Road traffic noise, Air pollution and Cardio-respiratory Health in European Cohorts: a Harmonised Approach in the BioSHaRE Project

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Summary

Background and aims: Few studies have investigated joint effects of road traffic noise and air pollution on cardiorespiratory 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 cohorts. Residential road traffic noise exposures for each participant are estimated using a European noise model based on Common Noise Assessment Methods in Europe (CNOSSOS-EU). Road traffic air pollution estimates at home address were derived from Land Use Regression models. Cross-sectional and incident epidemiological analyses are in progress, using individual level data, virtually pooled using DataSHIELD methodology.

Results: In total, 742,950 men and women are included from all five cohorts, mostly >40 years. Prevalence of self-reported myocardial infarction from these five cohorts is 2.1% (N=15,031) while prevalence of self-reported stroke is 1.4% (N=10,077). Initial pooled analysis of EPIC-Oxford, HUNT and Lifelines showed median day-time (07:00-19:00) noise estimate of 51.8 dB(A) and night-time (23:00-07:00) noise estimate of 43.5 dB(A). Correlations between noise estimates and NO_2 are generally low (r=0.1 to 0.4).

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

1. Introduction

Traffic-related noise and air pollution are suggested as the leading environmental risk factors for health in Europe. Traffic noise (road, rail, air) was associated with ~400-1500 disability-adjusted life years (DALYs) per one million people in six European countries, the second highest ranking after particulate air pollution[1]. An earlier report commissioned by World Health Organization also estimated that at least one million healthy life years were lost from traffic-related noise in the western part of Europe annually[2].

Among the noise studies in the literature, health effects in relation to road traffic noise are primarily investigated partly because this source of noise exposure potentially affects a large part of the population, particularly those residing in urban areas. Long-term exposure to road traffic noise has been linked to several cardiovascular outcomes in adult populations[3-4]. A meta-analysis in 2012 of 24 cross-sectional studies showed a pooled odds ratio of 1.03 (95%CI: 1.01 to 1.06) for the association between hypertension prevalence and averaged day-time road traffic noise level (Laeq16hr)[3]. Another meta-analysis in 2014 of 14 studies on coronary heart diseases reported a pooled estimate of relative risk 1.08 (95%CI: 1.04 to 1.13) per 10 dB(A) increase of weighted day-night road traffic noise level[4]. It should be noted that for both meta-analyses, the studied noise ranged from 45 to 77 dB(A), indicating that even relatively low noise level (<50 dB(A)) may potentially pose a cardiovascular health risk and there may be no threshold of effect.

While there is evidence that road traffic noise may be a risk factor for hypertension and ischemic heart disease (IHD), other cardiovascular endpoints, for instance stroke, need more robust investigation. 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[5], but the 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 reported the first evidence for an effect of road traffic noise on incident stroke 1.14 (95%CI: 1.03 to 1.25) per 10 dB(A) increase of Lden (weighted by day, evening and night noise level), independent of air pollution exposures[6].

Previous studies have adopted different study designs and exposure assessment methodologies. The quality of the exposure as well as the health outcomes differed across studies. Moreover, adjustments were made for different sets of covariates. These limitations may add statistical noise to the meta-analysis studies[4]. We have identified several gaps in this area of research. First, more data are needed to strengthen evidence supporting the previously presented dose-response relationships between road traffic noise and cardiovascular endpoints[2]. Second, other endpoints, in particular stroke, need more careful investigation given its clinical importance. Third, only a few studies have also investigated the role of traffic air pollution on the association between noise and cardiovascular health. Since both exposures may affect cardiovascular health through a range of underlying mechanisms, the independent and joint effect of these exposures needs to be explored further. Fourth, data are scarce regarding the associations between road traffic noise and biochemical markers for cardiovascular diseases. Noise is generally seen as an environmental stressor, which activates the autonomous nervous system and the endocrine system[7-8]. 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 diseases[2] and work to assess the associations between noise/air pollution exposure and these preclinical markers could provide insights into these mechanisms. Fifth, to our best knowledge, we are not aware that any study has investigated associations between road traffic noise and respiratory outcomes, particularly asthma in relation to noise-induced stress.

Within the framework of the 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 health by pooling the individual-level data from five European cohorts, after using a state-of-the-art harmonisation approaches to standardise both study variables and exposure assessments.

2. Methods

2.1 Study cohorts

Five European cohorts across different geographical regions are contributing to this study (Table I) and details of each cohort profile have been published elsewhere[9-13]. Participants were recruited at different time periods, starting in 1990s in EPIC-Oxford (UK), EPIC-Turin(Turin, Italy) and HUNT2 (Nord-Trøndelag region, Norway) cohorts to 2006-2007 in Lifelines (Northern part of the Netherlands) and UK Biobank (UK). Individual data on socio-demographic characteristics, lifestyle, long-term illness, physical and biological measurements were collected for each cohort. Linkage to health registers (diseases and mortality) is possible for each cohort except for Lifelines which will not be available within the timeframe of this study.

Table I. Baseline and follow-up periods and recruitments from participating cohorts.

Cohorts	Baseline	Follow-up(s)	Participants included in this study
EPIC-Oxford[9]	1993-1999	2007(2nd) 2010 (3rd)	57,446
EPIC-Turin[10]	1993-1998	1998-2006	10,604
HUNT[11]	1995-97 (HUNT2)	2006-08 (HUNT3)	65,215 at HUNT2 50,807 at HUNT3
Lifelines[12]	2007-2013	n/a	95,432
UK Biobank[13]	2006-2010	ongoing	502,656

2.2 Harmonisation of road traffic noise and air pollution

Road traffic noise at an individual's home address was modelled using the Common Noise Assessment Methods in Europe (CNOSSOS-EU) across the five cohorts[14]. 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 but similar 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[15].

Five annual A-weighted noise indicators for the year 2009 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 standardised Land Use Regression (LUR) models used in the ESCAPE (European Study of Cohorts for Air Pollution Effects) project[16-17]. Study areas of the HUNT cohort were not covered by the ESCAPE monitoring/modelling campaign and hence an alternative LUR model, covering western Europe with satellite-enhanced NO_2

(Nitrogen dioxide) and $PM_{2.5}$ (Particulate Matter with aerodynamic diameter $\leq$2.5μm) data was adopted[18]. Estimates for NO_2 and PM_{10} from 2005 to 2007 will be modelled for the HUNT cohort and other four cohorts. Estimates for NO_2 and PM_{10} from 2005 to 2007 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).

2.3 Harmonisation of covariates and outcome variables

A set of core covariates including age at recruitment, sex, height, weight, Body Mass Index (BMI), employment status, education level, smoking, alcohol drinking, blood pressure and self reported chronic conditions of hypertension, diabetes, stroke, myocardial infarction and asthma was identified in each cohort. These data were respectively harmonised across all cohorts through a rigorous protocol developed from the DataSHaPER (The DataSchema and Harmonisation Platform for Epidemiological Research)[19].

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. Biochemistry data of blood lipids, C-reactive protein and blood glucose (fasting and/or non-fasting), self-reported asthma and current asthma medications data were available for only three cohorts (HUNT, Lifelines, UK Biobank), so these variables were harmonised in these three cohorts.

2.4 Statistical analyses

Analyses are currently in progress. A pooled individual-level analysis is proposed in this study using a BioSHaRE-developed tool named DataSHIELD[20]. DataSHIELD has the ability to virtually but not physically pool the individual-level harmonised data from each local cohort and to perform analyses based on the R statistical environment. This tool will enable the creation of a very large, highly integrated database for epidemiological analysis.

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. Cross-sectional analyses using multivariate regression techniques (linear and logistic) will be performed to investigate the associations between exposures and the levels of biochemistry markers and prevalence of current asthma.

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 piecewise regression techniques, 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, education level, smoking history, alcohol consumption and working status. Additional sensitivity analyses may include further adjustments for chronic conditions, environmental tobacco exposures.

It may not be possible to harmonise area-level socioeconomic variable because of the variability of indicators used in different countries. Cohort-specific analyses with additional adjustment for cohort-specific area-level socioeconomic variables will be performed, and then cohort-specific results will be meta-analysed to obtain a pooled estimate, adjusted for area-level deprivation, which can then be compared to estimates 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 Study populations

In total, data from 742,950 individuals were successfully pooled from the five cohorts (Table II). Most participants were aged over 40 years, and 56% female. According to the

BMI categories, 41% of participants were overweight while 22% obese. About 13% of the study populations were current-smokers at the time of recruitment. Prevalence of self-reported hypertension (26%) and high blood lipids (15.4%) were relatively high among other chronic conditions in all study populations. Overall, there were 71,794 self-reported doctor-diagnosed asthma cases from the three cohorts of HUNT, Lifelines and UK Biobank.

Table II. Characteristics of pooled study populations from EPIC-Oxford, EPIC-Turin, HUNT, Lifelines and UK Biobank.

	N	%
Sex:		
Males	323,923	43.6
Females	419,027	56.4
Age group:		
<40 years	64,407	9.0
40-60 years	391,337	54.8
>60 years	259,052	36.2
BMI (kg/m^2):		
<25	268,276	37.7
25-30	289,464	40.7
>=30	153,520	21.6
Smoking status:		
Current-smoker	90,385	12.9
Ex-smoker	236,445	33.8
Never-smoker	372,094	53.3
Self-reported health at baseline:		
Hypertension	164,369	25.6
Myocardial infarction	15,031	2.1
Stroke	10,077	1.4
Diabetes	31,714	4.5
High blood lipids	79,779	15.4
Asthma*	71,794	11.1

*data only available for HUNT, Lifelines, UK Biobank

3.2 Road traffic noise

At the time of writing this report, noise estimates are only available for EPIC-Oxford, HUNT and Lifelines. Therefore, we herein only report results from these three cohorts.

The median (inter-quartile range, IQR) day-time noise (L_{day}) for EPIC-oxford, HUNT and Lifelines was 54.4 (3.6), 47.4 (6.6), and 53.9 (4.2) dB(A) respectively, and for night-time noise (L_{night}), 45.6 (3.6), 40.2 (5.0), and 45.1 (4.2) dB(A) respectively. Noise estimates for HUNT participants were lower than those of EPIC-Oxford and Lifelines. However, within-cohort variations in both L_{day} and L_{night} were larger in HUNT than the other two cohorts. Pooling day-time noise estimates from all three cohorts, the pooled median (IQR) was 51.8(4.9) dB(A) while the pooled median (IQR) for night-time noise was 43.5(4.3) dB(A). Correlations between noise estimates and NO_2 are generally low (r=0.1 to 0.4).

4. Conclusions

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

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