Original Article

Aircraft Noise and the Risk of Stroke

A Systematic Review and Meta-analysis

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Summary

Background: There have been many individual studies on the question whether aircraft noise is a risk factor for stroke, but until now there has not been any summary of the current state of the evidence of adequately high methodological quality.

Methods: In a systematic review and meta-analysis (PROSPERO registry number CRD42013006004), we evaluated the relation between address-based aircraft noise exposure and the incidence of stroke. A systematic literature search was performed in the MEDLINE, EMBASE, and BIOSIS databases including publications up to August 2017. Two of the authors, working independently of each other, screened the titles, abstracts, and full texts for eligible articles and evaluated the quality of the included studies on a three-level scale. The change of risk per 10 dB increase in the weighted mean aircraft noise level (L_{DEN}) was calculated. L_{DEN} is a noise level indicator with additional weighting of evening and nighttime noise.

Results: Of the nine studies that met the inclusion criteria, seven were suitable for inclusion in the meta-analysis. The result of the meta-analysis indicated a relative stroke risk of 1.013 (95% confidence interval, [0.998; 1.028]) per 10 dB increase in L_{DEN}, corresponding with an estimated 1.3% increase in the risk of stroke for each additional 10 dB of aircraft noise. The underlying studies were of poor to medium quality. The analyses of the studies included adjustments for various combinations of confounders, including age, sex, ethnicity, and socioeconomic status.

Conclusion: The present meta-analysis indicates that aircraft noise increases the risk of stroke, even if the overall finding just fails to reach statistical significance. The differing measures of exposure in the included studies, the lack of differentiation between ischemic and hemorrhagic stroke, and the lack of consideration of maximum noise levels are all factors that may have led to a marked underestimation of the risk of stroke.

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The health effects of noise are a highly relevant problem for the population. The World Health Organization (WHO) estimates that in the European Union and Western Europe the number of healthy life years lost due to environmental noise exceeds one million (disability-adjusted life years, DALYs) (1). Environmental noise-related sleep disturbances are presumably the greatest problem with more than 900 000 DALYs; the WHO report estimates that noise-related ischemic heart disease accounts for 61 000 DALYs. The WHO report does not provide a corresponding estimate for cerebrovascular events. Furthermore, the various individual sources of noise are not considered separately in the WHO report.

The German Federal Environmental Agency set as an average target to reduce noise pollution to 55 dB during the day and 45 dB during nighttime to prevent considerable annoyance (e1). Based on noise mapping information (e2), 8.7 million people in Germany are exposed to road noise of day–evening–night noise levels (L_{DEN}) of more than 55 dB. For 6.4 million people, an L_{DEN} of 55 dB is exceeded by rail traffic and for 0.8 million by air traffic. According to a representative survey from 2016 (e3), 76% of the German population feels disturbed or annoyed by road noise, and the same applies to 44% and 34% for aircraft noise and rail traffic noise, respectively.

Pathophysiologically, the cardiovascular effects of noise have been attributed to an activation of the autonomous nervous system with subsequent release of stress hormones (norepinephrine, epinephrine, cortisol); most of the supporting data are from experimental studies. These neuroendocrinological mechanisms can trigger or promote abnormal processes, such as increases in blood pressure and insulin resistance (e4). Disturbed sleep at night with subsequent daytime sleepiness and impaired regenerative processes may be of special importance in chronic stress reactions caused by noise pollution (e5, e6). While a causal relationship between noise and cardiovascular morbidity appears biologically plausible, it remains unclear whether the postulated effects can cause a measurable increase in stroke incidence that is also potentially detectable at the population level.

There is no current systematic review of the evidence on the relationship between aircraft noise and stroke incidence available at present. The design and methodological quality of the available individual studies are as heterogeneous as their results. Both

TABLE 1

Inclusion and exclusion criteria

Category	Inclusion criteria	Exclusion criteria
Population	General population (children and adults, male and female)	Vocationally exposed persons; self-selected persons (who offer to participate in the study of their own accord, e.g. volunteers, recruitment via newspaper ads, etc.)
Exposure	Environmental aircraft noise, annoyance by environmental aircraft noise	Noise from industrial activities, road traffic, rail traffic, neighborhood; exclusively military aircraft noise
Endpoints	Overall project*: ● non-auditory health problems and diseases ● effects on human health (incidence/prevalence) ● mixed and non-diagnosis-specific health endpoints (e.g. health problems in general) ● stress (e.g. Lewis Child Stress Scale, stress hormone measurement)	Auditory noise effects (e.g. hearing loss, tinnitus)
	Subproject*: fatal and nonfatal cerebrovascular accident (stroke)	
Study design/ publication	Cohort studies, case-control studies, cross-sectional studies, ecological studies	Reviews, editorials, letters to the editor

* The study is part of a large review project, evaluating effects of aircraft noise on a broad spectrum of non-auditory endpoints and diseases. The results for the endpoint "stroke" are the subject of this article.

cohort studies (for example [2]) and cross-sectional studies (for example [3]) have been reported. Some studies evaluate noise exposure as a continuous variable, other studies as a categorical variable with various intervals and cut-offs. In some studies, the endpoints were recorded as ICD-coded (ICD, International Classification of Diseases and Related Health Problems) hospital diagnoses or deaths determined by physicians (for example [4, 5]), while other studies rely solely on patient-reported information (for example [3]). Reviewing the individual studies identified mostly statistically non-significant risk estimates. The aim of this systematic review is to present the currently available evidence on the aircraft noise-related stroke risk.

Methods

Research question and inclusion criteria

This systematic review addresses the question whether noise due to civil air traffic or the perceived annoyance caused by it has an effect on the risk of fatal or nonfatal stroke (cerebrovascular accident) in humans. The research question was operationalized by means of a detailed *a priori* specification of the population, exposure and assessed endpoints. The inclusion and exclusion criteria are detailed in *Table 1*.

Search strategy

We performed a systematic electronic literature search in the MEDLINE (publications from 1947), EMBASE (publications from 1974) and BIOSIS (publications from 1969) bibliographic databases up to 31 August 2017, and complemented this with a manual search. Only original studies with an available abstract were included. No language limitations were imposed. With regard to study design, the search included cohort studies, case-control studies, cross-sectional studies, and ecological studies.

For the database search, the search strategy was adapted to the respective database, and is shown in *eBox 1*. In addition, a manual search was conducted in references of included publications, narrative reviews and key publications, as well as an online search using the citation-tracking function of the Google Scholar search engine (6, 7).

Literature screening

The screening of the titles, abstracts and full-text articles of the publications identified was performed by two authors independently of each other (VMW, AS); in case of diverging judgment, a third person (UE) was consulted. The reasons for excluding full-text articles were documented for each publication not included.

Data extraction

The data of the included studies were entered into an extraction table created *a priori*. The authors responsible for screening the literature (VMW, AS) performed the data extraction. Differences were discussed in consensus conferences. In case of incomplete data, the authors of the corresponding publication were contacted and asked to provide additional information.

Quality evaluation

The study quality was also assessed by two authors (VMW, AS) independently of each other, using an instrument which had been developed based on SIGN (Scottish Intercollegiate Guidelines Network 2004) and CASP (Critical Appraisal Skills Program 2004/2006) and which had been successfully used in several earlier reviews (among others in [8–13]). The instrument was adapted to the aircraft noise topic. The assessment included a summary quality rating on a three-step scale (++, +, −). In cases where the potential effect of methodological weaknesses on the core results of the study appeared to be significant, the respective studies were classified as "of low methodological quality (−)".

Data synthesis and statistical analysis

In preparation of the quantitative analysis, data were processed and converted. This included, among others, transformation of noise metrics of all studies included in the meta-analysis to the average noise level L_{DEN}. L_{DEN} is the weighted day-evening-night level with an extra 5 dB being added to noise in the evening hours and 10 dB to the nighttime hours. For the transformation, the conversion rules of the WHO working paper by Brink (14) were used. These rules are based on aircraft noise measurements. An overview of the noise metrics and their definitions in provided in *eTable 1*.

The statistical software Stata (version 14.1) was used to determine the potential dose-response relationships from the studies' results and for the meta-analysis conducted using the random-effects model.

In the core analysis, the linear change of the effect estimate with each increase in the L_{DEN} noise level by 10 dB was assessed. For this, the data of the studies with continuous exposure measurements—after transformation to L_{DEN}, if necessary—were directly integrated into the model. In studies with categorical noise intervals and various corresponding risk estimates, the change in risk for each 10 dB increase in aircraft noise levels was first calculated using the Stata function glst (method of generalized least squares [16]). For this, the risk estimates reported in the studies were allocated to the mean dB of the respective exposure category. If it was not possible to specify the covariance matrix, the Stata vwls procedure was used instead. Next, the studies were pooled using a random-effects model (Stata metan [15]).

In order to assess the impact of individual studies on the pooled effect estimate, a sensitivity analysis was conducted excluding one study at a time from the meta-analysis (leave-one-out method) (17).

Further details on the methodology are provided in *eBox 2*.

Results

Study selection

The flowchart (*eFigure*) shows the literature selection process. Twenty-two publications (2–5, 18–34, e14), containing data of altogether 9 studies, met the inclusion criteria. The extracted study data with the characteristics of the included studies/publications are listed in *eTable 2*.

Results of the individual included studies

The results of the included individual studies are summarized in *Table 2*. For studies with categorical measurements of aircraft noise, the risk estimates are allocated to their corresponding intervals; for studies with continuous exposure data, reference intervals are reported in dB. The described noise metrics and effect estimates are the original data and have not yet been converted.

The included studies apply a cohort approach (2, 4, 20, 23), a case-control approach (32), a cross-sectional design (3, 18, 34) or an ecological design with case-control approach (19). The majority of the studies are secondary data analyses (2, 4, 18–20, 23, 32). The observation periods studied vary between two (20) and eight (2) years. With the exception of the study by Wiens (34), data of women and men are evaluated in the studies. The included age groups are very heterogeneous between the individual studies. Frequently, the lower limit is set at 30 to 45 years (2, 3, 23, 32, 34), presumably because the endpoint "stroke" would only be very sporadically observed in younger age groups.

Synthesis of the results

Seven of the 9 included studies (with 20 related publications) were included in the meta-analysis. The meta-analysis yielded a relative stroke risk of 1.013 (95% confidence interval [0.998; 1.028]) with each increase in the noise level L_{DEN} by 10 dB. This corresponds to a risk increase of 1.3% with each 10 dB increase. Formally, the significance level is not reached. However, the result is so close to the significance threshold that an actual effect seems likely. The results of the core analysis are shown in the *Figure*. With a heterogeneity measure I^2 of 0%, no formal indication of heterogeneity of the included studies was found.

In the leave-one-out sensitivity analysis, pooled effect estimates between 1.010 and 1.016 were found, corresponding to a risk increase of 1.0 to 1.6% with each 10 dB increase in the aircraft noise level L_{DEN} *(Table 3)*. Only when excluding the largest study, the NORAH study on health risks (35), a statistically significant risk increase of 1.6% with each increase in L_{DEN} by 10 dB (risk ratio [RR] = 1.016; [1.001; 1.032]) was found. This applies to studies with good quality ratings as well as for studies rated as low-quality studies in our review. Separate analysis of the cohort studies also found no substantially different effect estimate. The NORAH study on health risks reported no positive association between average 24-hour sound levels and the diagnosis of stroke; however, this study shows a statistically significant increased stroke risk of 7% when nighttime maximal levels exceed 50 dB (NAT6) and average 24-hour noise levels are below 40 dB (odds ratio [OR]: 1.07; [1.02; 1.13]).

Further information about the results is provided in *eBox 3*.

Discussion

Our systematic review with meta-analysis found a statistically nonsignificant increase in stroke risk of 1.3% with each increase of the weighted aircraft noise level L_{DEN} by 10 dB. If the largest study (the NORAH study) is excluded, this association is statistically significant.

Strengths and limitations

Special features of this review include the *a priori* defined and published procedure and the comprehensive systematic search of the literature.

A literature search update for the period from September 2017 to November 2018 performed in the PubMed database yielded 35 hits. These were screened by 2 authors (VMW, AS) independently of each other. No new publications meeting the inclusion criteria were identified in the process.

It is generally possible that confounding and temporality could have biased the risk estimation. The 3 methodologically sound cohort studies included (2, 4, 23) found risk increases between 1.3% (2) and 9.2% (4) with each 10 dB increase in aircraft noise level. Thus, it seems to be rather unlikely that the risk was underestimated due to the above mentioned methodological aspects. The—in comparison to the pooled risk estimates of all studies—equal or higher risk estimates of the methodologically sound cohort studies also suggest that no relevant publication bias was present. Another important limitation is that the actual exposure of the subjects can deviate from the exposure assumed in the studies because the latter is based on the place of residence, but presumably many study participants spend much of their time elsewhere.

A large proportion of the studies is based on collections of secondary data which may harbor a higher risk of systematic bias, because these data were not collected directly from the subjects and not generated for research purposes. On the other hand, analyses of secondary data can counteract various biases: Selection mechanisms affecting the recruitment of research participants (selection bias) are usually negligible and recall bias can generally be avoided.

Comparison with the results of other studies

The meta-analysis of a Bulgarian working group (e16), investigating the association between various types of traffic noise and stroke has several issues related to the selection of the included studies. Among other things, the results of Gan et al. (23) were only analyzed collectively in the "mixed noise" category. Depending on the model used, this meta-analysis arrived at a risk estimate of 1.04 or 1.05 for each 10 dB increase in noise levels.

The meta-analysis published by Vienneau et al. (36) included 4 aircraft noise studies with stroke as the endpoint (4, 5, 18, 23). However, the aircraft-noise risk estimates were not reported separately from the risk estimates for other types of traffic noise. The

TABLE 2

Exposure parameters and endpoints of included studies

First author, publication year (additional associated publications)	Exposure metrics	Categorical or continuous exposure reporting[*1] (range)	Effect estimates, endpoint data collection	Confounders considered	Value	95% confidence interval
Correia et al., 2013 (18)	L_{DN}[*2]	per 10 dB (≥ 45–71.59 dB)	RR, ICD-coded hospital admissions for stroke	Age, sex, ethnicity	1.039[*3]	[0.995; 1.084][*3]
Evrard et al., 2015 (19)	L_{DEN}AEI[*2]	per 10 dB (≥ 42.0–46.1 dB)	MRR, ICD-coded stroke mortality rate	Adjusted on municipal level for sex, age, population density, lung cancer mortality, and a deprivation index[*4]	1.08[*4]	[0.97; 1.21][*4]
Frerichs et al., 1980 (20–22)	L_{Day} (17.5 hours)[*2]	45–50 dB	SMR, ICD-coded cerebrovascular deaths	Age, sex, ethnicity	1.06[*5]	[0.86; 1.29][*5]
		90 dB			0.92[*5]	[0.71; 1.17][*5]
Gan et al., 2012 (23)	L_{DEN}[*2]	not exposed	RR, ICD-coded stroke mortality	Age, sex, neighborhood, socioeconomic status, and comorbidity (diabetes, COPD, hypertensive heart disease)	1.00[*3]	[1.00; 1.00][*3]
		0.01–21.3 dB			1.30[*3]	[1.11; 1.53][*3]
		21.4–35.2 dB			1.29[*3]	[1.10; 1.51][*3]
		35.3–44.4 dB			1.07[*3]	[0.90; 1.26][*3]
		44.5–71.0 dB			1.16[*3]	[0.98; 1.36][*3]

First author, publication year (additional associated publications)	Exposure metrics	Categorical or continuous exposure reporting*1 (range)	Effect estimates, endpoint data collection	Confounders considered	Value	95% confidence interval
Hansell et al., 2013 (4)	L_{Day} (7–23 hrs)*2	≤ 51 dB	RR, ICD-coded hospital admissions for stroke	Age, sex, ethnicity, deprivation (Carstairs index), lung cancer (ecological variables)	1.00	[1.00; 1.00]
		>51 – 54 dB			1.03	[0.98; 1.09]
		>54 – 57 dB			1.04	[0.98; 1.12]
		>57 – 60 dB			1.04	[0.95; 1.14]
		>60 – 63 dB			1.10	[0.96; 1.25]
		>63 dB			1.24	[1.08; 1.43]
	L_{Night} (23–7 hrs)*2	≤ 50 dB			1.00*4	[1.00; 1.00]*4
		>50–55 dB			0.99*4	[0.92; 1.07]*4
		>55 dB			1.29*4	[1.14; 1.46]*4
Héritier et al., 2017 (2, 5)	L_{DEN}*2	per 10 dB (≥ 30 dB)	HR, ICD-coded stroke mortality	Sex, neighborhood index of socioeconomic status, marital status, education level, first language, nationality, and NO_2 exposure	1.013	[0.993; 1.033]
Floud et al., 2013 (HYENA study: [3, 24–31, e14])	$L_{Aeq,\ 16\ hours}$*2	per 10 dB (<35 – 76 dB)	OR, self-reporting of a physician's stroke diagnosis	Age, sex, ethnicity, education level, body mass index; additionally assessed but not included in the final regression (≤ 10% change in exposure coefficient): alcohol consumption, exercise, smoking	1.08	[0.82; 1.41]
	L_{Night}*2	per 10 dB (<30 – 70 dB)			1.18	[0.89; 1.56]
Seidler et al., 2016 (NORAH study: [32, 33])	L_{DEN}*2	<40 dB	ICD-10-coded hospital diagnosis of stroke	Age, sex, education level, job title (if available) and local proportion of persons receiving unemployment benefits	1.0*3	[1.00; 1.00]*3
		≥ 40 to <45 dB			1.04*3	[1.01; 1.08]*3
		≥ 45 to <50 dB			0.99*3	[0.96; 1.03]*3
		≥ 50 to <55 dB			1.03*3	[0.98; 1.08]*3
		≥ 55 to <60 dB			0.99*3	[0.93; 1.06]*3
		≥ 60 dB			0.86*3	[0.76; 0.97]*3
Wiens. 1995 (34)	Annoyance	Little, moderately annoyed	POR, self-reporting of a physician's stroke diagnosis	None	0.94*4	[0.44; 2.04]*4
		Rather, very annoyed			0.66*4	[0.66; 1.49]*4

*1 All aircraft noise information is based on calculated exterior noise levels which were established using noise maps. Personalized interior noise measurements were not included in any of the studies.

*2 L_{Aeq}: A-weighted average of an energy-equivalent continuous sound level over a period of time (A-weighting: in noise research typically the A filter is used which adjusts for deep and high frequencies, as these are perceived as less loud);
L_{Day}: L_{Aeq} for the day (usually 7:00 am – 7:00 pm) for all day periods of a year; L_{Night}: L_{Aeq} for the night (usually from 11:00 pm – 7:00 am) for all night periods of a year; L_{DN}: all 24 h L_{Aeq} periods of a year with additional 10 dB for nighttime noise annoyance (usually from 11:00 pm – 7:00 am); L_{DEN}: all 24h L_{Aeq} periods of a year with additional 5 dB for the evening hours (8:00 pm – 10.00 pm or 7:00 pm – 11:00 pm) and additional 10 dB for nighttime hours (10:00 pm – 6:00 am or from 11:00 pm – 7:00 am); L_{DEN}AEI: see L_{DEN}, but in addition weighted average exposure on municipal level

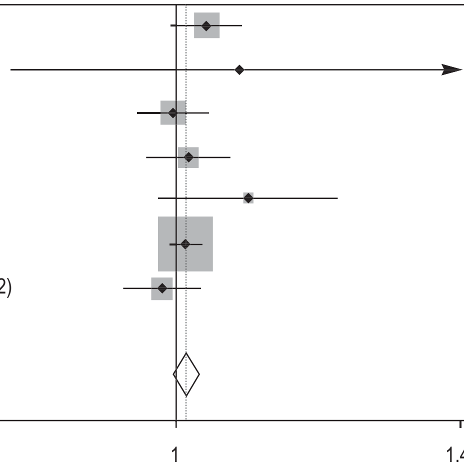
*3 Additional data from correspondence with study authors

*4 Data extraction of cerebrovascular events, but these data were not suitable for meta-analysis

*5 Self-calculated as described by Ulm, 1990 (e15)

COPD: chronic obstructive pulmonary disease ; HR: hazard ratio; ICD: International Classification of Diseases and Related Health Problems; MRR: mortality rate ratio; OR: odds ratio, POR: prevalence odds ratio; RR: risk ratio, SMR: standardized mortality ratio

FIGURE



Study	EE	[95% CI]	% weights*
Correia et al., 2013 (18)	1.039	[0.995; 1.084]	11.92
Floud et al., 2013 (HYENA study) (3)	1.080	[0.820; 1.410]	0.30
Frerichs et al., 1980 (20)	0.997	[0.955; 1.042]	11.47
Gan et al., 2012 (23)	1.016	[0.965; 1.069]	8.33
Hansell et al., 2013 (4)	1.092	[0.980; 1.217]	1.86
Héritier et al., 2017 (2)	1.013	[0.993; 1.033]	56.11
Seidler et al., 2016 (NORAH study)(32)	0.984	[0.939; 1.031]	10.00
Total **(I^2 = 0.0 %; p = 0.498)**	**1.013**	[0.998; 1.028]	100.00

Forest plot with the included risk estimates of the individual studies per increase in aircraft noise-related L_{DEN} by 10 dB and the pooled risk estimate (overall). With calculation of the fixed-effects model instead of the random-effects model, no change in the effect estimates and no relevant change in the width of the confidence intervals were found.

* The weights are from the random-effects analysis.

EE: effect estimate, CI: confidence interval; L_{DEN}: noise level with all 24h L_{Aeq} periods of a year with additional 5 dB for the evening hours (8:00 pm–10:00 pm or 7:00 pm–11:00 pm) and additional 10 dB for nighttime hours (10:00 pm–6:00 am or from 11:00 pm–7:00 am)

Swiss working group found a pooled overall effect estimate of 1.014 ([0.96; 1.066]) with each increase in L_{DEN} by 10 dB. This result is very close to the result of our meta-analysis.

The 2018 WHO review on the association between traffic noise and cardiovascular disease (37, 38) reported a pooled risk estimate with each increase in L_{DEN} by 10 dB for the stroke risk due to aircraft noise for:

- prevalence studies of 1.02 ([0.80; 1.28]),
- incidence studies of 1.05 ([0.96; 1.15]),
- mortality studies of 1.07 ([0.98; 1.17]).

However, the search period is limited to January 2000 until August 2015 and thus does not include older (for example, Frerichs et al. [20]) and, most importantly, newer analyses (for example, the NORAH study on health risks [32]).

The systematic review by Vienneau et al. (36, e12) and the WHO review (37, 38) allow a comparison between the traffic noise–related risk estimates for the “stroke” outcome with the corresponding risk estimates for the “ischemic heart disease” outcome . In both systematic reviews, the risk estimates for stroke are considerably lower compared to those for ischemic heart disease. At least to some extent, this could be explained by the fact that the diagnosis “stroke” includes both the ischemic and the hemorrhagic stroke. These two types of stroke can differ in their etiology (e17, e18). Thus, the separate analyses of the NORAH study on health risks indicated potential differences with regard to the traffic noise–related risks between hemorrhagic and ischemic stroke (e19).

Overall, our systematic review with meta-analysis provided evidence in support of an association between aircraft noise and the occurrence of stroke. Although the risk increase did not reach statistical significance when all identified studies were included in the analysis, the NORAH study on health risks—with the lowest risk estimates of all included studies—indicated that stroke risks may not be adequately described based solely on average sound levels. Accordingly, the NORAH study showed an association between the diagnosis of stroke and maximum aircraft noise levels at night. In recent years/decades, night flight restrictions, or even bans on night flights, have been introduced at many airports. A comparatively lower proportion of night flights in the NORAH study on health risks compared to several older studies may explain why the increased stroke risks observed with maximum nighttime aircraft noise levels are not apparent with the weighted average sound levels. Consequently, future studies on stroke risks associated with aircraft noise should not be limited to average sound levels, but should also take maximum nighttime levels into account.

Even if all uncertainties are taken into account, significantly less strokes are caused by aircraft noise compared to unhealthy lifestyle patterns. Based on the INTERSTROKE study by O´Donnell et al. (39), approximately 39% of strokes can be attributed to hypertension and 36% to being overweight. Even if all people were exposed to very high levels of aircraft noise (60 dB), less than 3% of all strokes could be attributed to aircraft noise, based on a 1.3% risk increase with every 10 dB increase in aircraft noise (the lifetime prevalence of stroke is 2,9% [40]).

Although the cerebrovascular accidents which could be prevented by noise-reducing measures only account for a comparatively small proportion of all strokes, the authors of this review believe that traffic noise-related health risks are important for the health of the population. Unlike the exposure to lifestyle factors, it is hardly possible for individuals to change their exposure to traffic noise. Consequently, effective noise reduction is a social responsibility.

Conclusion

All in all, our systematic review with meta-analysis indicates that there is an association between aircraft noise and the occurrence of stroke. Especially differences between the individual studies and in some cases inaccurate exposure estimations, the lack of differentiation between ischemic and hemorrhagic stroke, as well as the failure to take into account maximum levels could have resulted in a significant underestimation of the stroke risk. Given the large number of individuals exposed to environmental noise and the high prevalence of stroke in the population, more studies with improved methodology should be conducted. This would further strengthen the scientific evidence that serves as the foundation for effective noise protection—and thus effective health protection—of the population.

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Conflict of interest statement
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The remaining authors declare no conflicts of interest.

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Translated from the original German by Ralf Thoene, MD.

TABLE 3

Results of the leave-one-out analysis

Study left out (first author, year of publication)	RR	95% confidence interval
Correia et al., 2013 (18)	1.0097	[0.9940; 1.0258]
Frerichs et al.,1980 (20–22)	1.0152	[0.9994; 1.0313]
Gan et al., 2012 (23)	1.0130	[0.9957; 1.0306]
Hansell et al., 2013 (4)	1.0118	[0.9968; 1.0270]
Héritier et al., 2017 (2, 5)	1.0137	[0.9901; 1.0378]
HYENA study (3, 24–31, e14)	1.0130	[0.9975; 1.0288]
NORAH study on health risks (32, 33)	1.0165	[1.0007; 1.0324]

RR: risk ratio

References

1. WHO: Burden of disease from environmental noise – quantification of healthy life years lost in Europe. Copenhagen: WHO Regional Office for Europe 2011.
2. Héritier H, Vienneau D, Foraster M, et al.: Transportation noise exposure and cardiovascular mortality: a nationwide cohort study from Switzerland. Eur J Epidemiol 2017; 32: 307–15.
3. Floud S, Blangiardo M, Clark C, et al.: Exposure to aircraft and road traffic noise and associations with heart disease and stroke in six European countries: a cross-sectional study. Environ Health 2013; 12: 89.
4. Hansell AL, Blangiardo M, Fortunato L, et al.: Aircraft noise and cardiovascular disease near Heathrow airport in London: small area study. BMJ 2013; 347: f5432.
5. Huss A, Spoerri A, Egger M, et al.: Aircraft noise, air pollution, and mortality from myocardial infarction. Epidemiology 2010; 21: 829–36.
6. Giles J: Science in the web age: start your engines. Nature 2005; 438: 554–5.
7. Bakkalbasi N, Bauer K, Glover J, Wang L: Three options for citation tracking: Google Scholar, Scopus and Web of Science. Biomed Digit Libr 2006; 3: 7.
8. Seidler A, Euler U, Muller-Quernheim J, et al.: Systematic review: Progression of beryllium sensitization to chronic beryllium disease. Occup Med (Lond) 2012; 62: 506–13.
9. Seidler A, Jähnichen S, Hegewald J, et al.: Systematic review and quantification of respiratory cancer risk for occupational exposure to hexavalent chromium. Int Arch Occup Environ Health 2013; 86: 943–55.
10. Seidler A, Thinschmidt M, Deckert S, et al.: The role of psychosocial working conditions on burnout and its core component emotional exhaustion—a systematic review. J Occup Med Toxicol 2014; 9: 10.
11. Wagner M, Bolm-Audorff U, Hegewald J, et al.: Occupational polycyclic aromatic hydrocarbon exposure and risk of larynx cancer: a systematic review and meta-analysis. Occup Environ Med 2015; 72: 226–33.
12. Seidler A, Steputat A, Drössler S, et al.: Determinanten und Auswirkungen von Informationsüberflutung am Arbeitsplatz. Zentralblatt für Arbeitsmedizin, Arbeitsschutz und Ergonomie 2018; 68: 12–26.
13. Thinschmidt M, Deckert S, Then F, et al.: Systematischer Review: Der Einfluss arbeitsbedingter psychosozialer Belastungsfaktoren auf die Entstehung psychischer Beeinträchtigungen und Erkrankungen. Dortmund, Berlin, Dresden: Bundesanstalt für Arbeitsschutz und Arbeitsmedizin 2014; p. 189.
14. Brink M: Conversion of transportation noise exposure metrics Leq24h, LDay, LEvening, Ldn, and Lden to LNight. WHO Environmental Noise Guidelines for the European Region. Bern: Federal Office for the Environment 2015; p. 9.
15. Harris R, Bradburn M, Deeks J, Harbord R, Altman D, Sterne J: Metan: fixed-and random-effects meta-analysis. Stata J 2008; 8: 3–28.
16. Orsini N, Bellocco R, Greenland S: Generalized least squares for trend estimation of summarized dose-response data. Stata J 2006; 6: 40–57.
17. Higgins JP: Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. Int J Epidemiol 2008; 37: 1158–60.
18. Correia AW, Peters JL, Levy JI, Melly S, Dominici F: Residential exposure to aircraft noise and hospital admissions for cardiovascular diseases: multi-airport retrospective study. BMJ 2013; 347: f5561.

Key messages

- With each increase of the noise level L_{DEN} by 10 dB, a statistically non-significant increase in stroke risk by 1.3% is found.
- One of the uncertainties with regard to the actual exposure of included subjects is that noise levels were measured at the place of residence, but study participants may have spent much of their time elsewhere.
- There is a need for further scientific studies evaluating whether linear models can provide an optimum description of the exposure-risk relationship between aircraft noise and the occurrence of stroke.
- Due to the specific characteristics of aircraft noise, future studies on the stroke risk associated with aircraft noise should also take maximum noise levels into account.

19. Evrard AS, Bouaoun L, Champelovier P, Lambert J, Laumon B: Does exposure to aircraft noise increase the mortality from cardiovascular disease in the population living in the vicinity of airports? Results of an ecological study in France. Noise Health 2015; 17: 328–36.
20. Frerichs RR, Beeman BL, Coulson AH: Los Angeles airport noise and mortality—faulty analysis and public policy. Am J Public Health 1980; 70: 357–62.
21. Meecham WC, Shaw NA: Increase in mortality rates due to aircraft noise. Schriftenreihe des Vereins fur Wasser-, Boden- und Lufthygiene 1993; 88: 428–41.
22. Meecham WC, Shaw N: Effects of jet noise on mortality rates. Br J Audiol 1979; 13: 77–80.
23. Gan WQ, Davies HW, Koehoorn M, Brauer M: Association of long-term exposure to community noise and traffic-related air pollution with coronary heart disease mortality. Am J Epidemiol 2012; 175: 898–906.
24. Floud S, Vigna-Taglianti F, Hansell A, et al.: Medication use in relation to noise from aircraft and road traffic in six European countries: results of the HYENA study. Occup Environ Med 2011; 68: 518–24.
25. Jarup L, Babisch W, Houthuijs D, et al.: Hypertension and exposure to noise near airports: the HYENA study. Environ Health Perspect 2008; 116: 329–33.
26. Jarup L, Babisch W, Houthuijs D, et al.: Acute and long-term effect on blood pressure of exposure to noise near airports-The HYENA study. INTER-NOISE and NOISE-CON Congress and Conference Proceedings: Institute of Noise Control Engineering 2008; p. 562–78.
27. Babisch W, Houthuijs D, Pershagen G, et al.: Association between noise annoyance and high blood pressure. Preliminary results from the HYENA study. INTER-NOISE and NOISE-CON Congress and Conference Proceedings. Istanbul, Turkey 2007.
28. Babisch W, Swart W, Houthuijs D, et al.: Exposure modifiers of the relationships of transportation noise with high blood pressure and noise annoyance. J Acoust Soc Am 2012; 132: 3788–808.
29. Babisch W, Pershagen G, Selander J, et al.: Noise annoyance—a modifier of the association between noise level and cardiovascular health? Sci Total Environ 2013; 452: 50–7.
30. Dimakopoulou K, Koutentakis K, Papageorgiou I, et al.: Is aircraft noise exposure associated with cardiovascular disease and hypertension? Results from a cohort study in Athens, Greece. Occup Environ Med 2017.
31. Jarup L, Dudley ML, Babisch W, et al.: Hypertension and Exposure to Noise near Airports (HYENA): study design and noise exposure assessment. Environ Health Perspect 2005; 113: 1473–8.
32. Seidler A, Wagner M, Schubert M, Dröge P, Hegewald J: Band 6: Sekundärdatenbasierte Fallkontrollstudie mit vertiefender Befragung. Verkehrslärmwirkungen im Flughafenumfeld. Kelsterbach: Gemeinnützige Umwelthaus GmbH 2016.
33. Seidler AL, Hegewald J, Schubert M, et al.: The effect of aircraft, road, and railway traffic noise on stroke—results of a case-control study based on secondary data. Noise Health 2018; 20: 152–61.
34. Wiens D: Verkehrslärm und kardiovaskuläres Risiko. Eine Fall-Kontrollstudie in Berlin (West). Institut für Wasser-, Boden- und Lufthygiene des Bundesgesundheitsamtes 1995.
35. Seidler A, Wagner M, Schuber M, et al.: Myocardial infarction risk due to aircraft, road and rail traffic noise—results of a case-control study based on secondary data. Dtsch Arztebl Int 2016; 113: 407–14.
36. Vienneau D, Perez L, Schindler C, et al.: Years of life lost and morbidity cases attributable to transportation noise and air pollution: A comparative health risk assessment for Switzerland in 2010. Int J Hyg Environ Health 2015; 218: 514–21.
37. van Kempen E, Casas M, Pershagen G, Foraster M: WHO Environmental noise guidelines for the European region: a systematic review on environmental noise and cardiovascular and metabolic effects: a summary. Int J Environ Res Public Health 2018; 15.
38. van Kempen E, Casas M, Pershagen G, Foraster M: Cardiovascular and metabolic effects of environmental noise: systematic evidence review in the framework of the development of the WHO environmental noise guidelines for the European region. Bilthoven, The Netherlands: National Institute for Public Health and the Environment 2017; p. 300.
39. O'Donnell MJ, Chin SL, Rangarajan S, et al.: Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet 2016; 388: 761–75.
40. Busch MA, Schienkiewitz A, Nowossadeck E, Gosswald A: [Prevalence of stroke in adults aged 40 to 79 years in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2013; 56: 656–60.

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► **Supplementary material**
For eReferences please refer to:
www.aerzteblatt-international.de/ref1419

eBoxes, eTables, eFigure:
www.aerzteblatt-international.de/19m0237

Supplementary material to:

Aircraft Noise and the Risk of Stroke

A Systematic Review and Meta-analysis

by Verena Maria Weihofen, Janice Hegewald, Ulrike Euler, Peter Schlattmann, Hajo Zeeb, and Andreas Seidler

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eReferences

e1. Umweltbundesamt: Belästigung durch Verkehrslärm: www.umweltbundesamt.de/themen/verkehr-laerm/verkehrslaerm#textpart-1 (last accessed on 18 December 2018).

e2. Umweltbundesamt: Belastung der Bevölkerung durch Umgebungslärm: www.umweltbundesamt.de/daten/umwelt-gesundheit/belastung-der-bevoelkerung-durch-umgebungslaerm (last accessed on 18 December 2018).

e3. Umweltbundsamt: Umweltbewusstsein in Deutschland 2016 – Ergebnisse einer repräsentativen Bevölkerungsumfrage. Berlin/-Dessau-Roßlau: Umweltbundesamt 2017; p. 88.

e4. Münzel T, Gori T, Babisch W, Basner M: Cardiovascular effects of environmental noise exposure. Eur Heart J 2014; 35: 829–36.

e5. Halonen JI, Vahtera J, Stansfeld S, et al.: Associations between nighttime traffic noise and sleep: the Finnish public sector study. Environ Health Perspect 2012; 120: 1391–6.

e6. Badran M, Yassin BA, Fox N, Laher I, Ayas N: Epidemiology of sleep disturbances and cardiovascular consequences. Can J Cardiol 2015; 31: 873–9.

e7. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. Ann Intern Med 2009; 151: 264–9.

e8. Seidler A, Weihofen V, Wagner M, et al.: Systematic review: environmental aircraft noise and non-auditory health complaints and diseases. PROSPERO. University of York: International prospective register of systematic reviews 2013.

e9. Roerecke M, Rehm J: Chronic heavy drinking and ischaemic heart disease: a systematic review and meta-analysis. Open Heart 2014; 1: e000135.

e10. Pearce N: Effect measures in prevalence studies. Environ Health Perspect 2004; 112: 1047–50.

e11. Koo DL, Nam H, Thomas RJ, Yun CH: Sleep disturbances as a risk factor for stroke. J Stroke 2018; 20: 12–32.

e12. Vienneau D, Schindler C, Perez L, Probst-Hensch N, Roosli M: The relationship between transportation noise exposure and ischemic heart disease: a meta-analysis. Environ Res 2015; 138: 372–80.

e13. Seidler A, Wagner M, Schubert M, et al.: Aircraft, road and railway traffic noise as risk factors for heart failure and hypertensive heart disease–a case-control study based on secondary data. Int J Hyg Environ Health 2016; 219: 749–58.

e14. Babisch W, Houthuijis D, Kwekkeboom J, et al.: HYENA-Hypertension and exposure to noise near airports. A European study on health effects of aircraft noise. INTER-NOISE and NOISE-CON Congress and Conference Proceedings: Institute of Noise Control Engineering 2005; p. 1376–85.

e15. Ulm K: A simple method to calculate the confidence interval of a standardized mortality ratio (SMR). Am J Epidemiol 1990; 131: 373–5.

e16. Dzhambov AM, Dimitrova DD: Exposure-response relationship between traffic noise and the risk of stroke: a systematic review with meta-analysis. Arh Hig Rada Toksikol 2016; 67: 136–51.

e17. O'Donnell MJ, Xavier D, Liu L, et al.: Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. Lancet 2010; 376: 112–23.

e18. Blomstrand A, Blomstrand C, Ariai N, Bengtsson C, Bjorkelund C: Stroke incidence and association with risk factors in women: a 32-year follow-up of the Prospective Population Study of Women in Gothenburg. BMJ Open 2014; 4: e005173.

e19. Seidler A, Steputat A, Drössler S, et al.: Determinanten und Auswirkungen von Informationsüberflutung am Arbeitsplatz. Zentralblatt für Arbeitsmedizin, Arbeitsschutz und Ergonomie 2018; 68: 12–26.

eBOX 1

Search strategy in MEDLINE (via PubMed)

((Noise[tw] OR noise[MH]) AND (aircraft OR jet OR flight OR "air traffic")) AND (Epidemiologic Studies[MH] OR Odds Ratio [MH] OR observational stud*[tw] OR cohort stud*[tw] OR cohort analy*[tw] OR follow up stud*[tw] OR prospective stud* OR incidence stud*[tw] OR Longitudinal[tw] OR Case control[tw] OR Case-control[tw] OR Retrospective stud*[tw] OR cross-sectional stud*[tw] OR prevalence stud*[tw] OR ecological stud*[tw] OR correlation analys*[tw] OR incidence OR prevalence) NOT (letter[tw] OR editorial[tw] OR comment [tw]) NOT ((animals[Mesh:noexp]) NOT (humans[Mesh])) AND ("1"[PDat] : "2017/08/31"[PDat]) eBOX 2

Supplementary methodology information

General

This review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (e7).

The study protocol was published in advance in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42013006004 (e8).

Data synthesis and statistical analysis

Similar to the approach taken in other meta-analyses (e.g. [e9]), the various effect estimates (risk ratio [RR], standardized mortality ratio [SMR], hazard ratio [HR], odds ratio [OR]) of the individual studies were altogether regarded as estimates of the risk ratio. They were included unchanged in the creation of an aggregated risk estimate. Since stroke is a comparatively rare event on the population level (incidence far below 10%), it was possible to interpret odds ratios as risk ratios (e10) and include them in the meta-analysis.

In order to be able to perform a quantitative meta-analysis, the various exposure measures of the individual studies had first to be transformed, using conversion formulas, to the exposure measure L_{DEN}, i.e. to a weighted average level which adds a "penalty" for the evening and especially night hours, based on the assumption that during these times the negative effect of noise is particularly strong. Such "penalties" are normally specified in directives. The directive 2002/49/EC of the European Parliament and of the Council, for example, defines the noise measure L_{DEN} and prescribe for evening hours a "penalty" of 5 dB and night hours a penalty of 10 dB. Thus, the definition of L_{DEN} combines the objectively measured aircraft noise with the subjective component of perceived annoyance (penalties for evening and night hours). Pathophysiologically, these "penalties" are justified in particular by the disturbance of sleep architecture which has also been discussed as a risk factor for stroke (e11). On the other hand, when data from studies using different exposure measures are transformed into L_{DEN} for the sake of pooling and comparability, this inevitably means that information is lost: The conversion formulas cannot adequately reflect the peculiarities of an aircraft noise-exposed area (e.g., the existence of a ban on night flights or the number of flights in the evening and morning "shoulder" hours).

Furthermore, the precision of exposure identification varies between the studies included in this review with the magnitude of the noise map resolutions (e.g. 10 × 10 m grid in the study by Hansell et al. [4] vs. spatial resolution of 250 × 250 m in the HYENA study [3]) and how the noise data were linked to the population (e.g. very rough—and thus susceptible to bias—postcode-based allocation in the studies by Correia et al. [18] and Gan et al. [23]). In addition, exposure allocation based on place of residence is associated with considerable uncertainty with regard to the actual exposure, because especially during the day a large proportion of the population is not at home. These exposure-related uncertainties typically apply equally to persons with and without health effects. This so-called non-differential bias tends to result in conservative bias—i.e. an underestimation—of aircraft noise-related stroke risks.

Our meta-analysis is based on the assumption of a linear change of the risk of disease with increasing aircraft noise. This basic assumption is grounded on previous studies on cardiovascular aircraft noise risks (e.g. [e12, e13]). However, in the large NORAH study it was not possible to adequately match the association between aircraft noise and risk of stroke with a linear model (33, 35). Consequently, at this point it is not yet supported by conclusive scientific evidence that a linear model best describes the exposure-risk relationship between aircraft noise and the occurrence of stroke.

In particular, it is conceivable that there is a lower noise level threshold which has to be exceeded before the risk starts to increase. Here it should be noted that most of the individual studies de-facto introduced such a lower threshold by setting a "starting point"; however, the starting points of the various studies range between 0 and 45 dB. For comparison: 40–65 dB correspond to the usual sounds at home (e.g. a fridge: 40–43 dB) and a normal conversation (approx. 55–65 dB). Consequently, the question of a lower threshold cannot be answered by means of meta-analysis. Similarly, a starting point which is set too high in an individual study can result in biased risk estimates if risks of disease are already present at noise levels below the starting point. Thus, the different starting points of the individual studies would lead to underestimating rather than overestimating the pooled stroke risk.

eBOX 3

Supplementary information about the results

- **Results of the individual included studies:**
  - The research question of our review comprised, besides the effects of measurable noise exposure, the effects of noise-related annoyance. However, this question could not be answered, because the aspect of annoyance was evaluated in one study only (36).
  - The majority of exposure data used in the individual studies were address-specific average noise levels (in some cases limited to certain times of the day/night or to noise levels weighted according to the time of the day). One study described the exposure in an ecological way by using the L_{DEN}AEI measure (L_{DEN}AEI: weighted average exposure to aircraft noise on the municipal level) (19). In its core analysis, the NORAH Study on health risks reported the effect estimates for maximum nighttime levels above 50 dB separately (at 24-hour continuous noise levels below 40 dB) (33). Only the study by Wiens (34) used noise-related annoyance as the exposure variable.
  - The spectrum of endpoint data collection ranges from self-reported information (3,34) to ICD-coded medical or hospital diagnoses (4, 18, 32) to death-certificate diagnoses (2, 19, 20, 23).
  - All studies took age and sex as confounders into account. However, the analyzed studies differ with regard to the number and selection of additional confounders considered.
  - Three studies modeled the exposure-effect relationship continuously (2, 3, 18) using 10 dB increments, while the remaining studies reported the effect estimates based on noise intervals of variable size. The reported effect estimates include risk ratio (4, 18, 23), hazard ratio (2), odds ratio (3, 32, 34), mortality rate ratio (19), and standardized mortality rates (20).
  - Since almost all of the included studies were publicly funded, this source of bias is unlikely. Only one study (32) received indirect mixed funding with a small portion stemming from the aviation industry (11.4%) and otherwise mainly public funding; for a second study (20), funding information was unavailable.

- **Quality of the included studies:**
  - Four studies (2, 4, 23, 32) were of adequate quality (rating: +). The methodological quality of the remaining 5 studies (3, 18–20, 34) was inadequate (rating: −). None of the included studies reached the highest of the 3 quality rating levels (rating: ++). Further information about the methodological strengths and weaknesses of the individual studies is provided in the data extraction table (*eTable 2*).

eTABLE 1

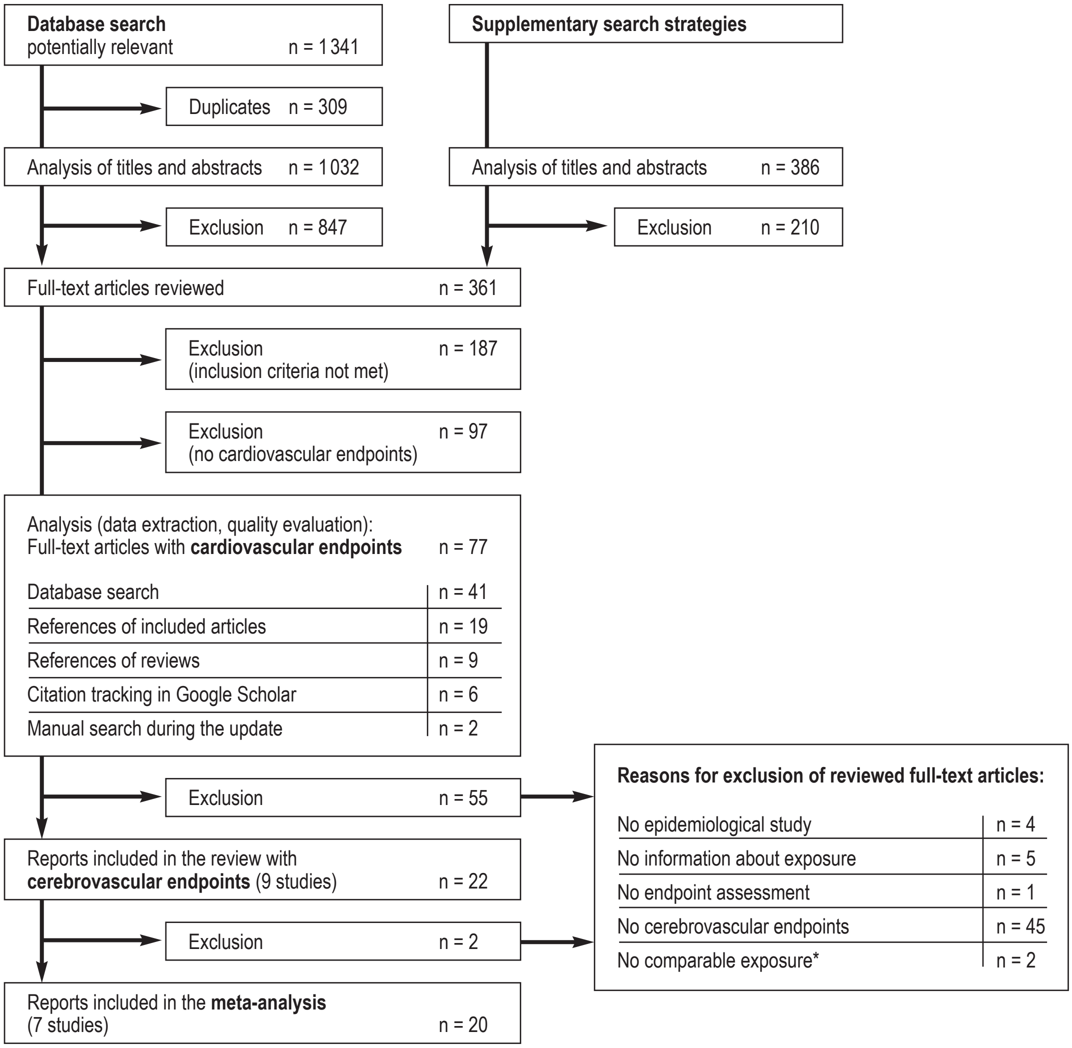
Noise metrics and their definitions*[1]

Abbreviation	Definition
dB	Logarithmic scale for sound pressure levels
L_{eq}	Average value of an energy-equivalent continuous sound level over a period of time
L_{Aeq}	A-weighted L_{eq}
L_{Day}	L_{Aeq} for daytime hours (usually 7:00 am – 7:00 pm)*[2] for all day periods of a year
$L_{Evening}$	L_{Aeq} for evening hours (usually 7:00 pm – 11:00 pm)*[2] for all evening hours of a year
L_{Night}	L_{Aeq} for nighttime hours (usually 11:00 pm – 7:00 am)*[2] for all nighttime hours of a year
L_{DN}	All 24 h L_{Aeq} periods of a year with additional 10 dB for nighttime noise annoyance (usually from 11:00 pm –7:00 am)*[2]
L_{DEN}	All 24 h L_{Aeq} periods of a year with additional 5 dB for evening hours (8:00 pm – 10:00 pm or 7:00 pm – 11:00 pm)*[2] and additional 10 dB for nighttime hours (10:00 pm – 6:00 am or from 11:00 pm – 7:00 am)*[2]
NAT6	Maximum level which is exceeded six times above 50 dB without upper limit during the night (from 10:00 pm – 6:00 am). At the same time, the 24 h continuous sound level is below 40 dB.

*[1] adapted according to directive 2002/49/EC (European Parliament and European Council, 2002)

*[2] In Germany, normal sleeping hours are defined in the respective federal states immission control legislation and usually encompasses the period from 10:00 pm – 6:00 am. Therefore, German studies (e.g. NORAH study) sometimes deviate from the periods for L_{Day}/$L_{Evening}$/L_{Night} listed in *eTable 1* and instead use the periods stipulated in the legislation.

eFIGURE



Flowchart of the selection process (based on the PRISMA Statement [e7])

* The exposure information in the studies by Wiens (27) and Evrard (19) differs considerably from the exposure information of the remaining studies and thus were not included in the meta-analysis: Wiens (27) only collected data on perceived annoyance, but not aircraft noise levels; Evrard (19) did not perform any individual, address-based estimation of the aircraft noise.

PRISMA, preferred reporting items for systematic reviews and meta-analyses *eTable 2: Extracted study data of the included studies/publications (n = 9 studies and 22 publications, respectively)*

Reference	Study design	Population					Exposure		Outcome & Results	Comments
(First author, publication year, country, airport)		**no. of subjects** (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		(study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
Correia et al., 2013										
Correia et al., 2013 USA (89 airports, not further specified)	cross-sectional	enrolled: M+F: 6,027,363 linkage of data: 90th centile of noise exposure with population: M+F: 5,523,788	≥ 65 years thereof 42.7% > 75 years	hospital admission rates per 100,000 population: **Stroke:** 1,343	2009	Secondary data linkage of data: 90th centilenoise exposure with population: 91.6%	L_{dn} for 2,218 zip codes close to 89 airports (Night = 10pm-7am, which adds a 10 dB "penalty")	Population weighted noise: ≥ 45 - 71.59[1] dB 90th centile of noise exposure categorized 90th centile of noise exposure ≤50 dB, 50-55 dB, >55 dB	POPULATION WEIGHTED NOISE: **Stroke:** Hospital admissions for primary diagnosis of stroke: relative rate (RR) per 10 dB increase (hierarchical Poisson regression model): 1.039 (95% CI 0.995-1.084)[1] adj. for age, sex, race (model 1) "after controlling for SES, demographic and pollution variables (models 2 and 3) this association was no longer statistically significant" 90TH CENTILE OF NOISE EXPOSURE: **Stroke:** % CATEGORIZED 90TH CENTILE OF NOISE EXPOSURE: **Stroke:** %	**study quality:** (-) **conflict of interest:** stated (no support from any commercial entities, no financial relationships/other relationships or activities that might have influenced the work) **funding:** stated (financed from public funds [Federal Aviation Administration]) **confounding (adjusted for):** (see left column) **strengths/ weaknesses:** + low potential for differential (e.g. recall) bias + ICD-coded exposition data - cross-sectional design without chronological information - maybe overestimation of potential risk, because private health insurance not included - very rough exposure information (just

[1] see e-mail correspondence with one of the authors (Andrew Correia), January 19th 2016

Reference (First author, publication year, country, airport)	**Study design**	**Population**					**Exposure**		**Outcome & Results**	**Comments** (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
										for zip code) - partly ecological confounders (e.g. SES)
Evrard et al., 2015										
Evrard et al., 2015 France (Paris-Charles de Gaulle, Lyon Saint-Exupéry, Toulouse-Blagnac)	ecological study design with case control approach	no statement can be made, because of ecological study design	not reported	Cerebrovascular deaths; ICDI60-I64, excluding I63.6). No. of cases not reported	2007-2010 mortality data	Sec. data No information on performance of linkage of data	L_{den}AEI aircraft noise data: 2008 for Paris-Charles de Gaulle, 2003 for Lyon Saint-Exupéry, 2004 for Toulouse-Blagnac Integrated noise model noise indicator L_{den}, with 1dB-resolution with a minimum of 50 dB for the Paris area	Average L_{den}AEI was estimate as 49.6 dB, range: ≥ 42.0 – 46.1 dB Avarage L_{den}AEI for Paris-Charles de Gaulle: 51.6 dB; for Lyon Saint-Exupéry: 45.3 dB and for Toulouse-Blagnac area: 45.7 dB	**Stroke:** ICD-coded stroke mortality rate ratio (MRR) per 10 dB increase: 1.08 (95% CI 0.97-1.21) adj. at the commune level for gender, age, log-population density, lung cancer mortality, and a deprivation index When NO_2 concentration was taken into account in the models including L_{den}AEI, the results did not change: 1.06 (95% CI 0.93-1.21). Introducing PM_{10} concentration in the model instead of NO_2 concentration did not change the results: 1.08 (95% CI 0.95-1.22).	**study quality:** (-) **conflict of interest:** stated (no conflicts of interest) **funding:** financed from public funds **confounding (adjusted for):** extra column (see left). **strengths/ weaknesses:** + ICD-coded exposition data - ecological study design do not allow any conclusions to individual level - exclusively consideration of ecological confounder - data for additional adjusting for air pollution exposure were only available for Paris and Lyon area

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
							and 45 dB for Lyon and Toulouse area Noise levels were then weighted for a given commune (L_{den} by the number of inhabitants living within this noise level and the total number of inhabitants in the commune) = L_{den}AEI			
Frerichs et al.,1980										
Frerichs et al., 1980	cohort	M+F: 216,921	not reported	low-noise control area (n=	1970-1971	Secondary data (1970	Meecham and Smith,	low-noise control	**Stroke:** ICD-coded cerebrovascular deaths: SMR	**study quality:** (-)

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
California, USA (Los Angeles International)	re-analysis of Meecham and Shaw, 1979	(population of extended boundaries)		92,101): Cerebrovascular deaths; ICDA-8 430-438: n=120 high-noise area (n= 124,820): Cerebrovascular deaths; ICDA-8 430-438: n=220		census data) not reported	1977 are cited, the report suggests an exposure assessment of L_{day} (17,5hr)	area: 45-50 dB high-noise area: 90 dB noise contour	Observed deaths: 45-50dB: 1.06 (95% CI 0.86-1.29)[2] 90dB: 0.92 (95% CI 0.71-1.17)[2]	**conflict of interest:** not stated **funding:** not stated **confounding (adjusted for):** age, ethnicity, sex **strengths/ weaknesses:** + low potential for selection bias as census data were used + ICD-coded outcomes - unclear exposure assessment - unclear population characteristics - migration-related aspects not considered - very short "follow-up" - mortality study - SES not considered as potential confounder - no confidence intervals/p-values are given in publication, therefore self-calculation of SMR an confidence intervals was necessary
Meecham and Shaw, 1979 airport [see Frerichs et	cohort	M+F: 164,168 Large "overlaps"	not reported	test area (n= 86,200): mortality due to	1970-1971	Secondary data (1970 census data)	not reported	test area: 90 dB noise contour	**Stroke:** ICD-coded cerebrovascular deaths ("crude" SMR[3]): among exposed O/E= 98/92.4 = 1.06	**study quality:** (-) **conflict of interest:** not stated

[2] self-calculated according to Ulm, 1990 (Ulm K: A simple method to calculate the confidence interval of a standardized mortality ratio (SMR). Am J Epidemiol 1990; 131: 373-5.)
[3] The "crude" SMR was determined by our calculations.

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
al., 1980]		with "re-analysis" of Frerichs et al., 1980		stroke n=98 control area (n= 77,968): mortality due to stroke n=64		not reported		control area: 45-50 dB	among non-exposed O/E=64/69.6 = 0.92 % increase [=1-(1.06/0.92)]=15%	**funding:** stated (financed from public funds: Academic Senate of the University of California Los Angeles) **confounding (adjusted for):** not adjusted **strengths/ weaknesses:** + low potential for selection bias as census data were used + ICD-coded outcomes - unclear exposure assessment - unclear population characteristics - migration-related aspects not considered - very short "follow-up" - mortality study - no adjustment for potential confounders - no confidence intervals/p-values are given - data driven presentation of results - considerable "risk elevation" for cirrhosis of the liver points to differences in alcohol consumption (and therefore potentially in SES) among "exposed" and "non-exposed" - Frerichs et al., 1980 "could not determine how they [Meecham and Shaw, 1979] identified 887 deaths in the airport area". According to Frerichs et al., 1980 "the original findings … were most likely based on faulty analysis"
Meecham and Shaw, 1993	cohort	M+F: 194.201	35-75+	test area: (n= 102,742)	1970-1977	Secondary data (mean of	"use of a combination of	test area: > 90 dB	**Stroke:** %	**study quality:** (-)

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
airport [see Frerichs et al., 1980]				control area: (n= 91,459)		1970 and 1980 census data) not reported	technical reports and on site measurements", Lane, 1974 is cited	control area: not stated, probably 45-50 dB (see Meecham and Shaw, 1979; Frerichs et al., 1980)		**conflict of interest:** not stated **funding:** not stated **confounding (adjusted for):** not adjusted **strengths/ weaknesses:** + SES considered: monthly income among exposed ($ 262) and non-exposed ($ 267) nearly identical + low potential for selection bias as census data were used + ICD-coded outcomes - very rough exposure information - unclear population characteristics - mortality study - no adjustment for potential confounders
Gan et al., 2012										
Gan et al., 2012 Canada (Vancouver International)	Cohort	study base: M+F: 466,727[4] Analysed: M+F: 445,868[4]	45-85 years	**Stroke:** n=1,288[6] n=1,309[5]	5-year exposure period (Jan. 1994-Dez. 1998), 4 year follow-up (Jan. 1999-Dec.	Secondary data	L_{den} calculate continuous noise levels for each area covered by a 6-	non-exposed[5] Quartile1: 0.01-21.3 dB[5] Quartile2: 21.4-35.2	**Stroke:** ICD-coded stroke mortality *non-exposed:* RR: reference category[5] persons: 165,959[5] cases: 402[5] *Quartile 1:* RR: 1.30 (95% CI 1.11-1.53)[5]	**study quality:** (+) **conflict of interest:** stated (no conflict of interest) **funding:** financed from public funds (inter alia: Health Canada via an agreement with the British Columbia Centre for Disease

[4] reported in the publication

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
		/// 471,626[5] persons exposed to aircraft noise: 294,783[4] /// 305,667[5] (471,626 analysed-165,959 non-exposed)			2002)		digit postal code obtained by Vancouver International Airport Authority	dB[5] Quartile3: 35.3-44.4 dB[5] Quartile4: 44.5-71.0 dB[5]	persons: 76,348[5] cases: 234[5] *Quartile 2:* RR: 1.29 (95% CI 1.10-1.51)[5] persons: 76,321[5] cases: 242[5] *Quartile 3:* RR: 1.07 (95% CI 0.90-1.26)[5] persons: 76,598[5] cases: 206[5] *Quartile 4:* RR: 1.16 (95% CI 0.98-1.36)[5] persons: 76,400[5] cases: 225[5]	Control to the Border Air Quality Study. Additional support was provided by the Centre for Health and Environment Research at The University of British Columbia, funded by the Michael Smith Foundation for Health Research, and the Canadian Institutes of Health Research) **confounding (adjusted for):** age, sex, neighborhood SES, and comorbidity (diabetes, COPD, or hypertensive heart disease) **strengths/ weaknesses:** + low potential for selection bias + ICD-coded outcomes + nine years observation period (five years exposure period plus additional four years follow-up) - mortality study - partly ecological confounders (neighbourhood SES) - adjustment for comorbidity (risk for overadjustment)
Hansell et al., 2013										
Hansell et al., 2013 UK (London Heathrow)	"cohort"	M+F: 3,591,719	unknown	Mortality (ICD-10 codes I61, I63, I64): **Stroke:**	2001 census	Secondary data	$L_{Aeq,07-23h}$ $L_{Aeq,23-07h}$ 2002	$L_{Aeq,07-23h}$: ≤ 51->63 dB $L_{Aeq,23-07h}$:	$L_{Aeq,07-23h}$: **Stroke** ICD-10 coded (I61, I63, I64) RR for hospital admissions [Model 2]:	**study quality:** (+) **conflict of interest:** stated (all authors declare: financial

[6] reported in web table 1 of the publication
[5] see e-mail correspondence with second author, January 29th 2016

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
				9,803; Hospital admissions (ICD codes see above): **Stroke**: 16,983	2001-2005 health data		aircraft noise data on 10m x 10m grids using the UK Civil Aircraft Noise Contour Model ANCON	≤ 50->55 dB	*≤ 51 dB:* RR: 1.0 persons: 2,619,350 cases: 12,200[7] *>51-54 dB:* RR: 1.03 (95% CI 0.98-1.09) persons: 436,790 cases: 2,121[7] *>54-57 dB:* RR: 1.04 (95% CI 0.98-1.12) persons: 283,234 cases: 1,354[7] *>57-60 dB:* RR: 1.04 (95% CI 0.95-1.14) persons: 131,956 cases: 670[7] *>60-63 dB:* RR: 1.10 (95% CI 0.96-1.25) persons: 60,637 cases: 318[7] *>63 dB:* RR: 1.24 (95% CI 1.08-1.43) persons: 59,752 cases: 320[7]	support for the submitted work through the funding of the UK Small Area Health Statistics Unit by Public Health England as part of the MRC-PHE Centre for Environment and Health, funded also by the UK Medical Research Council; financial support from the European Network for Noise and Health (ENNAH), EU FP7 grant No 226442; PE acknowledges support from the National Institute for Health Research (NIHR) Biomedical Research Centre based at Imperial College Healthcare NHS Trust and Imperial ollege London; PE is an NIHR Senior Investigator; ALH and HEL declare consultancy fees from AECOM as part of a Defra report on health effects of environmental noise; ALH declares a Greenpeace membership but has not received any money from the organisation nor been involved in campaigns; nor other relationships or activities that could appear to have influenced the submitted work.) **funding:** financed from public funds (inter alia: Public Health England, UK Medical Research Council, European Network for European Health) **confounding (adjusted for):** Model 2: age, sex, ethnicity, deprivation (carstairs index), lung cancer (ecological

[7] see e-mail correspondence with one of the authors (Rebecca E. Ghosh), January 14th 2016

<table>
<tr><th rowspan="2">Reference
(First author, publication year, country, airport)</th><th rowspan="2">Study design</th><th colspan="5">Population</th><th colspan="2">Exposure</th><th rowspan="2">Outcome & Results</th><th rowspan="2">Comments
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<td><table><tr><th>dB</th><th>RR</th></tr><tr><td>≤ 50</td><td>1.0</td></tr><tr><td>>50-55</td><td>1.04 (95% CI 0.99-1.08)</td></tr><tr><td>>55</td><td>1.08 (95% CI 1.02-1.14)</td></tr></table>
ICD-10 coded (I61, I63, I64) RR for mortality [Model 2]:
<table><tr><th>dB</th><th>RR</th></tr><tr><td>≤ 51</td><td>1.0</td></tr><tr><td>>51-54</td><td>1.06 (95% CI 0.97-1.16)</td></tr><tr><td>>54-57</td><td>1.03 (95% CI 0.93-1.15)</td></tr><tr><td>>57-60</td><td>0.86 (95% CI 0.74-1.00)</td></tr><tr><td>>60-63</td><td>1.11 (95% CI 0.88-1.40)</td></tr><tr><td>>63</td><td>1.21 (95% CI 0.98-1.49)</td></tr></table>
<table><tr><th>dB</th><th>RR</th></tr><tr><td>≤ 50</td><td>1.0</td></tr><tr><td>>50-55</td><td>1.10 (95% CI 1.02-1.17)</td></tr><tr><td>>55</td><td>1.02 (95% CI 0.93-1.12)</td></tr></table>
<hr>
$L_{Aeq,23-07h}$:
Stroke
ICD-10 coded (I61, I63, I64) RR for hospital admissions [Model 2]:

≤ 50 dB:
RR: 1.0
persons: 3,338,704
cases: 15,691[7]

>50-55 dB:
RR: 0.99 (95% CI 0.92-1.07)
persons: 180,335</td>
<td>variables)

strengths/ weaknesses:
+ relatively large census “cohort”
+ incidence and mortality outcome data
+ adequate exposure assessment
+ ICD-coded outcome measurement

- potential for unknown or residual confounding (as confounding was not considered on an individual level)
- multiple disease outcomes per study subject possible in incidence study (therefore, the study does not only reflect “etiology”, but the course of disease)
- no sex-specific data</td></tr>
</table>

Reference (First author, publication year, country, airport)	**Study design**	**Population**					**Exposure**		**Outcome & Results**	**Comments** (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
									cases: 877[7] *>55 dB:* RR: 1.29 (95% CI 1.14-1.46) persons: 72,680 cases: 415[7] ICD-10 coded (I61, I63, I64) RR for mortality [Model 2]: dB / RR ≤ 50 / 1.0 >50-55 / 0.92 (95% CI 0.81-1.05) >55 / 1.23 (95% CI 1.02-1.49)	
Héritier et al., 2017										
Huss et al., 2010 Switzerland (all airports)	cohort	M+F: 4,580,311	> 30 Mean: <45 dB: 50.7; 45-49 dB: 50.7; 50-54 dB: 50.2; 55-59 dB: 49.7; ≥ 60 dB: 49.1	cases total study population: **Stroke:** 25,231 ——— cases subgroup (residence ≥ 15 years): **Stroke:** 12,102	Dec. 2000 – Dec. 2005	95%	L_{dn}	<45-≥60 dB	total study population: **Stroke:** ICD-coded mortality from stroke: *<45 dB:* HR: 1.0 persons: 91.4% von 4,580,311 cases: 23,398 *45-49 dB:* HR: 0.97 (95% CI 0.90-1.04) persons: 3.5% von 4,580,311 cases: 842 *50-54 dB:* HR: 0.97 (95% CI 0.89-1.05) persons: 2.9% von 4,580,311 cases: 584 *55-59 dB:* HR: 1.06 (95% CI 0.95-1.18) persons: 1.9% von 4,580,311 cases: 366	**study quality:** (+) **conflict of interest:** not stated **funding:** financed from public funds (Swiss National Science Foundation) **confounding (adjusted for):** sex, age, civil status, nationality, educational level, setting (urban/rural), language region, type of building, socioeconomic status of the municipality, type of building, distance to major road, air pollution **strengths/ weaknesses:** + low potential for selection bias + rather adequate consideration of potential confounding (but smoking, BMI not directly considered)

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
									≥ 60 dB: HR: 0.83 (95% CI 0.91-1.13) persons: 0.3% von 4,580,311 cases: 41 subgroup (residence > 15 years): **Stroke:** ICD-coded mortality from stroke (HR): <45dB: 1.0 45-49dB: 1.03 (95% CI 0.92-1.14) 50-54dB: 1.02 (95% CI 0.90-1.15) 55-59dB 0.96 (95% CI 0.82-1.13) ≥ 60dB: 0.88 (95% CI 0.58-1.34)	- mortality study
Héritier, H. 2017 S/N 2503 Switzerland (all airports)	cohort	total cohort at baseline: M+F: 4.415.206 (males 47.9%)	> 30 yrs. mean 52.4 (SD 15.1) at baseline	See right column	Dec. 2000 – Dec. 2008	Sec. data	L_{den} generate Swiss-wide exposure models for 2001; noise from the most exposed façade was	≥ 30dB 67.1% censored observations (d.h. Werte kleiner 30 dB wurden auf den Default Wert 30dB	**Stroke:** ICD-coded stroke (I60-I64) HR (22,377 cases, n=4,415,206[8]): HR per 10 dB / adjusted for: 0.981 (95% CI 0.963-0.999) / crude 1.013 (95% CI 0.993-1.033) / adjusted ICD-coded hemorrhagic stroke (I60-I62) HR (5,354 cases, n=4,415,206[8]):	**study quality:** (+) **conflict of interest:** stated **funding:** financed from public funds (Swiss National Science Foundation and the Federal Office for the Environment) **confounding (adjusted for):** sex, neighborhood index of socio-economic position, civil status, education level, mother tongue, nationality and NO_2

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
							linked to geocodes at the residential floor height for each of the cohort participants	hoch gesetzt)[8]	HR per 10 dB / adjusted for: 0.990 (95% CI 0.955-1.026) crude; 0.991 (95% CI 0.951-1.032) adjusted ICD-coded ischemic stroke (I63) HR (n=2,991 cases, n=4,415,206[8]): HR per 10 dB / adjusted for: 1.052 (95% CI 1.006-1.099) crude; 1.074 (95% CI 1.020-1.127) adjusted	exposure **strengths/ weaknesses:** + low potential for selection bias + rather adequate consideration of potential confounding (but smoking, BMI not directly considered) - mortality study **Comment:** IR_{23-07h} does not differentiate between road, rail and air traffic noise and therefore could not be included in the meta-analysis
HYENA-Study[9]										
Floud et al., 2013 UK (London Heathrow), Germany (Berlin Tegel),	cross-sectional	Baseline: M+F: 4,861; M: 2,404; F: 2,457	45-70 years mean 58 (SD 7.0)	see right column see right column	2004-2006	after exclusions due to missing outcome and confoundi	$L_{Aeq,\ 07-23h}$ $L_{night\ 23-07h}$	<35-76 dB <30-70 dB	$L_{Aeq,\ 07-23h}$: **Stroke:** self-reporting of an physicians diagnosis of stroke (persons:4,712, cases:63): OR per 10 / adjusted for	**study quality:** (-) **conflict of interest:** stated (AH consultancy for Defra) **funding:**

[8] see e-mail correspondence with one of the authors (Prof. Martin Röösli), 27th March 2018

[9] Publications concerning the methodology of the HYENA-study were included in the data extraction of the papers reporting the results, see Jarup et al., 2005 (Jarup L, Dudley ML, Babisch W, et al.: Hypertension and Exposure to Noise near Airports (HYENA): Study Design and Noise Exposure Assessment. Environmental health perspectives 2005; 113: 1473-8, 37.) as well as Babisch et al., 2005 (Babisch W, Houthuijis D, Kwekkeboom J, et al.: HYENA-Hypertension and exposure to noise near airports. A European study on health effects of aircraft noise. INTER-NOISE and NOISE-CON Congress and Conference Proceedings: Institute of Noise Control Engineering 2005; p. 1376-85.).

Reference (First author, publication year, country, airport)	Study design	Population: no. of subjects (M, F, M+F)	age (mean, range)	no. of cases / no. of controls	time of cohort enumeration / follow-up (mean, range)	response rate (%) (baseline minus loss to follow-up)	Exposure: exposure assessment	exposure levels	Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
Netherlands (Amsterdam Schiphol), Sweden (Stockholm Arlanda & Bromma), Greece (Athen Elephtherios Venizelos), Italy (Milan Malpensa)						ng data: M+F: 4,712; M: 2,337; F: 2,375 39% response rate for aircraft noise <50 dB 45% (50 to < 65 dB) 45% (≥ 65 dB) large differences between countries			dB increase | – 1.07 (95% CI 0.82-1.39) | crude 1.08 (95% CI 0.82-1.41) | age, sex, BMI, education, ethnicity 1.08 (95% CI 0.82-1.41) | age, sex, BMI, education, ethnicity and other noise exposures heart disease and stroke (persons: 4,712; cases:276; subsample ≥ 20 years of residence): OR per 10 dB increase | adjusted for 1.17 (95% CI 0.97-1.40) | crude 1.11 (95% CI 0.92-1.34) | age, sex, BMI, education, ethnicity 1.11 (0.92-1.34) | age, sex, BMI, education, ethnicity and other noise exposures $L_{night\ 23\text{-}07h}$: **Stroke:** self-reporting of an physicians diagnosis of stroke (persons: 4.712; cases: 63): OR per 10 dB increase | adjusted for 1.17 (95% CI 0.89-1.55) | crude 1.18 (95 % CI 0.89-1.56) | age, sex, BMI, education, ethnicity	financed from public funds **confounding (adjusted for):** (see left column) additional information: alcohol intake, physical activity and smoking status proofed but not included in the final regression, because ≠ > 10% change in the coefficient of the exposure **strengths/ weaknesses:** + adequate consideration of potential confounding + adequate exposure assessment - self-reported outcome measurement - low response rate - cross-sectional design, however restriction to diagnoses whilst living at current address

Reference (First author, publication year, country, airport)	**Study design**	**Population**					**Exposure**		**Outcome & Results**	**Comments** (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
									1.18 (95% CI 0.89-1.57) — age, sex, BMI, education, ethnicity and other noise exposures heart disease and stroke (persons: 4.712; cases: 276; subsample ≥ 20 years of residence): OR per 10 dB increase — adjusted for 1.36 (95% CI 1.10-1.59) — crude 1.24 (95% CI 1.03-1.50) — age, sex, BMI, education, ethnicity 1.25 (95% CI 1.03-1.51) — age, sex, BMI, education, ethnicity and other noise exposures	
Floud, et al., 2011 airports [see Floud et al., 2013]	cross-sectional	Baseline: M+F: 4,861; M: 2,404; F: 2,457 Residence ≥ 5 years (Greece sample ≥ 3 years)	45-70 years mean 57.7 (SD 7.1)	evaluated (n=4,642) prevalences: **Stroke:** %	2004-2006	39% response rate for aircraft noise <50 dB 45% (50 to < 65 dB) 45% (≥ 65 dB) large differences between	$L_{Aeq,16h}$ = $L_{Aeq,07-23h \text{ or } 06-22h}$ L_{night} = $L_{Aeq,23-07h \text{ or } 22-06h}$ Annoyance ISO standard non-verbal 11 point scale (range: 0-10)	35-≥65 dB 30-≥60 dB ≥ 8 highly annoyed < 8 not highly annoyed	$L_{Aeq,16h}$: **Stroke:** % L_{night}: **Stroke:** % Annoyance due to aircraft noise in day: **Stroke:** % Annoyance due to aircraft noise at night: **Stroke:** %	**study quality:** (-) [see Floud et al., 2013] **conflict of interest:** stated (no competing interests) **funding:** financed from public funds **confounding (adjusted for):** $L_{Aeq,16h}$ and L_{night}: age, sex, BMI, alcohol intake, education, exercise, smoking status, road traffic noise; Annoyance due to aircraft noise (day and night): age, sex, BMI, alcohol intake, education, exercise, smoking status **strengths/ weaknesses:**

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
						countries	aircraft noise data [see Jarup et al., 2008]			+ adequate consideration of potential confounding + adequate exposure assessment - diagnoses defined by (self-reported) drug intake - low response rate - cross-sectional design, however restriction to diagnoses whilst living at current address - because of the high prevalence of outcomes, OR tend to considerably overestimate the "real risks" in antihypertensives
Jarup et al., 2008[10] airports [see Floud et al., 2013]	cross-sectional	[see Floud et al., 2011]	[see Floud et al., 2011]	unknown	[see Floud et al., 2011]	[see Floud et al., 2011]	$L_{Aeq, 16h} = L_{Aeq,07-23h}$ or 06-22h $L_{night} = L_{Aeq, 23-07h}$ or 22-06h 2002 aircraft noise data Integrated noise model (except UK:	cutoff level 35 dB cutoff level 30 dB	$L_{Aeq,16h}$: **Stroke:** % L_{night}: **Stroke:** %	**study quality:** (-) [see Floud et al., 2013] **conflict of interest:** stated (no competing financial interests) **funding:** financed from public funds **confounding (adjusted for):** "All noise indicators were included in the model, which was adjusted for country, age, sex, BMI, alcohol intake, education, and exercise." **strengths/ weaknesses:** + adequate exposure assessment

[10] together with: Jarup et al, 2008 (Jarup L, Babisch W, Houthuijs D, Pershagen G, Katsouyanni K, Velonakis M, Cadum E. 2008. Acute and long-term effect on blood pressure of exposure to noise near airports - The HYENA study. INTER-NOISE and NOISE-CON Congress and Conference Proceedings 2008:562-578.)

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
							national aircraft noise contour model [ANCON v 2]) spatial resolution 250x250 m 1dB-resolution, except for UK (5 dB-resolution)			+ hypertension diagnosis based on standardized measurements (mean of two BP measurements conducted by specially trained staff at home visits, validated and automated BP instruments) and self-reported diagnosis - low response rate - cross-sectional design, however restriction to diagnoses whilst living at current address - adjustment for L_{night} when analyzing $L_{Aeq,16h}$ or vice versa leads to results that are difficult to interpret
Babisch et al., 2007 airports [see Floud et al., 2013]	cross-sectional	[see Floud et al., 2011]	[see Floud et al., 2011]	prevalence of stroke: %	2003-2005	"Response rates differed between 30%-78% between the countries."	Annoyance ISO standard non-verbal 11 point scale (range: 0-10)	no cutoffs, continuous scale	Annoyance due to aircraft noise by day: **Stroke:** % Annoyance due to aircraft noise at night: **Stroke:** %	**study quality:** (-) [see Floud et al., 2013] **conflict of interest:** stated (no competing financial interests) **funding:** financed from public funds **confounding (adjusted for):** country, age, education, alcohol intake, BMI, exercise, sex (if not stratified) **strengths/ weaknesses:** + adequate consideration of potential

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		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
										confounding + adequate exposure assessment + hypertension diagnosis based on standardized measurements (mean of two BP measurements conducted by specially trained staff at home visits, validated and automated BP instruments) or a self-reported doctor-diagnosed hypertension in conjunction with use of antihypertensive medication (ATC-coding) - low response rate, but: participation rates differed not much between noise exposure categories, non-responder analyses conducted - cross-sectional design, however restriction to diagnoses whilst living for at least 5 yrs. at current address
Babisch et al., 2012 airports [see Floud et al., 2013]	cross-sectional	[see Floud et al., 2011]	[see Floud et al., 2011]	unknown	field work was carried out between 2003-2005	[see Floud et al., 2011]	L_{den} aircraft noise data [see Jarup et al., 2008]	> 40 dB	**Stroke:** %	**study quality:** (-) [see Floud et al., 2013] **conflict of interest:** not stated **funding:** financed from public funds **confounding (adjusted for):** Adjusted for: age, gender, alcohol consumption, BMI, physical activity at leisure, school education and country (airport) **strengths/ weaknesses:** [see Jarup, et al. 2008]

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
Babisch et al., 2013 airports [see Floud et al., 2013]	cross-sectional	Baseline: M+F: 4,861; M: 2,404; F: 2,457 Residence ≥ 5 years “Due to missing values the actual number of subjects varied slightly from analysis to analysis“	45-70 years	unknown	field work was carried out between 2003-2005	[see Jarup et al., 2008]	L_{den} Annoyance non-verbal 11 point “ICBEN scale” (range: 0-10) aircraft noise data [see Jarup et al., 2008]	> 40 dB	L_{den}: **Stroke:** % Annoyance: **Stroke:** %	**study quality:** (-) [see Floud et al., 2013] **conflict of interest:** stated (no conflict of interest) **funding:** financed from public funds **confounding (adjusted for):** see left column **strengths/ weaknesses:** [see Jarup, et al. 2008]
Dimakopoulou et al., 2017 Greece (Athen´s Elephtherios Venizelos)	Cohort	Sample: 21.488 Baseline: 780 Follow-up: 420, M: 186, F: 234	Baseline: 58 yrs. Follow-up: 67 yrs.	Prevalent at baseline: 7 Incident during follow-up: 5	Cohort enumeration: 2004-2006 Follow-up: 2013	40%	$L_{Aeq,\ 07\text{-}23h}$ $L_{night\ 23\text{-}07h}$ INM model	<35-76 dB <30-70 dB	$L_{Aeq,\ 07\text{-}23h}$: **Stroke:** self-reporting of an physicians diagnosis of stroke: OR per 10 dB: 0.84 (95% CI 0.36-1.59); Model: Including all subjects regardless of whether they were prevalent cases at baseline	**study quality:** (-) **conflict of interest:** stated (none declared) **funding:** financed from public funds **confounding (adjusted for):** age, sex, body mass index, alcohol intake, education, exercise, smoking habits and salt intake at baseline

Reference (First author, publication year, country, airport)	Study design	Population: no. of subjects (M, F, M+F)	age (mean, range)	no. of cases / no. of controls	time of cohort enumeration / follow-up (mean, range)	response rate (%) (baseline minus loss to follow-up)	Exposure: exposure assessment	exposure levels	Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
									1.02 (95% CI 0.30-3.54) – excluding the prevalent cases at baseline $L_{night\ 23\text{-}07h}$: **Stroke:** self-reporting of an physicians diagnosis of stroke: OR per 10 dB – Model 1.30 (95% CI 0.32-5.31) – Including all subjects regardless of whether they were prevalent cases at baseline 1.99 (95% CI 0.23-17.2) – excluding the prevalent cases at baseline	**strengths/ weaknesses:** + adequate consideration of potential confounding + adequate exposure assessment + adequate follow-up period - self-reported outcome measurement - approximate 54% of subjects was available for follow-up
NORAH-Study										
Seidler et al., 2016 Germany (Frankfurt International Airport) together with: Seidler et	Case-control Secondary data of three health insurance funds from	included in the study: 1,026,670 (M+F) after linkage of traffic noise and address	≥ 40 years	no. of cases: 25,495 (M: 44.9%, F: 55.1%) no of control subjects: 827,601 (M:	2006-2010	Secondary data	$L_{Aeq,24h}$ $L_{night\ 22\text{-}06h}$ NAT6 L_{DEN} historical radar data from the German flight	$L_{Aeq,24h}$ & $L_{night\ 22\text{-}06h}$ & L_{DEN}: ≥40-≥70 dB, reference category <40 dB NAT6: continuous sound	$L_{Aeq,24h}$: **Stroke:** ICD-10 coded hospital diagnosis of stroke (ICD-10: I61, I63 and I64): dB / OR / cases / controls <40 / 1.0 / 10,595 / 325,613 ≥40-<45 / 0.98 (95% CI 0.95- / 7,304 / 247,877	**study quality:** (+) **conflict of interest:** stated **funding:** major part of funding by the state of hessen, 11.4% funding of industry (airline, airport operator) **confounding (adjusted for):**

<table>
<tr><th rowspan="2">Reference
(First author, publication year, country, airport)</th><th rowspan="2">Study design</th><th colspan="5">Population</th><th colspan="2">Exposure</th><th rowspan="2">Outcome & Results</th><th rowspan="2">Comments
(study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])</th></tr>
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(M, F, M+F)</th><th>age (mean, range)</th><th>no. of cases / no. of controls</th><th>time of cohort enumeration / follow-up (mean, range)</th><th>response rate (%) (baseline minus loss to follow-up)</th><th>exposure assessment</th><th>exposure levels</th></tr>
<tr><td>al., 2018</td><td></td><td>data:
907,736 (M+F)</td><td></td><td>43.8%, 56.2%)</td><td></td><td></td><td>safety operator (DFS), analysis according to guidelines for calculations of noise abatement zones (AzB)</td><td>levels <40 dB, but more than six single incidents of noise exposure ≥50 dB between 22h and 6h at night, reference category <40dB, Max. <50dB</td><td>
<table>
<tr><td></td><td>1.01)</td><td></td><td></td></tr>
<tr><td>≥45-<50</td><td>1.02 (95% CI 0.98-1.06)</td><td>3,973</td><td>133,244</td></tr>
<tr><td>≥50-<55</td><td>0.97 (95% CI 0.92-1.03)</td><td>1,470</td><td>52,507</td></tr>
<tr><td>≥55-<60</td><td>0.86 (95% 0.77-0.95)</td><td>413</td><td>15,792</td></tr>
<tr><td>≥60-<65</td><td>1.62 (95% CI 0.79-3.34)</td><td>8</td><td>195</td></tr>
</table>
<table>
<tr><td>per 10 dB</td><td>0.976 (95% CI 0.953- 1.000)</td></tr>
</table>
Results of sensitivity analyses analysing ischemic and haemorrhagic stroke separately are available.
$L_{night\ 22-06h}$:
ICD-10 coded hospital diagnosis of stroke (ICD-10: I61, I63 and I64):
<table>
<tr><td>dB</td><td>OR</td><td>cases</td><td>controls</td></tr>
<tr><td><40</td><td>1.0</td><td>12,006</td><td>376,860</td></tr>
</table>
</td><td>age, sex, education, job title (when available), and local proportion of persons receiving unemployment benefits
strengths/ weaknesses:
+ adequate definition of cases
+ adequate exposure assessment
+ consideration of maximum nightly aircraft levels (NAT6)
+ adequate definition of outcome disease (ICD classification)
+ high number of cases and controls
- limited differentiation between incident and prevalent cases, therefore temporality cannot be totally established
- lack of adjustment for air pollutants (particularly relevant for aircraft noise)</td></tr>
</table>

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(M, F, M+F)</th><th>age (mean, range)</th><th>no. of cases / no. of controls</th><th>time of cohort enumeration / follow-up (mean, range)</th><th>response rate (%) (baseline minus loss to follow-up)</th><th>exposure assessment</th><th>exposure levels</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>≥40-<45</td><td>1.02 (95% CI 0.98-1.05</td><td>4,209</td><td>139,373</td></tr>
<tr><td>≥45-<50</td><td>1.00 (95% CI 0.95-1.06)</td><td>1,804</td><td>65,201</td></tr>
<tr><td>≥50-<55</td><td>0.99 (95% CI 0.91-1.07)</td><td>741</td><td>24,541</td></tr>
<tr><td>≥55-<60</td><td>1.00 (95% CI 0.68-1.46)</td><td>28</td><td>1,131</td></tr>
</table>
NAT6 (24 hrs. sound levels):
ICD-10 coded hospital diagnosis of stroke (ICD-10: I61, I63 and I64):
<table>
<tr><td>dB</td><td>OR</td><td>cases</td><td>controls</td></tr>
<tr><td><40, max. <50</td><td>1.0</td><td>10,595</td><td>325,613</td></tr>
<tr><td><40, max. ≥50</td><td>1.07 (95% CI 1.02-1.13)</td><td>1,732</td><td>52,373</td></tr>
</table>
NAT6 (Night time period 22-06h):
ICD-10 coded hospital diagnosis of stroke (ICD-10: I61, I63 and I64):
</td><td></td></tr>
</table>

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
									see below	

dB	OR	cases	controls
<40, max. <50	1.0	12,006	376,860
<40, max. ≥50	1.01 (95 % CI 0.98-1.04)	6,707	220,495

Results of sensitivity analyses analysing ischemic and haemorrhagic stroke separately are available.

L_{DEN}:

ICD-10 coded hospital diagnosis of stroke (ICD-10: I61, I63 and I64, n=):

dB	OR[11]	cases[11]	controls[11]
<40	1.0	7,126	220,667
≥40-<45	1.04 (95% CI 1.01-1.08)	7,170	222,033
≥45-<50	0.99 (95% CI 0.96-1.03)	6,729	229,302

11 see e-mail correspondence with one of the authors (Janice Hegewald), 27th March 2018

Reference (First author, publication year, country, airport)	Study design	Population					Exposure		Outcome & Results	Comments (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
									≥50-<55 | 1.03 (95% CI 0.98-1.08) | 2,937 | 100,433 ≥55-<60 | 0.99 (95% CI 0.93-1.06) | 1,236 | 43,630 ≥60 | 0.86 (95% CI 0.76-0.97) | 284 | 11,133	
Wiens, 1995										
Wiens, 1995 Germany (Berlin, all airports)	cross-sectional	random sample: 6,002 Baseline: M: 3,865 after linkage with noise data: M: 3,390 participati	31-70 years		1990	64%	Annoyance	category 1: not or littler annoyed + category 2: moderate annoyed vs. category	**Stroke:** self-reporting of stroke: category | POR[12] 1+2 | 0.94 (95% CI 0.44-2.04) 3 | 0.66 (95% CI 0.66-1.49)	**study quality:** (-) **conflict of interest:** not stated **funding:** financed from public funds (in part Senate Administration for Health Berlin) **confounding (adjusted for):** no adjusting **strengths/ weaknesses:** + acceptable response rate + population-based study base - self-reported outcomes

[12] POR calculated using logistic regression analysis, but no adjusting ("crude" data) – see e-mail correspondence with author, 3rd November 2015

Reference (First author, publication year, country, airport)	**Study design**	**Population**					**Exposure**		**Outcome & Results**	**Comments** (study quality [overall assessment according to SIGN/CASP], conflict of interest [stated vs. not stated], funding [financed from public funds vs. financed from industry], confounding, strengths / weaknesses [potential bias, over- or underestimation of potential effects])
		no. of subjects (M, F, M+F)	**age** (mean, range)	**no. of cases / no. of controls**	**time of cohort enumeration / follow-up** (mean, range)	**response rate (%)** (baseline minus loss to follow-up)	**exposure assessment**	**exposure levels**		
		on: M: 2,193 (residence ≥15 years)						3: rather or very annoyed		- cross-sectional design - no adjusting („crude“ data)

Legend:

Grey coloured text: data extraction of cerebrovascular events without preference for the meta-analysis

In this table, we separated each study with a grey crossbar. This means: everything that stands between the grey bars (= sometimes several publications on a study) was evaluated together.