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Associations of night-time road traffic noise with carotid intima-media thickness and blood pressure: The Whitehall II and SABRE study cohorts

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ABSTRACT

Background: Road traffic noise has been linked to increased risk of stroke, for which hypertension and carotid intima-media thickness (cIMT) are risk factors. A link between traffic noise and hypertension has been established, but there are few studies on blood pressure and no studies on cIMT.

Objectives: To examine cross-sectional associations for long-term exposure to night-time noise with cIMT, systolic blood pressure (SBP), diastolic blood pressure (DBP) and hypertension.

Methods: The study population consisted of 2592 adults from the Whitehall II and SABRE cohort studies living within Greater London who had cIMT, SBP and DBP measured. Exposure to night-time road traffic noise (A-weighted dB, referred to as dBA) was estimated at each participant's residential postcode centroid.

Results: Mean night-time road noise levels were 52 dBA (SD = 4). In the pooled analysis adjusted for cohort, sex, age, ethnicity, marital status, smoking, area-level deprivation and NOx there was a 9.1 μ m (95% CI: −7.1, 25.2) increase in cIMT in association with 10 dBA increase in night-time noise. Analyses by noise categories of 55–60 dBA (16.2 μ m, 95% CI: −8.7, 41.2), and >60 dBA (21.2 μ m, 95% CI: −2.5, 44.9) vs. <55 dBA were also positive but non-significant, except among those not using antihypertensive medication and exposed to >60 dBA vs. <55 dBA (32.6 μ m, 95% CI: 6.2, 59.0). Associations for SBP, DBP and hypertension were close to null.

Conclusions: After adjustments, including for air pollution, the association between night-time road traffic noise and cIMT was only observed among non-medication users but associations with blood pressure and hypertension were largely null.

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1. Introduction

There is growing interest in the potential link between exposure to traffic noise and various cardiovascular health outcomes (Babisch, 2014; Babisch et al., 2014; Barcelo et al., 2016; Bodin et al., 2016; Munzel et al., 2014, 2016; Stansfeld, 2015). We recently reported an area-level association between road traffic noise and increased risk of

strokes in London, UK (Halonen et al., 2015b). The observed association is biologically plausible based on an established link between noise exposure and hypertension (van Kempen et al., 2012), a major risk factor for stroke (Elliott et al., 2005). Increasing carotid intima-media thickness (cIMT) reflects changes in the vascular walls due to plaque formation as part of the atherosclerotic process. These changes, when severe, increase the risk of occlusion that may result in acute atherothrombotic events such as myocardial infarction and stroke (Eikendal et al., 2015; O'Leary et al., 1999). Although associations between air pollution and cIMT have been investigated (Perez et al., 2015; Tonne et al., 2012; Wilker et al., 2013), we are not aware of studies examining associations between exposure to road traffic noise and cIMT. This association could be on the stress-related pathway between traffic noise exposure and

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cardiovascular events (Basner et al., 2014; Munzel et al., 2014) as systolic blood pressure stress reactions, for example, have been linked to progression of cIMT (Jennings et al., 2004).

In this cross-sectional study, we examined whether long-term exposure to night-time road traffic noise is associated with higher cIMT and blood pressure or higher odds of hypertension among participants of the Whitehall II (WHII) cohort study of British civil servants and the participants of tri-ethnic population-based Southall and Brent REvisited (SABRE) cohort study who lived within Greater London in 2002–2012. We hypothesized that higher road noise exposure at the participants' residential postcodes is associated with higher cIMT, higher blood pressure and higher odds of hypertension.

2. Methods

2.1. Study population

The study population consisted of participants of two UK cohorts: participants included in the phase 7 clinic visit (2002–2004) of the WHII study of civil servants in England, (Marmot et al., 2005) and participants of the phase 2 (2008–2012) clinic visit of the SABRE tri-ethnic population-based cohort (Tillin et al., 2012). We included participants from both cohorts who had cIMT and blood pressure measured, lived within Greater London and whose residential postcode was available for noise exposure linkage, a total of 3270 adults. Residential addresses were not available due to confidentiality. After excluding those with missing data on any of the covariates the analytical sample size was 2592. The University College London Medical School Committee on the Ethics of Human Research and NHS Health Research Authority NRES London-Harrow Committee (ref. 85/0938) provided ethical approval for the Whitehall II study, and written informed consent was obtained from all participants. Approval for the SABRE study at baseline was obtained from Ealing, Hounslow and Spelthorne, and University College London research ethics committees, and at follow-up from St Mary's Hospital Research Ethics Committee (ref. 07/H0712/109).

2.2. Carotid intima-media thickness

For the participants of the WHII cohort in Phase 7 clinical examination, ultrasound vascular measures were performed at the Vascular Physiology Unit, Institute of Child Health, London UK. Measurements were taken in a temperature controlled (22–26 degrees centigrade), quiet room using a non-invasive, high-resolution ultrasound system, the Aloka 5500 with a 7.5 MHz transducer. Participants were examined in a supine position, with the head turned to a 45 degree angle away from the side to be scanned. Intima-media thickness was measured in the right and left common carotid arteries. Longitudinal images of the

common carotid artery, triggered on the R-wave of the ECG, were magnified and recorded in DICOM format as a cine loop, on the hard drive of the ultrasound machine for later analysis. The common cIMT was measured at its thickest part 1 cm proximal to the bifurcation. A measurement was taken between the leading edge of the intima and the media adventitia on three separate images on each side using electronic calipers and the mean of the six measures was used for analysis.

For all participants of the SABRE cohort who attended for a clinic visit, cIMT was measured by an experienced sonographer at St Mary's hospital in London, UK, using an iE33 ultrasound machine with a 7.5 MHz transducer (Philips UK Ltd., Guildford, UK) and concurrent recording of 3-lead ECG. Participants were in supine position on the scan bed. The distal 1 cm of the (left and right) common carotid artery was imaged after identifying the plane containing the bifurcation of the carotid bulb into the internal and external carotid arteries. Two additional angles, approximately 45 degrees anteriorly and posteriorly, were also used. Three to five cardiac cycles were stored as cine loops for analysis.

2.3. Blood pressure

In the WHII study, blood pressure was measured at the same clinic visit as cIMT. SBP and DBP were measured twice in the sitting position after five minutes of rest with an Omron HEM 907 digital blood pressure monitor (Omron Healthcare, Inc., Bannockburn, Illinois). The average of the two readings was taken to be the measured SBP and DBP (Kivimaki et al., 2009).

Blood pressure of the SABRE cohort participants was measured at St Mary's hospital in London, UK. Resting SBP and DBP were measured three times using an Omron 705IT (Omron Healthcare, Inc., Bannockburn, Illinois). For both SBP and DBP, the average of the second and third measurements was retained as the measured SBP and DBP.

Because 34% of the study sample had medication for hypertension (Table 1), we adjusted their measurement for SBP with an additional 10 mmHg, and DBP with an additional 5 mmHg (Cui et al., 2003).

2.4. Hypertension

Use of hypertension medication was requested in the study questionnaires in both cohorts. For the analyses hypertension was defined as taking hypertension medication and/or having SBP > 140 and DBP > 90.

2.5. Road traffic noise

Annual, A-weighted road traffic noise levels (all dB are A-weighted and hereafter referred to as dBA) for the years 2003–2009 were modelled at geometric centroids of the 2592 participants' residential

Table 1
Characteristics of the study participants included in the analysis.

Variable	All participants*	Included participants*		
	Pooled n = 3270	Pooled n = 2592	WHII n = 1965	SABRE n = 627
Outcomes				
SBP (mean (sd)) [mmHg]	135.3 (20.4)	133.1 (19.8)	128.4 (17.6)	147.5 (19.4)
DBP (mean (sd)) [mmHg]	76.4 (10.9)	75.7 (11.0)	74.2 (10.8)	80.7 (10.0)
cIMT (mean (sd)) [μm]	840 (192.9)	823.2 (180.8)	791.6 (155.9)	922.3 (214.6)
Covariates				
Age (mean (sd)) [years]	64.1 (7.4)	62.8 (7.0)	60.8 (5.9)	69.4 (6.2)
Sex = male (%)	2235 (68.3)	1800 (69.4)	1315 (66.9)	485 (77.4)
Hypertension treatment = yes (%)	1311 (40.1)	890 (34.3)	460 (23.4)	430 (68.6)
Marital status = non-married (%)	804 (25.8)	682 (26.3)	471 (24.0)	211 (33.7)
Smoking = current smoker (%)	251 (7.7)	199 (7.7)	154 (7.8)	45 (7.2)
Ethnicity = non-Caucasian (%)	975 (29.8)	593 (22.9)	269 (13.7)	324 (51.7)

* All participants are those participants from both cohorts who had cIMT and blood pressure measured, lived within Greater London and whose residential postcode was available for noise exposure linkage. Included participants are those among all participants without missing data on any of the covariates.

postcode locations using the Traffic Noise EXposure (TRANEX) model with 0.1 dBA noise level resolution (Gulliver et al., 2015). As the geometric centroid of the postcode falls on a building, we moved all centroids to 1 m from the facade facing the road. TRANEX uses detailed information on traffic for ~63,000 road links including varying flows and speeds for each study year, and detailed information on land cover and heights of individual buildings. Validation studies conducted in two UK cities showed Spearman's correlation between modelled and measured noise levels to be high: 0.90 (p -value < 0.0001), suggesting good model performance (Gulliver et al., 2015).

Exposures to day- and night-time noise were estimated. Due to the high correlation of 0.99 between day- and night-time road noise, we chose to focus on night-time noise only, as potential exposure misclassification is reduced in night-time when the majority of people are more likely to be at home. We report health effects of night-time road noise independently from day-time road noise as suggested by WHO (2011). For the TRANEX model, night-time exposure was L_{night} , which is an average of hourly measures from 23:00 to 6:59. For the categorical analyses, night-time road noise estimates were categorized by 5 dBA increments: <55 (reference), 55–60, and >60 dBA, like in our previous work (Halonen et al., 2015b). We also conducted supplementary analyses using daytime road noise ($L_{Aeq16\text{ hour}}$, from 7:00 to 22:59) and report the effects independently of night-time road noise. For the WHII participants we linked noise level from year 2003 or 2004, whichever was closer to each participant's clinical measurements. For the SABRE participants noise levels from 2009 were used.

2.6. Covariates

Data for the individual-level covariates were obtained from the study questionnaires and clinic visits. The following individual-level variables were used in the analyses: sex, age, ethnicity (categorized as white vs. other), marital status (married/cohabiting vs. other) and smoking status (current smoker vs. other). In addition to sex and age, we included smoking and ethnicity a priori given they are strongly associated with cardiovascular health (Martin et al., 2015; Messner et al., 2014), and may plausibly show spatial variability that could be associated with that of noise, given highly diverse composition of the London population, the spatial variability of ethnic groups within London and different smoking prevalences between different ethnic and social groups. Of other individual-level variables available, only marital status was found to be predictive of cIMT and associated with noise exposure and was not a potential intermediate, satisfying the definition of a confounder. In SABRE, ethnicity was described at baseline by the interviewer based on appearance and parental origin. In WHII, self-reported

ethnicity at phase 5 was mainly used; missing data were complemented by observer-assigned ethnicity from phase 1. Marital status and smoking status were based on responses to questionnaires in both cohorts. Other possible individual-level confounders such as body mass index, alcohol drinking and physical activity were not available in both cohorts and thus could not be included in the analyses.

To adjust for traffic-related air pollution like in prior studies (Monrad et al., 2016; Sorensen et al., 2011), annual nitrogen oxide (NOx) concentrations within WHII participants' postcode centroids were estimated for 2003 and 2004 using a dispersion model (Beevers et al., 2013). NOx estimates for the SABRE participants were for year 2009 and modelled for each participant's postcode using a Land Use Regression (LUR) model developed as part of the European Study of Cohorts for Air Pollution Effects (ESCAPE) (Beelen et al., 2013). NOx was weakly associated with exposure, although not predictive of outcomes. To control for possible confounding by area deprivation we used the Index of Multiple Deprivation (IMD). Lower Layer Super Output Area (LSOA) IMD was assigned to postcodes within the LSOA (Office for National Statistics, 2014). Information from 2004 (Noble et al., 2004) was linked to the WHII participants and from 2010 (McLennan et al., 2011) to the SABRE participants. In the analyses we used continuous IMD scores, where higher values indicate greater deprivation.

2.7. Statistical analyses

We used linear regression models to examine pooled associations for night-time road traffic noise with cIMT, SBP, and DBP, and logistic regression models for hypertension. Results for these analyses are presented in two complementary ways: 1) using noise as a continuous variable, as μm change in cIMT and as mmHg change in SBP and DBP per 10 dBA increase in noise level, 2) using noise as categorical variable (<55 dBA (reference), 55–60 dBA, and >60 dBA), as mean differences in cIMT (in μm), and SBP and DBP (in mmHg) between the reference category and the other two categories. For hypertension, we present odds ratios (OR) and 95% confidence intervals (CI). We repeated these analyses using daytime road traffic noise.

To examine the effects of adjustments for individual- and area-level covariates on the associations under study we used three different models: Model 1 was adjusted for cohort, age and sex; Model 2 in addition to Model 1 for individual-level ethnicity, marital status and smoking status; and Model 3 in addition to Model 2 for area-level deprivation and NOx. Adjustment for cohort was needed to account for differences in how the outcomes and NOx were measured. To explore potential differences in effect we ran sensitivity analysis including only those not taking anti-hypertensive medications. We also stratified

Table 2
Descriptive statistics of the environmental variables used in the pooled and cohort-specific analyses.

Environmental variables	Minimum	10th percentile	Median	Mean	90th percentile	Maximum	SD
Night-time noise (dBA)							
Pooled	49.2	49.3	49.8	51.7	59.2	75.4	4.3
WH II	49.2	49.3	49.7	51.4	58.4	75.4	4.0
SABRE	49.2	49.3	50.3	52.7	61.4	74.0	4.9
Daytime noise (dBA)							
Pooled	54.8	54.9	55.3	57.2	64.4	78.1	4.1
WH II	54.8	54.9	55.2	56.9	63.5	78.1	3.8
SABRE	54.8	54.9	55.7	58.1	66.3	77.5	4.7
NOx ($\mu\text{g}/\text{m}^3$)							
Pooled	25.0	44.4	57.1	60.0	78.2	227.5	15.7
WH II	36.1	47.2	60.7	62.5	79.8	143.4	13.2
SABRE	25.0	39.9	48.3	52.1	63.7	227.5	19.7
IMD ^a							
Pooled	1.0	5.1	15.5	18.2	35.2	70.4	12.3
WH II	1.0	4.4	12.1	15.5	31.8	70.4	11.0
SABRE	2.97	12.3	25.0	26.7	44.3	62.3	12.2

^a IMD = Index of Multiple Deprivation standardised using all Lower Layer Super Output Areas in England. Higher value indicates higher area-level deprivation.

Table 3

Pooled and cohort-specific associations for 10 dBA increase in night-time noise with cIMT, SBP and DBP.

Outcome	Model 1 ^a			Model 2 ^b			Model 3 ^c		
	Estimate	95% CI		Estimate	95% CI		Estimate	95% CI	
cIMT (μm)									
Pooled	9.8	−5.0	24.7	8.0	−6.9	22.8	9.1	−7.1	25.2
SABRE	6.6	−26.0	39.1	4.9	−27.8	37.5	14.3	−22.6	51.1
WHII	12.4	−4.1	28.8	11.5	−4.9	27.9	8.8	−8.7	26.4
SBP (mmHg)									
Pooled	0.1	−1.5	1.7	0.0	−1.6	1.6	0.3	−1.4	2.1
SABRE	−0.5	−3.6	2.5	−1.3	−4.3	1.7	−1.1	−4.5	2.3
WHII	0.5	−1.4	2.4	0.7	−1.2	2.6	1.1	−0.9	3.1
DBP (mmHg)									
Pooled	−0.3	−1.3	0.6	−0.3	−1.2	0.7	−0.2	−1.2	0.9
SABRE	−0.2	−1.8	1.3	−0.3	−1.9	1.3	−0.2	−2.0	1.6
WHII	−0.4	−1.6	0.8	−0.2	−1.4	1.0	0.0	−1.3	1.2

^a Model 1 adjusted for cohort (in pooled analyses), sex and age.^b Model 2 adjusted for cohort (in pooled analyses), sex, age, ethnicity, marital status and smoking.^c Model 3 adjusted for cohort (in pooled analyses), sex, age, ethnicity, marital status, smoking, area-level deprivation and NOx.

the models by sex as air pollution has been linked to greater progression of cIMT among females than males (Adar et al., 2013).

In addition to the pooled associations, fixed effects meta-analysis was performed based on Model 3 to investigate both cohort-specific and pooled estimates of the associations. Even though cIMT, SBP and DBP were approximately normally distributed, plots of residuals were examined to assess potential violations of linear regression assumptions. No violations were observed.

3. Results

Mean age of the total study population was 63 years ($SD = 7$), in the WHII cohort it was 61 years ($SD = 6$), and in the SABRE cohort 69 years ($SD = 6$). Other descriptive statistics of the participants (pooled and by cohort) are presented in Table 1. There were no differences in demographic variables and outcome variables between the cohort of all eligible participants and the cohort of participants without missing data. Distributions of night- and daytime road traffic noise, NOx and IMD scores, in the pooled sample and by study cohorts are presented in Table 2. In the pooled dataset, the correlation for night-time road noise and NOx was 0.33. The correlation for daytime against night-time road noise was 0.99. Results using daytime noise were unsurprisingly comparable to results using night-time noise (Supplemental Tables 1–3) and are not discussed further.

In the pooled and cohort-specific linear regression analyses we observed non-significant positive associations between road noise exposure and cIMT. In the fully adjusted model (Model 3), cIMT increased by 9.1 μm (95% CI: −7.1, 25.2) per 10 dBA increase in night-time noise (Table 3). According to the fixed effects meta-analysis, a 10 dBA increase in night-time noise was associated with an increased cIMT of 9.8 μm (95% CI: −6.0, 25.6) (Fig. 1), which is comparable to the estimate from the pooled regression. Results for both cohorts were very similar. Sex-stratified results are presented in Supplemental Table 4. A slightly

larger increase in cIMT per 10 dBA increase in night-time noise were seen among females (13.9 μm , 95% CI: −12.1, 39.8) than among males (8.2 μm , 95% CI: −12.1, 28.6).

Pooled association between night-time road noise and SBP was also positive although not statistically significant, the WHII cohort having a stronger indication of a positive association than SABRE (Table 3 and Fig. 2). Pooled and cohort-specific fully adjusted estimates for DBP were close to null (Table 3 and Fig. 2). The fixed effects meta-analysis resulted in similar effect estimates as the pooled analysis (Fig. 2). The sex-stratified analyses for SBP and DBP did not provide evidence of a differential effect by gender (Supplemental Table 4). There were no pooled associations between 10 dBA increase in night-time road noise and hypertension but with wide confidence intervals: odds ratio 0.98 (95% CI: 0.78, 1.23). The odds ratios from the fixed effects meta-analysis were similar (Supplemental Fig. 1). No significant associations were seen between NOx and any of cIMT, SBP or DBP when adjusted for the covariates and noise levels (Supplemental Table 5).

In analyses of noise by 5 dBA categories, pooled mean differences in cIMT between participants exposed to night-time road noise levels 55–60 dBA and >60 dBA vs. <55 dBA were 16.2 μm (95% CI: −8.7, 41.2) and 21.2 μm (95% CI: −2.5, 44.9), respectively, after adjustment for the confounders (Table 4). Results were similar between cohorts (Table 4). A somewhat greater increase in cIMT was seen among females (36.9 μm , 95% CI: 0.1, 73.7) than among males (15.1 μm , 95% CI: −15.2, 45.5) in the >60 dBA vs. <55 dBA night-noise category (Supplemental Table 6). Mean differences in SBP between participants exposed to night-time road noise level 55–60 dBA and >60 dBA vs. <55 dBA were also positive (1.1 mmHg, 95% CI −1.6, 3.8 and 0.1 mmHg, 95% CI: −2.5, 2.6), but statistically non-significant (Table 4). Odds ratios for hypertension in the 55–60 dBA and >60 dBA vs. <55 dBA category were 0.86 (95% CI: 0.60, 1.21) and 0.94 (95% CI: 0.68, 1.32), respectively.

In the subset of participants not taking anti-hypertensive medications, the associations between night-time road noise levels and SBP

Fig. 1. Fixed effects meta-analysis for associations between 10 dBA increase in night-time road traffic noise and carotid intima media thickness (cIMT).

Fig. 2. Fixed effects meta-analysis for associations between 10 dBA increase in night-time road traffic noise and diastolic (DBP) and systolic (SBP) blood pressure.

and DBP were mostly null. However, the association with cIMT was slightly more pronounced than in the overall cohort. In the fully adjusted model for the pooled sample (Model 3), cIMT increased by 14.1 μm (95% CI: -3.1, 32.6) per 10 dBA increase in night-time noise (Table 5). Mean differences in cIMT between these participants exposed to night-time noise levels 55–60 dBA and >60 dBA vs. <55 dBA were 16.9 μm (95% CI: -10.7, 44.5), and 32.6 μm (95% CI: 6.9, 59.0), respectively.

4. Discussion

This analysis using participants of two study cohorts from the Greater London, UK, found a positive association between long-term night-time road traffic noise exposure and carotid intima-media thickness among a sub-set of non-medication users after adjustment for individual-level risk factors, air pollution and area-level deprivation. We observed no associations between traffic noise exposure and blood

Table 4
Pooled and cohort-specific mean differences in cIMT, SBP and DBP by night-time road traffic noise categories.

		Model 1 ^a			Model 2 ^b			Model 3 ^c		
Night-time noise (dBA)	n	Estimate	95% CI		Estimate	95% CI		Estimate	95% CI	
cIMT (μm)										
Pooled										
<55 dBA	2187	Ref			Ref			Ref		
55–60 dBA	178	17.5	−7.4	42.5	15.7	−9.2	40.6	16.2	−8.7	41.2
>60 dBA	227	20.3	−2.1	42.6	18.8	−3.5	41.1	21.2	−2.5	44.9
SABRE										
<55 dBA	491	Ref			Ref			Ref		
55–60 dBA	59	18.7	−36.0	73.4	16.3	−38.5	71.0	19.9	−35.3	75.1
>60 dBA	77	16.2	−32.5	64.9	14.1	−34.7	62.9	26.0	−27.0	78.9
WHII										
<55 dBA	1696	Ref			Ref			Ref		
55–60 dBA	119	18.0	−9.6	45.5	17.6	−9.8	45.0	17.1	−10.4	44.6
>60 dBA	150	23.7	−1.0	48.5	23.7	−0.9	48.3	21.2	−4.8	47.2
SBP (mmHg)										
Pooled										
<55 dBA	2187	Ref			Ref			Ref		
55–60 dBA	178	0.9	−1.8	3.62	1.0	−1.7	3.7	1.1	−1.6	3.8
>60 dBA	227	−0.3	−2.7	2.11	−0.4	−2.8	2.0	0.1	−2.5	2.6
SABRE										
<55 dBA	491	Ref			Ref			Ref		
55–60 dBA	59	−1.1	−6.2	4.0	−1.7	−6.8	3.3	−1.7	−6.7	3.4
>60 dBA	77	−2.1	−6.7	2.5	−2.8	−7.3	1.7	−2.7	−7.6	2.2
WHII										
<55 dBA	1696	Ref			Ref			Ref		
55–60 dBA	119	2.0	−1.2	5.2	2.3	−0.9	5.5	2.4	−0.8	5.6
>60 dBA	150	0.6	−2.3	3.5	0.8	−2.1	3.6	1.4	−1.6	4.4
DBP (mmHg)										
Pooled										
<55 dBA	2187	Ref			Ref			Ref		
55–60 dBA	178	−0.4	−2.1	1.2	−0.3	−1.9	1.3	−0.3	−1.9	1.4
>60 dBA	227	−0.3	−1.8	1.1	−0.3	−1.7	1.2	−0.1	−1.6	1.5
SABRE										
<55 dBA	491	Ref			Ref			Ref		
55–60 dBA	59	−1.8	−4.5	0.8	−1.9	−4.5	0.7	−1.8	−4.5	0.8
>60 dBA	77	−0.6	−3.0	1.7	−0.7	−3.1	1.6	−0.7	−3.2	1.9
WHII										
<55 dBA	1696	Ref			Ref			Ref		
55–60 dBA	119	0.4	−1.6	2.4	0.6	−1.4	2.6	0.6	−1.4	2.6
>60 dBA	150	−0.2	−2.0	1.6	−0.1	−1.8	1.7	0.3	−1.6	2.2

^a Model 1 adjusted for cohort (in pooled analyses), sex and age.

^b Model 2 adjusted for cohort (in pooled analyses), sex, age, ethnicity, marital status and smoking.

^c Model 3 adjusted for cohort (in pooled analyses), sex, age, ethnicity, marital status, smoking, area-level deprivation and NO_x.

pressure or hypertension. Differences between the pooled and meta-analysis estimates were small, supporting the generalizability of our findings.

To our knowledge, this is the first study to examine associations between road traffic noise exposure and cIMT. Some previous studies have examined road proximity in relation to intermediate cardiovascular markers, which may reflect both noise and air pollution exposures. One earlier cross-sectional study examined coronary artery calcification (CAC) and found 1.63 times higher odds of having a high amount of CAC among individuals living ≤ 50 m compared to those living > 200 m from a major road (Hoffmann et al., 2009). Studies with longitudinal data have suggested that living within 100 m from a highway is associated with progression of atherosclerosis, indicated as an increase in cIMT (Kunzli et al., 2010), and long-term exposure to black carbon, another proxy for exposure to traffic, has been linked to an increase in cIMT in elderly men (Wilker et al., 2013). In the WHII cohort, increase in particulate matter has also been associated with extent of subclinical atherosclerosis measured by cIMT (Tonne et al., 2012). However, in these studies traffic noise was not measured or included as a separate exposure variable. Although positive associations between particulate air pollution and cIMT have been reported (Tonne et al., 2012; Wilker et al., 2013), inverse non-significant associations were observed with NO_2 or NO_x in a study with four European cohorts (Perez et al., 2015), which agrees with our findings.

We did not observe robust associations between long-term exposure to road traffic noise and systolic or diastolic blood pressure, or hypertension. Previous studies, including a meta-analysis of 24 studies, have shown associations between traffic noise and hypertension (Babisch et al., 2014; Barcelo et al., 2016; van Kempen et al., 2012), but other studies have not (Sorensen et al., 2011) or found that associations lost statistical significance after adjustment for air pollution (Babisch et al., 2014). Results for blood pressure have been less frequently reported. Similarly to our findings, studies on the long-term effects of traffic noise exposure on SBP or DBP have reported no (Dratva et al., 2011; Fuks et al., 2011) or weak associations (Sorensen et al., 2011). Two possible reasons for this are exposure misclassification and modifying effect of medication, discussed below. One study that used night-time traffic noise exposure estimated at the façade of the participants' residences suggested a positive association with SBP and DBP. They also reported that night-time traffic noise exposure estimated for indoors was associated with increased SBP (Foraster et al., 2014). This suggests that exposure misclassification may exist when using only outdoor traffic noise estimates, which attenuates the possible associations. In this study, we had no information about the direction of the bedroom

window in relation to the streets. It has also been suggested that high correlation (0.7 or higher) between noise and an air pollutant used as a covariate would have prevented researchers from seeing associations between noise and blood pressure in previous studies (Foraster et al., 2014). In our data correlation between road traffic noise and NO_x was around 0.30, indicating that this cannot explain the weak findings. Also, other studies have suggested noise is an independent contributor to health risks (Stansfeld, 2015). Overall, it is more difficult to assess a relationship between traffic noise and blood pressure, than hypertension, given the modifying effect of medication. Although we, and others (Dratva et al., 2011; Foraster et al., 2014; Fuks et al., 2011), attempted to adjust for the medication use, this may be another possible reason resulting in the lack of a clear association for blood pressure.

We observed a positive non-significant association between night-time road traffic noise and cIMT that was slightly larger in the subset of participants not taking anti-hypertensive medications, and slightly larger among females than males, which agrees with findings for particulate air pollutants and cIMT (Adar et al., 2013). The small numbers of participants exposed to noise levels above 60 dBA may, however, have impaired our ability to detect significant associations. This relates to the use of postcode- and not address-level noise estimates that might have resulted in reduced exposure contrasts limiting statistical power. Nevertheless, we were able to conduct a small study using the TRAFFIC study (King's College London, 2014) estimates of day-time road traffic noise levels within the CHASE cohort (Whincup et al., 2010), covering most of the geographical area related to cohorts in this study, to assess the difference between postcode and address level noise estimates ($n = 4692$; $\sim 2.5\%$ of all postcodes). For 85% of the addresses, the differences between postcode and address level noise estimates were smaller or equal to 1 dBA. The differences were bigger than 3 dBA for only 3% of the addresses. Although pooling data increased the sample size and the heterogeneity in the noise range covered, which had a favourable impact on power, statistical power remained as an important limitation. In addition, the exposure model used is likely to have resulted in some exposure misclassification, with exposure at low noise levels being over-estimated and exposure in areas with heavily trafficked minor roads underestimated. Therefore, we used not only linear but also categorical exposure metrics which may have reduced the misclassification. Our study did not include noise from rail and aircraft traffic as in London these have different distributions from road traffic noise (Carey et al., 2016; Halonen et al., 2015a; Hansell et al., 2013). Rail and aircraft noise also have different acoustic characteristics and thus may not be simply additive with road noise (Basner et al., 2014). Another limitation is that we did not have information on residential history for all

Table 5

In participants not taking anti-hypertensive medications, pooled and cohort-specific associations per 10 dB increase in night-time noise and mean differences in cIMT, SBP and DBP by night-time road traffic noise categories in model 3^a.

		cIMT (μm)			SBP (mmHg)			DBP (mmHg)		
	n	Estimate	95% CI		Estimate	95% CI		Estimate	95% CI	
Continuous										
Pooled	1702	14.7	−3.1	32.6	0.4	−1.6	2.3	−0.2	−1.5	1.0
SABRE	197	25.1	−29.9	80.2	0.0	−5.1	5.1	−0.6	−3.2	2.1
WHII	1505	12.4	−6.6	31.4	0.7	−1.4	2.8	0.0	−1.4	1.4
Categorical										
Pooled										
<55 dBA	1444	Ref			Ref			Ref		
55–60 dBA	114	16.9	−10.7	44.5	2.0	−1.0	5.0	0.4	−1.6	2.3
>60 dBA	144	32.6	6.2	59.0	−0.4	−3.2	2.5	−0.4	−2.2	1.5
SABRE										
<55 dBA	148	Ref			Ref			Ref		
55–60 dBA	20	45.0	−36.3	126.3	−1.4	−9.0	6.1	−3.9	−7.8	−0.1
>60 dBA	29	36.8	−39.5	113.1	−0.7	−7.7	6.4	−0.2	−3.8	3.4
WHII										
<55 dBA	1296	Ref			Ref			Ref		
55–60 dBA	94	12.2	−17.3	41.8	3.0	−0.3	6.3	1.3	−0.9	3.5
>60 dBA	115	32.6	4.3	60.9	−0.1	−3.2	3.0	−0.3	−2.4	1.8

^a Model 3 adjusted for cohort (in pooled analyses), sex, age, ethnicity, marital status, smoking, area-level deprivation and NO_x .

participants, therefore exposure of those participants who had lived in the residential postcode area used for the exposure linkage for a short time period may have been misclassified. As in all epidemiological noise studies to date, information on daily activities of the participants was not available and was not accounted for in the exposure modelling, which may also have caused some exposure misclassification. However, in this study, we used the same road traffic noise model as in our previous ecological study on cardiovascular morbidity and mortality in London (Halonen et al., 2015b). The strengths of this study also include use of individual-level information on cIMT, blood pressure and hypertension from two London cohorts, as well as control for possible individual- and area-level confounders such as smoking, area-level deprivation and air pollution.

5. Conclusions

Our findings from Greater London suggest that after taking into account potential confounders, such as air pollution, the association between night-time road traffic noise and cIMT is only observed among persons who do not use antihypertensive medication, and the associations with blood pressure and hypertension are largely null. Thus, we found only weak evidence to support the hypothesis that associations between road traffic noise and stroke are via the cIMT or hypertension pathway. To confirm these findings, the associations between road traffic noise exposure and cIMT should be further examined in longitudinal settings with large study samples and in locations with more variation in the noise exposure levels.

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Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.envint.2016.09.023>.

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