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CLINICAL RESEARCH
Prevention and epidemiology

A systematic analysis of mutual effects of transportation noise and air pollution exposure on myocardial infarction mortality: a nationwide cohort study in Switzerland

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Aims The present study aimed to disentangle the risk of the three major transportation noise sources—road, railway, and aircraft traffic—and the air pollutants NO_2 and $PM_{2.5}$ on myocardial infarction (MI) mortality in Switzerland based on high quality/fine resolution exposure modelling.

Methods and results We modelled long-term exposure to outdoor road traffic, railway, and aircraft noise levels, as well as NO_2 and $PM_{2.5}$ concentration for each address of the 4.40 million adults (>30 years) in the Swiss National Cohort (SNC). We investigated the association between transportation noise/air pollution exposure and death due to MI during the follow-up period 2000–08, by adjusting noise [L_{den}(Road), L_{den}(Railway), and L_{den}(Air)] estimates for NO_2 and/or $PM_{2.5}$ and vice versa by multipollutant Cox regression models considering potential confounders. Adjusting noise risk estimates of MI for NO_2 and/or $PM_{2.5}$ did not change the hazard ratios (HRs) per 10 dB increase in road traffic (without air pollution: 1.032, 95% CI: 1.014–1.051, adjusted for NO_2 and $PM_{2.5}$: 1.034, 95% CI: 1.014–1.055), railway traffic (1.020, 95% CI: 1.007–1.033 vs. 1.020, 95% CI: 1.007–1.033), and aircraft traffic noise (1.025, 95% CI: 1.006–1.045 vs. 1.025, 95% CI: 1.005–1.046). Conversely, noise adjusted HRs for air pollutants were lower than corresponding estimates without noise adjustment. Hazard ratio per 10 $\mu g/m^3$ increase with and without noise adjustment were 1.024 (1.005–1.043) vs. 0.990 (0.965–1.016) for NO_2 and 1.054 (1.013–1.093) vs. 1.019 (0.971–1.071) for $PM_{2.5}$.

Conclusion Our study suggests that transportation noise is associated with MI mortality, independent from air pollution. Air pollution studies not adequately adjusting for transportation noise exposure may overestimate the cardiovascular disease burden of air pollution.

Keywords Noise • Road traffic • Railway • Aircraft • Air pollution • Myocardial infarction • Interaction air pollution and noise • NO_2 • $PM_{2.5}$

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Introduction

Several meta-analyses have highlighted the link between transportation noise and cardiovascular health. Babisch[1] reported a risk increase of 1.08 (95% CI: 1.04–1.13) for coronary heart diseases per 10 dB(A) increase in road traffic noise levels, and positive associations between myocardial infarction (MI) and exposure to road traffic and to aircraft noise have also been reported by Vienneau.[2] Air pollutants have also been shown to impact cardiovascular health. A meta-analysis focusing on MI reported a relative risk of 1.011 (95% CI: 1.006–1.016) and 1.025 (95% CI: 1.015–1.036) per 10 $\mu g/m^3$ increase in NO_2 and $PM_{2.5}$ concentrations, respectively.[3] Transportation noise and air pollution impact health through different pathways,[4] though they share many biological pathways.

Mutual confounding is also of concern, since transportation noise and air pollution mainly originate from traffic. NO_2 and road traffic noise are often highly spatially correlated; aircraft and railway noise are less correlated with air pollution[5,6] and thus offer the potential to elucidate their mutual independent impact on health. Correlations between long-term traffic noise and air pollution ranging from 0.16 to 0.72 were reported in a systematic review.[7] However, Fecht *et al.*[8] found that correlation depends on the spatial unit, with largest ranges seen when comparing across smaller vs. larger spatial units. Finally, correlation between transportation noise and air pollution has been shown to decrease with decreasing measurement error demonstrating the need of high quality exposure modeling.[9] Various studies have investigated the link between co-exposure to air pollution and noise, and CVD mortality. Some report independent noise effects,[6,10–14] whereas others suggest attenuation of the noise effect estimates after adjustment for air pollution thus indicating confounding or antagonistic interaction[15,16] or did not adjust for exposure to air pollutants.[17,18] A limitation in many of these studies, including our own previous analysis on this cohort,[19] is the fact that they do not model exposure at the same spatial scale. Depending on the main interest of a study, the model used for adjustment may be less accurate than the main exposure model which would then yield partial confounding adjustment. A systematic review of nine studies comprising outcomes such as hospital discharge registers, self-reported medication intake, and mortality found that less than 10% of the effect estimate of noise was attenuated after adjustment for air pollution or vice versa[7] and thus concluded that confounding of cardiovascular effects by noise or air pollution is low. However, improvements in exposure assessment may change the situation.

As per our previous cohort study,[19,20] we developed high-quality models to assess road, railway, and aircraft noise. In this study, we further included highly detailed NO_2 and $PM_{2.5}$ exposures to investigate the independent associations between transportation noise and air pollution at the participants' residence with MI mortality.

Methods

Study population

The SNC probabilistically links national census data with mortality and emigration records.[21] 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) as myocardial infarction mortality is very rare in this age group, observations for which residential co-ordinates were missing ($n = 0.19$ million) or no buffers for the prediction of the air pollution levels could be calculated ($n = 0.01$ million), subjects living in an institution such as special-care homes ($n = 0.25$ million), and observations for which the cause of death was imputed (0.03 million) leaving 4.40 million observations for the analyses. The outcome under investigation was primary causes of death from MI (ICD-10: I21–I22). Immediately after death, primary and underlying causes of deaths are recorded by a physician, possibly verified later by autopsy. Eventually, coding of causes is done centrally by the Federal Statistical Office using the German Modification of the ICD-10 system. 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 included the three major transportation noise sources in Switzerland: road traffic, railway, and aircraft noise.

The noise exposure database is described in detail elsewhere.[22] In brief, road traffic noise emissions were calculated using sonROAD[23] while propagation was computed via the propagation model of StL-86.[24] For railway noise, the emissions were calculated using sonRAIL[25] and propagation was computed using the Swiss railway noise model SEMIBEL.[26] Aircraft noise exposure estimates were calculated via FLULA2.[27]

For each building in Switzerland, transportation noise exposure was estimated at pre-defined façade points with a maximum of 3 per facade.[22] For each façade point, we calculated the L_{den} 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 was assigned on the basis of the façade point per dwelling unit with the highest L_{den} value. If information on the floor of residence was not available, we assigned the noise estimates corresponding to the middle floor of the building.

NO_2 exposure

The fine scale NO_2 model was based on data from cantonal air pollution monitoring authorities of Genève, Vaud, Neuchâtel, Jura, Fribourg, Berne, Basel-City, Basel-Country, Solothurn, Aargau, Ticino, the Inluft and Ostluft network, and the Sapaldia team.[28] The data comprised 9469 data points from 14 days passive measurements collected from 2000 to 2008 at a total of 1834 locations. Missing data was imputed by considering available values from other monitoring sites within the same network based on inverse distance weighting. Subsequently, annual mean concentration for each year and site were calculated and were regressed against various spatial predictors as outlined in Supplementary material online, *Table S1*.

The prediction for the SNC at residential address was performed for each year, from 2000 to 2008, and then averaged to obtain a long-term NO_2 exposure estimate for each participant.

$PM_{2.5}$ exposure

Daily $PM_{2.5}$ at 100 m grid cells across Switzerland was predicted for 2003–08 from satellite, land use, and meteorological data as described in detail in de Hoogh *et al.*[29] We used aerosol optical depth data for the period of 2003–08 at 1×1 km resolution and combined it in four-staged modelling approach[30] with various predictors (Supplementary material online) and with $PM_{2.5}$ ground measurements to refine model resolution to address level. The annual models for the period 2003–08 were used to

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Table 1 Study population characteristics

Characteristics at baseline		L_{den} road above median (54.1 dB)	NO_2 above median (27.0 μg/m^3)	$PM_{2.5}$ above median (18.7 μg/m^3)
Number of participants at baseline	4 404 046	2 202 848	2 202 744	2 202 025
Males (%)	48	48	47	48
Age, mean (SD)	52.4 (15.1)	52.47 (15.44)	52.57 (15.49)	52.51 (15.37)
Education level (%)				
Compulsory education or less	24	26	25	25
Upper secondary level education	52	50	50	50
Tertiary level education	22	21	23	22
Not known	2	3	3	3
Civil status (%)				
Single	14	15	17	16
Married	70	67	65	66
Widowed	8	8	8	8
Divorced	8	9	10	10
Neighbourhood socio-economic position (%)				
Low	33	37	32	33
Medium	33	33	32	33
High	33	29	36	34
Mother tongue (%)				
German and Rhaeto-Romanic	65	59	60	60
French	19	22	19	19
Italian	7	9	10	10
Other	8	10	11	11
Nationality (%)				
Swiss	82	78	76	77
Rest of Europe (inclusive ex-USSR)	16	19	21	20
Other /unknown	2	2	3	3
NO_2 concentration (μg/m^3), mean (SD)	27.7 (7.6)	30.3 (7.8)	33.7 (5.6)	31.5 (7.2)
$PM_{2.5}$ concentration (μg/m^3), mean (SD)	19.4 (3.7)	20.2 (4.1)	21.1 (4.1)	22.1 (3.1)

predict $PM_{2.5}$ exposure for each SNC study participant, and the average over the whole period was used as a long-term $PM_{2.5}$ exposure measure in the epidemiological analysis.

Statistical analysis

We analysed the data using the Cox proportional hazards model with age at date of entry into the cohort as the underlying time variable. Participants were followed until emigration, death, or end of follow-up. In order to capture long-term effects of noise and air pollution, exposure values representing the average during the follow-up period as described above were added as static covariates into the model. L_{den} variables were left censored at 35 dB (road traffic) or 30 dB (railway and aircraft noise). Linear hazard ratios (HRs) were computed using multipollutant models adjusted for potential confounders excluding NO_2 and $PM_{2.5}$ in a first step, and stepwise including them in a second step. Additional potential confounders included in the model were sex, neighbourhood index of socio-economic position,[31] civil status, educational level, nationality, and mother tongue using the categories depicted in *Table 1*. The latter was selected as it is expected to represent cultural variability in health behaviour in Switzerland.[32] To satisfy the Cox proportional hazard assumption, we stratified the baseline hazard function on the following variables; sex, neighbourhood index of socio-economic position, civil status, and education level. Potential multicollinearity between exposure variables in the Cox proportional hazards models was evaluated using the variance inflation factor (VIF).

In addition to linear HRs, we also conducted categorical noise analyses using L_{den}(Road) in 5 dB and L_{den}(Railway) and L_{den}(Air) in 10 dB categories to explore the effect of combined exposures of noise respectively with NO_2 and $PM_{2.5}$. All analyses were conducted with the statistical software R and the package 'survival'.[33,34]

Results

The cohort contained 4.40 million observations amounting to 33.67 million person-years. There were 19 261 deaths from MI. The characteristics of the study population are displayed in *Table 1*.

For the NO_2 exposure model, R^2 values independently validated with NABEL data for each year, ranged from 0.70 to 0.82 with highest value for the year 2002 (Supplementary material online, *Table S2*). R^2 values for 10-fold cross-validated elastic net models were ≥0.60 and the R^2 values for elastic net combined with kriged residuals were ≥0.84 (Supplementary material online, *Table S2*). For the $PM_{2.5}$

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Table 2 Spearman's rank correlation coefficients for road traffic, railway, and aircraft noise as well as for $PM_{2.5}$ and NO_2

	L_{den} road	L_{den} railway	L_{den} air	$PM_{2.5}$	NO_2
L_{den} road	1				
L_{den} railway	0.13	1			
L_{den} air	0.09	-0.04	1		
$PM_{2.5}$	0.27	0.20	0.24	1	
NO_2	0.44	0.18	0.27	0.62	1

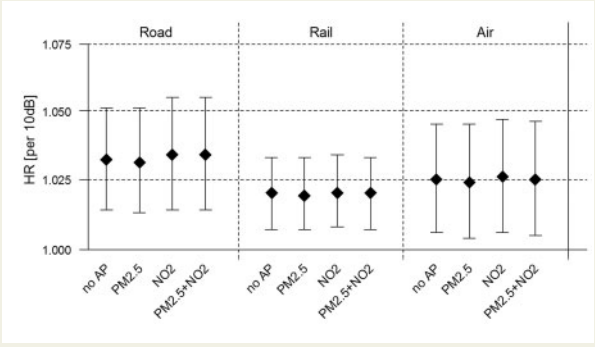

Figure 1 Linear hazard ratios for associations between road, railway, and aircraft noise exposure and myocardial infarction per 10 dB increase in L_{den}, not adjusted for air pollution (no AP), adjusted for $PM_{2.5}$ only ($PM_{2.5}$), adjusted for NO_2 only (NO_2), and adjusted for $PM_{2.5}$ and NO_2 ($PM_{2.5}$ + NO_2). All models were adjusted for age, sex, neighbourhood index of socio-economic position, civil status, education level, mother tongue, nationality, and the other noise sources.

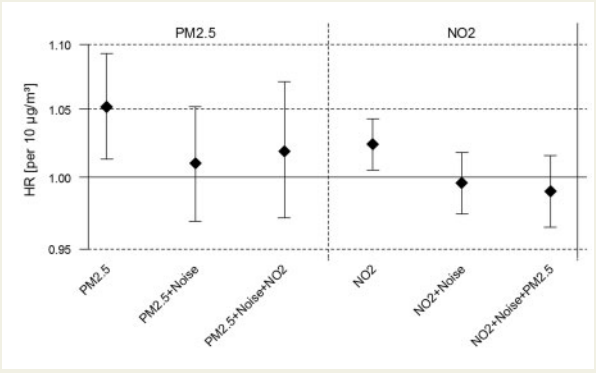

Figure 2 Linear hazard ratios for associations between $PM_{2.5}$ (left side) and NO_2 (right side) per 10 µg/m^3 and myocardial infarction in single exposure models, adjusted additionally for all noise sources, and adjusted for all noise sources and the complimentary air pollutant. All models were adjusted for age, sex, neighbourhood index of socio-economic position, civil status, education level, mother tongue, and nationality.

model, cross-validated temporal and spatial R^2 values ranged from 0.81 to 0.92 and 0.59 to 0.80.[29]

Mean NO_2 and $PM_{2.5}$ exposure levels were 26.1 and 20.2 µg/m^3 as depicted in Supplementary material online, *Figure S1*. The highest Spearman's correlation coefficient between the noise and the air pollution variables was 0.44, observed between L_{den}(Road) and NO_2 (*Table 2*). Correlation between $PM_{2.5}$ and road (0.27), railway (0.20), and aircraft noise (0.24) was rather low. The correlation coefficient between NO_2 and $PM_{2.5}$ was 0.62.

Without considering air pollution exposure, the HR for MI mortality per 10 dB noise increase was 1.032 (1.014–1.051) for road traffic, 1.020 (1.007–1.033) for railway traffic, and 1.025 (1.006–1.045) for aircraft traffic (Supplementary material online, *Table S3*). Adjustment for air pollution exposure had little impact on the HR of the linear exposure-response relationship for all three transportation noise sources (*Figure 1*). Categorical models showed no attenuation of the noise estimates for MI in all road traffic noise exposure categories after adjustment for both air pollutants (Supplementary material online, *Table S4*). A similar pattern was seen for the association between MI mortality and railway noise (Supplementary material online, *Table S5*) and aircraft noise (Supplementary material online, *Table S6*).

Without considering noise exposure, the HR for MI mortality per 10 µg/m^3 increase in NO_2 was 1.024 (1.005–1.043) and per 10 µg/m^3 increase in $PM_{2.5}$ 1.052 (1.013–1.093) (Supplementary material online, *Table S7*). In this case risk estimates for air pollution exposure unadjusted for noise tended to decrease upon adjustment for all noise sources (*Figure 2*).

Multicollinearity between noise and air pollution exposure measures was not critical. In fully adjusted multipollutant models VIF was 1.25 for road traffic noise, 1.06 for railway traffic noise, 1.10 for aircraft noise, 1.65 for $PM_{2.5}$, and 1.92 for NO_2.

Synergistic or antagonistic effects between road traffic noise and $PM_{2.5}$ or NO_2 could not be seen in linear-exposure response models including interaction terms. Similarly, testing interactions in categorical models to evaluate potential thresholds for interaction did not reveal any relevant interactions for $PM_{2.5}$ (*Table 3*) or NO_2 (Supplementary material online, *Table S8*) with road traffic noise exposure. For instance, interaction terms were close to unity for people exposed to high levels of noise and air pollutants.

Discussion

Using fine scale exposure modelling, this study demonstrates that the association between transportation noise and death from MI is stable to air pollution adjustment but not vice versa.

NO_2 originates mainly from road traffic while $PM_{2.5}$ arises from multiple sources including those not related to traffic such as industrial areas, power plants and wood burning and is thus less correlated to road traffic noise than NO_2. In multipollutant air pollution studies, the impact of NO_2 on mortality was independent from $PM_{2.5}$.[35] Strikingly many of the air pollution studies have not adjusted for transportation noise and thus noise as confounder in these studies cannot be ruled out, in particular for associations with NO_2. In the present study, we found that the effect estimates of both air pollutants were attenuated upon inclusion of the noise variables in the

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Table 3 Adjusted[a] hazard ratios (95% confidence intervals) and number of deaths (*N*) for $PM_{2.5}$ and road traffic noise for myocardial infarction in categorical (quartiles) interaction exposure models

		Road traffic noise (dB)			
		≤49.0 (main effect), *N* = 4249	49.0–54.1, *N* = 4775	54.1–60.3, *N* = 5016	>60.3, *N* = 5221
$PM_{2.5}$ ($\mu g/m^3$)	≤16.9 (main effect), *N* = 4524	1.00 (ref), *N* = 1509	1.04 (0.97–1.13), *N* = 1135	1.06 (0.98–1.15), *N* = 986	1.07 (0.98–1.16), *N* = 894
	16.9–18.7, *N* = 4667	1.07 (0.99–1.15), *N* = 1198	*0.97 (0.87–1.08), N = 1215*	*0.98 (0.87–1.10), N = 1159*	*1.01 (0.90–1.13), N = 1095*
	18.7–21.1, *N* = 5056	1.06 (0.98–1.15) *N* = 987	*1.02 (0.91–1.14), N = 1327*	*1.03 (0.92–1.16), N = 1389*	*1.04 (0.92–1.16), N = 1353*
	>21.1, *N* = 5014	1.09 (0.98–1.21), *N* = 555	*0.96 (0.85–1.09), N = 1098*	*0.97 (0.86–1.11) N = 1482*	*0.93 (0.82–1.06), N = 1879*

Cells with interaction terms are shown in italics.
[a]Age as the underlying time scale and additionally adjusted for sex, neighbourhood index of socio-economic position, civil status, education level, mother tongue, nationality, railway and aircraft noise.
ref, reference.

models, which indicates a confounding effect of transportation noise on air pollution. This finding would imply that many air pollution studies, which have not adjusted for transportation noise, may have overestimated the effects of air pollution on MI mortality.

On the other hand, our associations between noise and MI mortality were robust to $PM_{2.5}$ adjustment and only slightly attenuated if NO_2 was considered in the analyses. However, we were not able to evaluate the effects of ultrafine particles (UFP) due to lack of a national model. Of all air pollutants, UFP may have the most similar propagation behaviour to noise. Ultrafine particles are moderately correlated to road traffic noise[36–40] and are a known risk factor for cardiovascular morbidity.[41,42] Ultrafine particles, however, are poorly correlated with $PM_{2.5}$, and we cannot fully rule out that road traffic noise exposure is confounded by UFP. However, UFP are expected to be poorly correlated with railway noise in Switzerland, since railways are electrified, and thus the corresponding risk estimates are unlikely to suffer from such a bias.

Noise and air pollution exposure were both estimated at the residential address and thus bias due to different spatial resolution is expected to be minimized. Such bias may have occurred in our previous analysis[19,20] and other studies.[7,43–45] The models are further comparable in that both the noise and air pollution estimates reflect the ambient exposure, rather than indoor exposure, and therefore suffer similar bias. Nevertheless, bias cannot be completely excluded if accuracy of the models would differ; although R^2 in external validations available for NO_2 and road traffic noise were found to be similar (0.70–0.82 for all models).

In previous analyses conducted with the same cohort and noise data,[19] the noise effect models were adjusted for NO_2 derived from PolluMap, a 200 × 200 m dispersion model for the year 2010. Here, we improved the spatial resolution of the NO_2 exposure estimate, from the grid level to the address level, by further modelling with an extensive passive sampling network distributed across the country. PolluMap was included in this new NO_2 model as a predictor variable and was found to be the most relevant predictor for NO_2. However including additional factors like road and population density around the place of residence produced improved NO_2 exposure estimates (Supplementary material online, *Table S1*). The correlation between NO_2 estimates from PolluMap used in our previous study[19] and from the NO_2 estimates used here is 0.83. In contrast to our previous analyses we did not consider the intermittency ratio[46]—a measure of noise eventfulness—as an additional noise metric to the L_{eq}.

Our results for noise are in line with most of the criteria for evaluating causality proposed by Hill[47] such as consistency,[2,1] temporality, biological gradient, plausibility,[47] and coherence,[48] although specificity cannot be expected for the multifactorial disease MI. The effect sizes are small and not of clinical relevance for an individual. Overall, however, public health burden is relevant as many people are exposed to transportation noise and air pollution. A previous health impact assessment for Switzerland concluded that transportation noise and air pollution caused 6000 and 14 000 years of life lost in 2010.[49]

Strength and limitations

The strengths of this study include the large study population and the long follow-up time. We developed a detailed noise exposure model, which allowed for an individual exposure assessment at the address and floor level. Our air pollution models for NO_2 and $PM_{2.5}$ were both based on novel approaches using high resolution input data. Potential selection bias is minimal in this nationwide study based on census data. Finally, both the noise and air pollution models have been validated with independent data. The road traffic noise model for 2011 has been validated using 99 weekly measurements conducted in 2016 yielding an average difference between modelling and measurements of +0.5 dB(A) with a standard deviation of 4.0 dB(A).[50] This good agreement was obtained despite a time lag of five years between modelling and measurements demonstrating stable noise exposure in our study area. Similar stability is also expected for the time between baseline, time at which the noise exposure was assigned, and follow-up of this cohort study.

Though our models are adjusted for socioeconomic status and other demographic variables, we could not adjust for lifestyle and smoking as this information is not available in the SNC. We, therefore, cannot rule out that residual confounding of lifestyle may play a role for our analyses, although no indications for this were seen in a previous SNC noise study.[6] However, the non-significant effect estimates observed for NO_2 and $PM_{2.5}$ after noise adjustment may suffer from residual confounding. In Switzerland, mortality from cardiovascular diseases has been shown to be higher in rural areas,[32] where air

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pollution is lower on average. This mortality pattern is likely due to individual risk factors and the number of health facilities associated with urban areas, and thus correlated with NO_2 and $PM_{2.5}$, which may not be fully considered in our adjustment set. Since noise exposure varies on a very small scale, this type of bias is likely less relevant for these estimates.

Further, despite high quality exposure modelling, exposure misclassification is unavoidable due to uncertainty in the input data. For noise, uncertainty may arise from exposure assignment based on estimates for the loudest outdoor facade point while no information was available regarding indoor noise levels and noise attenuation factors. However, the impact of such misclassification on the study results are similar for noise and air pollution, and are more likely to dilute the association than introduce a spurious effect.

Conclusion

In this analysis on MI, mutually adjusted with fine-scale noise and air pollution modelling at address level, a consistent exposure-response association between long-term transportation noise exposure and MI mortality was observed. This association was independent from the effects observed for air pollution. Conversely, air pollution effects decreased upon adjustment for transportation noise exposure. Future studies need high quality exposure models for both air pollution and transportation noise to better understand their clinical and public health relevance for cardiovascular disease in various settings.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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