myocardial infarction: adjusted hazard ratios (HR) (95% CI) per 10 dB increase of exposure were 1.038 (1.019-1.058), 1.018 (1.004-1.031), and 1.026 (1.004-1.048) respectively for $L_{den}(\text{Road})$, $L_{den}(\text{Rail})$, and $L_{den}(\text{Air})$. In addition, total IR at night played a role: HRs for CVD were non-significant in the 1st, 2nd and 5th quintiles whereas they were 1.019 (1.002-1.037) and 1.021 (1.003-1.038) for the 3rd and 4th quintiles.

Conclusion: Our study demonstrates the impact of all major transportation noise sources on cardiovascular diseases. Mid-range IR levels at night (i.e. between continuous and highly intermittent) are potentially more harmful than continuous noise levels of the same average level.

Keywords: road traffic, railway, aircraft, noise, exposure, Lden, cardiovascular mortality, intermittency ratio

Introduction

There is growing epidemiological evidence that transportation noise affects health in various ways.

Transportation noise induces sympathetic and endocrine arousals that release stress hormones such as catecholamine and cortisol in the blood stream [1]. Further it induces annoyance [2], affects health-related quality of life [3-5], reduces sleep quality [6], and has been shown to affect physical activity levels [7]. All these effects are expected to increase the incidence and progression of hypertension and myocardial infarction (MI) [8, 9].

Blood pressure has been the most studied outcome in noise research so far. In a meta-analysis, Van Kempen and Babisch report a pooled odds ratio for hypertension prevalence of 1.03 (95% CI: 1.01, 1.06) per 5 dB increase in road traffic noise levels [10]. With respect to aircraft noise, meta-analyses on hypertension reported risk increase of 1.63 (95% CI: 1.14-2.33) [11] and 1.13 (95% CI: 1.00-1.28) [12] per 10 dB increase in exposure. For MI, a recent meta-analysis reports a linear exposure-response relationship within the range of 52-77 dB with a relative risk of 1.08 (95% CI: 1.04-1.13) per 10 dB increase in road traffic noise exposure [13], while another meta-analysis reported a relative risk for ischemic heart disease (IHD) of 1.04 (95% CI: 1.00-1.10) per 10 dB increase of road traffic noise exposure starting at a threshold of 50 dB [14]. For stroke, however, the few published studies do not show a consistent pattern; some point to an association with transportation noise [15, 16] whereas others do not [17-20].

Other cardiovascular outcomes such as heart failure have rarely been addressed, and studies on railway noise are scarce and restricted to outcomes like sleep medication intake [21], weight gain [22], waist circumference [23], blood pressure [24], heart failure [25] and hypertensive heart disease but cardiovascular mortality has not yet been investigated.

Further, most studies to date have considered a single noise source as the exposure variable. Thus, there is considerable uncertainty about the mutual independent exposure-response curve in the presence of multiple noise sources. Moreover, all previous studies on chronic diseases represent exposure using time-averaged noise levels, predominantly the L_{eq} -based metrics like L_{dn} , L_{den} , $L_{eq,Night}$ or $L_{eq,Day}$. However, there is evidence that temporal characteristics of noise also play an important role, e.g. when it comes to awakening reactions at night. There is evidence that the probability of event-related awakenings, body movements and cardiovascular arousals depend on the maximum sound pressure level and the slope of rise of individual events [26-28]. As a

consequence, such effects are less well predicted by average levels [29]. Since noise events during night have been linked with cardiac arousal on the short term [27, 30], we hypothesize that single but pronounced noise events during night are involved in the development of cardiovascular disease morbidity and mortality in the long run irrespective of the source of such events. Therefore, to describe the "eventfulness" of the noise exposure situation, we developed the noise metric "intermittency ratio" (IR in %), which quantifies the contribution of individual noise events above the background level to the total noise exposure [31].

By combining source specific nationwide noise models with the Swiss National Cohort (SNC) data, the aim of this study was to better understand the mutual independent link between cardiovascular mortality in adults and the residential exposure to the levels and intermittency of major transportation noise sources in Switzerland. In addition, we evaluated potential modifying effects of sex, age, socio-economic status, urbanization, building age, duration of residence and number of noise events.

Methods

Study population

The SNC probabilistically links national census data with mortality and emigration records [32]. The data used in our study is based on the 4 December 2000 census and on mortality and emigration data for the period 5 December 2000 to 31 December 2008 and contains 7.28 million observations. We excluded subjects below 30 years of age (n=2.59 million), observations for which residential coordinates were missing (n=0.19 million), subjects living in an institution (n=0.25 million), and observations for which the cause of death was imputed (n=0.03 million) leaving 4.41 million observations for the analyses.

The outcomes under investigation were primary causes of death from all cardiovascular diseases (CVD) (ICD-10: I00-I99), IHD (ICD-10: I20-I25), stroke in general (ICD-10: I60-I64), hemorrhagic stroke (ICD-10: I60-I62), ischemic stroke (ICD-10: I63), MI (ICD-10: I21-I22), heart failure (ICD-10: I50), and blood-pressure related death (BP) (ICD-10: I10-I15).

The SNC was approved by the cantonal ethics boards of Bern and Zurich.

Noise exposure data

Within the framework of the SiRENE project (Short and Long Term Effects of Transportation Noise Exposure), we built a Swiss-wide noise exposure database for the year 2001 which includes the three major transportation noise sources in Switzerland: road traffic, railway and aircraft noise.

The noise exposure database is described in detail elsewhere [33]. In brief, road traffic noise emissions were calculated using sonROAD [34] while propagation was computed via the propagation model of StL-86 [35]. For railway noise, the emissions were calculated using sonRAIL [36] and propagation was computed using the Swiss railway noise model SEMIBEL [37]. For aircraft noise, the three major civils airports; Zürich, Geneva and Basel, and the military airport located in Payerne were considered. Noise exposure estimates were calculated via FLULA2 [38], based on radar data for Zürich while for Geneva and Basel exposure was calculated on the basis of traffic statistics from the Federal Office of Civil Aviation along with available acoustic footprints from the years 2000 and 1999, respectively. For the military airport of Payerne, noise exposure estimates were computed based on idealized flight paths, number of flights and approximate operation times.

IR calculation has already been described elsewhere in detail [31]. In brief, the event-based sound pressure was computed for all vehicle pass-bys obtained from traffic flow statistics. All event-based sound pressure levels that exceed the background level, defined as the modeled hourly L_{eq} , by 3 dB were classified as perceivable events (level L_{eq} , T, Events). The ratio of these perceivable events and the overall sound pressure level $L_{eq,T,tot}$ is termed the intermittency ratio (IR) as follows:

$$IR \equiv \frac{10^{0.1L_{eq,T,Events}}}{10^{0.1L_{eq,T,tot}}} * 100$$

IR takes values in the range 0% to 100%, where 0% IR means that no single events can be perceived above background and 100% IR means that all noise energy is produced by “individual” noise events. In this study we only considered IR at night (23 to 7h) from all transportation sources combined.

For each building in Switzerland, noise exposure was estimated at pre-defined façade points. A maximum of three façade points, spaced by at least 5 meters, were assigned to each building façade by floor. For each façade point, we calculated the L_{den} (defined as the weighted logarithmic average of $L_{eq,day}$, $L_{eq,evening}$ and $L_{eq,night}$ with a penalty of 5 dB and 10 dB respectively applied to the latter exposure variables) for each noise source. Using the available geocodes and the information about floor of residence, we linked participants to their respective dwelling unit to assign noise exposure. Exposure, including IR, was assigned on the basis of the façade point per

dwelling unit with the highest L_{den} value. If information on floor of residence was not available, we assigned the noise estimates corresponding to the middle floor of the building.

Statistical Analysis

We analyzed the data using the Cox proportional hazards model with age as the underlying time variable. Participants were followed until emigration, death or end of follow-up. L_{den} exposure variables were censored at 35 dB (road traffic) or 30 dB (railway and aircraft noise). Hazard ratios for the outcomes of interests were computed using multipollutant models, i.e. including linear terms for each noise source shown in the following equation.

$$Outcome = L_{den}(Road) + L_{den}(Rail) + L_{den}(Air) + adjustments$$

The linearity assumption was evaluated in models with categorical exposure data. We included quintiles of IR night as a categorical variable in the model based on a significant log-likelihood ratio test. Each model was adjusted for sex (female/male), neighborhood index of socio-economic position (low, medium, high), civil status (single, married, widowed, divorced), education level (compulsory education or less, upper secondary level education, tertiary level education, not known), annual average NO_2 concentration ($\mu g/m^3$, estimated outdoor residential levels using PolluMap, a 100x100m dispersion model for Switzerland for year 2010 [39]), mother tongue (German and Rhaeto-Romansch, French, Italian, other language) and nationality (Swiss, rest of Europe (inclusive ex-USSR), rest of the world/unknown). Stratification analysis was conducted by sex (female vs. male), age (<65 vs. \geq 65 years old), building age (newer than 30 years or renovated vs. older than 30 years without renovation), movers (more than 5 years of residence vs. less than 5 years of residence), number of events that exceed the background level (median split), socio-economic position (median split), and urbanization (urban vs. rural).

Results

The study population amounted to 4.41 million observations, with 33.85 million person-years for the period 5th December 2000 to 31st December 2008. Characteristics of the study population are displayed in Table 1. In general, populations highly exposed to road and railway noise ($L_{den} > 55$ dB, IR > 80%) had a lower socioeconomic position and education than the total population, whereas it was the other way around for people highly exposed to aircraft noise. For all three highly noise exposed populations, the proportion of non-Swiss residents and the NO_2 concentration tended to be increased.

The cohort contained 142,955 deaths from CVD, of which 42.2%, 15.7% and 9.4% were deaths from IHD, stroke and BP-related diseases. Exposure to road traffic noise was most prevalent with >89% of the study population exposed to L_{den} above 45 dB. With respect to railway and aircraft noise, 25% and 14% of the study population were respectively exposed to L_{den} above 45 dB. The proportion of censored observations was 1.2%, 45.5% and 67.1% for road, railway and aircraft noise, respectively. The distribution of exposure to IR was skewed toward higher values with a mean of 69.5% and a median of 75.0%. More than 39% of the population was exposed to IR above 80%. These patterns are displayed on Figure 1.

Correlations between the three noise sources were low: Spearman's rank correlation for $L_{den}(\text{Air})$ vs $L_{den}(\text{Road})$: 0.09, $L_{den}(\text{Rail})$ vs $L_{den}(\text{Road})$: 0.12, $L_{den}(\text{Air})$ vs $L_{den}(\text{Rail})$: -0.04. Correlations for IR night with the transportation specific noise levels were also low: ($L_{den}(\text{Air})$): -0.07, $L_{den}(\text{Rail})$: 0.14 and $L_{den}(\text{Road})$: 0.04).

Table 2 shows the hazard ratios (HR) per 10 dB increase in L_{den} of all three transportation sources, included in one multipollutant model by outcome. The most consistent associations were observed for road traffic noise for which the HR for all CVD was 1.025 (95% CI: 1.018-1.032) per 10 dB. The only outcomes not related to road traffic noise were stroke in general (HR=1.011, 95% CI: 0.993-1.028) and hemorrhagic stroke (HR=1.004, 95% CI: 0.968-1.040). Ischemic stroke was significantly associated with road traffic noise (HR=1.050, 95% CI: 1.002-1.099). For railway noise exposure, significant positive linear associations were seen for IHD and MI with a borderline significant association for all CVD. Aircraft noise was not associated with all CVD (HR=0.994, 95% CI: 0.985-1.002). However, significantly elevated risks were observed for MI, heart failure and ischemic stroke. Categorical analyses demonstrated for most outcomes approximate linear associations, with the risk starting to increase as low as 40 dB (Supplementary Figures 2-9).

Night time IR was significantly associated with CVD (Table 3 and supplementary figures 10-17) in a bell shaped relationship where the HR for CVD were 1.019% (95% CI: 1.002-1.037) and 1.021% (95% CI: 1.003-1.038) in the 3rd and 4th quintiles. This trend was observed for all other outcomes although statistical significance was only reached for hemorrhagic stroke. Depending on the outcome, the highest HRs were located in the second (heart failure), third (stroke, ischemic stroke), or fourth (IHD, hemorrhagic stroke) quintile. This indicates that the health effects of noise are more pronounced in situations where the noise is between continuous and highly intermittent.

We evaluated a number of potential effect modifiers on all CVD, MI, ischemic stroke, BP and heart failure. For road and railway noise L_{den} , higher HRs for CVD were observed for men compared to women, although not

confirmed in the other outcomes. For all exposure sources and all outcomes, in tendency, HRs were larger in younger than in older individuals (≥ 65 year). For urbanization a mixed pattern was seen depending on outcome and exposure source. We did not find effect modification when considering building age, duration of living at the same residence, number of events that exceed background level, or socio-economic position (Supplementary Table 4-8).

Discussion

This study adds to the body of evidence linking transportation noise to CVD and, for the first time, addresses the impact of noise characteristics using a novel metric. In general, IR night appears to be non-linearly associated with the outcomes, which suggests that either continuous noise or highly intermittent noise with long quiet periods between events is less problematic than mid-range intermittency.

We observed a risk increase for heart failure, BP related, ischemic stroke and MI mortality in the road traffic noise levels independent of the other noise sources. Our exposure-response associations are fairly well in line with previous meta-analyses suggesting somewhat stronger risks but with a higher threshold [13, 10, 14].

Previous research on road traffic noise and stroke was inconsistent. Our study is the first to show that ischemic stroke but not hemorrhagic stroke is associated with road traffic noise. Of note, for hemorrhagic stroke IR was a significant predictor and we found borderline significant associations with railway noise, which is highly intermittent during night. This might indicate that for hemorrhagic stroke eventfulness of noise exposure is more relevant than the average level.

Most previous noise research on long-term transportation noise effects has not considered railway noise. In our study we observe an association between railway noise and death from IHD, MI and CVD as primary cause of death, but we cannot confirm a link with blood pressure and heart failure as seen in a German case control study [25]. Strikingly, categorical models suggest that the risk for CVD, IHD, and MI starts to increase at L_{den} levels as low as 30 dB (Supplementary Figures 2, 4, 5). Similar to Huss et al. [20], though with three additional years of SNC data and a greatly improved noise exposure model, we confirmed a significant association between aircraft noise and MI. In addition, aircraft noise was linked to heart failure and ischemic stroke. In general, effects of aircraft noise on all types of CVD were less pronounced than as seen for road and railway noise; a pattern which was also observed in the NORAH study [25]. In Switzerland there is a night ban on air traffic, meaning that during most of the night people are not exposed to aircraft noise, which may explain weaker associations for CVD. On the other hand this would imply that for MI, heart failure and ischemic stroke the

daytime, early morning or late night exposure to aircraft noise is involved in mechanisms triggering those particular outcomes. Further, self-selection may play a role in explaining the absence of association for aircraft noise exposure: subjects not able to cope with aircraft noise may tend to move away from noisy areas.

Alternative explanations include residual confounding (socioeconomic position and educational levels tended to be higher in people exposed to aircraft noise) and exposure misclassification in the high exposure range (since airports have to subsidize the installation of sound-proof windows in areas exceeding certain noise levels).

The recently published ESCAPE study reports a weak association between road traffic noise and hypertension that tended to be attenuated after adjustment for PM_{2.5} [41]. In our study, neither the direction nor the strength of association of any noise source substantially changed after adjustment for NO₂ (data not shown). However, we cannot rule out residual confounding from fine particles.

We did not find strong effect modification by sociodemographic factors. But higher relative risks observed for males, with respect to road and railway noise, are in line with an observational sleep study [42] and a recent meta-analysis on myocardial infarction [14].

Additional effect of noise intermittency

A particular asset of this study is the evaluation of the temporal noise exposure characteristics in addition to the noise levels. This IR night refers to the events above the background level and thus can be high even if L_{den} is low. The underlying hypothesis is that in quiet places even relatively low-level noise events during night may have an additional health effect compared to the average noise levels expressed as L_{den}. We found indications that a moderate IR night level (2nd-4th quintile) was more relevant than continuous noise (quintile 1) or highly variable noise (quintile 5) for increased risk of all CVD and IHD. This bell-shaped relationship indicates that subjects appear to be better able to cope with either continuous noise or highly variable noise. The latter may represent situations with very few distinct events and long quiet periods between. Interestingly, depending on the outcome different trends were apparent: for heart failure continuous levels with low level of intermittency seemed to be more problematic whereas for IHD it was the other way round.

Public health impact

While a risk increase of 2.5% per 10 dB road traffic noise exposure for cardiovascular mortality seems negligible, the public health impact is substantial. Transportation noise in 2010 in Switzerland was attributed to 6000 years of life lost which represents 1.8 billion CHF of external costs when also accounting for loss in

housing prices due to noise exposure [43]. Our study contributes to a better understanding of the role of noise characteristics; this should be considered in future noise regulation which currently focuses only on average noise levels.

Strengths and limitations

The strengths of this study are: the large study population without potential for selection bias; the large sample size combined with the long follow-up time which gives us high statistical power; and the very comprehensive noise modeling, for all three transportation sources, at the address level taking into account floor information. This allowed us to conduct an individual exposure assessment, and to assess the individual impact of all three sources concurrently which has rarely been done in previous large population studies. Finally, the IR metric allowed us to refine our exposure estimates, and in general this metric opens new research avenues in the field of noise epidemiology and in the regulation of noise.

While our models were adjusted for socioeconomic status and other demographic variables, there is no information about individual lifestyle and smoking in the SNC. Thus, we cannot rule out that residual confounding of lifestyle may have played a role for our analyses, although no indications for this were seen in a previous SNC noise study [20].

Our study further relied on death records, which may be considered a weakness as it does not represent incidence data. From a mortality perspective, bias would only be a problem if the quality of the death records is related to noise exposure. Given that noise exposure varies on a small scale this is unlikely. Furthermore, a meta-analysis of studies on MI and road traffic did not find systematic differences between mortality and incidence studies [14].

Although, substantial effort in historical exposure modeling was undertaken in the SiRENE project, the potential for exposure misclassification is a limitation in the present work, as it is in other epidemiological noise studies. Modeling errors of the three propagation models, e.g. from meteorology, was reported to be between 0.4 and 2.0 dB [44]. Additional uncertainty comes from the missing input data, missing information about residential history and location of bedroom, and personal behavior (such as window closing behavior and other coping strategies). However, these errors are more likely to be non-differential, thus resulting in an underestimation of the true risks.

In conclusion, this study confirmed previous results and generated new knowledge in the field of noise exposure epidemiology. Not only the nature of noise but its characteristics were found to be relevant for health. This finding may be of importance for noise protection policies.

Acknowledgements

We thank the Swiss Federal Statistical Office for providing mortality and census data and for the support which made the Swiss National Cohort and this study possible. The members of the Swiss National Cohort Study Group are Matthias Egger (Chairman of the Executive Board), Adrian Spoerri and Marcel Zwahlen (all Bern), Milo Puhan (Chairman of the Scientific Board), Matthias Bopp (both Zurich), Nino Künzli (Basel), Fred Paccaud (Lausanne) and Michel Oris (Geneva).

Sources of funding

This work was supported by the Swiss National Science Foundation (grant no. CRSII3_147635) and the Federal Office for the Environment.

Disclosure

Conflict of interests: None

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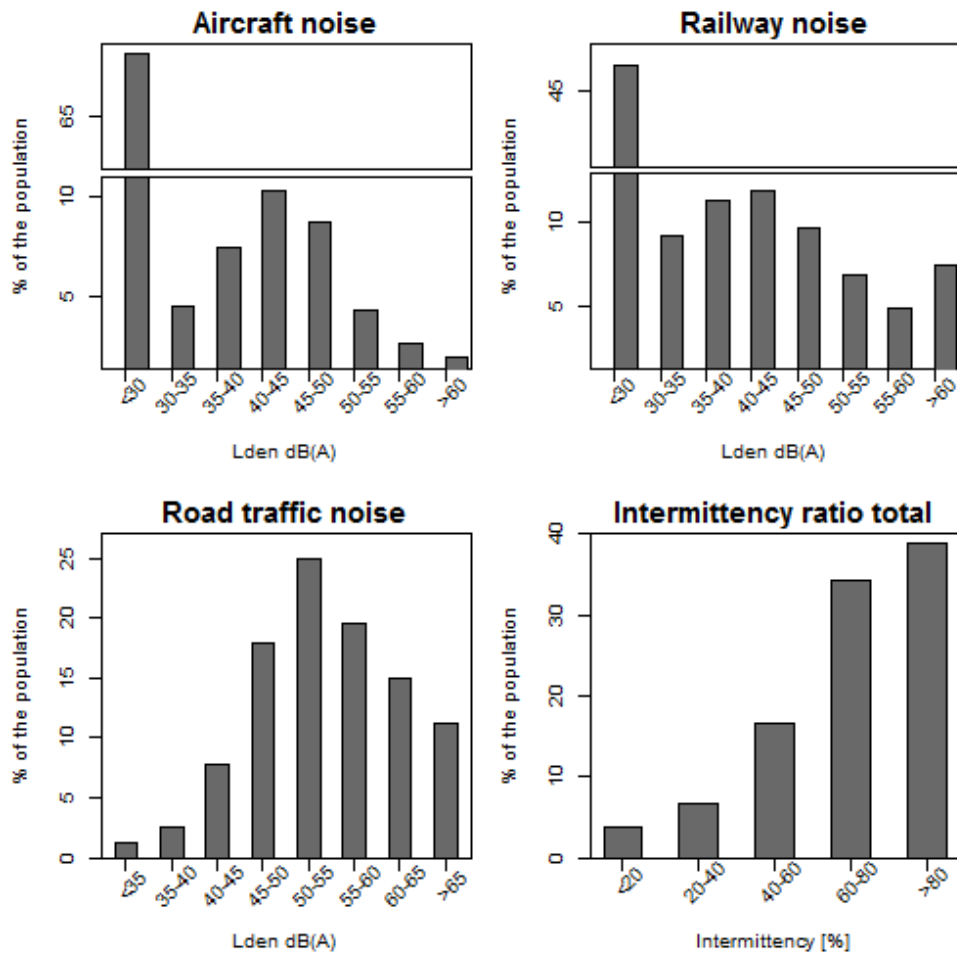


Fig 1: Distribution of noise exposure in the study population expressed as L_{den} in dB for aircraft, railway and road traffic noise levels and total IR at night in % (note different labelling for y-axis).

Table 1: Study population characteristics.

Characteristics at baseline	Total cohort (n=4,415,206)	>55 dB Road traffic noise (n=2,018,090)	>55 dB Railway noise (n=459,408)	>55 dB Aircraft noise (n=115,463)
Males (%)	47.9	47.9	48.2	48.7
Age: mean (SD)	52.4 (15.1)	52.4 (15.5)	52.1 (15.3)	51.1 (14.1)
Education level (%)				
• Compulsory education or less	23.8	26.7	27.9	20.7
• Upper secondary level education	51.6	49.9	50.5	51.7
• Tertiary level education	22.2	20.4	18.6	24.8
• Not known	2.2	2.8	2.9	2.6
Civil status (%)				
• Single	13.9	15.5	14.3	12.5
• Married	69.6	66.4	68.1	71.2
• Widowed	7.9	8.5	8.2	6.0
• Divorced	8.4	9.4	9.2	10.2
Socio-economic position (%)				
• low	50.4	54.5	61.0	35.2
• high	49.6	45.5	39.0	64.8
Mother tongue (%)				
• German and Rhaeto-Romansch	64.7	58.2	60.0	52.9
• French	19.4	22.6	19.5	28.4
• Italian	7.3	8.6	8.8	5.1
• Other	8.4	10.5	11.5	13.5
Nationality				
• Swiss	82.2	77.9	76.2	73.9
• Rest of Europe (inclusive ex-USSR)	15.9	19.5	21.3	22.2
• Other /unknown	1.9	2.5	2.4	3.9
NO ₂ concentration µg/m ³ : mean (SD)	20.4 (6.2)	22.1 (6.6)	21.6 (5.2)	24.3 (4.6)

Table 2: Hazard Ratios (HR) and 95% confidence intervals (CI) per 10 dB increase in noise levels for cardiovascular causes of death.

Outcome	ICD-10 code	N Cases	HR L _{den} (Road) (95% CI)		HR L _{den} (Rail) (95% CI)		HR L _{den} (Air) (95% CI)	
			Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
CVD	I00-I99	142955 (37.4% ^a)	1.012 (1.006-1.019)	1.025 (1.018-1.032)	1.006 (1.001-1.010)	1.005 (1.000-1.010)	0.949 (0.942-0.956)	0.994 (0.985-1.002)
BP	I10-I15	13549 (9.4% ^b)	1.02 (0.999-1.041)	1.053 (1.030-1.075)	1.008 (0.993-1.023)	1.011 (0.995-1.027)	0.930 (0.907-0.954)	1.012 (0.985-1.039)
IHD	I20-I25	60261 (42.2% ^b)	1.008 (0.997-1.018)	1.023 (1.012-1.034)	1.019 (1.011-1.026)	1.012 (1.005-1.020)	0.958 (0.947-0.969)	0.991 (0.978-1.003)
MI	I21-I22	19313 (13.5% ^b)	1.038 (1.020-1.056)	1.040 (1.021-1.059)	1.023 (1.011-1.036)	1.020 (1.007-1.033)	0.971 (0.952-0.990)	1.027 (1.006-1.049)
Heart failure	I50	12345 (8.6% ^b)	1.021 (0.999-1.043)	1.051 (1.027-1.074)	0.964 (0.948-0.980)	0.997 (0.980-1.014)	0.907 (0.882-0.932)	1.056 (1.028-1.085)
Stroke	I60-I64	22377 (15.7% ^b)	1.005 (0.989-1.022)	1.011 (0.993-1.028)	1.000 (0.988-1.012)	0.995 (0.983-1.008)	0.981 (0.963-0.999)	1.013 (0.993-1.033)
Hemorrhagic stroke	I60-I62	5354 (3.7% ^b)	1.029 (0.995-1.063)	1.004 (0.968-1.040)	1.028 (1.004-1.051)	1.020 (0.996-1.045)	0.990 (0.955-1.026)	0.991 (0.951-1.032)
Ischemic stroke	I63	2991 (2.1% ^b)	1.037 (0.992-1.083)	1.050 (1.002-1.099)	0.998 (0.966-1.031)	0.989 (0.956-1.023)	1.052 (1.006-1.099)	1.074 (1.020-1.127)

^a % of total causes of death, ^b% of all CVD causes of death, Multipollutant models adjusted for sex, neighborhood index of socio-economic

position, civil status, education level, mother tongue, nationality and NO₂ exposure.

Table 3: Hazard Ratios and 95% confidence intervals (CI) for cardiovascular causes of death and categorical IR night by quintiles.

	1st quintile (reference)	2nd quintile (IR night; 53.5-69.4%)	3rd quintile (IR night; 69.5-79.5%)	4th quintile (IR night; 79.6-87.3%)	5th quintile (IR night; 87.4-100%)	p-value for IR^a
CVD	1	1.001 (0.984-1.018)	1.019 (1.002-1.037)	1.021 (1.003-1.038)	0.994 (0.976-1.012)	0.003
BP	1	1.018 (0.992-1.045)	1.022 (0.995-1.049)	1.033 (1.006-1.061)	1.01 (0.982-1.039)	0.311
IHD	1	0.982 (0.94-1.025)	1.036 (0.993-1.082)	1.024 (0.98-1.069)	1.003 (0.958-1.05)	0.148
MI	1	1.019 (0.963-1.077)	1.045 (0.988-1.105)	1.018 (0.962-1.078)	0.987 (0.93-1.048)	0.290
HF	1	1.007 (0.949-1.068)	1.004 (0.947-1.065)	0.986 (0.929- 1.047)	0.954 (0.896-1.015)	0.370
Stroke	1	0.939 (0.861-1.025)	1.041 (0.955-1.135)	1.066 (0.977-1.163)	0.968 (0.881-1.063)	0.096
HS	1	1.023 (0.912-1.149)	1.044 (0.929-1.173)	1.008 (0.895-1.135)	0.926 (0.815-1.053)	0.024
IS	1	1.029 (0.982-1.077)	1.017 (0.971-1.066)	1.046 (0.999-1.097)	1.006 (0.957-1.057)	0.366

^a based on a likelihood ratio of models with and without IR. Models without IR presented in Table 2.

Multipollutant models including $L_{den}(\text{Road})$, $L_{den}(\text{Rail})$ and $L_{den}(\text{Air})$ adjusted for sex, neighborhood index of socio-economic position,

civil status, education level, mother tongue, nationality and NO_2 exposure.

