



# Road traffic noise, air pollution and cardio-respiratory health in European cohorts: a harmonised approach in the BioSHaRE project

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## ABSTRACT

**Background and aims:** Few studies have investigated joint effects of road traffic noise and air pollution on cardiovascular outcomes. This project aims to quantify the joint and separate effects of both exposures on prevalent and incident cardiovascular disease and asthma as part of the EU-funded BioSHaRE project involving five European cohorts (EPIC-Oxford, EPIC-Turin, HUNT, Lifelines, UK Biobank).

**Methods:** Health outcomes have been ascertained by self-report (prevalence) and medical record (incidence) and retrospectively harmonised across the five cohorts. Residential road traffic noise exposures for each participant are being estimated using a European noise model based on Common Noise Assessment Methods in Europe (CNOSSOS-EU). Cross-sectional epidemiological analyses are in progress, virtually pooled using DataSHIELD methods.

**Results:** In total, 716,945 men and women are included, mostly >40 years. Initial analysis of EPIC-Oxford and Lifelines showed prevalence of self-reported hypertension to be 26%, high blood lipids 15% and asthma 11% and mean annual 24-hour noise estimates of 56.4 dB(A) (EPIC-Oxford) and 65.8 dB(A) (Lifelines). Correlations between noise estimates and NO<sub>2</sub> are generally low ( $r \sim 0.1$  to 0.4).

**Conclusions:** Pooling of individual level harmonised data from established cohorts offers the large sample sizes needed to investigate effects of road traffic noise and ambient air pollution on cardio-respiratory diseases.

Keywords: Road traffic noise, air pollution, cardiovascular health, I-INCE Classification of Subjects Number(s): 62.5

(See <http://www.inceusa.org/links/Subj%20Class%20-%20Formatted.pdf> .)

## 1. INTRODUCTION

A survey conducted by European Commission in 2010 found that 44% of Europeans believed that noise affects their health to a “large extent”, and this had increased by 3% since the previous survey in 2006<sup>(1)</sup>. According to the WHO (2011) *Burden of Disease from Environmental Noise* study<sup>(2)</sup>, it was estimated that each year at least 1 million healthy life years were lost from traffic-related noise in the western part of Europe. More specifically, 61,000 healthy life years were lost from ischemic heart disease (IHD) alone as a result of exposure to environmental noise, the third highest ranking outcome after noise-induced sleep disturbance and annoyance (903,000 and 654,000 healthy life years lost

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respectively).

Road traffic is one of the main sources of noise in urban areas<sup>(3)</sup>. There is increasing evidence linking road traffic noise and cardiovascular diseases including hypertension and IHD. A meta-analysis of 24 studies<sup>(4)</sup> on cross-sectional associations between road traffic noise and prevalence of hypertension has reported a positive pooled odds ratio (OR) of 1.03 (95%CI: 1.01 to 1.06), per 5 dB(A) increase of average day-time noise level (L<sub>Aeq16hr</sub>) within a range of 45 to 75 dB(A). In a more recent meta-analysis of 14 prevalent and incident studies<sup>(5)</sup>, a 10 dB(A) increase of weighted day-night road noise level within the range of 52-77 dB(A) was associated with a statistically significant pooled OR for IHD (OR: 1.08, 95%CI: 1.04 to 1.13). Few studies have examined the association between road traffic noise and stroke. Self-reported heart disease and stroke (as a combined outcome) was associated with 24-hour average road traffic noise exposure (OR: 1.19, 95%CI: 1.00 to 1.41) in the Hypertension and Environmental Noise near Airports (HYENA) study<sup>(6)</sup>, but association was not seen in a subsample analysis in which further adjustments were made for air pollution exposures. A prospective cohort study of 57,053 participants (1881 incident stroke cases in 13 years of follow-up) reported the first evidence for a specific effect of traffic noise on stroke: the incident rate ratio for stroke was 1.14 (95%CI: 1.03 to 1.25) per 10 dB(A) increase of road traffic noise (L<sub>den</sub>, weighted by day, evening and night noise level), independent of air pollution exposures<sup>(7)</sup>.

Based on the current research evidence, the European Network on Noise and Health (ENNAH) project identified certain issues which need to be addressed in future studies<sup>(8)</sup>. First, more research is needed to strengthen and refine the previously established dose-response curves between noise and cardiovascular endpoints. Second, it is still unclear if effect estimates differ between sexes, day-time and night-time noise, in chronically ill, elderly or noise sensitive persons and how important exposure modifiers are (e.g. window opening habits, shielding effects). Third, road traffic is the common source of both noise and air pollution, but co-exposure of these two exposures in cardiovascular health has not been extensively explored<sup>(9)</sup>. While most studies have suggested an independent effect of noise, others did not. We are not aware of any study investigating associations between road traffic noise and respiratory outcomes, particularly asthma in relation to noise-induced stress.

The hypothesis for the underlying mechanisms that might explain associations between noise and cardiovascular disease is that noise is an environmental stressor, which activates the autonomous nervous system and the endocrine system<sup>(10-11)</sup>. Long-term exposure to noise might persistently activate these systems in a direct or indirect way and lead to biological responses and metabolic dysfunction (e.g. release of stress hormones, increased blood pressure) leading to subsequent cardiovascular disease<sup>(2)</sup>. If noise is a general stressor, then it might increase the possibility of asthma attacks, therefore impacting on reporting of current asthma (as those with mild asthma or susceptibility to asthma might be more likely to experience wheezing).

Cardiovascular and respiratory diseases are the leading causes of mortality in Europe. Continuing urbanization in Europe means more populations are exposed to noise from various sources<sup>(3)</sup>, the long-term cardio-respiratory health effects of which need to be carefully examined. Within the framework of Environmental Core Project of Biobank Standardisation and Harmonisation for Research Excellence in the European Union (BioSHaRE-EU), we jointly investigated the long-term effects of both road traffic noise and ambient air pollution on cardio-respiratory morbidity by pooling the data from five European cohorts, using a state-of-the-art harmonized approach for both study variables and exposure assessments.

## 2. METHODS

### 2.1 Study cohorts

Five European cohorts across different geographical regions, namely EPIC-Oxford<sup>(12)</sup> (UK), EPIC-Turin<sup>(13)</sup> (Italy), HUNT<sup>(14)</sup> (Norway), Lifelines<sup>(15)</sup> (the Netherlands) and UK Biobank<sup>(16)</sup> (UK), are contributing to this study (Table 1). Participants had been recruited at different time periods, starting in 1993 in both EPIC cohorts to 2006-2007 in Lifelines and UK Biobank. Individual data on socio-demographic characteristics, lifestyle, chronic illness, physical and biological measurements were collected for each cohort. Cardio-respiratory diseases and mortality status are available by linkages through medical and death records in each cohort except for Lifelines which will not be available within the timeframe of the study as reported at Internoise 2014.

Table 1-Baseline and follow-up periods and recruitments from participating cohorts

<b>Cohorts</b>	<b>Baseline</b>	<b>Follow-up(s)</b>	<b>Participants included in this study</b>
EPIC-Oxford	1993-1999	2007(2nd), 2010 (3rd)	57,446 at baseline recruitment
EPIC-Turin	1993-1998	1998-2006	10,604 at baseline recruitment
HUNT	1984-86 (HUNT1)	1995-97 (HUNT2), 2006-08 (HUNT3)	65,215 at HUNT2 50,807 at HUNT3
Lifelines	2007-2013	Follow up for 30 years	95,432 at baseline recruitment
UK Biobank	2006-2010	2012-2013 (20,000 participants only) and every few years in the future	502,656 at baseline recruitment

Of the 57,446 participants of EPIC-Oxford (the Oxford component of the European Prospective Investigation into Cancer and Nutrition) who provided information, most (87%) are a “health-conscious” group consisting of mainly vegetarians and vegans. Questionnaires were sent to these participants throughout the UK by post. The remaining 7,421 participants are general populations which were recruited through their general practices in Manchester, Oxfordshire and Buckinghamshire. EPIC-Turin (the Turin component of EPIC study) cohort recruited 10,604 men and women including blood donors and other healthy volunteers living in the Turin city area. The HUNT study constitutes three health surveys to date, the first commencing in the mid-1980s in Nord-Trøndelag region in central Norway, however only the 65,215 participants of HUNT2 (1995-1997) and 50,807 of HUNT3 (2006-2008) will be included in this analysis because of the availability of hospital and mortality data. The Lifelines study was launched in the three northern provinces in the Netherlands in 2007 for which 95,432 participants have provided completed information. The UK Biobank is the largest single cohort in this study, which has recruited 502,656 participants across the UK from 2006-2010.

## 2.2 Harmonisation of covariates and outcome variables

A set of core covariates including age at recruitment, sex, height, weight, body mass index (BMI), waist circumference, employment status, educational level, smoking, alcohol drinking, blood pressure, chronic conditions of hypertension, diabetes, stroke, myocardial infarction and high blood lipids is available in each cohort. These data were respectively harmonized across the five cohorts through a rigorous protocol developed from DataSHaPER (The DataSchema and Harmonization Platform for Epidemiological Research)<sup>(17)</sup>.

The DataSHaPER consists of two main platforms for data harmonization across participating cohorts. First, a DataSchema platform was developed to document and annotate harmonized variables with standard definitions and/or measuring procedures. Second, a harmonization platform was then used to derive these defined harmonized variables from each cohort, using systematic and scientifically-based information and procedures. These harmonization procedures will eventually provide a common set of harmonized, scientifically valid variables in each cohort, which will be used for individual pooled analysis.

Incident cardiovascular diseases (ICD10 codes I00-I99) during follow-up have been ascertained by record-linkage with hospital databases and mortality records in all cohorts except for Lifelines. Occurrence of asthma was self-reported on the questionnaire in only three cohorts (HUNT, Lifelines,

UK Biobank), with additional information on age onset, asthma-related symptoms and asthma medications also available. Asthma outcome was harmonized in these three cohorts.

### 2.3 Harmonisation of road traffic noise and air pollution

Road traffic noise at individual home address was modelled by using the Common Noise Assessment Methods in Europe (CNOSSOS-EU) across the five cohorts<sup>(18)</sup>. The CNOSSOS-EU method can handle extremely detailed inputs concerning multiple reflections and diffractions from individual buildings and barriers, meteorology, variability in ground terrain, characteristics of the road network and traffic fleet. However, for a national level application, the aforementioned input data may not be available to this degree of detail. Therefore, within the BioSHaRE project, a national version of CNOSSOS-EU model was applied in each cohort, with less-detailed inputs, but such that the accuracy of noise estimates should not be compromised. For example, for the UK, input data that were used for the BioSHaRE/CNOSSOS-EU model included road network geography, hourly vehicle flows, land cover, building heights, air temperature, and prevailing wind direction. Detailed methodology and validation of BioSHaRE/CNOSSOS-EU noise modelling is currently being prepared for publication and will not be presented in this paper.

Five annual A-weighted noise indicators were produced for each cohort, namely  $L_{day}$  (noise level over the 12-hour day time period from 0700 to 1900 hours),  $L_{eve}$  (noise level over the 4-hour evening period from 1900 to 2300 hours),  $L_{night}$  (noise level over the 8-hour night time period from 2300 to 0700 hours),  $L_{den}$  (The average sound level over a 24 hour period, with a penalty of 5 dB added for the evening hours and a penalty of 10dB added for the night time hours), and  $L_{Aeq16}$  (noise level between 7:00 and 23:00 hours).

Ambient air pollution at home address for EPIC-Oxford, EPIC-Turin, Lifelines and UK Biobank were estimated by using the Land Use Regression (LUR) models used in the ESCAPE (European Study of Cohorts for Air Pollution Effects) project. The ESCAPE standardized exposure assessment campaigns were conducted during 2008-2011 in 36 European study areas including those in the UK, Italy and the Netherlands, where four cohorts of this study are based<sup>(19-20)</sup>. Annual nitrogen dioxide ( $NO_2$ ), Nitrogen Oxides ( $NO_x$ ),  $PM_{10}$  (Particulate matter (PM) with aerodynamic diameter  $\leq 10\mu m$ ),  $PM_{2.5}$  (PM with aerodynamic diameter  $\leq 2.5\mu m$ ), the coarse fraction of PM ( $PM_{coarse}$ , as  $PM_{10}$  minus  $PM_{2.5}$ ) and the  $PM_{2.5abs}$ , light absorbance of  $PM_{2.5}$  (similar to black carbon) were estimated for each cohort, together with two indicators of local exposures to traffic: traffic intensity on the nearest road and total traffic load on major roads in a 100 metre buffer. Study areas of HUNT cohort were not covered by the ESCAPE modelling campaign and hence an alternative LUR model covering western Europe with satellite-enhanced  $NO_2$  and  $PM_{10}$  data will be adopted<sup>(21)</sup>. Estimates for  $NO_2$  and  $PM_{10}$  from 2005 to 2007 will be modelled for the HUNT cohort. Estimates produced from this alternative model and the ESCAPE model showed moderate to high correlations in the Lifelines cohort in an initial analysis ( $r$ : 0.650 for  $PM_{10}$  and 0.887 for  $NO_2$ , both modelled for the year 2007).

### 2.4 Statistical analyses

A pooled individual-level analysis is proposed in this study using a BioSHaRE-developed tool named DataSHIELD<sup>(22)</sup>. DataSHIELD has the ability to virtually but not physically pool the individual-level harmonized data from each local cohort and to perform analyses based on the R statistical environment. This tool will form a very large, highly integrated database for epidemiological analysis.

Analyses are currently in progress. Both road traffic noise and air pollution estimates are treated as a main exposure as well as co-adjusted for each other. Both will be examined on a continuous scale, assuming a linear effect. Additionally for noise, categorical noise levels will also be used to identify any possible threshold above which increased risk may be seen. For the prevalence of asthma in relation to air pollution and/or road traffic noise exposures, a cross-sectional logistic regression model will be built, adjusting for potential confounders identified *a priori*. The incident events of total cardiovascular diseases (ICD10 I00-99) as well as specific CVDs of ischemic heart diseases (ICD10 I20-25) and stroke (ICD10 I60-69) in relation to road traffic noise and air pollution will be examined by Cox proportional hazards regression models, with age as the time variable and with adjustment for confounders identified *a priori*. Potential key confounders or effect modifiers in the main model may include age, sex, height, weight, educational level, smoking history and working status. Additional sensitivity analyses may include further adjustments for chronic conditions, environmental tobacco exposures and alcohol consumption. Analyses may also be stratified by age group, sex, BMI, smoking status and education level based on previous studies. Area-level socioeconomic variable may not be

possible to harmonize because of the variability of indicators used in different countries. If that is the case, a cohort-specific analysis with additional adjustment for cohort-defined area-level socioeconomic variable will be performed, and then cohort-specific results will be meta-analyzed to obtain a pooled estimate for comparisons with those obtained from individual-level pooled analysis. To model differences and commonalities across countries taking into account uncertainties we will explore random effect by cohort in a multilevel model, assuming that people within the same cohort are more similar than people across the cohorts.

### 3. RESULTS

As analyses are in-progress, all results presented here are preliminary and subject to final corrections.

#### 3.1 Characteristics of study populations

In total, 716,945 participants will be included in this study. Table 2 shows the study population characteristics for the four cohorts with currently available data. 57% of all participants are female and most participants are over 40 years of age. 40% of participants are overweight and 21% obese. Prevalence of self-reported tobacco smoking (13%), hypertension (26%), high blood lipids (15%) and asthma (11%) are relatively high.

Table 2- Characteristics of study populations of EPIC-Oxford, EPIC-Turin, Lifelines and UK Biobank

	N	%
<b>Sex</b>		
Males	287,827	43.2
Females	378,311	56.8
<b>Age</b>		
<40 years	53,305	8.0
40-60 years	370,404	55.6
>60 years	242,429	36.4
<b>BMI (kg/m<sup>2</sup>)</b>		
<25	252,409	38.1
25-30	268,086	40.4
>=30	142,504	21.5
<b>Current tobacco smoker</b>	823,42	12.5
<b>Self-reported health</b>		
Hypertension	164,369	25.6
Myocardial infarction	134,17	2.0
Stroke	8760	1.3
Diabetes	296,40	4.5
High blood lipids	797,79	15.4
Angina	172,98	3.1
Asthma	659,95	11.1

#### 3.2 Road traffic noise

BioSHaRE/CNOSSOS-EU noise models have been applied to both EPIC-Oxford and Lifelines cohorts at the time of writing this manuscript. A pooled histogram of mean annual 24-hour noise level from both cohorts is shown in Figure 1. The mean annual 24-hour noise estimates in EPIC-Oxford and

Lifelines are 56.4 dB (A) and 65.8 dB (A) respectively. The mean pooled noise level across these two cohorts is 62.3 dB (A), with inter-quartile range 57.9 to 67.0 dB (A). Correlations between 24-hour noise estimates and NO<sub>2</sub> are generally low ( $r=0.1044$  and  $0.471$  for EPIC-Oxford and Lifelines respectively).

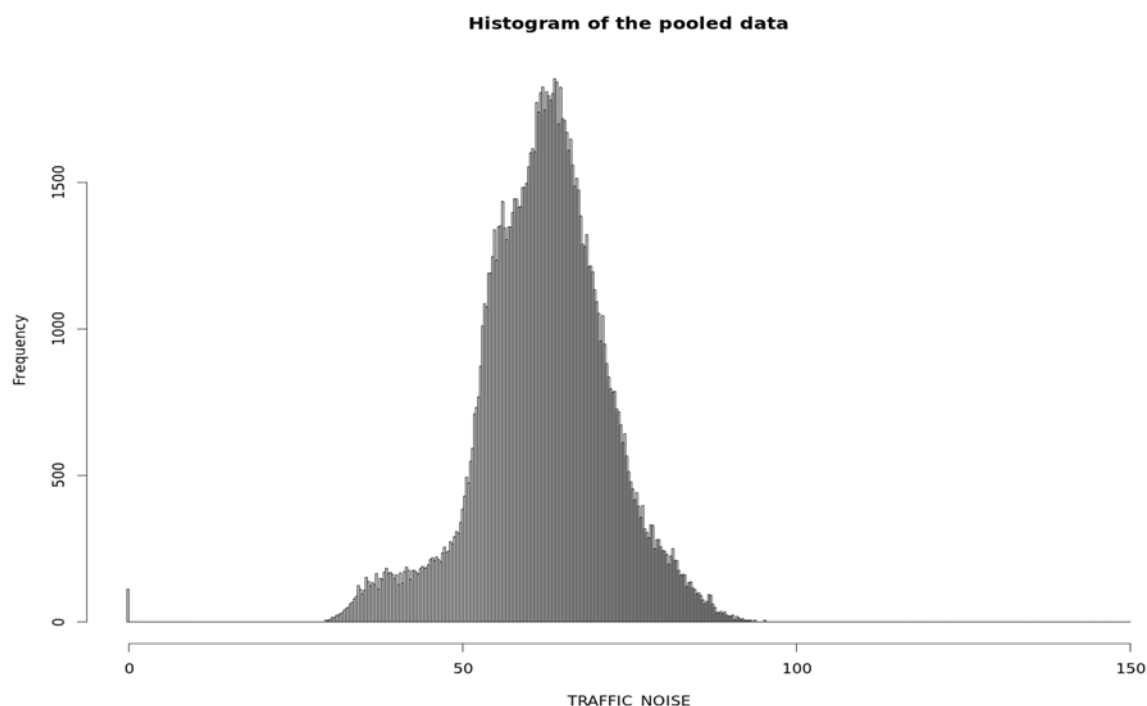


Figure 1-pooled histogram of mean annual 24-hour noise level (dB (A)) for participants from both EPIC-Oxford and Lifelines

### 3.3 Incident cardiovascular events

Incident CVD events have been ascertained for EPIC-Oxford and EPIC-Turin, and include 350/196 first ischemic heart disease events; 418/68 first strokes for EPIC-Oxford/EPIC-Turin respectively. 6421 total incident cardiovascular disease events were recorded for EPIC-Oxford. Total number of person-years of follow-up is 534,192 and 117,518 for EPIC-Oxford and EPIC-Turin respectively. Record-linkage for HUNT and UK Biobank is currently in-progress. All being well, it is hoped to have more results available for discussion at the Internoise meeting in November 2014.

## 4. CONCLUSIONS

The pooling of harmonized data from established cohorts offers the large sample sizes needed to investigate effects of road traffic noise and ambient air pollution on cardio-respiratory diseases.

## ACKNOWLEDGEMENTS

The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n°261433 (Biobank Standardisation and Harmonisation for Research Excellence in the European Union-BioSHaRE-EU).

We thank study participants, data collection teams, and scientific research teams in each cohort.

We also thank Eric Johnson, Federico Fabbri (Imperial College, UK) for IT support and Daniela Fecht (Imperial College, UK) for technical support in exposure modelling; Stephane Mbatchou (P3G, Canada) for data harmonization work; Yannick Marcon (Obiba, Canada) for OPAL installation support; and Paul Burton, Amadou Gaye (Bristol University, UK) for DataSHIELD tools.

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