Road traffic noise and incident cardiovascular disease: a joint analysis of HUNT, EPIC-Oxford and UK Biobank

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ABSTRACT

Background: Traffic noise has been associated with cardiovascular disease (CVD) in particular hypertension and ischemic heart disease (IHD), but evidence was not entirely consistent and population-based cohort studies on other CVD outcomes are lacking.

Objectives: This study aimed to investigate the effects of long-term exposure to road traffic noise on incident CVD in three large cohorts.

Methods: In a complete-case sample (N=361,699), 4,014 IHD and 2,109 cerebrovascular incident cases were ascertained between baseline periods 1993-2010 and end of follow-up 2008-2015 through medical record linkage. Annual mean road traffic noise exposure at baseline address was modelled for 2009 using a simplified version of the Common Noise Assessment Methods in Europe (CNOSSOS-EU). Individual-level data were harmonised and physically pooled across the three cohorts. Cox proportional hazard model was used for the analyses with adjustments for potential confounders, including air pollution.

Results: For an interquartile range (IQR) (3.9 A-weighted dB) higher daytime noise, a non-significant association with incident IHD was seen for the overall population (Hazard ratio (HR): 1.015, 95% Confidence Interval (CI): 0.989-1.042), fully adjusted. The association was not confounded by air pollution. Statistically significant associations were seen among women (HR: 1.057, 95%CI: 1.012-1.103, $P_{interaction}$: 0.346), those with a BMI ≥30kg/m^2 (HR: 1.099, 95%CI: 1.029-1.174, $P_{interaction}$: 0.013), and current-smokers (HR: 1.054, 95%CI: 1.007-1.103, $P_{interaction}$: 0.014). No associations were found for neither ischemic nor hemorrhagic stroke.

Conclusions: Our study strengthens the evidence base of road traffic noise effects on incident IHD, whilst the association with incident stroke remains unclear and needs further investigations.

Words: 250

Introduction

Traffic noise is one of the leading environmental risk factors for health in Europe. It was estimated that noise from road, rail and air traffic was associated with 400-1,500 disability-adjusted life years (DALYs) per one million Europeans, the second highest ranking after particulate air pollution(Hanninen et al. 2014).

As an environmental stressor, traffic noise is hypothesized to exert adverse health effects via both direct (e.g. sleep disturbance) and indirect (e.g. annoyance) pathways(Babisch 2014). In acute response to noise, via activations of the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic-adrenal-medulla axis, stress hormones such as adrenalin and cortisol are excessively released to help mitigate damages that noise may cause(Munzel et al. 2016a; Recio et al. 2016). In the long term, these adaptive physiological responses may result in adverse pathophysiologic changes including to blood pressure, lipids and glucose, which ultimately contribute to manifest cardiovascular disease (CVD)(Babisch 2014).

Beyond findings on annoyance and sleep disruption, the evid**e**nce base for cardiovascular effects of long-term traffic noise, particularly those of road transport sources, has been substantially strengthened in the past decade. Of note, most evidence to date has linked noise exposure to hypertension(van Kempen and Babisch 2012) and ischemic heart disease(IHD)(Babisch 2014; Vienneau et al. 2015), although for the latter more evidence is needed to strengthen the dose-response curve. Evidence on associations with other CVD outcomes such as stroke(Halonen et al. 2015; Sorensen et al. 2011), atherosclerosis(Kalsch et al. 2014) and atrial fibrillation(Monrad et al. 2016) is emerging but more studies are needed given the paucity of data at this stage. Relative to air pollution, the contribution of road traffic noise to CVD outcomes warrants more investigation(Stansfeld 2015) since both exposures share a common source and similar mechanistic pathways leading to CVD(Babisch 2014; Brook et al. 2010).

In this study, analysing harmonised noise and health data from three large cohort studies (HUNT, EPIC-Oxford and UK Biobank), we aimed to investigate the associations between residential road traffic noise exposure and incident CVD, in particular IHD and stroke, taking into account the effects of potential confounders and ambient air pollution. We also examined possible effect modification of these associations by a range of *a priori* selected variables in this large study sample.

Methods

Study population

Three population-based cohorts, EPIC-Oxford(Davey et al. 2003), HUNT(Krokstad et al. 2013) and UK Biobank(Sudlow et al. 2015), were included in this study as part of the BioSHaRE-EU (Biobank Standardisation and Harmonisation for Research Excellence) project.

EPIC-Oxford is a component of the European Prospective Investigation into Cancer and Nutrition (EPIC) study(Riboli and Kaaks 1997). During 1993-1999, 57,446 participants aged ≥20 years living throughout the United Kingdom (UK) were recruited through general practices or via postal methods and completed baseline assessments(Davey et al. 2003). The HUNT (Helseundersøkelsen i Nord-Trøndelag) study is a population-based health survey conducted in the whole county of Nord-Trøndelag in central Norway, targeting all residents aged ≥20 years. We used data from the second survey (HUNT2) undertaken in 1995-1997, during which 65,232 residents participated and provided data(Krokstad et al. 2013). UK Biobank, established during 2006-2010, recruited 502,649 participants aged 40-69 years across the UK(Sudlow et al. 2015).

Incident CVD outcomes

Since baseline recruitment, follow-up of first CVD event up to 2008-2015 was based on record linkages to hospital and mortality registries using the unique National Health Service (NHS) number for participants of EPIC-Oxford and UK Biobank in the UK and Personal Identification Number (PIN) for HUNT2 participants in Norway.

International Classification of Diseases (ICD) codes revisions 9 and 10 were used in the registries in both UK and Norway. The outcomes examined in this study were all CVD (ICD9:390-459; ICD10: I00-I99), IHD (ICD9: 410-414; ICD10: I20-I25) and cerebrovascular disease (ICD9: 430-438; ICD10: I60-I69). Incident cases were ascertained if one of the above codes appeared in the linked medical records between baseline recruitment and death, emigration or end of follow-up, whichever came first (event/censoring). Subsequently, acute coronary events (ICD9:410,411; ICD10:I20.0, I21, I23, I24), ischemic stroke (ICD9:433,434; ICD10:I63), and hemorrhagic stroke (ICD9: 431; ICD10: I60, I61, I62) were also ascertained.

Participants who reported prevalent CVD, including hypertension, heart attack, angina and stroke at baseline questionnaire, were excluded from analyses. Further, by screening medical

records, participants who had CVD diagnosed prior to baseline recruitment were also excluded (Supplement-1).

Exposure assessment

A simplified version(Morley et al. 2015) of the CNOSSOS-EU (Common noise assessment methods in European Union) noise modelling framework(Kephalopoulos et al. 2014) was developed and run for each cohort.

Noise sound pressure level was estimated on all roads within 500 meters of home address at recruitment. Noise propagation due to refraction and diffraction, absorption from buildings, distance and angle of view were considered in the model. Road network geography, hourly vehicle flows, building heights, land cover and meteorological data were obtained for the respective study areas. To account for participants living on minor roads that were not captured in the national level traffic datasets, a fixed low-level baseline flow (600 vehicles per day) was assigned(Gulliver et al. 2015). Traffic data were for the year 2009 and land cover data were for the year 2006. Annual mean A-weighted sound pressure level in decibels (dB(A)) for daytime noise (averaged sound level from 07:00 to 19:00), night-time noise (averaged sound level from 23:00 to 07:00) and 24-hour noise (Lden) were modelled at baseline address of participants in all three cohorts.

For all three cohorts, annual mean PM_{10} (particulate matter with aerodynamic diameter $\leq 10\mu m$) and NO_2 (nitrogen dioxide) air pollution estimates at baseline addresses for the year 2007 were assigned from a harmonised European Land Use Regression (LUR) model at a resolution of 100x100m(Vienneau et al. 2013).

Statistical analyses

We used Cox proportional hazards models with age as the underlying time-scale(Thiebaut and Benichou 2004), which allows comparison of individuals of the same age, to explore the associations between road traffic noise exposures on a continuous scale and each of the incident CVD outcomes. Harmonised individual-level data from each cohort were physically pooled in Stata (v12.1).

Adjusted models were defined *a priori* as follows: Model0: adjusted for cohort; Model1: further adjusted for sex; Model2(**main model**): further adjusted for education level (low, medium, high), employment (yes or no) and smoking status (never-, ex- and current-).All these covariates were retrospectively harmonised across all three cohorts (Supplement-2),

following a validated protocol(Fortier et al. 2011). Noise estimates was also assessed in tertiles (Lday: ≥38.5 to ≤52.9, >52.9 to ≤55.1, >55.1 to ≤86.4 dB(A) and Lnight: ≥34.6 to ≤44.1, >44.1 to ≤46.3, >46.3 to ≤77.6 dB(A)). Only participants with complete information on noise exposures and main model covariates were included in all the analyses.

Continuous variables including PM_{10}, NO_2, smoking pack-years, body mass index (BMI), weekly consumption of alcohol in grams and a binary variable of ever-had diabetes were each added to the main model in sensitivity analyses. We also conducted cohort-specific analyses (main model) and pooled cohort-specific hazard ratios (HR) via meta-analysis methods.

Subgroup analyses were conducted by sex, age (<60 and ≥60 years), BMI (<25, 25-30, ≥30 kg/m^2), smoking status, education level and ever-had diabetes based on the main model. Effect modifications were investigated by adding to the main model an interaction term between noise exposure and each of these variables.

All the results were presented as hazard ratio (HR) and 95% confidence interval (CI) per an interquartile range (IQR) higher of noise estimate.

Meta-analysis

We further updated meta-analytical evidence of road traffic noise effects on incident IHD by adding most recent evidence from a large study(Bodin et al. 2016) and those of the present study to that compiled by Vienneau et al (Vienneau et al. 2015). Both fixed-effect and random-effect meta-analysis was conducted by using Stata 'metan' package(Harris et al. 2008), with between-study heterogeneity being assessed by the I^2 statistics(Higgins and Thompson 2002).

Results

Pooling data from the three cohorts, a total of 361,699 participants with complete information were included in the analyses. The mean age of the pooled population was 53 years and 58% were women (Table 1). During follow-up, 23,401 incident CVD cases were recorded, with 4,014 cases of incident IHD and 2,109 cases of incident cerebrovascular disease.

The distributions of daytime noise and night-time noise by cohort and in the pooled data are shown in Table 2. In the pooled data, daytime noise ranged from 38.5 to 86.4 dB(A), with a median (IQR) of 54.0 (3.9) dB(A). The respective range for night-time noise was 34.7-77.6 dB(A), with a median (IQR) of 45.2 (3.9) dB(A). Spearman correlations between daytime

noise and PM_{10} or NO_2 were moderate (r=0.33) whilst correlation between daytime noise and night-time noise was close to unity (r=0.99) in the pooled data and in each cohort.

In the main model (Model 2), no significant associations were observed between daytime noise and any of the incident CVD outcomes in the pooled analysis (Table 3). A non-significant association was found with incident IHD (HR: 1.015, 95%CI: 0.989-1.042, per IQR increase). Further adjusting for air pollution, smoking pack-year, BMI or diabetes status did not materially change the main findings (Supplement-3) for all outcomes, except that after adding weekly alcohol consumption to the main model, the null associations with ischemic stroke became positive but remained non-significant (HR: 1.023, 95%CI: 0.953 to 1.099, per IQR increase). Pooling cohort-specific results via meta-analysis yielded similar HRs as those presented in Table 3 and heterogeneity across cohorts were not detected (Supplement-3).

No significant associations were found with either daytime or night-time noise in tertiles in the main model (Supplement-4).

In the subgroup analyses for incident IHD, significant positive associations were observed for women (HR: 1.057, 95%CI: 1.012-1.103), individuals with a BMI $\geq$30kg/m^2 (HR: 1.099, 95%CI: 1.029-1.174) and current smokers (HR: 1.054, 95%CI: 1.007-1.103) for an IQR increase daytime noise (Figure 1), with significant interactions also detected for the latter two associations ($P_{interaction}$ was 0.013 and 0.014 respectively). No significant associations were found in any subgroups for incident cerebrovascular disease nor all CVD (Supplement-5).

We included our estimate for daytime noise in the updated meta-analysis for Lden effects on incident IHD, as the two noise indicators was almost perfectly correlated (r=0.99). Overall, a significant association between per 10 dB(A) higher Lden and incident IHD (HR: 1.04, 95%CI: 1.00-1.07, p-value=0.04) was observed, with no heterogeneity detected across studies (I^2=9.9%, $P_{heterogeneity}$= 0.325) (Figure 2).

Discussion

To our knowledge, this is the largest cohort study to date examining the associations between road traffic noise and both incident IHD and stroke events. Our analyses suggested an overall non-significant increased risk for incident IHD, with associations reaching statistical significance among women, obese persons and current-smokers. An updated meta-analysis which included the estimate for IHD of the present study showed a significant positive

association between 24-hour road traffic noise and incident IHD. However, no associations were found for cerebrovascular disease, nor for all CVD events. Our study further suggested that road traffic noise effects on incident CVD outcomes were not confounded by ambient air pollution.

Findings on ischemic heart disease

Our finding on a possible link between road traffic noise and incident IHD is consistent with some previous studies, which reported a positive but non-significant association either in men-only samples(Babisch et al. 2005; Babisch et al. 1994) or in populations of both sexes(Selander et al. 2009). However, some studies also reported null associations with incident IHD(Babisch et al. 1999; Bodin et al. 2016) or IHD mortality(Beelen et al. 2009). To date, only one prospective cohort study has reported a statistically significant association with incident myocardial infarction (MI) (RR: 1.12, 95%CI: 1.02 to 1.22, per 10 dB(A) Lden) among 50,614 participants in Denmark(Sorensen et al. 2012). Studies published after year 2005 were all adjusted for traffic-related air pollution (NO_2 or black smoke) and suggested no confounding effects(Babisch et al. 2005; Beelen et al. 2009; Bodin et al. 2016; Selander et al. 2009; Sorensen et al. 2012). In our study, ambient rather than traffic-specific air pollution was adjusted for, but we would draw the same conclusion regarding confounding.

We further updated the meta-analytical evidence from Vienneau et al (Vienneau et al. 2015), by adding findings of the present study and those of Bodin et al(Bodin et al. 2016). Previously, based on eight road traffic noise studies, Vienneau et al reported a pooled effect of 1.04 (95%CI: 1.00-1.10) per 10 dB(A) Lden on IHD incidence. Herein we reported a same effect estimate but with a narrower confidence interval (1.04, 95%CI: 1.00-1.07), a more precise estimate due to the inclusion of our large study. Two very large ecological studies were also recently published. A small-area study of 8.6 million Londoners found daytime noise was significantly associated with IHD mortality, but not with hospital admissions, comparing areas with an annual mean noise level of 55-60 vs. <55 dB(A)(Halonen et al. 2015). A study in the Rhine-Main region of Germany identified 19,632 incident MI cases and 834,734 controls through health insurance databases and reported a statistically significant association between 24-hour road noise level and MI (2.8% per 10 dB increase, 95%CI: 1.2-4.5)(Seidler et al. 2016). Both studies were only adjusted for age, sex and a range of area-level variables, hence are not directly comparable to those of individual level cohort studies including ours. Nevertheless, including these two studies in the meta-analysis gave a pooled

effect estimate of 1.02 (95%CI: 1.00-1.04), with evidence for heterogeneity (*P-value*: 0.043) also being detected (figure not shown).

Unlike some previous studies which either found a stronger association with IHD in men(Babisch et al. 2005; Sorensen et al. 2012) or no effect modification by sex(Beelen et al. 2009; Selander et al. 2009), we found a significant association in women although the interaction term by sex was not statistically significant. It remains inconclusive whether there exists a sex difference of noise exposure on IHD. We did not consider the possible confounding effects of the intake of sex hormones or menopausal status of these women participants, which may plausibly influence the stress response either positively or negatively(Babisch et al. 2005). Also, it was reported in a UK study that women were more sensitive to noise(Stansfeld and Shipley 2015), but it is unclear whether noise sensitivity will modify the associations with IHD morbidity. We found a stronger association among current-smokers, but other studies have reported an effect in ex-smokers only(Selander et al. 2009) or no effect modification by smoking(Beelen et al. 2009). Emerging studies also reported positive significant associations between traffic noise and obesity markers(Oftedal et al. 2015; Pyko et al. 2015), lending further support to our finding of a stronger association between traffic noise and IHD among obese persons. Although the subgroup findings were incompatible with some previous studies, our study benefited from a very large sample size to explore interactions.

Findings on cerebrovascular disease

Very few studies have investigated road traffic noise effects on incident stroke. The aforementioned study in Denmark firstly reported a positive significant association between Lden and incident stroke (HR: 1.14, 95%CI: 1.03-1.25, per 10 dB(A) increase)(Sorensen et al. 2011). The same research group later reported that this association was mainly confined to ischemic stroke but not hemorrhagic stroke(Sorensen et al. 2014). In contrast to this, our much larger study did not find an association with any category of stroke events.

The small-area study in London found a significantly elevated risk for stroke hospital admissions among adults in areas exposed to annual mean daytime noise >60 vs. <55 dB(A)(Halonen et al. 2015). However, no significant associations with stroke mortality were observed in the London study, in line with the findings of the Dutch study(Beelen et al. 2009). Two other studies investigating stroke incidence in combination with other heart diseases reported either null associations(de Kluizenaar et al. 2013) or that the observed

significant association was confounded by air pollution(Floud et al. 2013). Heterogeneity was found across these studies in a recent review, in which the authors suspected that road traffic noise effects on stroke may follow a non-linear trend(Dzhambov and Dimitrova 2016). The nature of any dose-response relationship however remains to be established.

In the cohort-specific analyses, a positive but non-significant association was observed in UK Biobank with an effect estimate similar to that of Sorensen et al(Sorensen et al. 2011). Given the relatively short period of follow-up (mean 1.3 years), future studies will be needed to explore this possible link between noise exposure and incident stroke events in UK Biobank.

Aircraft noise

In this study, data for aircraft noise exposure were not available. Of note, aircraft noise is qualitatively different from road traffic noise and may therefore have different associations with health outcomes(Munzel et al. 2016b). Vienneau et al summarised findings from only three studies to date on aircraft noise and found a somewhat stronger association with IHD than that of road traffic noise. However, heterogeneity existed across these three studies, among which only one study observed a significant association with hospital admissions for IHD(Hansell et al. 2013), the other two studies showed a borderline significant association with IHD hospital admissions(Correia et al. 2013) or with MI mortality(Huss et al. 2010). Similar findings were also observed for stroke outcomes in these three studies(Dzhambov and Dimitrova 2016).

Strengths and limitations

Strengths of this study include its prospective design, a very large sample size with harmonised noise, health and covariate data, and adjustment for air pollution exposures in relation to CVD morbidity.

There are several limitations to this study. First, our model-based noise assessment approach at baseline residential address is inevitably associated with exposure misclassification, for example, due to time spent away from home, travel during the day, housing characteristics and window-opening. These misclassifications are believed to be non-differential for cases and non-cases and therefore only likely bias the risk estimates towards null. In addition, the current noise model used in this study tends to over-estimate noise exposures for those at low exposure levels due to the assumed national baseline value and to under-estimate exposure for those living in areas with heavily trafficked minor roads. Both scenarios contributed to the

uncertainty of continuous noise estimates and limited our ability to detect a noise effect, if present. Second, noise from railway, aircraft and occupation may all have impacts on health(Munzel et al. 2014), and by not considering these noise sources, our risk estimates may have been underestimated. Vienneau et al combined risk estimates from road and aircraft noise studies on IHD in the meta-analysis and indeed reported a higher, more precise effect estimate, compared to that of road traffic noise alone(Vienneau et al. 2015). However, the authors also suggested that failing to consider different noise sources in the analyses is likely not a major problem as the pooled estimate for road and aircraft noise alone on IHD was similar. This arguably may not be the case for other CVD outcomes such as stroke(Dzhambov and Dimitrova 2016).Third, road traffic noise was estimated using traffic data input from year 2009 and then applied to participants' home addresses across the three cohort at baseline during 1993-2010. Assumptions have to be made that whilst the absolute traffic volumes may have changed between baseline periods and 2009, the relative difference of road traffic noise will have been stable. Fourth, although our analyses were adjusted for a key set of covariates including lifestyle, individual-level socioeconomic status and air pollution, we cannot rule out the possibility of residual confounding by other unaccounted factors such as physical activity and area-level deprivation. Finally, selection bias may exist as we only included 58% of the original sample in the complete-case analysis. Across the three cohorts, participants included in the analyses were younger and in relatively better socioeconomic positions in terms of employment and education, which could be one of the reasons to explain our weak findings.

Conclusions

This study provides further suggestive evidence between residential road traffic noise exposure and incident ischemic heart disease, particularly in obese individuals and current-smokers. Evidence for incident stroke events remains inconclusive and more prospective cohort studies are needed to investigate this potentially important link.

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Tables

Table 1 Baseline characteristics and incident CVD cases by tertiles of daytime road traffic noise

	Daytime noise, dB(A)			
	Pooled data* (N=361,699)	[38.5 to 52.9]	(52.9 to 55.1]	(55.1 to 86.4]
Age≥60 years, %	31.3	29.2	33.4	31.4
Women, %	58.4	57.2	59.0	59.2
BMI ≥30kg/m^2, %	16.7	15.8	17.0	17.3
High education level, %	57.4	48.8	61.2	62.2
Currently employed, %	66.4	67.1	65.4	66.7
Current smokers, %	13.2	16.5	10.9	12.1
Follow-up of CVD events				
Average follow-up years	3.9	6.4	2.6	2.7
Incident CVD cases	23,401	16,437	3,627	3,337
Incident IHD cases	4,014	2,908	606	500
Incident acute coronary events	1,605	1,231	214	160
Incident cerebrovascular cases	2,109	1,615	249	245
Incident ischemic stroke	999	820	95	84
Incident hemorragphic stroke	360	238	61	61

*participants with complete information on noise exposure, incident outcomes and covariates in the main model. CVD: cardiovascular disease; IHD: ischemic heart disease. BMI: body mass index;
Associations between daytime noise and each variable or outcome presented in this table all have a p-value<0.05, based on chi-square test.

Table 2 Distribution of road traffic noise metrics in each cohort and in the pooled data

Distributions of road traffic noise exposure, dB(A)											**Spearman correlation**	
Daytime noise	N	Min	5%	25%	50%	75%	95%	Max	Mean (SD)	IQR	PM_{10}	NO_2
HUNT2	43,264	38.5	39.1	43.6	47.4	50.3	54.6	68.4	47.0 (4.9)	6.7	0.05	-0.05
EPIC-Oxford	29,067	50.9	51.1	53.0	54.5	56.6	66.1	84.1	55.6 (4.3)	3.6	0.10	0.11
UK Biobank	289,368	50.9	51.1	52.8	54.3	56.3	65.9	86.4	55.4 (4.2)	3.5	0.09	0.10
Pooled data	361,699	38.5	46.4	52.1	54.0	56.0	65.1	86.4	54.4 (5.1)	3.9	0.33	0.33
Night-time noise	N	Min	5%	25%	50%	75%	95%	Max	Mean (SD)	IQR		
HUNT2	43,264	34.7	35.1	37.5	40.2	42.5	46.4	60.0	40.3 (3.7)	5.0		
EPIC-Oxford	29,067	42.1	42.2	44.2	45.7	47.8	57.3	75.3	46.8 (4.3)	3.6		
UK Biobank	289,368	42.1	42.3	44.0	45.5	47.5	57.1	77.6	46.6 (4.2)	3.5		
Pooled data	361,699	34.7	39.4	43.3	45.2	47.2	56.3	77.6	45.8 (4.7)	3.9		

Daytime (07:00-19:00) noise; night-time (23:00-07:00) noise; IQR: inter-quartile range

Table 3 Association (hazard ratios, 95%CI) between daytime noise (per IQR (3.9 dB(A)) increase) and each incident CVD outcome: pooled analyses from all three cohorts of 360,881 participants

	ischemic heart disease	**acute coronary events**	**cerebrovascular disease**	**ischemic stroke**	**hemorrhagic stroke**	**all CVD**
Model 0	1.025(0.998-1.052)	1.039(0.997-1.082)	0.986(0.952-1.022)	1.000(0.950-1.052)	0.941(0.859-1.030)	1.002(0.991-1.013)
Model 1	1.021(0.995-1.048)	1.033(0.992-1.076)	0.985(0.951-1.021)	1.001(0.951-1.053)	0.940(0.858-1.030)	1.002(0.991-1.012)
Model 2	1.015(0.989-1.042)	1.026(0.985-1.068)	0.983(0.948-1.019)	0.998(0.948-1.050)	0.935(0.853-1.025)	0.999(0.988-1.010)

Model 0: adjusted for cohort; Model 1: further adjusted for sex; Model 2: further adjusted for employment, education, smoking status. IQR: inter-quartile range

Figure Legends

Figure 1 Associations between per IQR (3.9 dB(A)) higher daytime noise and incident ischemic heart disease: subgroup analyses based on main model (adjusted for cohort, sex, employment, education, smoking status).

Figure 2 Updated forest plot of effect estimates for incident ischemic heart disease per 10 dB(A) increase of road traffic noise (Lden)