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

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## ABSTRACT

Aims: This study aimed to investigate the effects of long-term exposure to road traffic noise on incident CVD in three large cohorts: HUNT, EPIC-Oxford and UK Biobank.

Methods: In a complete-case sample (N=361,699), 4,014 IHD and 2,109 cerebrovascular incident cases were ascertained between baseline (1993-2010) and end of follow-up (2008-2015) through medical record linkage. Annual mean road traffic noise exposure was modelled at baseline address. Individual-level covariate data were harmonised and data were pooled. Analyses used Cox proportional hazards model with adjustments for confounders, including air pollution.

Results: For an interquartile range (IQR) (3.9 dBA) higher daytime noise, a non-significant association with incident IHD was seen (Hazard ratio (HR): 1.015, 95% Confidence Interval (CI): 0.989-1.042), fully adjusted. Statistically significant associations and interaction terms were seen in obese individuals (HR: 1.099, 95%CI: 1.029-1.174), and current-smokers (HR: 1.054, 95%CI: 1.007-1.103). No associations were found for ischemic or hemorrhagic stroke.

Conclusions: Our study strengthens the evidence base for an effect of road traffic noise on incident IHD, whilst the association with incident stroke remains unclear.

## Introduction

There is good evidence that environmental noise causes annoyance and disturbs sleep and there is increasing awareness of the potential long-term impacts on health (1). Hanninen et al (2014) estimated that noise from road, rail and air traffic was associated with 400 to 1,500 disability-adjusted life years (DALYs) per one million Europeans, the second highest ranking after particulate air pollution (2).

Traffic noise is hypothesised to exert adverse health effects via both direct (e.g. sleep disturbance) and indirect (e.g. annoyance) pathways. Acute response to noise involves activation of the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic-adrenal-medulla axis leading to release of stress hormones such as adrenalin and cortisol are excessively released (3, 4). In the long term, these adaptive physiological responses may result in adverse pathophysiologic changes to cardiovascular risk factors such as increases in blood pressure, lipids and glucose.

The evidence base for cardiovascular effects of long-term traffic noise, particularly those of road transport sources, has been substantially strengthened in the past decade. However, the largest numbers of studies to date relate to blood pressure. A meta-analysis of 24 studies published in 2012 found noise exposure was linked to increased risk of hypertension (5). A meta-analysis of 14 studies published in 2014 also found increased risk of incident cardiovascular disease (CVD) (6). The CVD meta-analysis was based on five cross-sectional and four case-control studies, together with five cohort studies (of which two of the cohorts could be considered large, with >10,000 participants). The authors commented that the age range of study subjects and the lower limit cut-off of noise levels used affected the effect estimates of different studies. More cohort studies are needed to better define the dose-response relationships.

Evidence on associations with other CVD outcomes such as stroke (7, 8), atherosclerosis (9) and atrial fibrillation (10) is emerging but more studies are needed for these outcomes given the paucity of data at this stage. While air pollution from road traffic is well recognised to increase CVD risk, road traffic noise and air pollution share a common source and the independent contribution of road traffic noise to CVD outcomes warrants more investigation (11).

This study analysed 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

Data were obtained from three cohorts: two UK based cohorts, EPIC-Oxford and UK Biobank, and one Norwegian cohort, HUNT. Ischaemic heart disease (IHD) and cerebrovascular disease incident cases were ascertained between baseline (1993-2010) and end of follow-up (2008-2015) through medical record linkage. Follow-up processes for each cohort are described in more detail below.

*Cohort details*

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.

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.

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.

*Road and air pollution exposure data*

Annual mean road traffic noise exposure was modelled at baseline address, using a simplified versionof the CNOSSOS-EU (Common noise assessment methods in European Union) noise modelling framework was developed and run for each cohort (12). Air pollution data were obtained from a harmonised European Land Use Regression (LUR) model at a resolution of 100x100m (13).

*Statistical analyses*

We harmonized individual-level confounder data from each cohort and physically pooled the data. We used Cox proportional hazards models with age as the underlying time-scale, 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, using Stata (v12.1). Models were adjusted for cohort, sex, employment, education and smoking status. Analyses were conducted using a complete-case sample.

## Results

The total number of individuals in the complete-case sample was 361,699. Through medical record linkage, 4,014 IHD and 2,109 cerebrovascular incident cases were ascertained between baseline (1993-2010) and end of follow-up (2008-2015), with average follow-up of 3.9 years. Cerebrovascular disease cases were also analysed by subset of ischaemic (n=999) and haemorrahgic (n=366) stroke.

In the pooled data, daytime noise ranged from 38.5 to 86.4 dB(A), with a median of 54.0 dB(A) and interquartile range (IQR) 3.9 dB(A).

For each IQR (3.9 dBA) increase in daytime noise, a non-significant but positive association with incident IHD was seen (Hazard ratio (HR): 1.015, 95% Confidence Interval (CI): 0.989-1.042) in fully adjusted models (Table 1), but there was no obvious association with cerebrovascular disease. Also, no associations were observed when analysing outcomes of ischemic or hemorrhagic stroke (Table 1).

In further analyses for IHD, statistically significant associations and interaction terms were seen in obese individuals (HR: 1.099, 95%CI: 1.029-1.174), and current-smokers (HR: 1.054, 95%CI: 1.007-1.103).

Table 1: Hazard ratios (95%CI) between daytime noise per InterQuartile Range (3.9 dB(A)) increase) and outcome: pooled analyses from all three cohorts of 360,881 participants

| **Model** | **Ischaemic heart disease** | **Cerebrovascular disease** | **Ischaemic stroke** | **Haemorrhagic stroke** |
|---|---|---|---|---|
| Noise exposure only | 1.015 (0.989-1.042) | 0.983 (0.948-1.019) | 0.998 (0.948-1.050) | 0.935 (0.853-1.025) |
| Noise adjusted for $PM_{10}$ | 1.015 (0.989-1.042) | 0.981 (0.946-1.017) | 0.997 (0.947-1.050) | 0.934 (0.852-1.024) |
| Noise adjusted for $NO_2$ | 1.015 (0.989-1.042) | 0.982 (0.948-1.018) | 0.998 (0.948-1.050) | 0.936 (0.854-1.025) |

Models adjusted for cohort, sex, employment, education, smoking status

## Discussion

This large prospective study using pooled data from >300,000 individuals in cohorts in the UK and Norway found some evidence for increased risk for incident IHD in relation to exposure to daytime traffic noise, with statistically significant increased risk in current smokers and in the obese but no increased risk of stroke. The results were robust to adjustment for traffic-related air pollutants.

Our findings for IHD are consistent with those reported in the literature. A meta-analysis of cohort, cross-sectional and case-control studies of road traffic noise effects on both prevalent and incident IHD was published by Babisch in 2014 (6). The analyses included 14 studies (3 in men only) and found a significant pooled estimate of the risk for IHD (OR: 1.08, 95%CI: 1.04 to 1.13) per 10 dB(A) increase of weighted day-night road noise level within the range of 52-77 dB(A) – the confidence intervals just overlap with the estimates in our study. Vienneau et al later updated the Babisch review by including eight incidence studies only and reported a pooled effect of 1.04 (95%CI: 1.00-1.10) per 10 dB(A) higher of Lden on IHD incidence (13), which provides results much closer to the range seen in our study. The Vienneau review suggested a possible threshold of 50 dB, above which a linear dose-response was seen.

Very few studies have investigated road traffic noise effects on incident stroke and findings have been mixed. We found no evidence for associations with ischaemic or haemorrhagic stroke. This is consistent with a London-based study based on general practice registry data that did not find an association between night-time road traffic noise and incident stroke (14). A Dutch cohort followed for 13 years through record linkage also did not find associations between noise and hospital admissions for cerebrovascular disease (ICD9 430-438) adjusted for air pollution (15). Cross-sectional associations between self-reported 'heart disease and stroke' using data from the Hypertension and Environmental Noise near Airports (HYENA) study did find some evidence associations with 24 hour average road traffic noise exposure (OR: 1.19 (95% CI 1.00, 1.41), but adjustment for air pollution in the subsample for which this was available suggested this may have been due to confounding by air pollution (16). However, a Danish study reporting in 2011 found a positive significant association between Lden and incident stroke (HR: 1.14, 95%CI: 1.03-1.25, per 10 dB(A) increase) (8) and later reported that this association was mainly confined to ischaemic stroke but not haemorrhagic stroke (17). Also, a small area ecological study in London (17) found elevated risks for stroke hospital admissions in areas exposed to annual mean daytime noise >60 vs. <55 dB(A) in adults (RR:1.05, 95%CI: 1.02 to 1.09), adjusted for air pollution exposures.

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. However, we did not have information on personal behaviour, daytime location or building characteristics (e.g. window-glazing) and behaviours (e.g. window opening) that may have modified exposures. Despite the large size in terms of numbers of individuals, the average follow-up time was short (3.9 years) and the number of incident stroke events was relatively small, which may have restricted ability to detect significant associations particularly if adverse effects if noise exposure act over a long time period.

This study provides contributes further evidence to associations between residential road traffic noise exposure and incident ischemic heart disease but evidence for associations with incident stroke remains inconclusive.

**Acknowledgements**

Acknowledgements: The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between HUNT Research Centre (Faculty of Medicine, Norwegian University of Science and Technology NTNU), Nord-Trøndelag County Council, Central Norway Health Authority, and the Norwegian Institute of Public Health. We thank all the participants in the EPIC-Oxford cohort for their invaluable contribution to the study. This research has been conducted using the UK Biobank Resource.

Acknowledgements also given to Dany Doiron and Stephane Mbatchou (McGill University, Montreal, Canada) for their help in preparing the data harmonisation work.

P.E. is an NIHR Senior Investigator and acknowledges support from the Imperial College Healthcare NHS Trust and Imperial College London Biomedical Research Centre, the National Institute for Health Research (NIHR) Health Protection Research Unit on the Health Effects of Environmental Hazards, the Medical Research Council and Public Health England (MRC-PHE) Centre for Environment and Health. The views expressed are those of the authors and not necessarily those of the Department of Health, the NHS or the NIHR.

Funding: This work was supported by funding from the European Union Seventh Framework Programme (FP7/2007-2013) Biobank Standardisation and Harmonisation for Research Excellence in the European Union-BioSHaRE-EU (grant number 261433).

EPIC-Oxford is funded by UK Medical Research Council (grant number MR/M012190/1) and Cancer Research UK (grant number C8221/A19170).

UK Biobank was established by the Wellcome Trust medical charity, Medical Research Council, Department of Health, Scottish Government and the Northwest Regional Development Agency. It has also had funding from the Welsh Assembly Government, British Heart Foundation and Diabetes UK.

The Medical Research Council - Public Health England (MRC-PHE) centre for Environment and Health is funded by the UK Medical Research Council and Public Health England (grant number MR/L01341X/1).

The funders had no involvement in the study design, analysis and interpretation of data, nor did they have any input into the preparation, review or approval of this manuscript.

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