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Traffic noise and hypertension – results from a large case-control study

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ABSTRACT

Background: Environmental traffic noise is a potential cause of hypertension. We aimed to study the association between hypertension as recorded in health insurance claims data and the exposure to three sources of traffic noise (aircraft, road and rail).

Methods: This large case-control study was conducted among persons aged 40 and above in 2010 and living in the region around Frankfurt airport in Germany. Individual residential noise exposure for the index year 2005 was assessed using standard noise algorithms. Cases were all newly diagnosed cases of hypertension recorded in three large health insurances databases in the period 2006–2010. Controls had no hypertension diagnosis. Categorical and continuous analyses were conducted with binary logistic regression models adjusted for sex, age and residential area-based socioeconomic information.

Results: The main analysis included 137,577 cases and 355,591 controls. There were no associations with any of the traffic noise sources. Odds ratios (OR) per 10 dB noise increase were 0.99 (95% confidence interval: 0.98;1.01) for aircraft noise, and 1.00 (0.99;1.01) both for road and railway noise. Similarly, nighttime noise levels showed no associations with hypertension. Odds ratios were increased for the subgroup of newly diagnosed hypertension cases with a subsequent diagnosis of hypertensive heart disease: per 10 dB aircraft noise there was a 13.9% OR increase (6.0% for road traffic, 5.4% for rail traffic). Increases were also noted when we analyzed cases with a longer exposure-outcome time window.

Conclusion: Our results are suggestive of an association of noise exposure with clinically more severe hypertension diagnoses, but not with uncomplicated hypertension. The absence of individual confounder data, however, adds to the risk of bias. The results contribute to evidence on traffic noise as a cardiovascular risk factor.

1. Introduction

Traffic noise is a recognized environmental risk factor. Cardiovascular diseases, and particularly hypertension, have received the most attention as clinical outcomes possibly associated with diverse sources of traffic noise. Due to the high public interest in large-scale infrastructural developments such as airports, and the concomitant burdens on nearby communities, aircraft noise has been at the center of epidemiologic research (Eriksson et al., 2014; Evrard et al., 2015, 2016). However, noise associated with road and railway traffic is even more ubiquitous in many countries and particularly road traffic noise has been researched intensely over the past years (Babisch, 2014; Babisch et al., 2014; Meline et al., 2015; Recio et al., 2016b).

In Germany, the prevalence of hypertension in adults aged 18–79 years is about 30% for women, and 33% for men, with highest values of above 70% in the oldest age group (65–79 years) (Neuhauser and Sarganas, 2015). A cumulative hypertension incidence of 26.2% over a 12-year period was reported recently (Diederichs and Neuhauser, 2017). A possible relationship between noise and hypertension is often explained by a chronic stress response to noise, involving the sympathetic nervous system as well as endocrine responses (Babisch et al., 2014; Recio et al., 2016a).

Epidemiological studies on aircraft noise and hypertension have yielded inconsistent results. The cross-sectional "Hypertension and Exposure to Noise around Airports (HYENA)" study investigated associations between aircraft and traffic noise exposure and hypertension in 4861 people residing in the vicinity of six large European airports (Jarup et al., 2008). A 10 dB increase in nighttime aircraft

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noise levels increased the odds of hypertension by 14% (95%CI: 1.2;28.6%), while for average daytime road traffic noise exposure the OR per 10 dB increase was elevated by 9.7% (95%CI:0.3;20.1%). Sex-specific analyses of the HYENA data indicated significant increases in odds ratios with increasing road traffic noise for men but not for women, while for nighttime aircraft noise no sex differences were apparent. The absolute blood pressure increase due to nighttime aircraft noise measured among study participants was in the order of 6 mmHg systolic and 7 mmHg diastolic pressure. In Sweden, Eriksson (Eriksson et al., 2010) found no overall association between aircraft noise exposure and incident hypertension in a cohort of residents near airports; in subgroup analyses, non-smoking men, but not women showed a statistically significant relative risk increase of 21% (95%CI 5;39%) per 5 dB. Looking at traffic noise overall including aircraft noise, the "Residential Environment and Coronary heart Disease (RECORD)" study indicated increased hypertension risks associated only with combined road, rail and air traffic noise at the workplace, but not in the residential setting (Meline et al., 2015). A 2009 review estimated a pooled 13% risk increase per 10 dB (95%CI 0;28%) of aircraft noise based on five studies, but also noted limited validity of measurements taken in several of the included studies (Babisch and Kamp, 2009). A recent meta-analysis summarized data from three cross-sectional studies and one cohort study and computed an OR of 1.63 for hypertension among residents with aircraft noise exposure (Huang et al., 2015). This increase was significant only for men.

Overall the evidence appears inconclusive, but with a tendency towards a positive association between hypertension and aircraft traffic noise. Looking at road traffic only, van Kempen and Babisch (van Kempen and Babisch, 2012) reported a statistically significant 3.4% increased OR per 5 dB based on the pooling of 24 studies.

We therefore investigated the association between physician-diagnosed hypertension as recorded in health insurance claims data and the exposure to three sources of traffic noise in a large case-control study, deriving study participants from a database of about 1 million persons with individual health and residential noise information. The current analysis is embedded in the NORAH (noise-related annoyance, cognition and health) case-control study conducted in the region around Frankfurt airport in Germany.

2. Materials and methods

We analyzed case-control data from health insurance claims databases for persons residing in the vicinity of Frankfurt airport, using individual residential noise data for three sources of noise: air, rail and road traffic. The detailed study design and methods are available from (Seidler et al., 2017, 2016a, 2016b). We provide a summary overview of the general methods and a detailed description of specific approaches to hypertension.

2.1. Study population

The study population from which cases and controls were identified included 1,026,670 persons aged 40 years or above in 2010 who were members of one of three large statutory health insurance funds in the period 2005–2010, representing some 23% of all residents of this age group in the study region situated around Frankfurt airport. The study region included all administrative areas with substantial aircraft noise exposure of the population.

2.2. Cases of hypertension

Requirements for the classification as a newly diagnosed case were a recorded main or secondary hospital discharge diagnosis of hypertension (ICD 10: I10.-), or two confirmed I10.- diagnoses in the ambulatory setting within a time period of 12 months. A further requirement was that no hypertension diagnosis was recorded in the 12 months prior to the first diagnosis date during the study period. Thus, 137,577 individuals qualified as cases based on this definition.

Using a predefined restrictive case definition, we additionally analyzed all persons with a confirmed hypertension diagnosis as above who also had a further diagnosis of hypertensive heart disease (I 11.-) during the study period (n =7031).

2.3. Controls

Control subjects were all persons in the claims database without any new or prevalent hypertension diagnosis as described above during the study period. They had to be aged 40 years or above in 2010 and have an insurance period of at least 12 months in one of the participating health insurance funds. 355,591 persons served as controls for the main analysis.

2.4. Exposure assessment

Extensive steps to map aircraft, rail and road noise data to individual residential addresses were undertaken. Immission sites per noise source were selected (aircraft: center of building; road, rail: main exposed outer surface of residence) and average and maximum noise levels for the index year 2005 calculated based on most appropriate data sources. These were historical radar data and input data provided by German Flight Safety Operator (DFS) for aircraft noise and traffic count or operation data from relevant official sources (traffic count data; German Railway Operator and Federal Railway Authority). Noise models included sound propagation scenarios from source to immission site as well as data on noise barriers and walls along car traffic and railway routes, covering day- and nighttime exposures. All calculations were done using national or EU algorithms for noise mapping. Aircraft noise data were compared for consistency with measurements from local monitoring stations (Möhler, 2016). A graphical overview of aircraft noise exposure and the geographical study area has been published earlier (Seidler et al., 2017).

Several independent databases were designed to assure that no single institution had access to personal identifiers (addresses) together with sensitive health claims data. The data linkage office in Bremen merged address-specific noise and address data from health insurances (one insurance fund performed this step independently). Address data were then replaced by study ID, and the merged data set forwarded to the data analysis office in Dresden where claims information from the three health insurances was linked to the noise data via the common study ID. All procedures followed a strict data protection protocol approved beforehand by federal and state authorities.

2.5. Data analysis and adjustment for confounding

We initially performed extensive descriptive analyses of the large case-control data set, using 2005 as the index year for exposure, and the period 2005–2010 as analysis window for relevant health and confounder information. We then built logistic regression models to calculate OR and 95%CI with hypertension as outcome and noise exposure per 5 dB category as explanatory variable, using the 24 h average noise exposure (LpAeq. 24 h) category < 40 dB as reference. 24 h average noise exposure was also modelled as a continuous variable and presented as OR per 10 dB increase in noise exposure. Separate models were run to study nighttime (22–6 h) traffic noise. We included sex (male, female) and age (in 5-year categories, starting at 40 years) in the models. Data on education and job title were available for a proportion of cases (32.1%, n =44,188) and controls (50.9%, n =180,881) in the health insurance funds database. We included this information in the final regression model, along with an area-based measure of socioeconomic status (SES) (= proportion of persons on long-term unemployment benefit) available for all study participants. A separate analysis was restricted to all persons for whom SES informa-

tion was recorded in the database. The same models were also applied to the subset of cases of hypertension with an additional diagnosis of hypertensive heart disease.

2.6. Sensitivity analyses

As first sensitivity analysis, we used a less restrictively defined analysis set where all confirmed prevalent hypertension diagnoses in the period 2005–2010 were included as cases (n = 397,424). The control set was not changed (n = 355,591). This was done to assess how the requirement of being free of any hypertension diagnosis 12 months prior to the first confirmed diagnosis influenced the analysis population and regression results.

The second sensitivity analysis included a restriction of cases to those who had a confirmed (incident) diagnosis of hypertension and who died during the period 2006–2010. Notably, no specific cause of death information was included in the claims databases. Additional sensitivity analyses included a) regression models combining all three noise sources, b) an analysis using medication prescription data where, in addition to the case definition used in our main analysis, also cases with an ambulatory main HPT diagnosis combined with prescription of antihypertensive medication (Anatomic Therapeutic Chemical (ATC) Code: C02-03;C07-09) within 12 consecutive months were considered, c) analyses of cases residing at least 5 years at the same place at the time of the incident diagnosis (for control subjects; residing at the same place for at least 5 years in 2008), and d) an analysis using only persons with newly recorded hypertension in 2009/2010.

Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine of the Technische Universität Dresden. The study concept was also approved by the Federal Commissioner for Data Protection and Freedom of Information (BfDI) as well as by the data protection authorities of the federal states of Hesse and Rhineland-Palatinate.

3. Results

Table 1 provides an overview of our population for the main analysis. The overall study population comprised about 23% of all residents aged 40 years and above in the study area. The analysis population included slightly more women than men in both case and control groups. The control group of non-hypertensive persons was expectedly somewhat younger. The mean (SE) age of cases at diagnosis of hypertension was 63.8 (± 0.03) years; the mean (SE) age of control subjects in 2008 (reference date) was 53.0 (± 0.02) years. Data were derived from health insurance sources and included many pensioners or persons co-insured with other insurees, thus education or occupational information was not available for many study group members. In terms of the area-based socioeconomic measure, an even distribution between cases and controls was observed. Median 24 h noise exposure was highest for road traffic (about 49 dB), followed by aircraft (about 41 dB) and railway noise (about 38 dB), without obvious differences between cases and controls.

We found no association between 24 h average aircraft, railway or road traffic noise and hypertension in the regression analyses (Table 2). The adjusted OR was close to 1 (OR range: 0.86–1.02) in all categories of noise levels, with the lowest OR in the sparsely populated group with aircraft noise levels above 60 dB. Similar null results were obtained for the association between road traffic noise and railway noise. The OR per 10 dB noise increase were 0.997 (95%CI 0.985;1.010) for aircraft noise, and 1.003 both for road (95%CI 0.995;1.011) and railway noise (95%CI 0.994;1.011). Separate analyses for women and men generally did not reveal any sex-specific differences, as almost all ORs remained very close to unity. For aircraft noise, the only exception was the small group with levels above 60 dB: here, men showed an increased OR and women a decreased OR, both with wide confidence intervals due to sparse data. For railway noise, women had slightly increased OR in the category 50- < 55 dB (OR = 1.04; 95%CI 1.01;1.07) and in the category ≥ 60 dB (OR = 1.06; 95%CI 1.00;1.12).

For nighttime noise levels, the results for aircraft noise remained unchanged, with OR close to 1 in all incremental 5 dB categories above 40 dB, and a slightly reduced OR in the highest category (here: 55- < 60 dB). For the other noise sources, all OR for nighttime noise were close to unity.

Including the three different health insurance databases as dummy

Table 1
Characteristics of cases with hypertension and control subjects, main analysis.

	Cases		Control subjects	
	n	%	n	%
Total	137,577	100.0	355,591	100.0
24 h noise levels [dB; median, int.quart. range]				
Aircraft	40.6	9.8	40.9	10.1
Road	48.7	11.8	49.0	11.9
Railway	37.6	12.9	38.2	13
Sex				
Males	62,843	45.7	163,645	46.0
Females	74,734	54.3	191,946	54.0
Age [yrs.]				
35 - < 45	8823	6.5	105,418	29.6
45 - < 50	12,909	9.4	68,444	19.2
50 - < 55	15,101	11.0	50,624	14.2
55 - < 60	17,555	12.8	38,862	10.9
60 - < 65	16,082	11.7	27,325	7.7
65 - < 70	19,508	14.2	25,389	7.1
70 - < 75	17,533	12.7	17,516	4.9
75 - < 80	12,488	9.1	9118	2.6
80 - < 85	9466	6.9	6039	1.7
≥ 85	5392	3.9	3901	1.1
Statutory health insurance funds				
Health insurance 1	88,263	64.2	221,959	62.4
Health insurance 2	10,123	7.4	24,844	7.0
Health insurance 3	39,191	28.5	108,788	30.6
Education				
Primary/sec. education, no vocational educ.	10,280	7.5	37,939	10.7
Primary/sec. education & vocational educ.	20,815	15.1	81,946	23.0
High school graduate, no vocational educ.	662	0.5	2122	0.6
High school graduate & vocational educ.	2011	1.5	7929	2.2
College degree	1598	1.2	5968	1.7
University degree	1327	1.0	7928	2.2
Education unknown	100,884	73.3	211,759	59.6
Occupation				
Agricultural occupations	423	0.3	1926	0.5
Unskilled manual occupations	5492	4.0	21,358	6.0
Skilled manual occupations	5026	3.7	20,029	5.6
Technicians, Engineers	1068	0.7	4584	1.3
Simple services	9626	7.0	36,410	10.2
Qualified services	1642	1.2	7425	2.1
Semiprofessionals	2.518	1.8	13,253	3.7
Professionals	245	0.2	1585	0.4
Simple commercial & admin. occupations	3481	2.5	14,953	4.2
Qualified commercial & admin. occupations	7809	5.7	36,226	10.2
Managers	767	0.6	3481	1.0
Other	964	0.7	4860	1.4
Unknown	98,516	71.6	189,501	53.3
Local proportion of persons receiving unemployment benefits (quintiles[a])				
≤ 6.7%	46,075	33.5	115,324	32.4
> 6.7- ≤ 7.5%	22,750	16.5	53,056	14.9
> 7.5- ≤ 8.7%	15,374	11.2	38,650	10.9
> 8.7- ≤ 12.7%	39,713	28.9	112,528	31.6
> 12.7%	13,665	9.9	36,033	10.1

[a] Calculation of quintiles: frequent duplication of values led to an uneven distribution.

Table 2
Case-control analysis of hypertension and exposure to three sources of traffic noise, results of main analysis stratified by 24 h noise levels (LpAeq. 24 h), nighttime noise, and for the subgroup of persons with available individual socioeconomic status (SES) information.

	Aircraft noise				Road traffic noise				Railway noise			
Noise Exposure	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**
24 h LpAeq; Hypertension I.10 (N = 137,577)												
< 40 dB.	63,415	156,517	1.00		14,592	34,961	1.00		73,621	186,233	1.00	
40- < 45 dB	40,799	109,054	0.98	[0.96,1.00]	29,269	73,344	0.99	[0.96,1.01]	17,145	45,468	1.00	[0.98,1.02]
45- < 50 dB	22,080	59,143	1.01	[0.99,1.03]	33,146	85,354	0.98	[0.96,1.01]	21,689	57,935	1.00	[0.98,1.02]
50- < 55 dB	8742	23,558	1.01	[0.98,1.04]	24,410	64,955	0.99	[0.96,1.02]	15,254	39,905	1.02	[0.99,1.04]
55- < 60 dB	2508	7219	0.97	[0.92,1.02]	15,191	39,482	1.01	[0.99,1.05]	5997	15,712	1.00	[0.96,1.03]
60- < 64 dB (≥60 for aircr.)	33	100	0.86	[0.57,1.32]	11,348	30,189	1.02	[0.99,1.05]	2319	5962	1.04	[0.98,1.09]
65- < 70 dB					7523	21,117	0.98	[0.98,1.01	1002	2748	1.03	[0.95,1.12]
≥70 dB					2098	6189	0.96	[0.91,1.02]	550	1628	0.93	[0.84,1.03]
Continuous (per 10 dB)			0.997	[0.985,1.010] p = 0.668			1.003	[0.995,1.011] p= 0.428			1.003	[0.994,1.011] p = 0.539
Nighttime 22–6; Hypertension ICD I.10												
< 40 dB	99,465	253,893	1.00		55,729	138,769	1.00		72,945	185,061	1.00	
40- < 45 dB	23,217	60,309	1.02	[1.00,1.03]	27,902	73,113	0.99	[0.97,1.01]	16,995	44,643	1.01	[0.98,1.03]
45- < 50 dB	10,648	29,711	1.00	[0.97,1.02]	21,739	57,085	1.01	[0.99,1.04]	21,051	56,287	1.02	[1.00,1.04]
50- < 55 dB	4071	11,087	1.01	[0.97,1.05]	15,913	41,458	1.03	[1.01,1.05]	15,516	40,645	1.01	[0.98,1.03]
55- < 60 dB	176	591	0.81	[0.67,0.97]	10,998	30,033	1.01	[0.99,1.04]	6838	17,784	1.00	[0.97,1.03]
≥60 dB					5296	15,133	0.99	[0.95,1.02]	4232	11,171	1.02	[0.98,1.07]
24 h LpAeq; Hypertension ICD I.10; only cases (N = 44,188) and controls (N = 180,881) with SES information												
< 40 dB	19,933	80,382	1.00		4562	18,209	1.00		23,606	96,514	1.00	
40- < 45 dB	13,319	55,561	0.99	[0.97,1.02]	9303	37,897	0.99	[0.95,1.03]	5621	22,956	1.02	[0.98,1.05]
45- < 50 dB	7100	29,488	0.99	[0.97,1.03]	10,492	43,630	0.97	[0.94,1.02]	6984	28,577	1.02	[0.99,1.06]
50- < 55 dB	3014	11,819	1.07	[1.02,1.12]	7936	32,797	0.98	[0.94,1.02]	4820	19,993	0.99	[0.96,1.03]
55- < 60 dB	813	3575	0.96	[0.89,1.05]	4947	19,747	1.02	[0.97,1.07]	1918	7754	1.02	[0.96,1.08]
60- < 64 dB (≥60 for aircr.)	9	56	0.68	[0.33,1.40]	3778	15,203	1.02	[0.97,1.08]	710	2948	1.00	[0.92,1.09]
65- < 70 dB					2466	10,365	0.96	[0.91,1.02]	337	1330	1.08	[0.97,1.22]
≥70 dB					704	3033	0.97	[0.88,1.06]	192	809	0.97	[0.83,1.15

OR: Odds Ratio, ICD: International Classification of Diseases, 10th revision; * adjusted for age, sex, education, and job title (when available), local proportion of persons receiving unemployment benefits; 95%CI: 95% confidence intervals.

variables in the regression model resulted in somewhat better model fit, but numeric values of OR and CI were essentially unchanged. When we restricted the analysis to the subset of cases and controls with available individual SES information, the results also remained unchanged (Table 2, bottom), with no association found between aircraft, railway or road traffic noise (24 h average and nighttime 22–6 h) and hypertension diagnosis. Exceptions were an elevated OR of 1.07 (95%CI 1.02; 1.12) for 24 h aircraft noise in the category 50- < 55 dB and a slightly increased OR (3.6%) for railway nighttime noise in the category 45- < 50 dB. All OR per 10 dB increase were close to unity (data not shown). Similar results with no elevations in the OR were found in a model combining all traffic noise sources, thus controlling for exposure to other than the noise type of interest.

When we merged individual noise exposure from different sources in one categorical exposure term, the OR for most of the combinations were close to 1, with the exception of exposures ≥50 dB both for aircraft & railway noise (1855 cases, 4820 controls) where an OR of 1.07 (95%CI 1.00;1.14) was found.

For the subset of hypertension cases with an additional, consecutive diagnosis of hypertensive heart disease (Table 3), for the 24 h average noise levels for aircraft noise we found an OR increase of 13.9% per 10 dB (95%CI 9.0;19.0). Similarly, for road traffic there were significant increases in the OR in all categories from 40 dB onwards, with a linear increase of 6.0% (95% 3.1;8.9) per 10 dB. For railway noise, a linear increase of 5.4% (95%CI 2.3;8.5) was estimated (Table 3). Thus, for this restrictively defined case group of patients with subsequent hypertensive heart disease, significant associations with traffic noise were found, with highest linear increases for aircraft noise. Focusing on nighttime noise, several categories were sparsely populated and associations somewhat lower for road traffic noise. Most other estimates were of similar magnitude compared to 24 h noise level.

In the sensitivity analysis using prevalent cases (and thus an almost tripled case set when compared to the main analyses), noise level categories for all noise types were generally not positively associated with case status; the estimated OR were mostly lower when compared to the analysis of newly diagnosed cases. The OR per 10 dB increase was 0.99 for aircraft, road traffic and railway noise. Thus, the inclusion of prevalent cases did not improve the differentiation between cases and controls with regard to noise exposure. Using prescription data for antihypertensive medication in the case definition resulted in estimates of OR per 10 dB of 1.006 (95%CI 0.991;1.021) for aircraft, 1.007 (95% CI0.999;1.016) for road traffic, and 1.009 (95%CI 0.999;1.019) for railway noise, again very close to the results of our main analysis.

A further sensitivity analysis assessed a case definition restricted in terms of severity/co-morbidity, including only newly diagnosed hypertensive patients who died of any cause in the period 2006–2010 (n = 12,856). For this case group, all OR were generally close to unity or slightly below 1, and the linear OR per 10 dB was 0.96 (95%CI 0.925;0.997) for aircraft noise and 1.010 (95%CI 0.986;1.035) for railway noise. For road traffic (OR 1.034; 95%CI 1.011;1.057) slight increases per 10 dB were found (Table 4).

To study whether a longer disease-free interval influences our findings, we restricted the analysis population to cases with a first hypertension diagnosis recorded in 2009 or 2010. The results are shown in Table 5. Overall, there is an indication for a weak positive dose-response association in this analysis, which is stronger for aircraft noise than for the other noise types. The OR increase per 10 dB was 3.5% (95%CI 1.5;5.6) for aircraft noise against 1.5% (95%CI 0.2;2.7) for road traffic and 1.3% (95%CI −0.1;2.7) for railway noise. Results for cases and control subjects who had not changed residence in the 5 years prior to the diagnosis (or 2008 for controls) were generally similar; particularly higher road traffic noise exposure seemed to be more consistently associated with a diagnosis of hypertension, although most results were not statistically significant (Supplementary table S1).

Table 3
Case-control analysis of 24 h (LpAeq) and nighttime noise levels, with restriction to cases with HPT and subsequent hypertensive heart disease diagnosis (7031 cases, 355,591 controls).

	Aircraft noise				Road traffic noise				Railway noise			
Noise Exposure	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**
24 h LpAeq; Hypertension ICD I.10 and subsequent hypertensive heart disease ICD I.11 (N = 7031)												
< 40 dB	2901	156,517	1.00		621	34,961	1.00		3562	186,233	1.00	
40- < 45 dB	2223	109,054	1.14	[1.07,1.21]	1445	73,344	1.14	[1.03,1.25]	965	45,468	1.13	[1.05,1.22]
45- < 50 dB	1259	59,143	1.23	[1.14,1.32]	1739	85,354	1.19	[1.08,1.30]	1167	57,935	1.10	[1.02,1.17]
50- < 55 dB	510	23,558	1.25	[1.13,1.38]	1308	64,955	1.21	[1.09,1.33]	806	39,905	1.10	[1.02,1.20]
55- < 60 dB	138	7219	1.16	[0.97,1.39]	744	39,482	1.14	[1.02,1.27]	314	15,712	1.08	[0.96,1.22]
≥60 dB	0	100	–	–	1174	57,495	1.28	[1.16,1.42]	217	10,338	1.18	[1.03,1.36]
Continuous (per 10 dB)			1.139	[1.090,1.190]			1.060	[1.031,1.089]			1.054	[1.023,1.085]
				p = 0.000				p = 0.000				p = 0.001
Nighttime 22–6; Hypertension ICD I.10 and subsequent hypertensive heart disease ICD I.11												
< 40 dB.	4839	253,893	1.00		2704	138,769	1.00		3520	185,061	1.00	
40- < 45 dB	1317	60,309	1.14	[1.07,1.21]	1453	73,113	1.05	[0.98,1.12]	977	44,643	1.17	[1.09,1.26]
45- < 50 dB	630	29,711	1.16	[1.06,1.26]	1163	57,085	1.09	[1.02,1.17]	1142	56,287	1.12	[1.05,1.21]
50- < 55 dB	240	11,087	1.17	[1.02,1.34]	797	41,458	1.04	[0.96,1.12]	831	40,645	1.11	[1.03,1.20]
55- < 60 dB	5	591	0.43	[0.18,1.05]	599	30,033	1.12	[1.02,1.23]	338	17,784	1.03	[0.92,1.16]
≥60 dB					315	15,133	1.19	[1.05,1.34]	223	11,171	1.12	[0.98,1.29]

OR: Odds Ratio, ICD: International Classification of Diseases, 10th revision; * adjusted for age, sex, education, and job title (when available), local proportion of persons receiving unemployment benefits; 95%CI: 95% confidence intervals.

4. Discussion

In this large observational epidemiological study on hypertension and noise comprising approximately 135,000 cases and 355,000 controls, we found no association between a diagnosis of hypertension and residential traffic noise exposure in the main analysis, but significant positive exposure-disease associations in persons with an initial hypertension diagnosis and subsequent hypertensive heart disease, as well as in selected sensitivity analyses. We used secondary data from three health insurances and individual residential traffic noise estimates for aircraft, road traffic and railway noise.

Noise exposure and hypertension have been linked in several previous studies. The best estimate so far, derived from a pooled analysis of two earlier meta-analyses (Babisch and Kamp, 2009; van Kempen and Babisch, 2012), is a 7.6% odds ratio increase (95% CI 3.2;12.1) per 10 dB for traffic noise (Vienneau et al., 2015a). However, it should be noted that this is a joint estimate based on studies of aircraft and of road traffic noise. Evrard and colleagues (Evrard et al., 2016) recently analyzed cross-sectional data of 1244 adults residing in the vicinity of French airports. They found a significant OR of 1.34 per 10 dB for hypertension and noise exposure at nighttime for men, but not for women. Overall, there is marked heterogeneity in epidemiological results on noise exposure and hypertension, partly deriving from the fact that different designs were used to study the association, but also due to differences in exposure, confounder and outcome assessment. In principle, the most reliable effect estimate should be derived from longitudinal studies of populations with varying levels of noise exposure, well-defined information on exposure duration and intensity and extensive ascertainment of potential confounders such as socioeconomic status. Very few cohort studies are available, and no case-control studies using health insurance data or primary data for disease and confounder ascertainment and location-specific noise data were identified during our searches, as most studies rely on cross-sectional designs. The cohort study by Eriksson (Eriksson et al., 2010, 2007) found a positive association of incident hypertension and aircraft noise only in the subgroup of non-smoking men. In a Danish cohort study including some 57,000 participants, no association between transport noise and hypertension was found (Sorensen et al., 2011a). For road

Table 4
Sensitivity analyses of 24 h (LpAeq) noise levels and a) inclusion of prevalent HPT diagnoses and b) with restriction to cases with HPT and subsequent death from any cause until 2010.

	Aircraft noise				Road traffic noise				Railway noise			
Noise Exposure	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**
24 h LpAeq; Hypertension ICD I.10, prevalent and new diagnoses (N = 397,424)												
< 40 dB	187,307	156,517	1.00		44,167	34,961	1.00		217,352	186,233	1.00	
40- < 45 dB	116,485	109,054	0.97	[0.96,0.99]	86,721	73,344	0.97	[0.95,0.99]	48,560	45,468	0.98	[0.97,1.00]
45- < 50 dB	62,303	59,143	1.00	[0.99,1.02]	95,388	85,354	0.95	[0.93,0.97]	61,507	57,935	0.98	[0.97,1.00]
50- < 55 dB	24,219	23,558	1.00	[0.97,1.02]	69,080	64,955	0.96	[0.94,0.98]	42,744	39,905	0.99	[0.97,1.01]
55- < 60 dB	7032	7219	0.95	[0.91,0.99]	43,086	39,482	0.97	[0.95,1.00]	16,658	15,712	0.95	[0.93,0.98]
≥60 dB	78	100	0.77	[0.55,1.09]	58,982	57,495	0.97	[0.95,0.99]	10,603	10,338	0.98	[0.94,1.01]
Continuous (per 10 dB)			0.989	[0.980,1.000]			0.994	[0.988,1.000]			0.987	[0.980,0.993]
				p = 0.040				p = 0.062				p = 0.000
24 h LpAeq; Hypertension ICD I.10 and subsequent death from any cause (N = 12,856)												
< 40 dB	6255	156,517	1.00		1437	34,961	1.00		6993	186,233	1.00	
40- < 45 dB	3703	109,054	0.95	[0.91,1.00]	2753	73,344	0.96	[0.89,1.03]	1481	45,468	0.96	[0.91,1.03]
45- < 50 dB	1998	59,143	0.99	[0.93,1.06]	3200	85,354	1.00	[0.93,1.08]	2078	57,935	1.02	[0.96,1.08]
50- < 55 dB	696	23,558	0.92	[0.84,1.00]	2087	64,955	0.97	[0.89,1.04]	1350	39,905	0.99	[0.93,1.06]
55- < 60 dB	201	7219	0.87	[0.74,1.02]	1481	39,482	1.07	[0.99,1.16]	566	15,712	0.99	[0.90,1.09]
≥60 dB	3	100	0.94	[0.27,3.25]	1898	57,495	1.04	[0.96,1.12]	388	10,338	1.10	[0.98,1.23]
Continuous (per 10 dB)			0.960	[0.925,0.997]			1.034	[1.011,1.057]			1.010	[0.986,1.035]
				p = 0.033				p = 0.004				p = 0.425

OR: Odds Ratio, ICD: International Classification of Diseases, 10th revision; * adjusted for age, sex, education, and job title (when available), local proportion of persons receiving unemployment benefits; 95%CI: 95% confidence intervals.

Table 5
Case-control analysis of hypertension and exposure to three sources of traffic noise, results of analysis including only cases first diagnosed in 2009/10, stratified by 24 h noise levels (LpAeq. 24 h).

	Aircraft noise				Road traffic noise				Railway noise			
Noise Exposure	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**	**Cases**	**Controls**	**OR***	**95% CI**
24 h LpAeq; Hypertension I.10 cases (N = 39,811) and controls (N = 355,591)												
< 40 dB.	17,867	156,517	1.00		4077	34,961	1.00		21,049	186,233	1.00	
40- < 45 dB	11,893	109,054	1.01	[0.98,1.04]	8421	73,344	1.01	[0.97,1.06]	4923	45,468	0.99	[0.96,1.03]
45- < 50 dB	6627	59,143	1.06	[1.03,1.10]	9536	85,354	1.00	[0.96,1.04]	6433	57,935	1.03	[0.99,1.06]
50- < 55 dB	2616	23,558	1.06	[1.01,1.11]	7110	64,955	1.02	[0.98,1.06]	4506	39,905	1.04	[1.00,1.08]
55- < 60 dB	796	7219	1.08	[0.99,1.17]	4417	39,482	1.04	[0.99,1.09]	1761	15,712	1.02	[0.96,1.07]
60- < 65 dB (≥60 for aircr.)	12	100	1.12	[0.64,2.08]	3412	30,189	1.08	[1.03,1.14]	695	5962	1.09	[1.00,1.18]
65- < 70 dB					2205	21,117	1.02	[0.96,1.08	281	2748	0.99	[0.88,1.13]
≥70 dB					633	6189	1.02	[0.93,1.12]	163	1628	0.96	[0.81,1.13]
Continuous (per 10 dB)			1.035	[1.015,1.056] p = 0.001			1.015	[1.002,1.027] p= 0.018			1.013	[0.999,1.027] p = 0.056

OR: Odds Ratio, ICD: International Classification of Diseases, 10th revision; * adjusted for age, sex, education and job title (when available), local proportion of persons receiving unemployment benefits; 95%CI: 95% confidence intervals.

traffic, a recent pooled cross-sectional analysis of data from 3 cohorts from the Netherlands, the UK and Norway, (LifeLines, Epic-Oxford and Hunt3) had inconsistent findings across data sets, ranging from a slight negative association in the Netherlands to a positive association for noise above 60 dB in the Norwegian Hunt3 - study (Zijlema et al., 2016). The European Study of Cohorts for Air Pollution Effects (ESCAPE) found a weakly positive association between road traffic noise and self-reported (relative risk (RR) =1.03) as well as newly treated (RR =1.05), but not with measured hypertension in the joint analysis of data from six cohorts (Fuks et al., 2016).

In our dataset, socioeconomic status information is based on job title and education data available only for a third of cases and half of all controls. This is partly due to the fact that many study participants were in retirement age and therefore had no registered job title. In the regression analysis, a further area-based variable capturing the proportion of persons on income support was used. The overall size of the data set allowed a subgroup analysis including only persons with SES information. The effect estimates in this analysis were not substantially different from the main analysis, apart from some results in individual categories with slightly elevated risks. From this comparison, substantial confounding by socioeconomic status in the main analysis seems less likely, however it should be noted that the quality of information in the claims databases is limited.

The noise exposure assessed in our study pertains to residential noise in the year 2005. We were able to use address-specific noise data differentiated by noise source. Thus, risk estimates for aircraft, road traffic and railway noise could be derived in a comparable manner, which has rarely been possible in earlier studies. Individual indoor noise measurements were done for several subprojects of the NORAH study, but for the large-scale case-control study this was not a feasible option. Other noise sources, notably occupational noise, were not available either.

We used energy-based noise exposure indicators such as LpAeq differentiated by time of day for our analyses. Other metrics including those that consider noise peaks for aircraft noise were available for the study, but showed no different exposure-risk patterns than those described for the main analysis. An assessment of combined individual exposures to all traffic noise types generally showed no statistically significant associations, except for a combination of higher (≥50 dB) aircraft and higher railway noise. The results in this regard were not as pronounced as those for depression and combined noise exposures (Seidler et al., 2017).

The temporal association of noise exposure and cardiovascular effects including hypertension is not known. Thus, it is possible that noise exposure in 2005 had not yet led to a clinical diagnosis of hypertension during 2006–2010, especially if noise levels were lower in subsequent years. Moreover, it is possible that noise effects on blood pressure are of a temporary nature and only rarely lead to sustained hypertension and a clinical diagnosis. In addition, noise-related blood pressure increases might also be small and not be deemed clinically significant, which would be a precondition for a medical diagnosis of hypertension and initiation of treatment. However, measurements taken in the HYENA study (Jarup et al., 2008) revealed changes above 5 mmHg, which - if sustained - should lead to diagnostic and clinical consequences. In our analysis limited to persons with hypertension identified only in 2009 or 2010, all noise types were positively associated with hypertension, with a statistically significant 3.5% per 10 dB increase for aircraft noise. This generally supports the notion that extended time intervals may be required for the development of a traffic-noise associated hypertension, and that longer diagnosis-free intervals may be needed to more precisely identify incident cases of hypertension.

The subgroup analysis of persons with hypertension and a diagnosis of hypertensive heart disease yielded marked increases in effect estimates for all traffic noise types. Highest linear increases were observed for aircraft noise (13.9% per 10 dB), for the other noise types category-specific estimates reached 30% in some instances. These results suggest that noise exposure could be either linked to more severe forms of sustained hypertension, or that non-differential disease misclassification for hypertension without complications in the insurance data obscures exposure-disease associations. Such misclassification could be due to the limited diagnostic accuracy of office-based methods as compared to ambulatory blood pressure monitoring as highlighted in a recent systematic review (Piper et al., 2014). The results for this subgroup of patients partly overlap with those reported by Seidler et al. (Seidler et al., 2016b) from the same study base, focused on heart failure. There, similarly elevated odds ratios were reported for hypertensive heart disease. The major difference lies in the case-definition employed for the current (subgroup) analysis: we required a diagnosis of hypertension followed by hypertensive heart disease to ensure that hypertensive patients with a defined course of disease were selected. The sensitivity analysis with a focus on hypertensive patients who died during the study period showed associations only for road traffic noise. Whether these persons died of cardiovascular deaths could not be ascertained. However, given the fact that they died in relative temporal proximity to the hypertension diagnosis, a poorer health status overall can be reasonably assumed.

4.1. Strengths and weaknesses

The strengths of our study lie in the large population base, the detailed, source-specific residential traffic noise assessment and the

opportunity to conduct a case-control rather than a cross-sectional analysis.

Hypertension as the outcome of interest in this study was not assessed with study-specific blood pressure measurements, but rather via a diagnosis from hospital discharge records or two ambulatory visits in a 12 months period as recorded in health insurance data. Hypertension diagnoses may remain unrecorded, or alternatively they may be false-positive findings that are not confirmed over time, particularly in the ambulatory setting. Studies with individual measurements provide better diagnostic information, but the included population is often restricted in size and may be subject to selection bias.

We aimed to include only newly registered hypertension diagnoses by using a hypertension-free time interval of 12 months prior to the first recorded diagnosis during the study period. However, there might be cases where hypertension was diagnosed earlier and not carried over in the records, or simply not recorded. The effect of this misclassification is hard to assess, but as it is not likely to be differential with regard to noise exposure, a bias towards null effects – if any – may be assumed. The sensitivity analysis including prevalent cases supports this assessment, as does the analysis with a longer time window between 2005 as index year for the noise assessment and the first recorded diagnosis of hypertension which yielded slightly elevated OR estimates across the different noise types. It is likely that the one-year diagnosis-free interval that we used for the newly diagnosed cases in our main analysis is too short to strictly exclude all prevalent hypertension cases.

Confounding in this study may be due to various sources including socioeconomic status. Individual information was available for 32% of the cases and 50% of controls, whereas area-based SES was included for all participants. The subgroup analysis for the group with available individual SES data did not yield different results as compared to the main analysis. This finding does not exclude confounding by SES, but suggests that SES had limited influence on the results. Overall, the lack of individual-level covariates is an important limitation for our study. The underlying databases were exploited to the best possible extent in this regard. An attempt for additional primary data collection via the participating health insurances was not successful overall. Thus, some existing associations between noise exposure and hypertension may be masked by the lack of confounder control, but this remains speculative.

With regard to duration and timing of exposure, we used 2005 as the index year for noise measurements. This is a limitation as noise exposure may change over time, which we cannot address with the currently available data. The analyses focusing on persons with long-term residence (minimum 5 years) at the same place seemed to indicate a tendency for more pronounced exposure-disease associations particularly for road traffic noise. Extended exposure to environmental (road) traffic noise – assuming that the 2005 noise levels are useful representations for the years prior to 2005 – thus could be of importance for the development of hypertension. This needs to be addressed in other data sets.

Other studies (Foraster et al., 2014; Sorensen et al., 2011b) included air pollution as potential confounder of a noise - hypertension association, which was not possible in our study. While these studies and two systematic reviews focusing on transportation noise and cardiovascular outcomes (Tetreault et al., 2013; Vienneau et al., 2015b) generally indicate no confounding effect of air pollution, the recent ESCAPE study found some attenuation of the association of hypertension and road traffic noise after adjustment for fine particulate matter (PM 2.5) exposure.

In summary, traffic noise from road, rail or aircrafts was not found to be associated with uncomplicated hypertension in both men and women around Frankfurt airport, however, our database lacked informative details in several respects. Positive associations were found for hypertension with a subsequent diagnosis of hypertensive heart disease, and also when a longer time window between residential traffic noise measurement and hypertension diagnosis was used. We regard these results as indicative of an effect of transportation noise on hypertension, which is pronounced among clinically more progressed cases in our data set. Hypertension is highly prevalent in the population, and is a major risk factor for subsequent cardiovascular and cerebrovascular events. Even though uncertainties remain, traffic noise reduction needs to be considered in the context of cardiovascular disease prevention.

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Ethical approval and data protection

Comments of the Ethics Committee of the Medical Faculty, TU Dresden (AZ: EK328102012; 21 February 2013 and 22 April 2014) were complied with. The Federal Commissioner for Data Protection and Freedom of Information (AZ: III-320/010#0011; reply of 11 June 2012) and the Data Protection Commissioners of the German states Hesse (AZ: 43.60-we; reply of 13 March 2012; amendments 7 February 2014) and Rhineland-Palatinate (AZ: 6.08.22.002; reply of 7 May 2012; amendments 4 February 2014) approved the study concept.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2017.05.019.

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