

Online Supplements

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

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- **Supplement-1**

EPIC-Oxford: Each participant was followed for first CVD admission to hospital following recruitment using the unique National Health Service (NHS) number. In England, information on hospital admissions for each patient are available from 1 April 1997 from the Hospital Episode Statistics (HES) database. In Scotland, the equivalent database is called the Scottish Morbidity Records (SMR) which started in 1 January 1981. Hospital admission data for each participant from England (from 1 April 1997 to 31 December 2012) and Scotland (from 1 January 1981 to 31 December 2008) were obtained via linkages to the respective database and provided by EPIC-Oxford. The diagnosis codes used WHO 9th revision of International Classification of Diseases (ICD9) before 1 April 1996, and since then the 10th revision (ICD10). The respective ICD codes used to identify incident cardiovascular diseases were ICD9 390-459 and ICD10 I00-I99. For participants dying during follow-up, cause of death up to 30 December 2009 was obtained from the NHS central register. Incident CVD death were ascertained when CVD (ICD9 390-459; ICD10 I00-I99) was either a primary or a secondary cause of death, providing that the participant had never had CVD diagnosed/reported prior to the death.

Following internal standard exclusions in EPIC-Oxford, linkages were not possible for 12,342 of the recruited 57,446 participants (*Email correspondence from the EPIC-Oxford team*). In addition, participants whose nations of residence was Wales or Northern Ireland as well as those participants who had pre-existing self-reported CVD-related history (heart attack, angina, stroke, hypertension and hyperlipidaemia) were excluded (N=4720), making record linkage possible for a total of 40,384 participants.

HUNT: The HUNT cohort has been further enhanced by linkage to registers covering all participants in all three surveys (HUNT1, HUNT2, HUNT3). Information from national or local registers is linked to each HUNT participant using the unique Norwegian Personal

Identification Number (PIN). After recruitment to HUNT2, participants were followed for first CVD admission to hospital up to 31 March 2015. Incident CVD cases were identified by linkages with medical record at the only two local hospitals serving the population of the county of Nord-Trøndelag. Before 1 January 1999, ICD9 codes were used as diagnosis codes in the medical records, and since then ICD10 codes were used. The respective ICD codes used to identify incident cardiovascular diseases are ICD9 390-459 and ICD10 I00-I99. Mortality data until 31 December 2013 were obtained from the National Cause of Death Registry. Participants were ascertained as incident deaths if CVD was one of the causes of death and participants had never had CVD diagnosed/reported before. Participants who reported at the time of HUNT2 recruitment that they had ever had heart attack, angina pectoris, stroke, previously taken medication for hypertension as well as those who were currently taking medication for hypertension were excluded (N=12,037), making record linkages for a total of 66,844 participants for all three surveys.

UK Biobank: As for EPIC-Oxford, data on any hospital admission for each participant are available from HES in England and SMR in Scotland. Hospital data were not yet available for Wales to be included in the timeframe of this study. As for the EPIC-Oxford and HUNT studies, participants were followed for first CVD admission to hospital or CVD death following recruitment. ICD10-coded hospital data were available for UK Biobank from 1996-1997 to March 2010 in England and to December 2012 in Scotland. The censored date for hospital CVD admission was defined as 31 March 2010 for UK Biobank. Cause of death up to 30 December 2013 was obtained from the Health & Social Care Information Centre (HSCIC) for each participant in England and Wales; while for Scotland, mortality data up to 30 November 2012 were obtained from Information Services Department (ISD). The respective ICD codes used to identify incident cardiovascular diseases from all registers are ICD10 I00-I99. After excluding those who had CVD diagnosed in their medical records before recruitment to UK

Biobank and those who reported in recruitment that they had ever had heart attack, stroke, hypertension and angina (N=165,426), record linkages were available for a total of 337,223 participants.

Table S1 Summary of CVD outcome ascertainment in each cohort

	EPIC-Oxford	HUNT2	UK Biobank
Baseline recruitment	1993-1999	1995-1997	2006-2010
Data source	Hospital Episode Statistics (HES); Scottish Morbidity Records (SMR); NHS central register for death;	Two local hospitals in the Nord-Trøndelag county; National Cause of Death Registry;	Hospital Episode Statistics (HES); Scottish Morbidity Records (SMR); NHS central register for death;
Start date of medical records	01-Apr-1997 (England HES) 01-Jan-1981 (Scotland SMR)	01-Jan-1995	01-Apr-1997 (England HES) 01-Jan-1981 (Scotland SMR)
Censored date for first hospital CVD admission	31-Dec-2012 (England HES) 31-Dec-2008 (Scotland SMR)	31-Mar-2015	31-Mar-2010 (England and Scotland)
Censored date for death	30-Dec-2009	30-Dec-2013	30-Dec-2013
Pre-existing CVD cases before recruitment	4,720	12,037	165,426
Record linkages available for this analysis	40,384	66,844 (includes participants from HUNT1, 2, and 3.	337,223

- **Supplement-2**

Table S2: harmonisation of each main variable

Harmonised name	Harmonised definition	Unit/Categories
AGE_YRS	Age of the Years participant in years (continuous) at recruitment	
GENDER	Sex of the participant	0: Male; 1:Female
ADM_YRINT	Calendar Year of the interview	calendar year
PM_HEIGHT	Measured height	cm
PM_WEIGHT	Measured weight	kg
PM_BMI_CONTINUOUS	Body Mass Index: calculated using measured or self- reported weight and height (kg/m ²)	kg/m ²
PM_BMI_CATEGORICAL	Body Mass Index calculated using measured weight and height (Mass in Kg / (Height in metre) ²) and stratified in 3 categories.	1: less 25 kg/m ² ; 2: 25 to 30 kg/m ² ; 3: over 30 kg/m ²

SMK_STATUS	Indicator of the participant's baseline and past smoking status, which includes use of cigarettes, cigars, pipes and other tobacco products.	0: Never-smoker; 1: Ex-smoker; 2: Current-smoker
WORK_STATUS_CURRENT	Indicator of whether the participant at baseline was in paid employment or is self-employed.	0: No paid employment or not self-employed; 1: Paid employment or self-employed
EDU_HIGHEST_1	Highest level of education completed by the participant. Categories are adapted from the UNESCO Revision of the International Standard Classification of Education, 2011	0: No education or primary education 1: Secondary education; 2: Vocational/college/university
ALC_CURRENT_QTY_TOTAL#	Baseline Quantity of Total Alcohol	Grams of alcohol consumed on average per week. Baseline

Consumed in Beer, quantity of total alcohol taken
Wine and Spirits per = (Baseline quantity of beer
week (7 days) taken * Average quantity of
alcohol in a bottle/glass/pint of
beer) + (Baseline quantity of
wine taken * Average quantity
of alcohol in a serving of wine)
+ (Baseline quantity of spirits
taken * Average quantity of
alcohol in a serving of spirits).

#Quantity of alcohol for the same drink type may vary between cohorts, as serving sizes may be different in each cohort's country. If information about serving size was not mentioned, then the average serving size for the cohort country was estimated and grams of alcohol determined

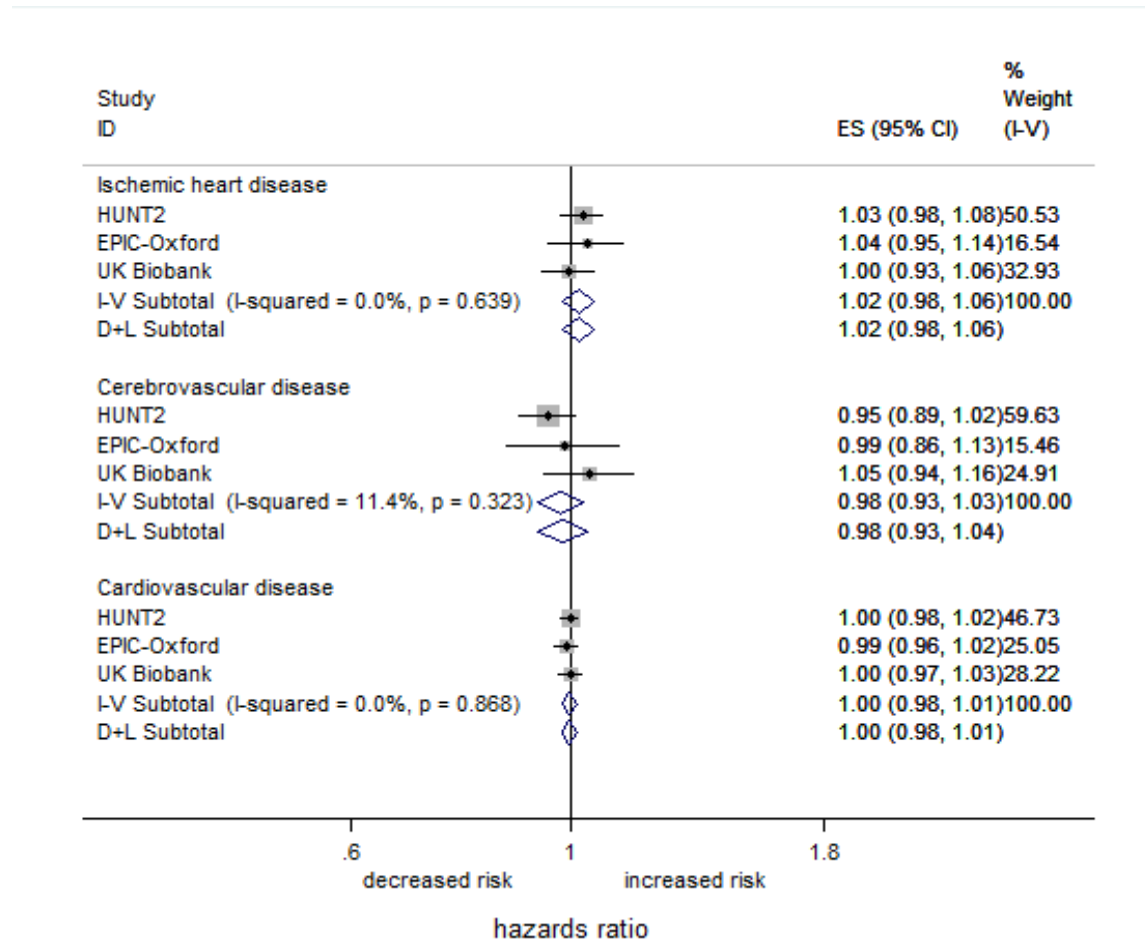
- Supplement-3

Table S3: Sensitivity analyses based on main model (Model 2): Association (hazard ratios, 95%CI) between daytime noise (per 3.9 dB(A) increase) and each of incident CVD outcome

	ischemic heart disease	acute coronary events	cerebrovasc ular disease	ischemic stroke	hemorrhagic stroke	ALL CVD
Model 2 (Main model)	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)
Sensitivity analyses						
Model 2+PM₁₀	1.015 (0.989-1.042)	1.026 (0.985-1.069)	0.981 (0.946-1.017)	0.997 (0.947-1.050)	0.934 (0.852-1.024)	0.997 (0.987-1.008)
Model 2+NO₂	1.015 (0.989-1.042)	1.026 (0.985-1.069)	0.982 (0.948-1.018)	0.998 (0.948-1.050)	0.936 (0.854-1.025)	0.998 (0.988-1.009)
Model2+BMI	1.014 (0.988-1.041)	1.024 (0.983-1.066)	0.982 (0.948-1.019)	0.997 (0.947-1.050)	0.935 (0.853-1.025)	0.998 (0.987-1.009)
Model 2+alcohol consumption	1.019 (0.985-1.055)	1.019 (0.965-1.076)	1.003 (0.956-1.054)	1.023 (0.953-1.099)	0.998 (0.892-1.117)	1.005 (0.991-1.019)
Model 2+ ever- had diabetes	1.015 (0.989-1.041)	1.025 (0.984-1.067)	0.981 (0.947-1.017)	0.997 (0.947-1.049)	0.934 (0.852-1.023)	0.998 (0.988-1.009)
Model 2+smoking pack-years	1.015 (0.987-1.044)	1.026 (0.983-1.072)	0.984 (0.947-1.023)	0.993 (0.940-1.049)	0.940 (0.854-1.035)	0.998 (0.986-1.010)

Model 2: cohort, sex, employment, education, smoking status

Figure S3: cohort-specific analyses of associations between per IQR* increase of daytime noise and incident CVD outcomes based on model 2 (adjusted for cohort, sex, employment, education, smoking status).



IQR for HUNT2, EPIC-Oxford and UK biobank was 6.7, 3.6, 3.5 dB(A) respectively.

- **Supplement-4**

Table S4 Association (hazard ratios, 95%CI) between daytime noise , night-time noise in tertiles and each of incident CVD outcome: pooled analyses from all three cohorts of 361,699 participants on Model 2

	ischemic heart disease	cerebrovascular disease	ALL CVD
Daytime noise, dB(A)			
>= 38.5 to <=52.9	1	1	1
>52.9 to <=55.1	1.06 (0.96-1.18)	0.91 (0.78-1.06)	1.00 (0.96-1.04)
>55.1 to <=86.4	0.94 (0.84-1.06)	0.99 (0.84-1.16)	0.96 (0.92-1.01)
Night-time noise, dB(A)			
>=34.6 to <=44.1	1	1	1
>44.1 to <=46.3	0.98 (0.89-1.09)	0.95 (0.83-1.10)	0.99 (0.95-1.03)
>46.3 to <=77.6	0.97 (0.87-1.08)	1.00 (0.86-1.17)	0.96 (0.92-1.01)

Daytime (07:00-19:00) noise; night-time (23:00-07:00) noise; Model 2: cohort, sex, employment, education, smoking status.

- **Supplement-5**

Table S5.1 Associations between per IQR (3.9 dB(A)) higher daytime noise and incident cerebrovascular disease: subgroup analyses based on Model 2 (adjusted for cohort, sex, employment, education, smoking status).

	n	cerebrovascular disease		
LDAY		HR	95%CI	
men	150354	0.976	0.926	1.028
women	211345	0.975	0.925	1.029
age<60years	248358	0.956	0.905	1.010
age>=60 years	113341	1.001	0.954	1.050
BMI<25kg/m²	151929	0.973	0.917	1.033
BMI: 25-30 kg/m²	144895	0.986	0.933	1.042
BMI>30 kg/m²	59490	1.026	0.925	1.138
never-smoker	201454	0.992	0.937	1.050
ex-smoker	109905	0.993	0.925	1.065
current-smoker	46326	0.957	0.894	1.025
low- education	52504	0.951	0.903	1.001
Medium- education	98658	1.020	0.955	1.089
High- education	206523	1.023	0.936	1.119
had diabetes	7049	1.220	0.875	1.702
not had diabetes	349966	0.979	0.943	1.015

Table S5.2 Associations between per IQR (3.9 dB(A)) higher daytime noise and incident cardiovascular disease: subgroup analyses based on Model 2 (adjusted for cohort, sex, employment, education, smoking status).

	n	All CVD			
LDAY		HR	95%ci		p
men	150354	1.003	0.987	1.019	0.002
women	211345	0.993	0.978	1.008	
age<60years	248358	0.997	0.983	1.010	0.085
age>=60 years	113341	1.003	0.985	1.022	
BMI<25kg/m²	151929	0.991	0.974	1.009	0.045
BMI: 25-30 kg/m²	144895	0.996	0.980	1.013	
BMI>30 kg/m²	59490	1.010	0.981	1.039	
never-smoker	201454	0.986	0.969	1.003	0.005
ex-smoker	109905	0.999	0.979	1.020	
current-smoker	46326	1.015	0.994	1.037	
low- education	52504	1.003	0.985	1.022	0.016
Medium- education	98658	1.000	0.982	1.018	
High- education	206523	0.992	0.970	1.014	
had diabetes	7049	1.078	0.974	1.193	0.002
not had diabetes	349966	0.997	0.986	1.008	