



National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

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

RIVM Report 2017-0078

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Colophon

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Synopsis

Cardiovascular and metabolic effects of environmental noise.

Systematic evidence review in the framework of the development of the WHO environmental noise community guidelines for the European Region

Environmental noise, especially from road traffic, increases the risk of ischaemic heart disease, primarily myocardial infarction. In addition, it might elevate the risk of high blood pressure and stroke. There is also suggestive evidence that road traffic noise increases the risk of diabetes and obesity. Both the cardiovascular and metabolic effects of noise may be mediated by stress-related mechanisms and sleep disturbance, possibly affecting the hormone balance.

These are the main conclusions of an evidence review of the literature dealing with studies on the impact of noise exposure on the cardiovascular and metabolic system. To this end, we evaluated the results and quality of 61 epidemiological studies. Not all studies were of good quality. Best substantiated are the effects of road traffic noise on ischaemic heart disease. The greatest number of studies concerned traffic noise and hypertension, but most were cross-sectional and of low quality.

The results of this review form input for the new environmental noise guidelines for the European Region, prepared by the World Health Organization (WHO).

Key words: noise exposure, blood pressure, hypertension, ischaemic heart disease, stroke, diabetes, obesity, meta-analysis

Publiekssamenvatting

Hart- en vaatziekten en metabole effecten van omgevingsgeluid

Een systematische review voor de nieuwe gezondheidskundige richtlijnen voor omgevingsgeluid in Europa door de WHO

Door omgevingsgeluid, vooral afkomstig van binnenstedelijk wegverkeer, hebben mensen een grotere kans op zogeheten coronaire hartziekten, zoals pijn op de borst of een hartinfarct. Daarnaast zou het een hoge bloeddruk of een beroerte kunnen veroorzaken. Ook zijn er aanwijzingen gevonden dat geluid van wegverkeer de kans op diabetes en overgewicht zou verhogen doordat omgevingsgeluid invloed heeft op de hormoonhuishouding. Omgevingsgeluid veroorzaakt vaak stress en een slechtere nachtrust. Als mensen 's nachts slechter slapen, raakt de aanmaak van cortisol verstoord.

Dit blijkt uit een uitgebreide review door het RIVM van onderzoeken naar de gezondheidseffecten van omgevingsgeluid. Hierin zijn de resultaten van 61 bestaande onderzoeken vergeleken en is de kwaliteit van deze studies beoordeeld. Niet alle studies bleken van even goede kwaliteit. Het beste onderbouwd zijn de effecten door geluid van wegverkeer op coronaire hartziekten. Het grootste aantal studies onderzocht de relatie tussen geluid van wegverkeer en hoge bloeddruk. Dit zijn echter vooral studies die onder andere door hun beperkte opzet van minder goede kwaliteit zijn.

Dit onderzoek is uitgevoerd op verzoek van de Wereldgezondheidsorganisatie (WHO). De resultaten van deze review vormen de basis voor de nieuwe gezondheidskundige richtlijnen voor omgevingsgeluid die de WHO voor Europa gaat opstellen.

Kernwoorden: omgevingsgeluid, bloeddruk, hypertensie, coronaire hartziekten, beroerte, diabetes, obesitas, meta-analyse

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Summary

Aim

In this report, we present the results of a systematic review of the literature dealing with observational studies on the association between noise exposure and the cardiovascular and metabolic systems. The aim was to update some of the existing exposure-response relationships, and to evaluate the overall quality of the evidence. The World Health Organization (WHO) commissioned this review. Its results form important input for the new environmental noise guidelines for the European Region. The WHO requires that new guidelines should be based on the latest scientific knowledge.

Evaluation of existing reviews

The first step in this review was to identify and select reviews of “sufficient” quality, that described the impact of exposure to environmental noise from several sources on the cardiovascular or metabolic systems, in different settings, and populations. Eventually, we identified 37 reviews evaluating available studies into the impact of exposure to environmental noise on the cardiovascular and metabolic systems. By means of the AMSTAR tool we selected 15 reviews. Evaluation showed that most of the studies covered by the selected reviews, reported on the impacts of road and aircraft noise exposure among adults. Nine reviews included one or more meta-analyses, resulting in more than 13 exposure-response relationships. For most of these relationships, the reviewers were not able to provide a quality judgement of the individual studies. For a number of (new) health end-points (e.g. obesity) and/or noise sources (e.g. rail traffic), no reviews or exposure response relationships were available. Following the results existing reviews, we decided to carry out a new systematic review.

Materials and methods

Identification and selection

We identified observational studies involving the impact of noise from air, road-, and rail traffic and wind turbines on the cardiovascular and metabolic systems published from 2000 until October 2014 in scientific literature databases and the grey literature. We supplemented the results of this search with (i) studies that had been identified within the existing reviews that were evaluated for the purpose of this evidence review. However, conducting a systematic review often takes a lot of time. While working on this review, new results became publically available. In order to keep our results more up to date, it was decided to extend our study material with more recent studies beyond the studies that we had already identified for the period 2000 – October 2014. However, only updated and new results of studies published between November 2014 and August 2015 were included. Overall, we identified more than 600 publications and we selected 61 studies (described in 113 records) for data extraction.

Data extraction

From the selected 61 studies, we systematically extracted data on the general study characteristics, the characteristics of the population under investigation, the assessment of exposure and health endpoints, the results of the study-, and the quality of the study. The data extraction was carried out in duplicate, with the exception of studies on the impact of wind turbine noise (n = 3), and studies on the impact of noise on children's blood pressure, where the data extraction was carried out by one person only.

The main effects under investigation were: a) hypertension, b) ischaemic heart disease (IHD), c) stroke, d) diabetes, e) change in body mass index (BMI), f) change in waist circumference, and g) change in children's mean blood pressure. In order to compare the results of the studies, we expressed their results in a uniform way. With the exception of the change in blood pressure in children, change in BMI, and change in waist circumference, we expressed the results as an RR per 10 dB (L_{DEN}).

Data aggregation

For data aggregation, we included only estimates from studies that were well matched, adjusted or stratified for at least age and sex. If more than one risk estimate was given by a study, we used the estimates for men and women separately and for separate age categories where possible. After selecting the study estimates, we calculated a pooled estimate using a random-effects model.

Assessment of the quality of evidence: GRADE

The WHO also required us to assess the quality of the evidence that had been retrieved in this review. To this end, we applied a modified version of the GRADE considerations. In summary, for every health outcome, we had to assess the quality of the evidence according to several criteria. To this end, we evaluated the design of the evaluated studies, quality of the studies, consistency and precision of the results, directness of the evidence derived from the studies, publication bias, whether a dose response gradient is present, the magnitude of the effect found, and whether the results could be explained by possible confounding. GRADE has four levels for the quality of evidence, ranging from "very low" to "high". The level of the quality of evidence will be linked with the guideline values and recommendations that the WHO includes in its environmental noise guidelines.

Main findings and weighing the quality of the evidence**Hypertension**

We evaluated 40 studies that investigated the impact of noise on the risk of hypertension. Thirty-seven investigated the effects of transportation noise. We found positive associations between noise from air, road, and rail traffic and hypertension. We observed the strongest associations in the cross-sectional studies, which formed the largest part (n = 38) of the available evidence. Only the association between road traffic noise and the prevalence of hypertension was statistically significant: after aggregating the results of 26 studies, we derived an RR of 1.05 (95%CI: 1.02 – 1.08) per 10 dB (L_{DEN}) for the association between road traffic noise and the prevalence of hypertension within the range of approximately 20 - 80 dB (L_{DEN}). Although there was evidence

for moderate to high heterogeneity among studies, meta-regression analyses could not reveal clear sources for this observed heterogeneity. Despite the fact that most studies adjusted for important confounders, and were able to ascertain individual exposure levels, we rated the quality of the evidence from the cross-sectional studies as “low” to “very low”. Among other reasons, this is because the response rate in many of the studies was lower than 60%. Furthermore, most studies ascertained hypertension by means of self-reporting only.

In the evaluated cohort studies ($n = 2$) investigating the association between transportation noise and the incidence of hypertension, no increased risk of hypertension due to transportation noise was observed. This is confirmed by a recent meta-analysis, including the individual data from six cohort studies on the association between road traffic noise and the incidence of hypertension. The reason for the apparent discrepancy in the findings between the cross-sectional studies and the cohort studies is unclear.

Overall, we consider the quality of the evidence supporting an association between traffic noise exposure and hypertension to be “very low”, indicating that any estimate of effect is very uncertain.

Ischaemic heart disease

We evaluated 22 studies that have investigated the association between exposure to noise from air, road, and rail traffic and ischaemic heart disease (IHD). Half of them ($n=11$) were of cross-sectional design. The studies ($n = 8$) that investigated the impact of air traffic noise found indications of an increased risk of IHD. Aircraft noise was associated with the prevalence of IHD, the incidence of IHD, and mortality due to IHD. Only the association between aircraft noise and the incidence of IHD was statistically significant. We estimated an RR of 1.09 (95%CI: 1.04 – 1.15) per 10 dB after aggregating the results of two studies. Since most studies on the impact of aircraft noise were of ecological and cross-sectional design, the quality of the evidence from these studies, was mostly rated as “very low”. However, the results of the current review are consistent with the results of new longitudinal studies (not included in this review), which reported positive associations between aircraft noise and mortality due to IHD.

Overall, we rate the quality of the evidence supporting an association between air traffic noise and IHD as “low”, indicating that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

We found evidence that noise from road traffic is associated with an increased risk of IHD. An increase in road traffic noise was associated with significant increases in the prevalence of IHD, and the incidence of IHD. The relationship between noise from road traffic and the incidence of IHD was the most robust: After combining the results of three cohort studies and four case-control studies, we found an RR of 1.08 (95%CI: 1.01 – 1.15) per 10 dB (L_{DEN}) for the association between road traffic noise and the incidence of IHD within the range of approximately 40 – 80 dB L_{DEN} . We rated the quality of the evidence that comes from these longitudinal studies as “high”. Supporting evidence came from studies on the association between road traffic noise and the prevalence of IHD. However, we rated the quality of the evidence from these studies as

low. The results of the current review are furthermore strengthened by the results of several recently published longitudinal studies.

A visualization of the shape of the association between road traffic noise and the incidence of IHD, indicated that the risk of IHD increases continuously for road traffic noise levels from about 50 dB (L_{DEN}). This is consistent with the findings of another recent meta-analysis on the association between road traffic noise and IHD.

Overall, taking into account all the evidence from road traffic noise on IHD, we rate the quality of the evidence supporting an association between road traffic noise and IHD to be “moderate”, indicating that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. However, for road traffic noise and the incidence of IHD, we rated the quality of the evidence as high.

Compared with noise from road and air traffic, we found only a few studies ($n = 4$) that investigated the impact of noise from rail traffic. These had a cross-sectional design. After aggregating the results of the studies on the association between rail traffic noise and the prevalence of IHD, we found a non-significant RR of 1.18 per 10 dB (L_{DEN}).

Overall, we rate the quality of the studies supporting an association between rail traffic noise exposure and IHD to be “very low”, indicating that any estimate of effect is very uncertain.

Stroke

Compared with the number of studies on the impact of noise on hypertension and IHD, relatively few studies were available that investigated the impact on stroke ($n = 9$).

According to the results of the ecological and cross-sectional studies, an increase in aircraft noise was associated with an increase in both the prevalence and the incidence of stroke. None of these associations was statistically significant.

The observations found for the prevalence and incidence of stroke were supported only by the results of the ecological studies on the association between air traffic noise and mortality due to stroke. No association between air traffic noise exposure and mortality due to stroke was observed in the evaluated cohort study. This is consistent with the results of recent longitudinal studies, which showed no clear indications of an association between aircraft noise and mortality due to stroke. Unfortunately, we were not able to include these studies in the current evidence review.

The results of the studies that investigated the impact of road traffic noise were not consistent. Only for the association between road traffic noise and the incidence of stroke did we find a statistically significant RR of 1.14 (95%CI: 1.03 – 1.25) per 10 dB (L_{DEN}). This result was based on one cohort study, comprising 51,485 participants, including 1,881 incident cases of stroke.

In the evaluated cross-sectional and ecological studies on the association between road traffic noise and the prevalence of stroke or mortality due to stroke, no increased risk of stroke due to road traffic noise was observed. This was not consistent with the results of recently published longitudinal studies, which showed that an increase in road

traffic noise was statistically significantly associated with an increase in mortality due to stroke. Unfortunately, we were not able to include these new studies in the current evidence review.

As part of the current review, only one cross-sectional study was evaluated that investigated the association between rail traffic noise and the prevalence of stroke.

Overall, we rate the quality of the evidence supporting an association between traffic noise and stroke to be "low". This indicates that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Diabetes

For the current review, we were able to evaluate seven studies that investigated the association between environmental noise and the risk of diabetes. Four studies investigated the possible impact of transportation (air, road, rail traffic) noise. We found two studies that investigated the impact of air traffic noise on diabetes occurrence. In a cross-sectional study on the association between air traffic noise and the prevalence of diabetes, a non-significant RR of 1.01 per 10 dB (L_{DEN}) was found. In the evaluated cohort study on the association between air traffic noise and the incidence of diabetes, no increased risk of diabetes due to air traffic noise was observed.

We found indications that noise from road traffic increases the risk of diabetes. The two evaluated cross-sectional studies showed a positive but non-significant trend of the prevalence of diabetes with road traffic noise exposure. In the evaluated cohort study, a statistically significant association was found between road traffic noise and the incidence of diabetes. We estimated an RR of 1.08 (95%CI: 1.02 – 1.14) per 10 dB (L_{DEN}) across a noise range of approximately 50 – 70 dB.

Remarkably, an increase in rail traffic noise was associated with a decrease in the risk of diabetes in one cross-sectional study, while a cohort study found no statistically significant association.

Overall, we rate the quality of the evidence supporting an association between traffic noise and diabetes to be "low". This indicates that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Obesity

The number of evaluated studies that investigated the impact of noise on markers of obesity was limited to four: one cohort study and three cross-sectional studies. All the studies showed that an increase in traffic noise was associated with an increase in the risk of obesity, although this was present only in subgroups according to one study. An increase in air traffic noise of 10 dB (L_{DEN}) was associated with a significant increase in waist circumference of 3.46 (95%CI: 2.13 - 4.77) cm during 8 to 10 years of follow-up. The evidence on traffic noise affecting obesity markers is strengthened by the results of two recent longitudinal studies. Unfortunately, we were not able to include these studies in the current evidence review.

Overall, we rate the quality of the evidence supporting an association between traffic noise and markers of obesity to be "low". This indicates

that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Blood pressure in children

In total, we evaluated eight studies investigating the impact of noise on children's blood pressure. Seven studies were cross-sectional; one study reported both the results of cross-sectional and longitudinal analyses. With the exception of the association between road traffic noise at school and systolic blood pressure, we observed positive but non-significant associations between exposure to road traffic noise and increase in blood pressure. No combined exposure-response estimate could be computed from the studies on the impact of aircraft noise, since no quantitative results were provided in any of the studies. Overall, we rate the quality of the studies supporting an association between traffic noise and blood pressure in children, to be "very low", indicating that any estimate of effect is very uncertain.

Wind turbine noise

Overall, we evaluated only three cross-sectional studies that investigated the impact of noise from wind turbines on the cardiovascular and metabolic system. Important limitations of these studies were the low response rates (two studies had response rates of less than 60%), and the fact that in all studies the cardiovascular or metabolic endpoint was ascertained by a questionnaire or interview. In the studies, we observed that an increase in wind turbine noise was associated with non-significant increases in self-reported hypertension and non-significant decreases in self-reported cardiovascular disease. For self-reported diabetes, the results were inconsistent. Overall, we rate the quality of the studies supporting an association between exposure from wind turbine noise and deteriorations of the cardiovascular or metabolic system to be "very low", indicating that any estimate of effect is very uncertain.

Conclusions and recommendations

The current review shows that, despite the fact that a large number of studies have investigated the impact of noise on the cardiovascular system, but applying the GRADE, the quality of the evidence is often rated as relatively low. This does not mean that exposure to noise has no effect on the cardiovascular system, but encourages further research to improve the quality of the evidence. After all, there is a strong biological plausibility that noise affects human health. Furthermore, in many of the evaluated studies, we observed statistically significant associations between noise and cardiovascular endpoints. The most robust were the effects of road traffic noise on IHD.

On the basis of the results of cohort and case-control studies, we found high quality evidence that exposure to road traffic noise is associated with increased incidence of IHD.

This review also addressed the possible impact of noise on the metabolic system. In comparison with the studies on the impact of noise on the cardiovascular system, the number of available studies was rather limited. The results of these studies were not always consistent. In addition, the quality of the evidence was rather low. However, it is at this moment, given the limited number of available studies in particular,

too early to draw definite conclusions with regard to the impact of noise on the metabolic system.

The results of the current review show that at this moment, not enough studies of good quality are available that have investigated the impact of noise on the cardiovascular and metabolic systems. The plausibility of an association calls for further efforts with improved research. In order to improve the quality of the existing evidence, more studies with a cohort or case-control design are needed.

In order to improve the quality of the existing evidence, we also recommend that more well designed studies on health effects in relation to wind turbines and rail traffic noise are set up and carried out.

List of abbreviations

95%CI	95% confidence interval indicates the level of uncertainty around the measure of effect
X_2	Chi square
AMSTAR	measurement tool for the Assessment of Multiple SysTemAtic Reviews
ANOVA	analysis of Variance
AWACS	Airborne Warning and Control System
BCC	Berlin Case Control study
BMI	Body Mass Index
CPRD	Clinical Practice Research Datalink
EEA	European Environmental Agency
EMBASE	literature database
END	European Noise Directive
dB(A)	A-weighted decibel
DCH	Danish Diet Cancer and Health cohort
DEBATS	Discussion sur les Effets du Bruit des Aeronefs Touchant la Santé. French study on the relationship between aircraft noise exposure and hypertension
Df	Degrees of freedom
FORM	Grading system
GES	Gezondheidskundige Evaluatie Schiphol or Health Impact Assessment Schiphol
GINIplus	Multicentre, population-based German prospective birth cohort
GIS	Geographic Information System
HR	Hazard Ratio
H_z	Hertz
HYENA	Hypertension and Exposure to Noise near Airports. European multicentre study
ICCBP	The Inner City Child Blood Pressure study
ICD-10	10th edition of the International Classification of Diseases, a clinical cataloguing system
IHD	Ischaemic Heart Disease
I ²	A statistic that reflects the percentage of between-study heterogeneity
IR	Intermittency Ratio
KORA	Kooperative Gesundheitsforschung in der Region Augsburg, a research platform to examine the links between health, disease and the living conditions of the population
L_{Aeq}	A-weighted sound pressure level, equivalent to the total sound energy over a given period.
$L_{Aeq6-22hr}$	A-weighted equivalent sound pressure level in dB measured between 6:00 and 22:00 hours.
$L_{Aeq7-19hrs}$	A-weighted equivalent sound pressure level in dB measured between 7:00 and 19:00 hours.
$L_{Aeq16hr}$	A-weighted equivalent sound pressure level in dB measured over a 16-hour period.
$L_{Aeq24hr}$	A-weighted equivalent sound pressure level in dB measured over a 24-hour period.

L _{DAY}	Day equivalent level: A-weighted equivalent sound level, measured over a day (7:00 – 19:00 hrs)
L _{DEN}	Day-Evening-Night equivalent level: A-weighted equivalent sound level, measured over a 24-hour period with a 10 dB penalty added to the levels between 23:00 and 7:00 hours and a 5 dB penalty added to the levels between 19:00 and 23:00 hours to reflect people's extra sensitivity to noise during the night and the evening
L _{DN}	Day-night equivalent level: A-weighted, equivalent sound level, measured over a 24-hour period, with a 10 dB penalty added to levels between 23:00 and 7:00 hours
L _{Night}	Night equivalent level: A-weighted equivalent sound level, measured overnight (23:00 – 7:00 hours)
L _{pA,eq,18-06h}	A-weighted equivalent sound pressure level in dB measured between 18:00 and 6:00 hours.
LISAplus	A German prospective birth cohort study
MID	Minimal Important Difference
mmHg	Millimetre Mercury
NARoMI	Noise and Risk of Myocardial Infarction
NHMRC	National Health and Medical Research Council
NO	Nitric Oxide
NO ₂	Nitrogen Dioxide
NO _x	Generic term for the mononitrogen oxides NO and NO ₂
NORAH	Noise Related Annoyance, Cognition and Health
OR	Odds Ratio: a relative measure of effect that allows the comparison of an exposure or intervention group of a study with a control or non-exposed group
P	p-value
PIAMA	Preventie en Incidentie van Astma, Mijt en Allergie, large, ongoing population-based Dutch cohort study with prenatal inclusion and follow-up until the current age of 18 years
PREVEND	The Prevention of Renal and Vascular End-stage Disease (PREVEND)
PubMed	Literature database
Q	Q–statistic, reflecting the consistency of the effect estimates across studies
RANCH	Road traffic and Aircraft Noise exposure and children's Cognition and Health
REGICOR	Registre Gironi del Cor (Girona Heart Registry).
RIVM	National Institute of Public Health and the Environment
RR	Relative Risk, proportional measure estimating the size of the effect of a treatment compared with other interventions of no treatment at all
SAPALDIA	Swiss study on Air Pollution and Lung Disease in Adults, a cohort study in the Swiss population studying the effects of air pollution on respiratory and cardiovascular health in adults
SAS	Statistical Package
SDPP	Stockholm Diabetes Prevention Programme study
SEHS	Stockholm and Environmental Health Study
SERA	Study on the Impact of Airport Noise

SES	Socio-economic status
SNC	Swiss National Cohort study
SPANDAU	Spandauer Gesundheitstest (Spandau Public Health) a prospective cohort study
SPL	Sound Pressure Level
STATA	Statistical Package
WHO	World Health Organization

1 Introduction

During the past decades, several national and international organizations have published reviews of the scientific evidence on noise and health, and made recommendations for protecting human health from the adverse effects of environmental noise exposure, originating from various sources and community settings. Some of these documents also contain evaluations of the impact of noise on the cardiovascular system. In 1994, an International Committee of the Dutch Health Council stated that, "there was sufficient evidence of an association between environmental noise exposure and hypertension and ischaemic heart disease". The Committee estimated that the observed threshold for hypertension corresponded to an L_{DN} value of 70 dB for outdoor environmental noise exposure. The same threshold was suggested for ischaemic heart disease (IHD) [1]. In 1999, the World Health Organization (WHO) stated: "Epidemiological studies show that cardiovascular effects occur after long-term exposure to noise with outdoor $L_{Aeq24hr}$ values of 65 - 70 decibel (dB). However, the associations are weak. The association is somewhat stronger for ischemic heart disease than for hypertension" [2]. Recently, the European Environmental Agency (EEA) published a "Good Practice Guide" in which it concluded that "for hypertension the level above which effects start to occur or start to rise above background was 50 dB (L_{DEN}) outdoors; for ischemic heart disease this level was 60 dB (L_{DEN})" [3].

Both the Dutch Health Council, and the WHO, also made statements with regard to the effects on the cardiovascular system of noise exposure during the night. Note that studies on the relationship between noise and cardiovascular disease often used L_{day} as the exposure measure. In 2004, a committee of the Dutch Health Council concluded that, although a relationship between night-time noise exposure and an increased risk of hypertension and cardiovascular disease is likely, "there is limited, indirect evidence of a causal relationship between exposure to night-time noise and high blood pressure and cardiac disease" [4]. In 2009, the WHO drew a similar conclusion in its "Night Noise Guidelines" [5]. It concluded that "there is limited evidence that night-time noise is related to hypertension and myocardial infarction; although the studies were few or not conclusive, a biological pathway could be constructed from the evidence". The guidelines recommended a general threshold of 55 dB (L_{night}) outdoors at night for protection from cardiovascular disease, and suggested an optimal target of 40 dB [5].

In recent years, new evidence on the impact of environmental noise on the cardiovascular system has accumulated. An important observation is that some of the results that were published were based on data analyses of existing or ongoing cohort studies [6]. Another observation is that an increasing number of studies were published that investigated the combined effects of noise and air pollution. In addition, during the last few years, several studies have been published that deal with the possible effects of noise on the metabolic system, in particular with regard to outcomes such as diabetes and obesity [6].

In the WHO's existing health guidelines, the main sources of concern was transportation noise: mainly, road traffic and air traffic. Hardly any of the published studies reported on the health impacts of other noise sources, such as rail traffic and wind turbines. Consequently, the current guidelines do not address the potential health impacts of these noise sources. However, with the ongoing extension of railway transport facilities, and the substantial growth of wind energy facilities, the number of studies on the impact of rail traffic noise and on wind turbine noise has increased.

For these reasons, the WHO decided to revise its existing health guidelines. To this end, we reviewed all pertinent literature systematically, using a protocol developed for this purpose. Before we present the results of this review, we give a summary of the existing evidence of possible mechanisms leading to impairment of the cardiovascular system. In the background document "Biological effects and plausibility" Pershagen et al. [7] present a more thorough overview of the potential mechanisms behind the association between environmental noise exposure and cardiovascular as well as metabolic effects. Since we present a summary of this background document in the next section, we do not include any references.

1.1 Possible ways in which noise exposure affects the cardiovascular system

The most common explanation for the effects of noise on the heart and circulatory system is stress. Stress can have direct impacts, but can also manifest itself in adverse behaviour (e.g. smoking, drug use, drinking) and thus indirectly contribute to health problems. Furthermore, in people who already suffer from cardiovascular disease, their health may deteriorate through exposure to noise, so subclinical disorders may become manifest.

First, exposure to noise can lead to *physiological* stress. This caused by physiological and biochemical reactions, which usually occur acutely, such as the increase of blood pressure and the excretion of stress hormones including cortisol and adrenaline.

The experimental studies that investigated the effects of short-term noise exposure found acute biochemical, physiological, and cardiovascular changes. These changes mark a common physiological stress reaction of short duration that occurs because of the activation of the autonomous nervous and endocrine systems. It appeared that these acute effects are the same as the effects caused by an ordinary stress reaction. Some authors assume that the effect of noise on the auditory system is transmitted to the Reticular Arousal System (RAS) and the hypothalamus, where both neuronal and hormonal (hypothalamic pituitary adrenal axis) may be activated. When stressed, the body secretes adrenal medullary hormones (catecholamines) such as noradrenaline. These hormones can raise peripheral resistance and increase blood pressure as well as heart rate. If these reactions are repeated, or last long enough, they can create chronic deregulations and become risk factors for cardiovascular disease.

Second, exposure to noise can cause *psychological* stress. Here it is of importance how a person perceives and appraises the different sounds

in their daily environment. Appraisal can be considered as a process in which a person determines whether a situation poses a threat, challenge or potential harm or loss, on the basis of which they choose a response strategy to deal with the situation. In other words, it is a process that determines whether sounds that are present in our environment are regarded as being "noisy". Earlier research suggested that the appraisal of the stressor is one of the essential factors predicting the short- and long-term health effects of exposure to daily repeated stressors such as environmental noise. Annoyance is an indicator that is often used in the appraisal of noise. The assumption is that a negative appraisal is manifest in a high annoyance score. The latest developments in the field of noise and annoyance can be found in the evidence review dealing with annoyance by Guski et al. [8].

The cardiovascular effects related to noise exposure might not only be a direct effect of the exposure itself; they may also be the consequence of a decrease in sleep quality, caused by noise exposure during the night. Chronic night-time noise exposure might disturb the secretion of stress hormones such as cortisol, which could affect health. The latest developments regarding the impact of noise on sleep are presented in the evidence review dealing with the effects on sleep written by Basner et al [9].

People living in a city or close to roads, are exposed not only to traffic noise, but also to air pollution generated by traffic. Several studies indicate that exposure to air pollution may affect the cardiovascular system. Air pollution and noise from road traffic share the same source, so the effects could be attributed to both exposure types. This may give rise to confounding, where it is difficult to ascribe observed effects to a specific exposure, as well as to effect modification, where the two exposures interact in causing cardiovascular effects.

Until now, high blood pressure (hypertension) and IHD have been the main outcomes of concern in observational studies on the impact of noise on the cardiovascular system. This is remarkable, given the fact that there is good evidence that hypertension and/or increased blood pressure is associated not only with a higher risk of IHD, but also with a higher risk of stroke.

1.2 The impact of noise on the metabolic system

Other health endpoints that could be associated with noise exposure, but are not often investigated, are obesity and diabetes. Stress may contribute to these effects: noise acts as a stressor and activates the hypothalamic pituitary adrenal axis, increasing cortisol levels and inhibiting insulin secretion as well as peripheral insulin sensitivity. In addition, disruption of normal sleep patterns and chronic sleep deprivation can induce diabetes via increased fasting glucose and appetite modulation as well as general dysregulation of the metabolic and endocrine functions.

1.3 Children

Children may be a vulnerable group in relation to the health effects of noise exposure, since they tend to spend more time outdoors than adults do, and because they behave differently. Furthermore, children might be more susceptible to noise exposure for different reasons: (i) their organs are not fully developed; (ii) they are not always aware of the dangers of such exposure; and (iii) they have not (fully) developed coping mechanisms and cannot change their exposure situation in the same way as adults. In addition, studies have demonstrated that many adult diseases may originate in childhood. Although there are guidelines available that aim to reduce environmental noise exposure in settings where most children spend part of their time, none of these guidelines takes into account cardiovascular or metabolic effects in children.

2 Existing reviews of studies on the impact of noise on the cardiovascular and metabolic systems

During the first step in our evidence review, we had to identify and select systematic reviews of sufficient quality that described the impact of exposure to noise from several sources on the cardiovascular system, in different settings and populations. To this end, the WHO carried out a bibliographic search. In addition, the literature files of the National Institute of Public Health (RIVM), and the proceedings of conferences on noise and health were scanned. In order to assess whether the identified publications investigated the impact of exposure to environmental noise on the cardiovascular system, we checked their titles and abstracts. In total, we identified and selected 33 papers and reports [10-42]. The quality of these selected reviews was assessed by two reviewers (EvK and MF) using the AMSTAR tool [43]. Of these 33 systematic reviews, we selected 12 reviews that were identified as of "sufficient quality" (AMSTAR score of 8/11 or higher) or "moderate quality" (AMSTAR score of 4-7/11) and relevant for our evidence review [11, 18-20, 22, 24, 27, 28, 33, 37, 38, 41]. During the process of data-extraction for the current evidence review, we observed that several new reviews have been published. We considered four of these newly published reviews [44-47] to be relevant and included them in the current review. One review was an update of a review that was already included [44]; therefore, we considered 15 systematic reviews in total.

Table 2.1 presents some characteristics of the selected reviews. The number of studies on the impacts of noise on the cardiovascular system that were evaluated in these reviews ranged from 3 to 62. The time range of the studies covered by the reviews was from 1965 to June 2014. Most of the participating studies were carried out among adults, investigating the impacts of road and aircraft noise exposure. Three reviews also aimed to include studies that investigated the impact of rail traffic noise exposure; two reviews included studies that investigated the impact of occupational noise exposure; and one review included studies that investigated the impact of wind turbine noise exposure. Nine reviews also included a meta-analysis.

Table 2.1: Characteristics of the 15 systematic reviews that were identified and selected, and that investigated the impact of aircraft, road, rail traffic, and/or wind turbine noise exposure on the cardiovascular system.

First author and reference	Studies included							Meta-analysis
	Number evaluated	Number of participants	Time range	Countries*	Population**	Noise source†	Health endpoint‡	
Argalášová-Sobotová [27]	18	22 - 3,622	1965 – 2012	CR, Lit, Sb, Mc, Slo, Rus	1	R, A	0, 1, 2	No
Babisch [23, 37]	62	94 – 145,000	NR	Worldwide	1, 2	R, A, T	0, 1, 2	Yes
Babisch [22]	~28		NR	Worldwide	1, 2	A	1	Yes
Babisch [28]	12	243 – 412,420	NR	Eur, Jap, Can	1	R	2	Yes
Banerjee [46]	12	417 – 809,379	1980 – 2010	Eur	1	R, A	2	Yes
Di Huang [47]	5	1,500 – 5,828	1977 – 2010	NL, Swe, Aus	1	A	1	Yes
Dzhambov [45]	9	875 – 57,053	Up to June 2014	Can, Den, Ger, Swe, SKor, USA	1	R, A, O	3	Yes
Hohmann [19]	11	43 - 1,542	Up to Apr 2011	Eur, USA	1, 2	R, A, T	0, 2	No
Merlin [33]	3	340 – 740	1980 – 2012	Swe, NL	1	W	1, 3, 4	No
Ndrepepa [20]	8	375 - 4,320	Up to November 2009	Ger, Au, Sb, UK, Eur	1	R	1, 2	No
Paunović [18]	13	115 - 1,542	1980 – 2010	USA, Ger, Aus, NL	2	R, A	0	No
Tétreault [11]	9	719 – 445,868	Up to Nov 2012	Eur, Can	1, 2	R	1, 2	No
Van Kempen [24]	43	46 – 35,150	1970 – 1999	Worldwide	1	O, R, A	0, 1, 2	Yes
Van Kempen [41]	27	357 – 38,849	Up to 2010	Eur, Jap	1	R	1	Yes
Vienneau [38, 44]	10	243 - ~22.5 million	1994 – 2014	Eur, Can, USA	1	R, A, T	2	Yes

Abbreviations: NR = Not Reported; *) Au = Austria, Aus = Australia, Can = Canada, CR = Czech Republic, Den = Denmark, Eur = Europe, Ger = Germany, Jap = Japan, Lit = Lithuania, Mc = Macedonia, NL = Netherlands, Rus = Russia, Sb = Serbia, SKor = South Korea, Slo = Slovakia, Swe = Sweden, UK = United Kingdom, USA = United States of America; **) 1 = Adults, 2 = Children; †) O = occupational noise, R = road traffic noise, A = air traffic noise, T = rail traffic noise, W = wind turbine noise; ‡) 0 = blood pressure, 1 = hypertension, 2 = Ischaemic Heart Disease (including myocardial infarction, angina pectoris), 3 = diabetes, 4 = cardiovascular disease.

2.1 Aircraft noise

2.1.1 Hypertension

Five reviews (described in six references) attempted to identify and include studies that investigated the impact of air traffic noise on hypertension [22-24, 27, 37, 47], of which three also included a meta-analysis [22-24, 37, 47].

In 2002, Van Kempen et al. published a review that aimed to gain insight into the potential impact of noise exposure on cardiovascular diseases in adults [24]. They carried out a meta-analysis in order to disentangle the sources of heterogeneity among the study results. From several bibliographic literature resources, they systematically observed more than 500 observational studies involving the association between noise exposure and blood pressure and/or IHD, published between 1970 and 1999, in English, Dutch or German. Finally, Van Kempen et al. selected 43 studies for data extraction. Although they presented the results of these studies in a systematic way, an evaluation of the quality of each study was lacking. It appeared that two of the selected studies investigated the association between aircraft noise exposure and hypertension [48, 49]. Based on the results of only one cross-sectional study which was carried out among people living around Schiphol-Amsterdam-Airport in the 1970s, Van Kempen et al. presented an exposure effect estimate of a Relative Risk (RR) of 1.59 (95%CI: 1.30 – 1.93) per 10 dB increase in noise level (expressed in $L_{Aeq7-19hrs}$) [49].

For his review, Babisch [23, 37] identified and selected 62 studies that investigated the cardiovascular effects of road, rail, and/or air traffic noise, and were published in the period between the 1960s and 2005. Babisch identified and selected the studies based on his own knowledge of the topic and the literature. Of these 62 studies, 16 investigated the effects of air traffic noise exposure on hypertension [48-64]. Babisch presented the results of the studies in a systematic way. The results showed consistently higher risks of hypertension in higher-noise-exposed areas. Although for five studies [49, 58-60, 62-64] quantitative estimates could be derived, Babisch [37] decided not to combine the results of these studies for an exposure response relationship. He based his decision on the result of an evaluation of the selected studies according to the following criteria: (1) peer-reviewed in the international literature, (2) reasonable control of possible confounding, (3) objective assessment of exposure, (4) objective assessment of outcome, (5) type of study, and (6) availability of (information for) exposure response assessment.

In response to the need for a quantitative risk assessment for burden of disease estimations, Babisch and Van Kamp [22] made an attempt to derive an exposure response relationship for the impact of air traffic noise on the cardiovascular system. They attempted this as part of their review on air traffic noise exposure and cardiovascular disease in adults and children. Together with the authors' knowledge about new publications until 2009, Babisch's earlier review [23, 37] formed the basis of the identification of studies. Eventually, Babisch and Van Kamp presented the results of more than 28 studies. For the meta-analysis of the effect of air traffic noise on hypertension in adults, they selected five

cross-sectional studies [49, 58-60, 65, 66]. According to the authors, these five studies full filled the minimum requirements regarding the validity of the exposure assessment, outcome, and statistical control for confounding factors. Further evaluation of the quality of each individual study was lacking, however. After combining the results, Babisch and Van Kamp estimated an RR (expressed as an OR) of 1.13 (95% CI: 1.00 – 1.28) per 10 dB increase of the noise level (expressed in L_{DN}) (see Figure 2.1).

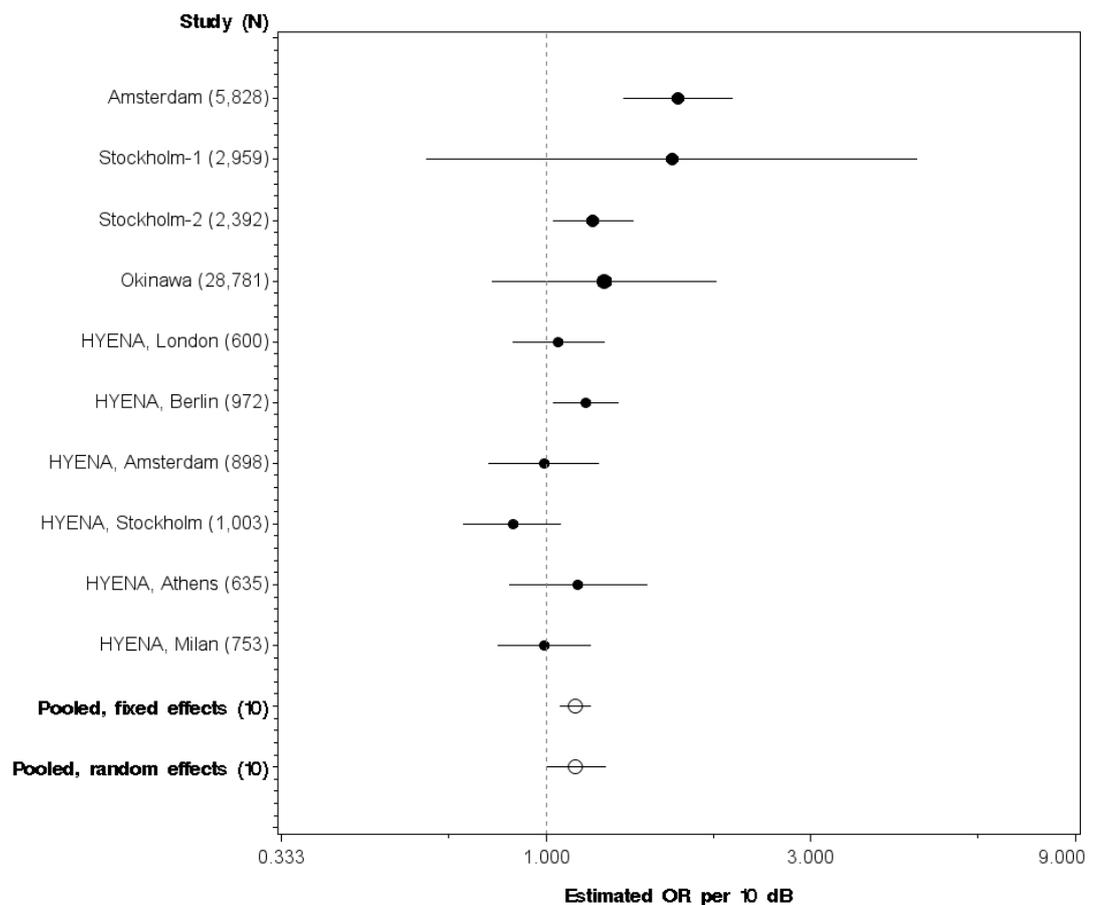


Figure 2.1 Association between air traffic noise exposure and the prevalence of hypertension. The dashed vertical line corresponds to no effect of noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI. The white circles represent the summary estimate and 95% CI. Derived from Babisch and Van Kamp (2009) [22].

In 2013, Argalášová-Sobotová et al. [27] published a systematic review of studies on the cardiovascular effects of environmental noise on adults, conducted since 1965 in Central, Eastern and South-Eastern Europe and Newly Independent States. By means of a systematic literature search of accessible bibliographic databases, the researchers identified 18 papers. Although four [67-70] of these studies investigated the impacts of aircraft noise exposure on the cardiovascular system, none of them investigated the impact on hypertension.

In 2015, Di Huang et al. published the results of a meta-analysis of the association between air traffic noise exposure and hypertension [47]. Of

the 156 articles that they systematically identified, they selected and evaluated five studies [49, 60, 61, 71, 72]. After combining the results of four cross-sectional studies, they estimated an odds ratio (OR) of 1.63 (95%CI: 1.14 – 2.33) for a contrast between non-exposed and exposed, meaning that persons “exposed” to air traffic noise exposure have a higher risk of hypertension than the reference group (see Figure 2.2). The problem however, is that the studies that were included in this meta-analysis were on different reference groups. Heterogeneity was assessed as significant ($I^2 = 81.2\%$, $p = 0.001$). As opposed to the other reviews investigating the impacts of aircraft noise, the review of Di Huang et al. included a quality assessment of each study evaluating among other things: (i) whether the study had been published in a peer-reviewed journal, (ii) the study design, (iii) the validity of the outcome assessment, (iv) whether confounding factors were controlled for, and (v) the response rate of the study. The higher a study scored, the better its quality. Di Huang et al. included in their meta-analysis only the studies that scored “good” and “very good”.

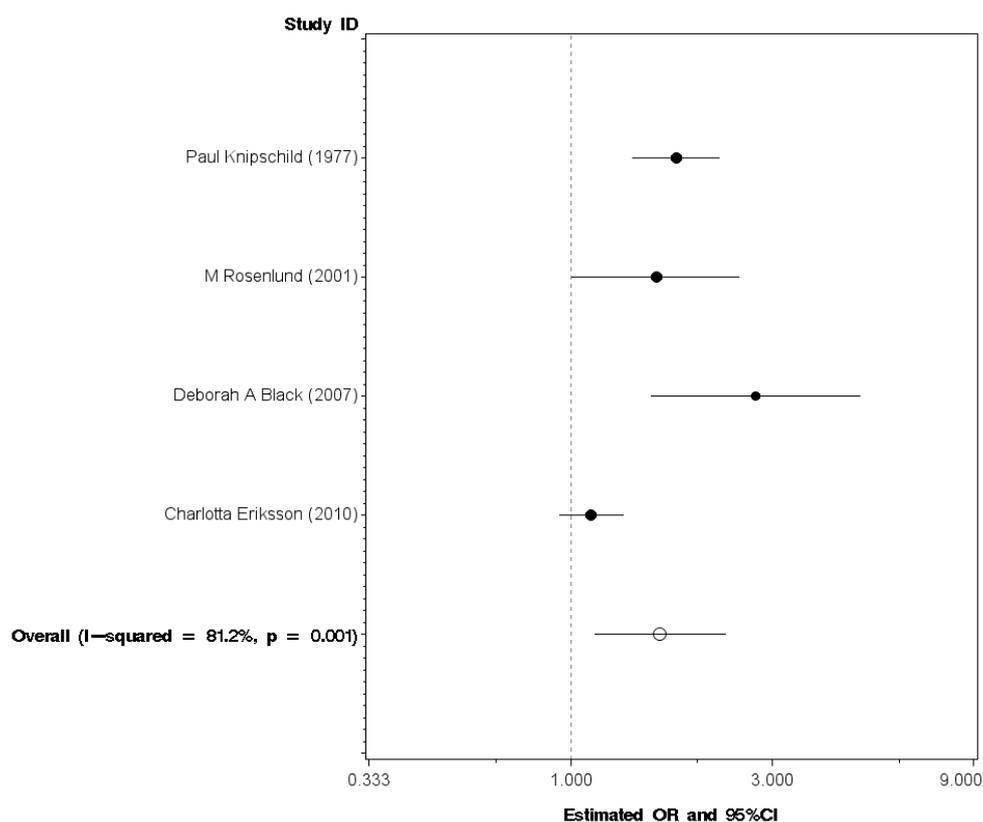


Figure 2.2 Forest plot of meta-analysis of studies on the impact of air traffic noise on hypertension. Individual studies represented by OR and 95%CI for the group exposed to air traffic noise versus a reference group (Source: [47]).

2.1.2 Ischaemic heart disease and other cardiovascular diseases

In total, we have identified six reviews that have attempted to identify and include studies that investigated the impact of air traffic noise on IHD [19, 24, 26, 27, 37, 44, 46]; three reviews also included a meta-analysis [24, 44, 46](see Table 2.1).

In their study, Van Kempen et al. [24] included four studies on the association between air traffic noise exposure and indicators of IHD [48, 49, 73, 74]. IHD indicators were angina pectoris, the use of cardiovascular medicines, and consultation of a specialist and/or general practitioner. None of these indicators was associated with exposure to air traffic noise. A quality judgement per study was lacking.

A few years later, Babisch [37] selected for review seven studies [48-50, 53, 54, 57, 63, 64] that investigated the effects of air traffic noise exposure (expressed in decibels) on IHD. Four of them investigated the effects of air traffic noise exposure on IHD prevalence, whereas three studies investigated the effects on the use of cardiovascular medication. In his study, Knipschild [48] reported positive associations between air traffic noise exposure and the prevalence of angina pectoris, heart trouble, and ECG ischaemia; the results of the other three studies were mixed: The Spandau study [62] found a positive and statistically significant association for angina pectoris, and a negative but not statistically significant association for myocardial infarction. Bluhm et al. [64] found the reverse: they reported a negative association for angina pectoris and a positive association for myocardial infarction. Neither of these associations was statistically significant. The results of the study carried out around a military airport did not show a clear trend. On the other hand, the results of the studies on the impact on the use of cardiovascular medication [49, 50, 57] were more consistent: all studies found a positive trend: air traffic noise exposure was related to a (sometimes statistically significant) increase in the prevalence of cardiovascular medication use. Babisch [37] decided not to combine the results of the studies on the impact of air traffic noise on IHD to generate an exposure response relationship. He based his decision on the result of an evaluation of the selected studies on several pre-defined criteria. These were already mentioned in section 2.1.1.

Argalášová-Sobotová et al. [27] identified only two studies that investigated the impact of air traffic noise on cardiovascular disease [67, 69]. They systematically evaluated and presented the characteristics and results of these studies; a judgement on the individual quality of the studies was lacking, however. Both selected studies were ecological studies. The results of these studies were consistent: both found a higher prevalence or incidence of cardiovascular disease in groups of people living close to an airport compared with people living further away.

For their meta-analysis on the relationship between traffic noise exposure and IHD, Vienneau et al. [44] selected five cohort studies, four case-control studies, and two ecological studies. The researchers identified these studies by means of a systematic search in PubMed and EMBASE. Three of the 11 identified studies investigated the effects of aircraft noise exposure on IHD [75-77]. After combining the results of these three studies, Vienneau et al. [44] found an RR of 1.06 (95%CI: 1.04 – 1.08) per 10 dB increase in aircraft noise level (L_{DEN}). A separate judgement of the quality of these studies was lacking.

More recently, Banerjee [46] published a meta-analysis of cross-sectional studies on the association between transportation noise exposure and cardiovascular disease endpoints among adult populations. The review identified 14 studies for data extraction.

Banerjee included twelve of the identified studies in a meta-analysis. Five of these studies investigated the effects of aircraft noise [53, 57, 62, 74, 78, 79]. Banerjee [46] found that persons exposed to air traffic noise have a non-significant higher risk of IHD compared with a reference group. The problem, however, is that the studies that were included in Banerjee's meta-analysis [46] used different reference groups. It was not possible to derive the increase in risk of IHD per increase in aircraft noise levels. As was the case in the other reviews investigating the impacts of aircraft noise exposure, a separate judgement of the quality of the selected and evaluated studies was lacking in the review.

2.2 Road traffic noise

2.2.1

Hypertension

Seven reviews have attempted to identify and include studies that have investigated the impact of exposure to road traffic noise on hypertension [11, 19, 20, 24, 27, 37, 41]. Two of these also included a meta-analysis, combining the results of studies on the association between road traffic noise and hypertension (see Table 2.1).

In their 2002 review, Van Kempen et al. [24] evaluated six studies that investigated the association between road traffic noise exposure and hypertension [80-87]. From these studies, they were able to derive only two effect estimates. After combining these, it appeared that exposure to road traffic noise was not associated with the *prevalence* of hypertension. Van Kempen et al. estimated an RR of 0.95 (95%CI: 0.84 – 1.08) per 5 dB(A). They did not provide an evaluation of the individual quality of the studies included in their review.

In his review, Babisch [37] included 15 studies that investigated the effects of road traffic noise exposure on hypertension in adults [62, 82-85, 87-106]. The results of these studies were not consistent. Compared with the older studies, the newer studies included in this review suggested a higher risk of hypertension in subjects exposed to high levels of road traffic noise. Consequently, Babisch [37] decided not to combine the results of these studies for an exposure response relationship.

In 2012, Van Kempen and Babisch published a meta-analysis of the relationship between road traffic noise exposure and hypertension [41]. To this end, they evaluated 27 observational studies [65, 82, 84, 85, 87-89, 91, 94, 95, 98, 103-105, 107-115]. After aggregating the results of 24 of these studies, they found that an increase in road traffic noise exposure was associated with a statistically significant increase in the prevalence of hypertension. Data-aggregation revealed an OR of 1.03 (95%CI: 1.01 – 1.06) per 5 dB increase in the 16-hour average road traffic noise level (see Figure 2.3). They did not provide an evaluation of the individual quality of these studies.

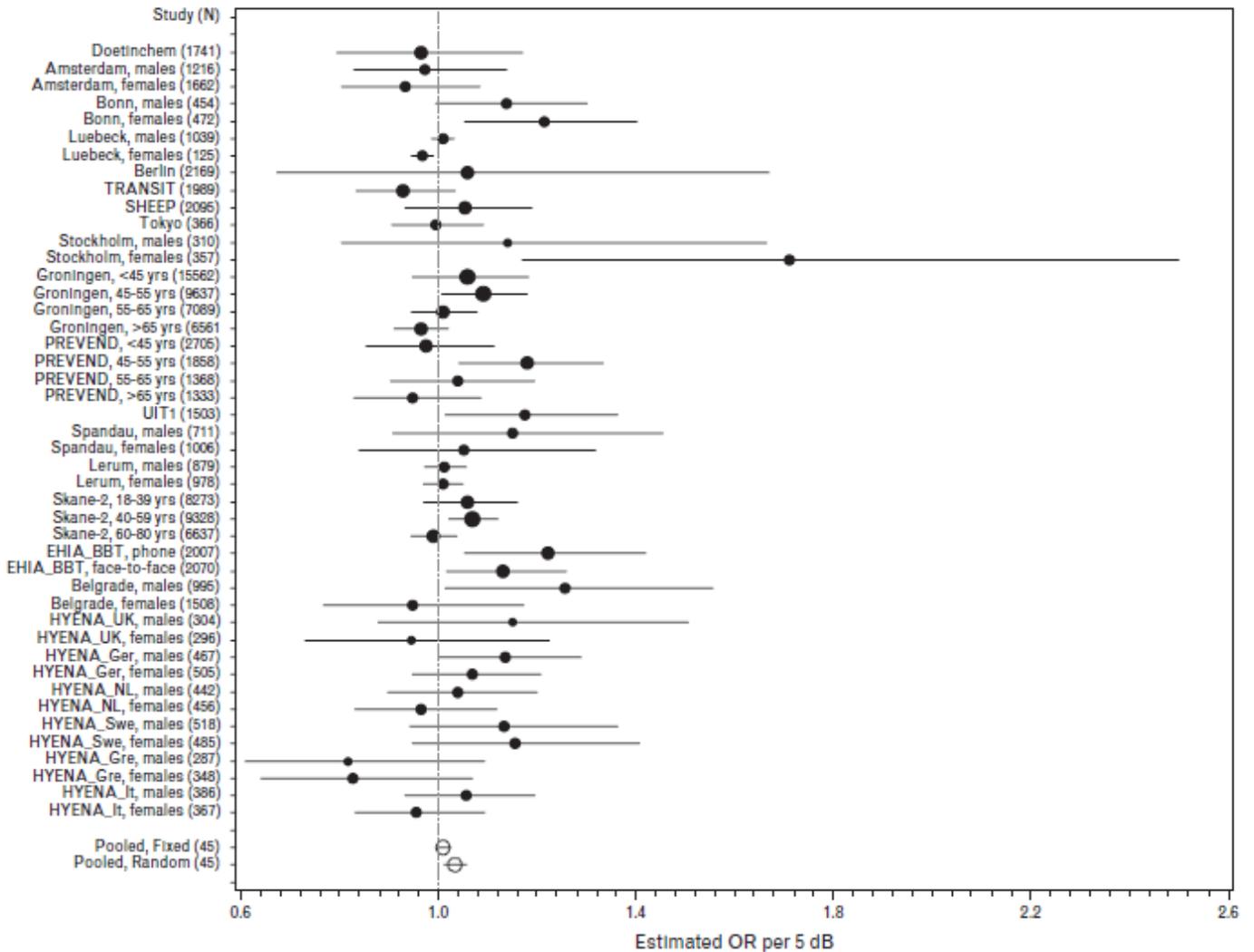


Figure 2.3 Association between road traffic noise exposure and the prevalence of hypertension. The dashed vertical line corresponds to no effect of noise exposure. The black circles correspond to the estimated OR per 5 dB and 95% CI. The white circles represent the summary estimates and 95% CI. Derived from Van Kempen and Babisch [41].

In 2013, several reviews were published: One of the aims of the review published by Hohmann et al. [19] was to evaluate studies on the association between long-term noise exposure and stress indicators, cardiovascular risk factors, and immune-mediated diseases in children and adolescents. Of the 447 articles that Hohmann et al. (2013) systematically identified, they selected 25 studies. None of these studies reported on the impact of road traffic noise exposure on the risk of hypertension.

For the purpose of their 2013 review, Tétreault et al. [11] identified studies that investigated the association between road traffic-related noise or air pollution exposure, and cardiovascular outcomes. They investigated the mutually confounding effect of noise or air pollution in these associations. Tétreault et al. identified more than 220 studies that

were published until November 2012. They selected nine studies for data extraction, using planned criteria. Eight studies (nine papers) reported on the impact of road traffic noise exposure [107, 109, 116-122]. Two studies (both described in [109]), included the association with hypertension. Both studies were cross-sectional and carried out in the Dutch city of Groningen. Tétreault et al. [11] classified both studies as having minor selection bias since the response rate was between 30% and 60%. Because the air pollution indicator was not specific to road traffic, Tétreault et al. also suspected the studies of minor exposure misclassification bias. However, both studies assessed exposure at the residential address only. The results of the studies were consistent: after adjusting for confounders, the studies reported positive associations between exposure to road traffic noise and the prevalence of hypertension. None of these associations was statistically significant.

As part of their systematic review, Argalášová-Sobotová et al. [27] identified three studies that had investigated the impacts of road traffic noise exposure on hypertension [115, 123, 124]: two cross-sectional studies and one case-control study. They did not include an evaluation of the quality of the individual studies. The results of the studies were consistent: all three studies found a positive association between exposure to traffic noise and hypertension.

In their review, Ndrepepa and Twardella [20] attempted to assess whether there was an association between annoyance from road traffic noise and cardiovascular diseases in adults. They identified 271 publications, published until November 2009, and selected eight studies for data extraction. Seven studies (six papers) reported on the association between annoyance due to road traffic noise exposure and hypertension [89, 101, 102, 125-127]. Three of these studies also assessed modelled or measured objective road traffic noise levels [89, 101, 126]. Unfortunately, Ndrepepa and Twardella [20] were not able to provide the associations between these objective road traffic noise levels and hypertension. The review by Ndrepepa and Twardella [20] included an assessment of the quality of each study, which included the following items: (i) whether the study had been published in a peer-reviewed journal, (ii) the study design, (iii) the validity of the outcome assessment, (iv) control for confounding factors, and (v) the response rate. The higher a study scored, the better its quality. Ndrepepa and Twardella [20] rated the quality of the evaluated studies investigating the association between road traffic noise annoyance and hypertension, and including actual road traffic noise levels, as "good".

2.2.2 *Ischaemic heart disease*

Nine reviews attempted to identify and include studies that have investigated the impact of exposure to road traffic noise on IHD [11, 19, 20, 23, 24, 27, 28, 37, 44, 46]. For their systematic review (including a meta-analysis), Van Kempen et al. [24] evaluated eight studies on the effects of road traffic noise exposure on IHD [73, 80, 81, 83, 86, 87, 96, 102, 103]. They found that road traffic noise exposure was positively but statistically not significantly associated with myocardial infarction. After aggregating the results of the cross-sectional studies on the impact of noise on the *prevalence* of myocardial infarction, they found an RR of 1.03 (95%CI: 0.99 – 1.09) per 5 dB increase in road traffic noise level

($L_{Aeq6-22hr}$). Unfortunately, it was not possible to aggregate the results of the cohort-studies. Van Kempen et al. found that road traffic noise exposure was positively associated with IHD. After combining the results of the cross-sectional studies on the impact on the prevalence of IHD, they found a statistically significant RR of 1.09 (95%CI: 1.05 – 1.13) per 5 dB increase in road traffic noise level ($L_{Aeq6-22hr}$). However, data aggregation of the results of the cohort studies [128-132] did not result in a statistically significant effect estimate (RR of 0.97 (95%CI: 0.90 – 1.04) per 5 dB). Van Kempen et al. [24] did not find an association between road traffic noise exposure and the prevalence of angina pectoris: data aggregation of the results of two cross-sectional studies revealed an RR of 0.99 (95%CI: 0.84 – 1.16) per 5 dB. The authors were not able to provide an evaluation of the individual quality of the studies.

For his review, Babisch [37] evaluated the results of 15 studies (20 papers) [53, 54, 62, 82, 83, 87, 89, 91-93, 96-105] that investigated the impact of road traffic noise on IHD. Babisch [37] found not much indication of a higher IHD risk among subjects living in areas with a daytime average sound pressure level of less than 60 dB(A) across the studies. For higher noise categories, he consistently found a higher IHD risk among the studies. However, the association rarely achieved statistical significance. As part of his review, Babisch [37] also carried out a meta-analysis on the association between road traffic noise exposure and the *incidence* of myocardial infarction. He selected four studies according to the following criteria: (1) whether the study had been peer-reviewed in the international literature, (2) whether there had been reasonable control of possible confounding, (3) whether the exposure had been assessed objectively, (4) whether the outcome had been assessed objectively, (5) type of study, and (6) whether the study included an exposure response assessment. Subsequently, he pooled the results of these four studies and derived a summarizing OR of 1.17 (95%CI: 0.87 – 1.57) per 10 dB ($L_{Aeq6-22hr}$).

Recently, Babisch [28] supplemented his meta-analysis [37, 133] with the results of new studies that had been published since 2008. This time, he included not only the results of cohort and case-control studies but also the results of cross-sectional studies. After pooling the results (seven effect estimates) of five cohort studies (presented in four papers) [116, 119, 122, 129] he estimated a statistically significant OR of 1.07 (95%CI: 1.01 – 1.14) per 10 dB increase in road traffic noise level (L_{DN}). After combining the results of the case-control studies (five effect estimates) Babisch [28] found an OR of 1.10 (95%CI: 0.99 – 1.22) per 10 dB; for the cross-sectional studies (five effect estimates) he found an OR of 1.11 (95%CI: 0.94 – 1.31) per 10 dB. Babisch [28] was not able to provide an evaluation of the individual quality of the studies included in his review.

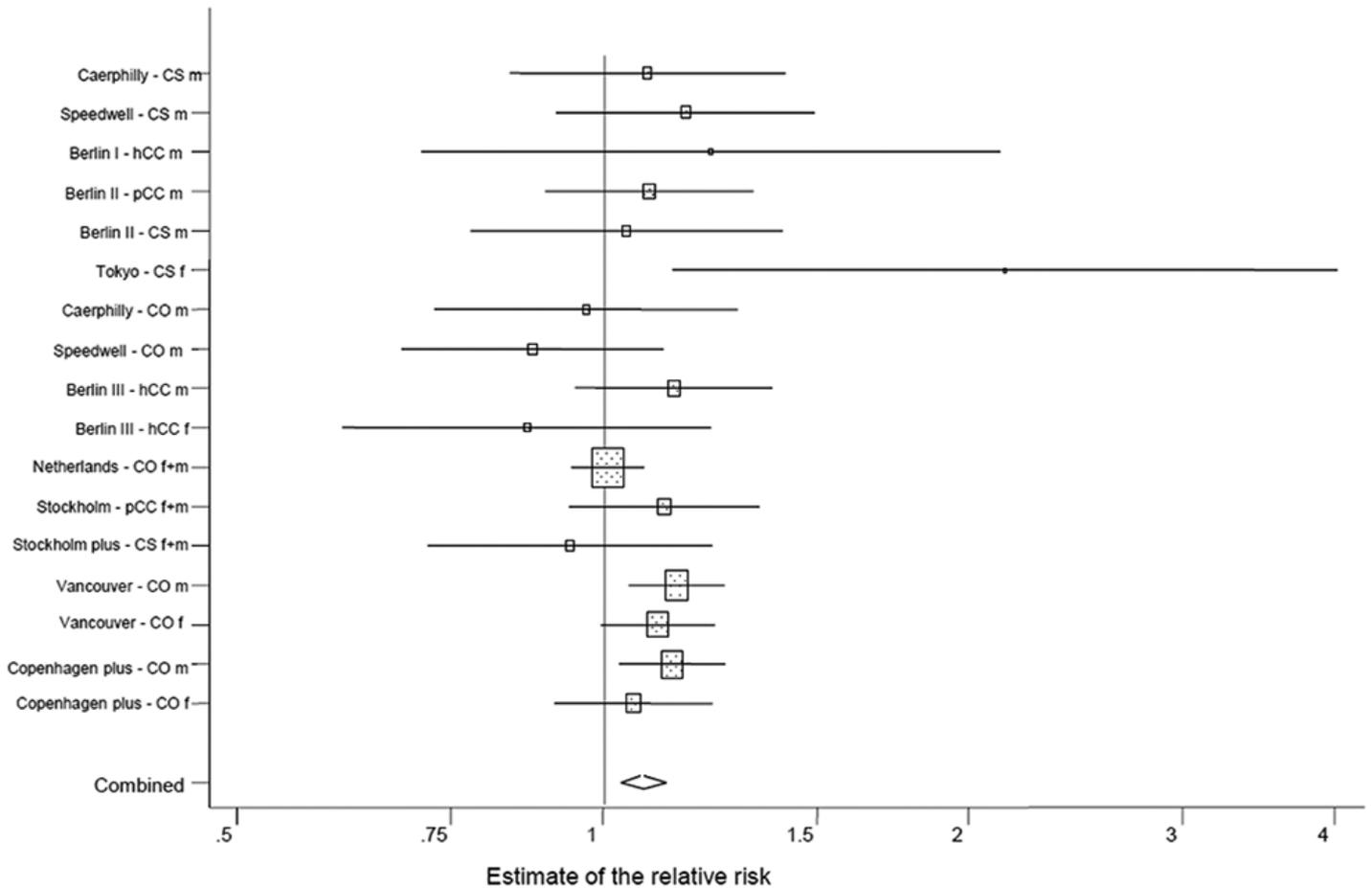


Figure 2.4: Forest plot of the Relative Risk per 10 dB(A) increase in noise level of the association between road traffic noise and coronary heart diseases (11 studies, 17 observations). Source: Babisch [28]

The results that were reported by Babisch [28] for road traffic noise, were comparable with the findings of a meta-analysis carried out by Vienneau et al. [38, 44]. For their study, Vienneau et al. [38, 44] identified 10 studies involving the association between road, rail or air traffic noise and myocardial infarction or coronary disease, published for the 20-year period prior to January 2014. To this end, they searched several bibliographical literature resources (including the grey literature). Seven of the identified studies (described in six papers) investigated the impact of road traffic noise [103, 107, 116, 122, 129, 131]. After pooling the results of these studies (eight estimates derived from seven studies), Vienneau et al. [38, 44] found an RR of 1.04 (95%CI: 1.00 – 1.10) per 10 dB (L_{DEN}). Like those of Babisch [28] and Van Kempen et al. [24], the meta-analysis of Vienneau et al. [38, 44] did not include a systematic judgement of the quality of the included studies.

More recently, Banerjee [46] published a meta-analysis including cross-sectional studies on the association between transportation noise exposure and cardiovascular disease endpoints among adult populations. Nine [53, 87, 89, 92, 97, 98, 102, 103, 126] of the 14

studies that were evaluated investigated the effects of road traffic noise. Banerjee [46] found that persons exposed to road traffic noise have a non-statistically significant higher chance of IHD than the reference group. The problem however, is that the studies that were included in Banerjee's meta-analysis [46] used different reference groups. It was not possible to derive the increase in the risk of IHD for a certain increase in road traffic noise level. Banerjee [46] did not provide a systematic assessment of the quality of the included studies.

For their review Tétreault et al. [11], identified eight studies (seven papers) that investigated the impact of road traffic noise exposure. Four of these studies investigated the impact on IHD (including myocardial infarction) [107, 116, 119, 122]. The results of the review suggested that after considering air pollution exposure in the association between road traffic noise exposure and cardiovascular disease, the effect estimates changed mostly less than 10%.

In 2013, Argalášová-Sobotová et al. [27], published a systematic review of studies on the cardiovascular effects of environmental noise in adults conducted since 1965 in Central, Eastern and South-Eastern Europe and Newly Independent States. They identified five studies that investigated the association between road traffic noise exposure and IHD [84, 134-137]. The results of these studies were quite consistent. All the studies reported positive, though not always statistically significant associations between exposure to road traffic noise and the different indicators for IHD.

In their review, Ndrepepa and Twardella [20] evaluated eight studies that investigated the association between annoyance from road traffic noise and IHD [89, 101, 102, 125-127, 130, 131]. Five studies [89, 101, 126, 130, 131] also reported the modelled and/or measured road traffic noise levels. The individual quality of these studies was very different, with quality scores ranging from 4 ("fair") [89] to 15 ("very good") [130]. Unfortunately, the associations between road traffic noise levels and IHD from the separate studies were not reported by Ndrepepa and Twardella [20].

2.3 Rail traffic noise

Three reviews attempted to identify and compare studies that investigated the impact of rail traffic noise on hypertension in adults [19, 37, 44]. In his review, Babisch [37] identified two studies that investigated the effects of exposure to rail traffic noise [88, 106]. Both were cross-sectional. Babisch was able only to report the results of the study that was carried out by Bluhm et al. [106]: After adjustment for a range of confounders, Bluhm et al. found that an increase in the exposure to rail traffic noise was associated with a decrease in the prevalence of hypertension. Unfortunately, Babisch [37] was not able to report the results of the study carried out by Lercher et al. [88]. Within their reviews, both Hohmann et al. [19] and Vienneau et al. [44] were not able to identify any studies that investigated the impact of rail traffic noise on hypertension. None of the three reviews [19, 37, 44] identified any studies that investigated the impact of rail traffic noise on IHD.

2.4 The impact of noise on stroke

None of the selected reviews reported on the effects of aircraft, or rail traffic noise on stroke. Only the review by Tétreault et al. [11] assessed the impact of road traffic noise exposure on stroke. They identified one study [138] in which a positive association was found between exposure to road traffic noise (L_{DEN}) and hospital admissions due to stroke. After adjustment for confounders, they estimated an OR of 1.18 (95%CI: 1.11 – 1.26) per 10 dB increase in road traffic noise level. After additional adjustment for NO_x ¹ the OR decreased to 1.14 (95%CI: 1.03 – 1.25) per 10 dB. According to Tétreault et al. [11] this study was suffering from minor selection bias, because the response rate was between 30% and 60%. Exposure misclassification bias could have affected the outcome of the study to a small extent, since the study ascertained exposure relative to residential addresses only.

2.5 The impact of noise on diabetes and obesity

More recently, Dzhambov presented the results of a review that investigated the association between noise exposure and the risk of type 2 diabetes [45, 139]. To identify epidemiological and experimental studies (including reviews) dealing with the effects of long-term noise on type 2 diabetes, he carried out two searches in PUBMED and EMBASE, and searched the internet, as well as the reference lists of all included studies. He excluded studies dealing with the effects of noise in people with already diagnosed diabetes and those without control group. Eventually, he identified and evaluated nine studies; two studies [140, 141] investigated the impact of aircraft noise; two studies investigated the impact of road traffic noise [107, 142]; Heidemann et al. [143] investigated the impact of reported traffic intensity on diabetes; the remaining studies [144-147] investigated the impact of occupational noise exposure.

The review by Dzhambov [45, 139] did provide an evaluation of the quality of the individual studies. He considered the following: (i) study design, (ii) time frame, (iii) the working and living conditions in the country where the study was carried out, (iv) the way the study population was selected, (v) the response rate, (vi) the sample size, (vii) the description of the study population, (viii) the representativeness of the study population, (ix) the assessment of both the outcome and the exposure, (x) whether noise exposure duration was considered, (xi) the noise metric, (xii) the biological plausibility given the noise levels in the studies, (xiii) adjustment for personal and/or environmental covariates, (xiv) the potential for deriving effect estimate(s) for a meta-analysis, and (xv) the impact of possible additional transformations with the data in order to assess an effect estimate. Dzhambov [45, 139] rated the overall quality score of the two evaluated studies [107, 142] as 29.5 and 37, respectively on a scale ranging from 0 to 49 (the higher the better).

For his meta-analysis, Dzhambov [45] combined the results of five studies. His results, suggested that people exposed at their homes to L_{DEN} values of more than 60 dB had a 22% higher risk of type 2 diabetes than those exposed to L_{DEN} values of less than 64 dB.

¹ NO_x is a generic term for the mononitrogen oxides nitric oxide (NO) and nitrogen dioxide (NO_2)

None of the selected reviews presented in Table 2.1, reported on the association between noise exposure and obesity.

2.6 Effects of air – and road traffic noise on blood pressure in children

Five of the selected reviews, reported on the results of studies that investigated the impact of air traffic noise on children's blood pressure [11, 18, 19, 22, 37]. For his review, Babisch [37] identified 11 studies (reported in 13 papers) that investigated the effects of *air traffic* noise on blood pressure in children [67, 148-159]. In addition, he identified four studies (reported in five papers) that investigated the effects of *road traffic* noise on children's blood pressure [160-164]. According to Babisch [37], the conclusions from these studies were inconsistent and difficult to interpret. He also found a number of methodological problems in these studies.

Babisch and Van Kamp [22] identified eight papers that investigated the effects of aircraft noise on children's blood pressure [148, 149, 156-159, 165, 166]. After presenting the results of these studies in a qualitative way, the researchers concluded that the evidence on the effect of noise exposure on children's blood pressure was limited and inconsistent. In their review, they addressed several methodological problems such as small study size, insufficient contrasts between noise levels, selection bias, and insufficient adjustment for potential confounders.

In their review Paunović et al. [18] explored the methodological differences between studies on the effects of noise on the blood pressure of children living in an urban environment, with a focus on differences in blood pressure measurement. They identified 13 papers that investigated the effects of aircraft and/or road traffic noise on children's blood pressure, published in the period 1980 – 2010. Seven of these papers reported on the effects of aircraft noise [148, 149, 156, 158, 159, 166, 167]. Another seven papers, investigated the impacts of road traffic noise [162, 163, 166, 168-171]. After presenting and discussing the different studies in a systematic way, Paunović et al. [18] concluded that there was a tendency toward a positive association between noise exposure and blood pressure in children, despite the discrepancies between the presented results. With regard to blood pressure measurement, they concluded that the methods for its measurement were diverse among the evaluated studies. Unfortunately, Paunović et al. [18] were not able to provide an assessment of the individual quality of the studies.

In their systematic review, Hohmann et al. [19], concluded that air traffic noise exposure was positively associated with systolic blood pressure. The researchers based their conclusion on two studies [149, 156] with a "moderate" and "low" evidence quality level, respectively. The level of evidence was measured by means of a tool developed by the Scottish Intercollegiate Guidelines Network [172]. For their review, Hohmann et al. [19] also evaluated eight other papers that investigated the impact of noise exposure on children's systolic blood pressure [148, 157, 162, 163, 166, 169, 173]. These papers reported on studies that were all cross-sectional with a low evidence level. The five largest studies reported a positive association between

aircraft or road traffic noise and systolic blood pressure. The results for the studies on the impact of noise on children's diastolic blood pressure were less consistent: in two cohort studies and three cross-sectional studies, air, road, and rail traffic noise exposure was not associated with diastolic blood pressure [149, 156, 157, 163, 169]. Four other (cross-sectional) studies found a positive association between exposure due to road and/or aircraft noise and diastolic blood pressure [148, 150, 162, 166].

In their review, Tétreault et al. [11] identified and evaluated only one relevant paper [117]. This paper examined whether air pollution at school (nitrogen dioxide) was associated with poorer child cognition and health and whether adjustment for air pollution explains or moderates the observed associations between aircraft and road traffic noise. To this end, the authors of this paper made use of a subsample of the United Kingdom RANCH sample that consisted of 719 children (aged 9-10 years) attending 22 schools around London's Heathrow airport. Both noise levels and air pollution data were available for these children. The paper reported that no associations were found between neither aircraft nor road traffic noise exposure at school and blood pressure. According to Tétreault et al. [11], the analysis reported by Clark et al. [117] suffered from minor selection bias due to the fact that 7 of the 29 schools were excluded for lack of air pollution exposure. Another possible reason for their not finding any association was classification bias, because only noise and air pollution at school was taken into account.

2.7 Effects of wind turbine noise on the cardiovascular system

Only Merlin et al. [33] systematically reviewed studies on the adverse health effects of audible noise (greater than 20 Hz) and infrasound and low-frequency noise (less than 20 Hz) from wind turbines or wind farms. From several bibliographic literature sources, they systematically identified 1,778 black references and 1,070 grey references published in the period from 1981 to October 2012 in English. Eventually, 11 references (reporting on seven studies) met their selection criteria, and were selected for data extraction.

Three of the seven selected studies reported on the association between audible noise (greater than 20 Hz) from wind turbines and effects on the cardiovascular system [34, 174-179]. Two studies were carried out in Sweden and one study was carried out in The Netherlands. All the studies had a cross-sectional design. Their sample sizes ranged from about 340 to 740 persons (1,830 participants in total); response rates ranged from 37% to 68%. In all the studies, respondents were adults from the general population who lived close to a wind turbine.

In the studies, the researchers expressed exposure to wind turbine noise as A-weighted sound pressure levels (SPL) in dB(A); they estimated exposure to wind turbine noise by means of noise propagation models. To this end, they used information on the manufacturer and the type of wind turbine from the years 2006 and 2007 as input. The studies investigated the association between wind turbine noise and three different health outcomes: (i) self-reported hypertension, (ii) self-reported cardiovascular disease, and (iii) self-reported diabetes.

Merlin et al. [33] categorized each study according to the National Health and Medical Research Council (NHMRC) Designation Levels of Evidence [180, 181]. This hierarchy is included in the FORM grading system [182] and indicates the degree to which study results are likely to be affected by different types of bias simply because of the way the study has been designed. Based on this system, the reviewers judged all studies as Level IV aetiology studies. They judged the evidence from these studies as inconsistent, and the population health impact as slight to moderate. Because response rates were low, the authors judged that the evidence from the three studies was not directly generalizable to the target population.

2.8 Conclusions

After an extended search, we identified 37 papers and report reviews that investigated the impact of exposure to environmental noise on the cardiovascular system. Only one review was available on noise and diabetes. Based on the AMSTAR score and their relevance for the total evidence review, we selected 15 reviews.

Most of the studies that were covered by the selected reviews reported on the impacts of road and aircraft noise exposure, among adults. Three reviews also aimed to include studies that investigated the impacts of rail traffic noise exposure; two reviews included studies that investigated the impacts of occupational noise; one review included studies that investigated the impacts of wind turbine noise. The time range of the participating studies in the reviews was from 1965 to June 2014. Nine reviews included one or more meta-analyses, resulting in more than 13 exposure-response relationships. However, some of these exposure-response relationships are already outdated. Since their publication, several more studies have been published, e.g. on the association between aircraft noise exposure and the prevalence of hypertension.

For most available exposure-response relations, including the most recent studies on the impacts of noise on the cardiovascular system, the reviewers were not able to provide a quality judgement of the individual studies. This was the case, for example, for the relationship between road traffic noise and IHD. In 2012, Van Kempen and Babisch [41] published a meta-analysis on the association between road traffic noise and hypertension. They included studies published until 2010. However, in the period 2010 - 2014 several new studies were published. Like the other meta-analyses, the meta-analysis of Van Kempen and Babisch [41] did not include a systematic judgment of the quality of the evaluated studies.

In the last few years, several new outcomes have been reported in relation to transportation noise exposure, including stroke, diabetes and obesity, but valid exposure-response relationships are not yet available. In addition, no exposure-response relationships describing the impacts of rail traffic noise and/or wind turbine noise on the cardiovascular system are available, although the results of several studies have been reported.

Finally, no exposure-response relationships are available describing the impact of noise on children's blood pressure. The degrees of blood pressure elevations found in relationship to noise exposure in children were small and the clinical significance of such minor changes in

childhood blood pressure is difficult to determine. Researchers assume that the extent of blood pressure elevations that was found was probably not clinically significant for children during their youth. However, it could portend elevations later in life that might be health-damaging [37]. The literature suggests that increased blood pressure in children strongly predicts hypertension in young adults. Indeed, essential hypertension and the precursors of cardiovascular disease might originate in childhood [183-187]. Therefore, the WHO decided to carry out a new systematic review in order to update some of the existing exposure-response relationships, and to assess the quality of the existing evidence.

3 Updated systematic review: Materials and methods

3.1 Data collection

The review described in the previous chapter constituted the starting point for the current systematic review. Based on the considerations reported in Chapter 2, we carried out an additional systematic search of the literature in order to identify the following five groups of observational studies (such as ecological studies, cross-sectional studies, case control studies, cohort studies):

1. Observational studies on the association between aircraft and/or rail traffic noise exposure and hypertension and/or high blood pressure, and/or IHD (including angina pectoris and/or myocardial infarction) in adults published from 2000 until October 2014 with no language restriction.
2. Observational studies on the association between aircraft and/or rail traffic and/or road traffic noise exposure and stroke and/or type 2 diabetes, and/or obesity in adults, published until October 2014 with no language restriction.
3. Observational studies on the association between road traffic noise exposure and hypertension and/or high blood pressure published from 2010 until October 2014 with no language restriction.
4. Observational studies on the association between road, rail and air traffic noise exposure and blood pressure in children published until October 2014 with no language restriction.
5. Observational studies on the association between audible noise (greater than 20 Hz) and infrasound and low-frequency noise (less than 20 Hz) from wind turbines or wind farms and blood pressure and/or cardiovascular disease published from October 2012 until October 2014 with no language restriction.

We identified all studies in Medline/PubMed, Scopus, Embase, and Scisearch. The different search profiles that we used, can be found in Appendix I. To ensure that most of the studies could be identified, we also manually scanned reports and proceedings in the field of epidemiology, noise and health. As can be seen, our search in Medline/PubMed, Scopus, Embase, and Scisearch did not include

- studies on the association between aircraft and/or rail traffic noise exposure and hypertension and/or high blood pressure, and/or IHD (including angina pectoris and/or myocardial infarction), published *before* 2000.
- studies on the association between road traffic noise exposure and hypertension and/or high blood pressure published *before* 2010.
- studies on the association between audible noise (greater than 20 Hz) and infrasound and low frequency noise (less than 20 Hz) from wind turbines or wind farms and blood pressure and/or cardiovascular disease published *before* October 2012.

The reason for this is that these studies were already identified in the reviews evaluated in the previous chapter. Therefore, we supplemented

the results of the search described in the above sections, with studies that were included in the reviews presented in the previous chapter [11, 18-20, 22, 24, 26-28, 33, 37, 38, 41, 44-47, 133, 139]. Because some of the authors were involved as researchers in studies that were identified with the searches described above, we were able to include the latest results for these studies published *after* October 2014. This was the case for the following studies (that were already selected), published between November 2014 and August 2015: DEBATS study [188], REGICOR study [189], SDPP [190], HUBRO [191], and DCH [192]. Overall, we identified more than 600 publications.

We included studies that meet the following criteria for data extraction:

- Studies should report on the following:
 - (i) the relationship between aircraft or rail traffic noise exposure and high blood pressure or hypertension, and/or IHD (including angina pectoris and/or myocardial infarction) in adult populations who were not identified with a certain illness or disorder; or
 - (ii) the relationship between aircraft or rail or road traffic noise exposure and stroke and/or type 2 diabetes and/or obesity in adult populations who were not identified with a certain illness or disorder; or
 - (iii) the relationship between road traffic noise exposure and high blood pressure or hypertension in adult populations who were not identified with a certain illness or disorder; or
 - (iv) the relationship between audible noise (greater than 20 Hz) and infrasound and low-frequency noise (less than 20 Hz) from wind turbines or wind farms and blood pressure and/or cardiovascular diseases in adult populations who were not identified with a certain illness or disorder; or
 - (v) the relationship between road, rail or air traffic noise exposure and blood pressure in child populations (infants, children and adolescents, people younger than 18 years) who were not identified with a certain illness or disorder.
- Studies must quantify and/or describe the relationship between objective exposure (expressed in equivalent sound levels (L_{Aeq}) in decibels (dB(A)) from:
 - (i) both civil and military aircrafts or rail traffic, and the prevalence or incidence or hospital admissions or mortality due to hypertension or high blood pressure and/or IHD (including angina pectoris and/or myocardial infarction);
 - (ii) both civil and military aircraft or rail or road traffic, and the prevalence or incidence or mortality due to stroke and/or type 2 diabetes;
 - (iii) road traffic, and the prevalence or incidence of hypertension or high blood pressure;
 - (iv) road, rail, or air traffic, and blood pressure (expressed in mmHg);
 - (v) road, rail, or air traffic, and the obesity markers body mass index (BMI) and waist circumference expressed in kg/m^2 and cm, respectively.

Studies on the association between audible noise (greater than 20 Hz) and infrasound and low-frequency noise (less than 20 Hz) from wind turbines or wind farms and blood pressure and/or cardiovascular disease must quantify and/or describe the relationship between objective exposure (expressed in e.g. Sound Pressure Levels (SPL) in decibels (dB(A)) to wind turbines or wind farms and blood pressure levels (in mmHg) or the prevalence or incidence of cardiovascular disease.

- We did not include studies that used hearing loss or defective hearing or distance from an airport or railway track or road, or from a wind turbine or wind farm as a proxy for exposure to aircraft or rail or road traffic or wind turbine noise. We also did not include studies that assess the noise exposure on the basis of subjective ratings, as given by the subjects in e.g. a questionnaire.
- Nor did we include studies involving a comparison between only two exposure groups (e.g. exposed vs control).

EvK and MF carried out the identification and selection of most of the studies. The team of GP carried out the identification and selection of the studies reporting on noise and obesity and/or type 2 diabetes.

3.2 Data extraction

From the 61 studies (described in 113 records) that met the above-mentioned criteria, we extracted the following data via a structured data extraction form:

- data on general study characteristics (authors, year of publication, study design, aim of the study, study period, study location)
- population characteristics (sampling of the study population, number of participants, response- and attrition rate, gender, age)
- exposure assessment,
- health outcome measurement, and
- the results of the study.

We carried out the data extraction in duplicate and then discussed the results, with the exception of studies on the impact of wind turbine noise ($n = 3$) and studies on the impacts of noise on children's blood pressure. For these studies, the data extraction was carried out by one person only (EvK).

The main effects under investigation were hypertension, IHD, stroke, type 2 diabetes, change in body mass index, change in waist circumference, and change in mean blood pressure in children. In order to make a comparison between the studies, we calculated the following outcome variables:

- For studies on the impact of noise on hypertension, IHD, stroke, or type 2 diabetes, we calculated the natural logarithm of the RR and its variance per 10 dB(A).
- For studies on the impact of noise on children's blood pressure, we calculated the blood pressure change (mmHg) for a noise

level increase of 10 dB(A) and its variance for both systolic and diastolic blood pressure.

- For studies on the impact of noise on the obesity markers BMI and waist circumference, we calculated the change (kg/m² and cm, respectively) per noise level increase of 10 dB(A) and its variance.

To retain the link with European Noise Directive (END) [193], we expressed noise exposure in L_{DEN}. However, most studies did not report an RR per 10 dB (L_{DEN}). Where noise exposure was expressed by means of another noise indicator than L_{DEN} (e.g. L_{Aeq16hr}, or L_{Aeq24hr}), a conversion to L_{DEN} was needed. Appendix II gives an overview of the conversion rules that we have applied.

For studies that reported an RR per 10 dB L_{DEN}, we derived the natural logarithm of the RR per unit of noise. We derived the variance per 10 dB from the reported 95% CI. In addition, without conversion we used the results of studies on the relationship between noise exposure and children's blood pressure that reported the (adjusted) betas and standard errors as a result of a linear regression analysis or an analysis of variance (ANOVA).

Several publications reported a series of grouped exposure-specific RR or blood pressure levels, with one noise exposure group as a reference group. We had to transform these data (RR or the blood pressure level per noise exposure category) into a risk estimate or blood pressure change per unit of noise. Before this was possible, we had to assign an exposure value to each noise exposure group, by assigning the midpoint of the cut points of the class as the exposure value. For example, if there was a noise exposure group of 50 - 55 dB, the assumed noise exposure level in this group would be 52.5 dB. For open-ended noise exposure classes (e.g. < 50 dB or >55 dB), we assigned a value that seemed to be most plausible. For the upper open-ended category (>55 dB), we assigned the value of its lower bound and half of the width of the previous (second highest) interval. So in the previous example, if the upper open-ended category was greater than 55 dB, we assigned a value of $55 + (55 - 50)/2 = 57.5$ dB; for the lower open-ended category, we assigned the value of its upper bound and half the width of the next (second-to-lowest) interval. So in the example: $50 - (55 - 50)/2 = 47.5$ dB.

Often, studies reported an OR per noise unit. In some cases, we needed to carry out a transformation: in studies where the incidence or prevalence of a health outcome was more than 10% and where the OR was more than 2.5 or less than 0.5, we assumed that the adjusted OR derived from a logistic regression could no longer approximate the RR; correction of the OR was desirable. To this end, we applied the formula developed by Zhang and Yu [194]:

$$RR = \frac{OR}{(1 - P_0) + (P_0 \times OR)}$$

Where: RR = Relative Risk, OR = Odds Ratio, P₀ = incidence (or prevalence) of the outcome of interest in the non-exposed group.

We used the statistical software packages STATA Special Edition 14.0 and SAS 9.4 to carry out all statistical calculations. In situations where the prevalence or incidence of hypertension, IHD, stroke, or type 2 diabetes between several noise exposure groups were compared, we calculated the natural logarithm of the RR using generalized least squares for the trend estimation of single studies based on the categorical data shown in the references (STATA command routine 'glst.ado') [195]. For the studies that compared blood pressure levels between several noise exposure groups, we carried out a linear regression weighted for the number of participants in each exposure group.

From each participating study, we extracted one or more estimates of the natural logarithm of the RR per 10 dB(A). Because not all the required data were directly available, we carried out recalculations. To this end, we used the reported data in the different papers and reports. In several studies, the authors provided us with additional information [42, 58, 59, 110, 114, 118, 120, 196-199]. If studies reported their results in more than one publication, we used the most suitable publication (most recent, highest number of participants, best adjustments).

It should be noted that a number of studies reported more than one health outcomes (e.g. [58, 65, 109]). In some cases, we considered more than one reference for a study in order to retrieve the necessary data.

3.3 Study quality: Assessment of risk of bias

In the selected studies, we evaluated the risk of bias by means of a checklist developed by the WHO [200]: (i) information bias due to exposure assessment, (ii) bias due to confounding, (iii) bias due to selection of participants, (iv) information bias I due to health outcome assessment, and (v) information bias II due to health outcome assessment. For each study, the evaluation was carried out by two of three independent reviewers (EvK, MC, GP). Table 3.1 shows how we scored the studies on these items. From these scores, we calculated a total risk of bias score. For studies where there was difference of opinion between the two reviewers, we attempted to reach consensus through discussion between them.

3.4 Data aggregation

Since the extracted estimates had to be un-confounded by at least age and/or sex, we included estimates only from studies that were well matched, adjusted or stratified for at least age and sex. If more than one risk estimate was available for a study, we used the estimates for men and women separately and for separate age categories, where possible. After selecting the study estimates, we calculated a pooled RR per 10 dB using the STATA-command METAN to fit a random-effects model [201]. A random-effects model acknowledges the occurrence of variation in true effects between studies, but regards them as unknown effects to be estimated, by assuming that the effects observed in the sample of studies analysed, are drawn from a population of studies [202]. To test the consistency of effect estimates across studies, we used the Cochran's Q-test [203]. If the Q-test was statistically

significant ($P < 0.05$), this indicated heterogeneity across populations. Since the Q-test has low statistical power in meta-analysis with few studies, we also used the I^2 statistic. With the I^2 statistic, we investigated whether the observed variance in study outcomes, comes from real differences between studies and could be explained by study-level covariates. The I^2 statistic reflects the percentage of between-study heterogeneity that is attributable to variability in the true exposure effect, rather than sampling variation [204]. A value of 0% indicates no observed heterogeneity, and larger values show increased heterogeneity. As suggested by Higgins et al. [205], we described I^2 values between 25% and 50% as “low”, values of 50%-75% as “moderate”, and values $\geq 75\%$ as “high”.

3.5 Heterogeneity

For some outcomes, we had at our disposal a relatively large number of effect estimates. In these cases, we were able to investigate how the summary estimates were affected by sources of heterogeneity. To this end, we carried out a meta-regression analysis using the STATA-command METAREG [206]. We tested a broad range of covariates:

- (i) Covariates regarding the design of the study: study period, sample size, response rate, noise source under investigation, adjustment for confounders, risk of bias, whether the study was originally set up to investigate the impact of noise, the way noise exposure was assessed and the outcome was ascertained.
- (ii) Covariates regarding the population under study: age, sex, and exposure duration.

We compared the between-study variances of the models with and without these covariates to see whether the heterogeneity in the covariates used in each study, could explain part of the between study variance.

3.6 Publication bias

One of the most important problems of a meta-analysis is that researchers are not always able to publish their results. If the reasons that studies remain unpublished are associated with their outcome, the validity of a meta-analysis can be seriously threatened. In order to indicate the extent of publication bias in the present study, we produced so-called funnel plots. A funnel plot is a scatter plot of the studies' effect estimates (RR per 10 dB) against the inverse of the standard error. It is based on the fact that the precision in estimating the underlying effect will increase as the sample size of studies increases. In the absence of bias, the plot should resemble a symmetrical funnel plot [207]. In order to test funnel plot asymmetry or the presence of small-study effects, we applied Egger's test of publication bias [208, 209] using the STATA commands METAFUNNEL and METABIAS. As a rule of thumb, Harbord et al. [210] recommend that tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis. When there are fewer studies, the power of these tests is too low to distinguish chance from real asymmetry.

Table 3.1: Scoring protocol used to assess the risk of bias

Characteristic/domain	Score (risk of bias)	Description/value label
Information bias/ bias due to exposure assessment	Low	Noise level is expressed in L_{DEN} , L_{night} , or components AND , (a) is based on modelled equivalent noise levels from noise models that used the actual traffic volume, composition, and speed per 24 hrs per road/railway/airport as input in which case the modelled noise levels are subsequently linked with the home and/or school address of the participant; OR , (b) is based on measurements at the façade of the participant's home and/or school for a minimum of 1 week by qualified staff, and adjusted for data under point (a) as well as meteorological conditions when necessary; OR , (c) is based on a noise map reported in a separate publication but which fulfils conditions (a) or (b).
	High	Noise level is not expressed in L_{DEN} , L_{night} , or components, OR (a) is based on modelled noise levels from noise models that did not use the actual traffic volume, composition, and speed per 24 hrs per road/railway/airport as input in which case the modelled noise levels are linked with the area (e.g. postal code area, town, output area) in which the participant lives or attends school; OR (b) is based on measurements of less than 1 week and the measured noise levels are linked with the area (e.g. postal code area, town, neighbourhood) in which the participant lives or attends school OR not adjusted for data under point (a) or meteorological conditions when necessary OR by unqualified staff; OR (c) is based on a noise map reported in a separate publication but which does not fulfil conditions (a) or (b).
	Unclear	If not enough information is available to judge the above
Bias due to confounding	Low	All important confounders are taken into account either through matching or, restriction or in the analysis. For hypertension and blood pressure an effect estimate should at least be adjusted for age and gender; for IHD, stroke, type 2 diabetes, and obesity an effect estimate should at least be adjusted for age, gender and smoking
	High	Only 1 or no confounder is taken into account; OR subjects in exposed and unexposed groups differ for one or more important confounders and there is no adjustment in the analysis
	Unclear	Less than all to > 1 important confounders taken into account, OR Insufficient information to decide on one of the above.
Bias due to selection of participants	Low	Participants randomly sampled from a known population, AND response rate higher than 60%, AND attrition rate less than 20% in follow-up studies.

Characteristic/domain	Score (risk of bias)	Description/value label
	High	No random sampling OR response rate less than 60% OR attrition rate higher than 20%.
	Unclear	No information to judge the above.
Bias due to health outcome assessment	Low	The health outcome of interest is objectively measured OR taken from medical records OR taken from questionnaire or interview using a known scale or validated assessment method.
	High	The health outcome of interest is self-reported and not assessed using a known scale or validated assessment method
	Unclear	Not sufficient information reported to assess the above.
Bias due to not blinded outcome assessment	Low	The health outcome of interest is assessed blind for exposure information in cohort and cross-sectional studies or exposure is assessed blind for being a case in case-control studies
	High	The health outcome and/or exposure assessment is not blinded.
	Unclear	Not sufficient information reported to assess the above.
Total risk of bias	Low	At least 4 at low risk of bias. One "high" or "unclear" out of five is allowed.
	High	Any other.

3.7 Results of the search

Our search (described in the section “Data collection”) yielded 480 references (after removal of duplicates) in total. The screening of references for the eligibility resulted in 167 references. Following further screening, 113 references ultimately fulfilled our inclusion criteria [34, 42, 48, 53, 54, 57-60, 62-66, 71, 73-77, 85-87, 94-97, 102-105, 107-114, 116-122, 128-132, 134, 135, 138, 141, 142, 159, 162, 166, 167, 174-179, 188-190, 192, 196-199, 211-248]. These references described 61 different studies. We included 57 of these studies in one or more of the different meta-analyses.

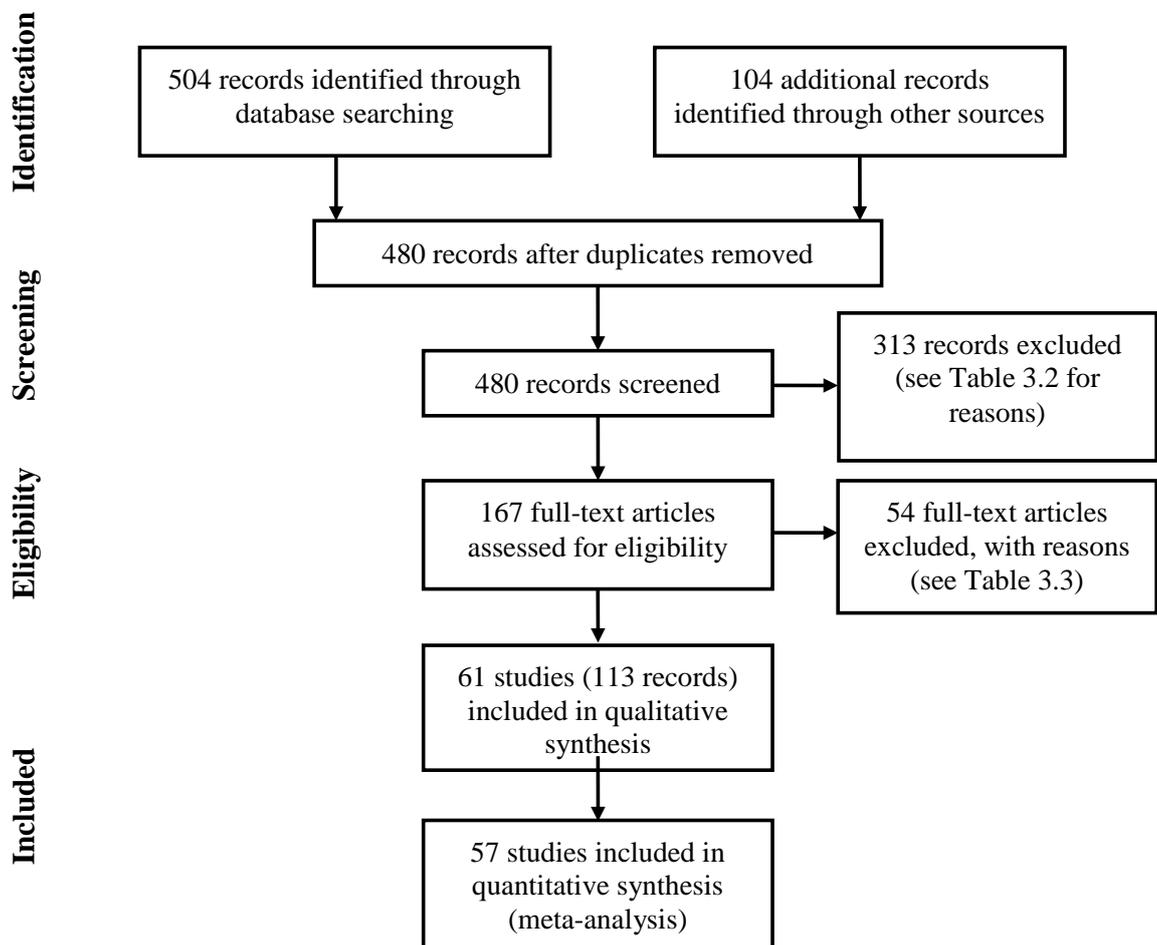


Figure 3.1: Flowchart of the study identification and selection for the meta-analysis

Table 3.2: Reasons for exclusion of references during screening phase

Reason for exclusion	Number of references excluded	Reference
Only title available	46	See appendix IX
Experiment dealing with short-term noise effects/in vitro/experiment	9	[249-257]
Complete proceeding book, meeting report	2	[258, 259]
Erratum	3	[139, 260, 261]
Measurement or simulation study without reporting health outcomes	43	[262-304]
Review (not a single study)	79	[10, 11, 14, 18-20, 22-24, 27, 28, 30, 32, 37, 38, 41, 44-47, 78, 99, 133, 305-360]
Editorial/discussion/comment/Letter to the editor	49	[361-409]
Health impact assessment	9	[410-418]
No relevant outcomes measured	36	[123, 164, 419-452]
Exposure characterization did not meet the criteria	23	[69, 115, 126, 127, 140, 143, 150, 453-468]
Occupational study	8	[469-476]
Study population did not meet criteria	6	[477-482]
Total excluded	313	

Table 3.3: Reasons for exclusion of references during eligibility phase

Reason for exclusion	Number of references excluded	Reference
Paper not accessible	9	[67, 124, 151-155, 158, 483]
Comparison of two exposure groups	27	[49, 50, 56, 80-82, 84, 90-93, 98, 100, 101, 106, 136, 148, 149, 156, 157, 160, 161, 163, 165, 168, 169, 484]
Not possible to extract effect estimate from reported data	11	[52, 55, 61, 72, 79, 83, 88, 485-488]
Not possible to distinguish between different disease outcomes	2	[51, 489]
Exposure characterization did not meet criteria	5	[137, 171, 490-492]
Total	54	

4 Studies investigating the impact of noise on hypertension

4.1 Aircraft noise

4.1.1 *Descriptive results*

We selected 12 studies for data extraction that investigated the association between aircraft noise exposure and hypertension. These studies were published between 1976 and 2015 [48, 58-60, 64-66, 71, 188, 199, 212-216, 223, 226, 235, 238, 242] [62, 63, 211, 224, 234, 236, 241]. Table 4.1 presents some characteristics of these 12 studies.

Of the 12 selected studies, 11 studies were cross-sectional and one study was a cohort study. All the studies - except one - were carried out in Europe. The sample sizes of the studies ranged from 85 to almost 29,000 persons. Most studies (n = 10) investigated the impact of civil aircraft noise exposure. The Okinawa study [58, 59, 242] investigated the impact of military aircraft noise exposure only, while the AWACS study [199] investigated the combination of civil and military aircraft noise.

Most of the studies (n = 10) estimated the aircraft noise levels by means of noise models that were incorporated in Geographic Information Systems (GIS). These models were able to predict equivalent noise levels as a function of traffic data provided by the authorities, under the condition that a number of parameters are known and acquired as input data (e.g. air traffic statistics, radar tracks, location of dwellings, meteorological conditions). The noise models predict equivalent noise levels at user-defined outdoor points, from which conventional noise indicators were calculated (e.g. L_{DEN} , $L_{Aeq16hr}$, and L_{DN}).

Two studies ascertained the noise exposure levels of their respondents by means of noise measurements. These measurements were carried out as part of a monitoring system positioned around the airport [48, 58, 59, 238, 242], which measured aircraft noise levels for residential areas, neighbourhoods, and/or villages in which the respondents live. Subsequently, the studies assigned the measured noise levels to everybody who is a member of that group, i.e. respondents living in that particular area. When noise exposure is ascertained in this way, the results of these studies may be sensitive to decisions about cut-off points used to categorize continuous exposure variables. We are concerned about the method used to assign scores to exposure categories [493]: we cannot rule out the possibility that the exposure assessment and the failure to apply individual exposure estimates to the study population have caused exposure misclassification.

Five of the evaluated studies ascertained hypertension by means of a self-report [60, 62, 63, 199, 224, 234, 236, 241]. The OKINAWA study [58, 59, 242] ascertained hypertension by means of measurements of blood pressure and/or a clinical interview. Six studies used a combination of self-report and blood-pressure measurements [48, 64-66, 71, 188, 212-216, 223, 226, 235, 238] [211].

Only 6 of the 12 studies [65, 188, 211-216, 224, 226, 234-236] presented in table 4.1 were originally set up to investigate the effects of aircraft noise. In the other 6 studies, the researchers made use of data that were gathered for other purposes.

Table 4.1: Overview of characteristics of the 12 selected studies on the association between aircraft noise and hypertension

Study [Ref]	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{††)}	Sex and age (yrs.)	Type ^{‡)}	Exposure range and characterization ^{Ⓛ)}	Ascertainment hypertension ^{**)}
Knipschild-1 [48, 238]	NL	CS	5,828 (NR)	MF, 35-64	C	50 – 70 dB (2)	1, 2
Okinawa [58, 59, 242]	Jap	CS	28,781 (NR)	MF, 20-79	M	< 50, 50-55, 55-60, > 60 dB (2)	1
SEHS [60]	Swe	CS	2,959 (74)	MF, 19-80	C	<50, 50-55, 55-60, > 60 dB (1)	2
HYENA [65, 212-216, 235]	Eur	CS	4,861 (24)	MF, 45-70	C	40 - 75 dB (1)	1, 2
SDPP [64, 66, 71, 223]	Swe	CO	5,712 ^{a)}	MF, 35-56	C	<50, 50-54, 55-59, ≥65 dB (1)	1, 2
DEBATS-pilot [226]	Fr	CS	85 (10)	MF, 21-84	C	<50, 50-54, 55-59, ≥ 60 (1)	1, 2
DEBATS-main [188]	Fr	CS	1,244 (NR)	MF, 18-90	C	NR (1)	1, 2
AWACS [199]	NL	CS	9,365 (36)	MF, 17-65	M,C	30 - 65 dB (1)	2
SERA [211]	It	CS	597 (50)	MF, 45-70	C	<60, 60-65, 66-75 (1)	1, 2
GES-2 [224, 234, 236]	NL	CS	5,873 (46)	MF, ≥ 18	C	30 – 75 dB (1)	2
GES-3 [224, 234, 236]	NL	CS	6,091 (49)	MF, ≥ 18	C	30 – 75 dB (1)	2
SPANDAU [62, 63, 241]	Ger	CS	1,718 (85)	MF, 18-90	C	62-67, 67-75, ≥75 (1)	2

*) Eur = Europe, Fr = France, Ger = Germany, It = Italy, Jap = Japan, NL = The Netherlands, Swe = Sweden, †) CS = cross-sectional study, Eco = ecological study, CO = cohort study; ††) N = number of participants and the response percentage in brackets; ‡) Type of aircraft noise: C = civil aircrafts, M = military aircraft; Ⓛ) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; **) The way hypertension was ascertained: 1 = measurement of blood pressure levels and/or by means of a clinical interview, 2 = by means of a question as part of a questionnaire or interview (self-reported); a) the attrition rate in the SDPP study probably exceeds 20% in the follow-up of the cohort.

4.1.2 *Study quality*

We judged that most of the studies have a high risk of bias (see Table 4.2). An important reason was that response rates of the evaluated studies were usually lower than 60%: in order to score “low” on the factor “Bias due to selection of participants”, the participants had to be randomly sampled from a known population *and* the response rate of the study had to be higher than 60%. For cohort studies, we took into account the loss to follow-up (i.e. attrition rate) when rating the factor “Bias due to selection of participants”. In the only evaluated cohort study (SDPP), the final baseline study group comprised 3,128 men and 4,821 women. After 8 - 10 years, the participants were invited to participate in a follow-up survey. The final follow-up study group comprised 2,383 men and 3,329 women, representing 76% and 69%, respectively, of the baseline study population. The true loss to follow-up is unclear, since exclusions were made of those with diabetes at recruitment and some died during the observation period. However, we suspect that the attrition rate probably exceeded 20% (see Table 7.1). Therefore, we rated the factor bias due to selection of participants as “high”.

In order to score “low” on the factor “Bias due to confounding”, a study should contain information that can be used to derive effect estimates that are at least adjusted for age and sex; we judged that this was the case for 10 of the selected studies. Furthermore, we often rated the bias due to health outcome assessment as “high”, since several studies ascertained hypertension by means of self-reporting only. For the OKINAWA study and the Knipschild-1 study, we rated the bias due to exposure assessment as “high”: both studies ascertained the exposure to aircraft noise of their participants by means of noise measurements, as part of a monitoring network. In the previous Paragraph, we have explained the problems that can result from this approach.

If we suspected that participants were aware that they were participating in a study on the impact of aircraft noise on the cardiovascular system, we rated the item “Bias due to not blinded outcome assessment” as “high”.

Table 4.2: Risk of bias: reviewer's judgements about each risk of bias item for each of the 12 studies on the association between aircraft noise and hypertension that were selected for data extraction

Study	Bias due to exposure assessment	Bias due to confounding *)	Bias due to selection of participants †)	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
SDPP	Low	Low	High	Low	Low	Low
HYENA	Low	Low	High	Low	High	High
SEHS	Low	Low	Low	High	Low	Low
DEBATS-pilot	Low	Low	High	Low	Unclear	High
DEBATS-main	Low	Low	Unclear	Low	Unclear	Unclear
AWACS	Low	Low	High	High	Low	High
Okinawa	High	Low	Unclear	Low	Low	High
Knipschild-1	High	High	High	Low	Low	High
SERA	Low	Low	High	Low	Unclear	High
GES-2	Low	Low	High	High	Low	High
GES-3	Low	Low	High	High	Low	High
SPANDAU	Low	Low	Low	High	Low	Low

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age and sex; †) In order to score "low" participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60% (cross-sectional studies) and attrition rate is less than 20% (follow-up studies). See the Materials and methods section for further explanation of the items.

4.1.3 Data aggregation

For the SPANDAU study, we were not able to derive an RR per 10 dB (L_{DEN}); consequently we were not able to include this study in the data aggregation. Since the Knipschild-1 study could not provide estimates that were adjusted for at least age and/or sex, we decided not to include this study in the data aggregation.

Figure 4.1 shows the estimates of the remaining studies. The figure shows that in the *cross-sectional studies* (comprising 60,121 residents and including 9,487 cases), aircraft noise exposure tended to be positively associated with the prevalence of hypertension: using a random effects model we estimated an RR of 1.05 (95% CI: 0.95 – 1.17) per 10 dB increase in aircraft noise (L_{DEN}). We based this estimate on the results of studies carried out within the aircraft noise level range of approximately 35 - 75 dB (L_{DEN}). We observed increased but moderate heterogeneity among the studies. We estimated a residual proportion of the between-study variance due to heterogeneity of $I^2_{residual} = 72.1\%$ (χ^2 test for heterogeneity: $Q = 53.7$, $Df = 15$, $p < 0.001$).

We found that only one *cohort study* investigated the association between aircraft noise exposure and the *incidence* of hypertension. This study (carried out in the aircraft noise level range of approximately 45 - 65 dB (L_{DEN})) reported the effect estimates for men and women separately. The corresponding RRs for the incidence of hypertension were 1.17 (95%CI: 0.90 – 1.51) and 0.85 (95%CI: 0.62 - 1.15) per 10 dB increase in aircraft noise, respectively.

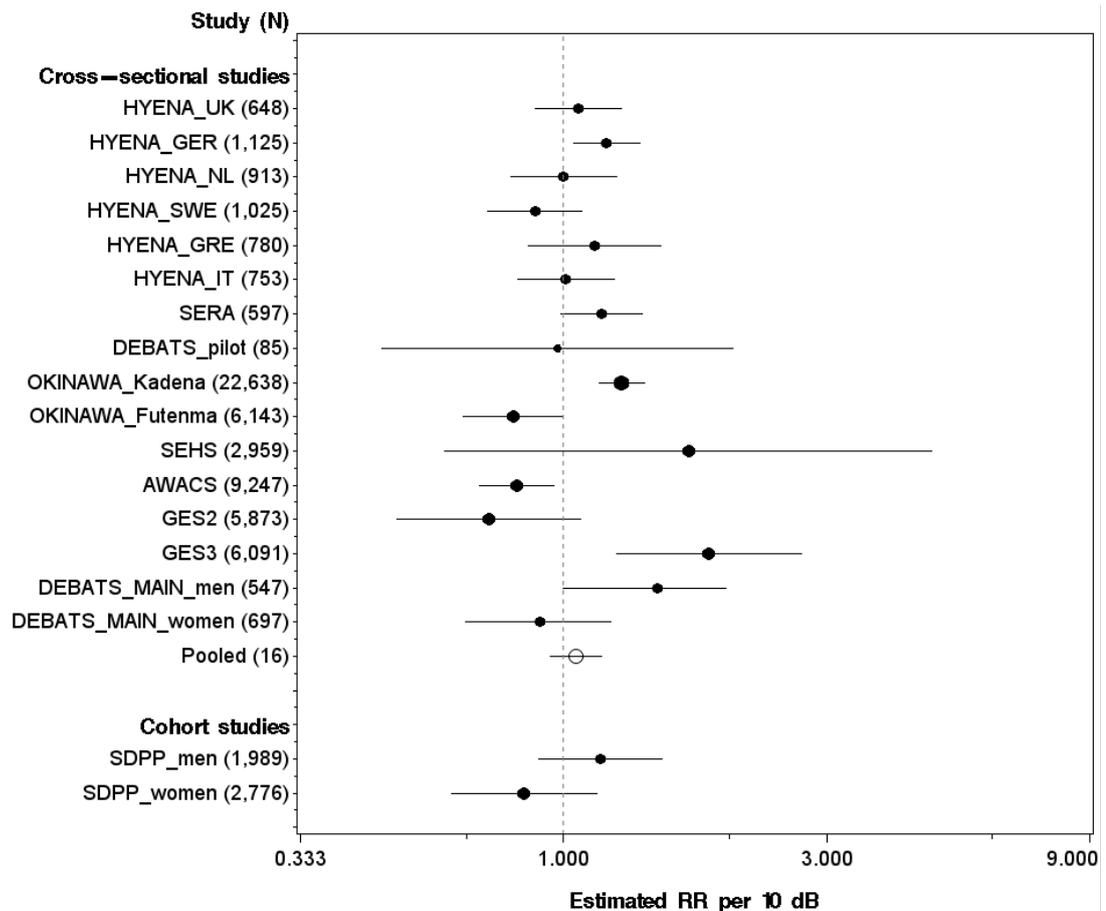


Figure 4.1: Association between aircraft noise exposure (L_{DEN} in dB) and hypertension in cross-sectional and cohort studies. The black vertical line corresponds to no effect of aircraft noise exposure. The black dots correspond to the estimated RR per 10 dB and 95% CI for the different studies. The white circle represents the summary estimate and 95% CI.

4.1.4 Publication bias

To assess the extent of publication bias among the cross-sectional studies, we plotted the estimated natural logarithm of the RR per 10 dB against the study precision (standard error). The result is presented in figure 4.2 (funnel plot). The figure indicates that there is no strong publication bias, and the result of the Eggers test for publication bias did not show evidence of the presence of small study effects ($p = 0.946$). We did not assess publication bias for cohort studies, because only one cohort study was included.

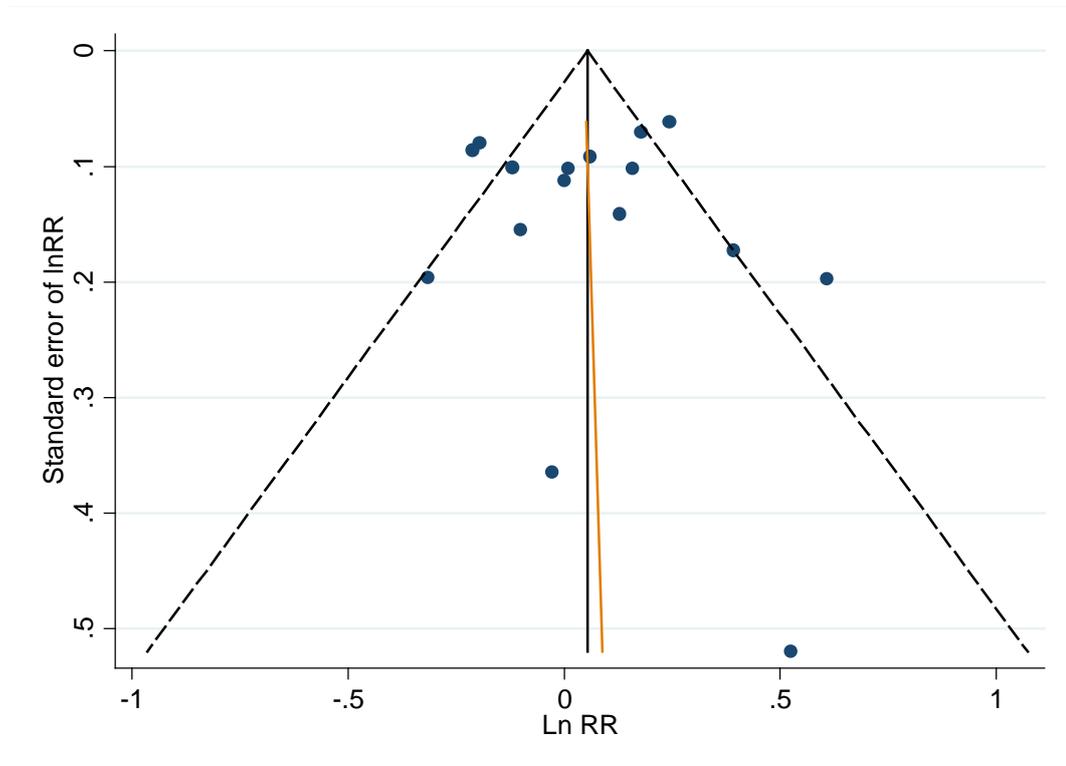


Figure 4.2: Funnel plot showing the natural logarithm of the RR per 10 dB for the relationship between aircraft noise exposure and the prevalence of hypertension in the individual cross-sectional studies plotted against the precision (standard error of lnRR), including the fitted regression line from the standard (Egger) test for small-study effects.

4.1.5

Heterogeneity

To study whether the heterogeneity between the cross-sectional studies observed in figure 4.1 might be due to differences in study characteristics, we carried out a meta-regression analysis, including one covariate at a time. Table 4.3 presents the results of this analysis. The table shows that there was no evidence of heterogeneity due to (i) sample size, (ii) whether the study adjusted for socio-economic status (SES), (iii) whether the study adjusted for a noise source other than air traffic, (iv) the response rate of the study, (v) the exposure duration of the population under investigation, (vi) whether the study was set up originally to investigate the impact of aircraft noise on hypertension. In addition, the rated quality (i.e. risk of outcome and total bias) of the study did not affect heterogeneity.

Table 4.3: Results of a meta-regression analysis for the cross-sectional studies analysing the association between aircraft noise and hypertension (16 effect estimates)

Adjustment for covariate	No of estimates	RR _{10dB}	95% CI	I ² _{Residual} Proportion of variation due to heterogeneity (%)	ΔI ² _{residual} Difference of residual variation*)	p-value of variable in meta-regression
Base model	16	1.05	0.95 - 1.17	72.1		
Sample size				73.8	0	0.65
<1,000 participants	8	1.08	0.99 - 1.17			
≥1,000 participants	8	1.03	0.85 - 1.25			
Type of aircraft				68.4	3.7	0.18
Civil	13	1.09	0.98 - 1.20			
Military	2	1.02	0.65 - 1.59			
Civil and military	1	0.82	0.70 - 0.96			
Adjustment for indicator of socio-economic status				73.4	0	0.87
No	4	1.08	0.81 - 1.43			
Yes	12	1.04	0.93 - 1.17			
Adjustment for other noise sources				71.8	0.3	0.57
No	14	1.07	0.95 - 1.20			
Yes	2	0.98	0.69 - 1.38			
Risk of outcome bias				70.7	1.4	0.76
High	4	1.08	0.69 - 1.70			
Low	12	1.06	0.96 - 1.18			
Risk of total bias				73.7	0	0.54
High	13	1.04	0.93 - 1.16			
Low	1	1.69	0.61 - 4.67			
Unclear	2	1.15	0.71 - 1.86			
Secondary analysis				73.1	0	0.45
No	12	1.08	0.97 - 1.20			
Yes	4	0.99	0.73 - 1.34			
Response rate				72.6	0	0.52
<45%	6	0.99	0.86 - 1.14			
≥45%	6	1.13	0.92 - 1.40			
Missing	4	1.08	0.81 - 1.43			
Exposure duration				73.9	0	0.72
3 years or less	3	1.00	0.68 - 1.48			
	6	1.06	0.97 - 1.17			

Adjustment for covariate	No of estimates	RR _{10dB}	95% CI	I ² _{Residual} Proportion of variation due to heterogeneity (%)	ΔI ² _{residual} Difference of residual variation*)	p-value of variable in meta-regression
More than 3 years Missing	7	1.09	0.87 – 1.37			
Gender of population under study				73.1	0	0.36
Men	1	1.48	1.06 – 2.08			
Women	1	0.90	0.67 – 1.23			
Men and women	14	1.04	0.93 – 1.17			
Age of population under study				73.6	0	0.89
Middle-age	7	1.07	0.99 – 1.16			
All ages	9	1.06	0.86 – 1.31			

*) Negative values are set to zero; negative signs are possible if the covariate explains less of the heterogeneity than expected by chance.

4.2 Road traffic noise

4.2.1 Descriptive results

We identified and selected 28 studies on road traffic noise exposure effects for data extraction. They were published between 1984 and 2014 [42, 62, 63, 65, 85-87, 94, 95, 102-105, 107-114, 118, 120, 121, 189, 196-199, 212-219, 225, 230-233, 235, 237, 241, 243, 244]. Table 4.4 gives an overview of the characteristics of these studies. All studies were cross-sectional, except the DCH study [120, 121], which was a cohort study. All studies, except two [105, 196, 197], were carried out in Europe. Sample sizes ranged from 366 to 45,271 persons.

Most of the studies (n = 19) estimated road traffic noise levels for the houses of the participants by linking their addresses to maps that were created by noise models incorporated in Geographic Information Systems (GIS). These models are able to predict equivalent noise levels at user defined outdoor points, as a function of traffic data and additional parameters such as the characteristics of the road network, characteristics of buildings, land-use along the road network, slopes, etc.

Four studies ascertained the noise exposure of their participants by means of noise measurements. In most cases, these noise levels were measured for a residential area or neighbourhood. This noise level was subsequently assigned to every participant living in that area or neighbourhood. Five other studies used a combination of noise measurements and noise models to ascertain the noise exposure levels to which individual participants were exposed.

Seventeen of the evaluated studies ascertained hypertension by means of a question that was part of a questionnaire or interview. The studies treated those who reported that they had (ever) been diagnosed with hypertension and/or used antihypertensive medication as cases. Five other studies ascertained hypertension by means of blood pressure

measurements (sometimes in combination with an anamnesis). Six studies used a combination of self-reporting and blood pressure measurements.

Only 13 of the studies presented in Table 4.4 were originally set up to investigate the effects of road traffic noise [42, 65, 86, 87, 94, 95, 102-105, 108, 110, 112, 114, 196, 197, 212-216, 219, 235]; for one study [111] we were not sure whether it was originally set up to investigate the impact of noise. The remaining 14 studies [62, 63, 85, 107, 109, 113, 118, 120, 121, 189, 198, 199, 217, 218, 225, 230-233, 237, 241, 243, 244] made use of data that were gathered for other purposes.

Table 4.4: Overview of characteristics of the 28 selected studies on the association between road traffic noise and hypertension

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs)	Exposure range and characterization ^{§)}	Ascertaining of hypertension ^{**)}
ALPNAP [42, 110, 114]	Aus	CS	1,653 (35)	MF, 20-74	31 – 74 dB (1,2)	2
Amsterdam [85]	NL	CS	2,878 (71)	MF, 41-43	<55, 55-59, 60-64, 65-69, 70-80 dB (2)	1
Caerphilly [86, 87]	UK	CS	2,512 (89)	M, 45-59	51-55, 56-60, 61-65, 66-70 (2)	1
Luebeck [94, 95]	Ger	CS	2,295 (83)	MF, 30-69	≤60, 61-65, ≥66 (2)	1
BCC3 [102-104]	Ger	CS	2,169 (86)	M, 31-70	≤60, 61-65, 66-70, 71-75, 76-80 (1)	2
SHEEP [107]	Swe	CS	2,095 (70-75)	MF, 45-70	42-68 dB (1)	1, 2
Tokyo [105]	Jap	CS	366 (73)	F, 20-60	45-49, 50-54, 55-59, 60-64, 65-69, 70-75 (1)	2
Stockholm Road [108]	Swe	CS	667 (77)	MF, 19-80	≤45, 45-50, 50-55, >55 (1, 2)	2
Groningen [109, 237]	NL	CS	38,849 (47)	MF, 28-75	<45 - >65 (1)	2
PREVEND [109, 237]	NL	CS	7,264 (NR)	MF, 28-75	<45 - >65 (1)	1
UIT1 [42]	Aus	CS	1,503 (NR)	MF, 18-74	50 -60 (1,2)	2
SPANDAU [62, 63, 241]	Ger	CS	1,718 (85)	MF, 18-90	<55, 55-60, 61 – 65, >65 (1,2)	2
Skane-1 [111]	Swe	CS	13,557 (54)	MF, 18-80	<50, 50-54, ≥55 (1)	2
Lerum [112]	Swe	CS	1,953 (71)	MF, 18-75	45-50, 51-55, 56-70 (1)	2
Skane-2 [113]	Swe	CS	24,238 (59)	MF, 18-80	<45 - 71 (1)	2
BBT-1 (phone) [42, 110]	Aus	CS	2,007 (80)	MF, 20-74	30 - 80 (1)	2
BBT-2 (face-to-face) [42,	Aus	CS	2,070 (62)	MF, 17-85	30 - 80 (1)	2

110]						
HYENA [65, 212-216, 235]	Eur	CS	4,861 (24)	MF, 45-70	45 - 70 (1)	1, 2
KORA [217, 218]	Ger	CS	4,261 (64)	MF, 25-74	≤45, 46-50, 51-55, 56-60, 61-65, ≥66 (1)	1, 2
Berlin-IV [219, 494]	Ger	CS	2,043 (23)	MF, 35-74	<45, 45-49, 50-54, 55-59, 60-64, ≥70 (1)	1, 2
Taiwan [196, 197]	Tw	CS	820 (NR)	MF, all ages	<77, 77-80, 80-83, ≥83 (2)	2
REGICOR [189, 230-232]	Sp	CS	2,067 (74)	MF, 36-82	NR (1,2)	1, 2
Heinz-Nixdorf Recall Study [233]	Ger	CS	4,291 (89)	MF, 45-75	<55, 55-60, 60-65, 66-70, 71-75, >75 (1)	1
Oslo Health Study [243, 244]	Nor	CS	13,174 (62)	MF, ?	20 - 70 (1)	1, 2
DCH [120, 121]	Den	CO	32,635 ^{a)}	MF, 50-64	<55, 55-65, >65 (1)	2
SAPALDIA-2 [118, 198]	Swi	CS	6,450 (74)	MF, 28-72	<50, 50-55, >55 (1)	2
Roadside study [225]	Swe	CS	2,498 (59)	MF, 18-80	<50, 50-55, 55-59, ≥60 (1)	2
AWACS [199]	NL	CS	9,247 (36)	MF, 17-65	30 - 65 (1)	2

*) Aus = Austria, Den = Denmark, Eur = Europe, Ger = Germany, Jap = Japan, NL = The Netherlands, Nor = Norway, Sp = Spain, Swe = Sweden, Swi = Switzerland, Tw = Taiwan, UK = United Kingdom; †) CS = cross-sectional study, Eco = ecological study, CO = cohort study; ‡) N = number of participants and the response percentage in brackets; □) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; **) The way hypertension was ascertained: 1 = measurement of blood pressure levels and/or by means of a clinical interview, 2 = by means of a question as part of a questionnaire or interview (self-reported); a) the attrition rate in the DCH study exceeds 20% in the follow-up of hypertension in the cohort.

4.2.2

Study quality

We judged that most of the evaluated studies have a high risk of bias. For the Tokyo study we were not able to judge the total risk of bias (see table 4.5): it was for example, not clear how exposure was assessed or how participants were selected [105].

An important reason for the fact that we judged most studies as having a high risk of bias was that response rates were usually lower than 60%. For cohort studies, we took into account the loss to follow-up (i.e. attrition rate) when rating the factor "Bias due to selection of participants". For the only cohort study (DCH), the original study group comprised 57,053 subjects who were enrolled in the cohort between 1993 and 1997. In the period 2000 – 2002, the cohort comprised 54,379 participants (95% of the original study group), of whom 45,271 (79% of the original study group) agreed to participate in the study on the impact of road traffic noise (when investigating hypertension, the cohort consisted of 32,635 persons). Since the attrition rate exceeded 20%, we rated the factor "Bias due to selection of participants" as "high".

Another reason that we judged studies to have a high risk of bias was that not every study contained information that can be used to derive effect estimates that are at least adjusted for age and sex; this was not the case for four of the selected studies (see Table 4.5). Furthermore, we often rated the bias due to health outcome assessment as “high”, since we observed that several studies ascertained hypertension by means of self-reporting.

Table 4.5: Risk of bias: reviewer’s judgements about each risk of bias item for each of the 28 studies on the association between road traffic noise and hypertension that were selected for data extraction

Study	Bias due to exposure assessment	Bias due to confounding*)	Bias due to selection of participants†)	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
Amsterdam	High	Low	Low	Low	Low	Low
Caerphilly	High	High	Low	Low	Low	High
Luebeck	High	Low	Low	Low	Unclear	High
BCC3	Low	Low	High	High	Low	High
SHEEP	Low	Low	Low	Low	Low	Low
Tokyo	Unclear	Low	Low	High	Unclear	Unclear
Stockholm Road	Low	High	Low	High	Low	High
Groningen	Low	Low	High	High	Low	High
PREVEND	Low	Low	High	Low	Low	Low
UIT1	Low	High	Low	High	Unclear	High
SPANDAU	Low	Low	Low	High	Low	Low
Skane-1	Low	Low	High	High	Unclear	High
Lerum	Low	Low	Low	High	High	High
Skane-2	Low	Low	Low	High	Low	Low
BBT-1 (phone)	Low	Low	Low	High	Unclear	High
BBT-2 (face-to-face)	Low	Low	Low	High	Unclear	High
HYENA	Low	Low	High	Low	High	High
KORA	Low	Low	Low	Low	Low	Low
Berlin-IV	Low	Low	High	Low	Low	Low
Taiwan	High	Low	Unclear	High	Unclear	High
REGICOR	Low	Low	Low	Low	Low	Low
Heinz-Nixdorf Recall Study	Low	Low	Low	Low	Low	Low
Oslo Health Study	Low	Low	Low	Low	Low	Low
DCH	Low	Low	High	High	Low	High
SAPALDIA-2	Low	Low	Low	High	Low	Low
Roadside	Low	High	High	High	Low	High
ALPNAP	Low	Low	High	High	Unclear	High
AWACS	Low	Low	High	High	Low	High

*) In order to score “low”, the study should contain information that can be used to derive effect estimates that are at least adjusted for age and sex; †) In order to score “low” participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%.

4.2.3 *Data aggregation*

For the ALPNAP study, we decided not to include an RR per 10 dB (L_{DEN}) in the data aggregation: the ALPNAP study researchers included several interaction terms for noise exposure and other factors in their statistical model. These interaction terms were the interaction between noise exposure and age, noise exposure and health status, and noise exposure and family history of hypertension. Since all these interaction terms were statistically significant, the effect of noise exposure differs across the different categories of these factors [42, 110, 114]. For the BBT study [42, 110], we were able to include the results of the phone study only.

For the data aggregation, we included only those estimates where hypertension was ascertained by means of self-reporting and/or blood pressure measurement and that were adjusted for both age and gender. Where it was possible to derive an estimate for separate age categories, we included both these separate estimates. We ended up with 47 effect estimates for the cross-sectional studies. After aggregating these 47 effect estimates (comprising 154,398 residents and 18,957 cases), we found that an increase in road traffic noise exposure is positively associated with an increase in the prevalence of hypertension: using a random effects model, we estimated an RR of 1.05 (95%CI: 1.02 – 1.08) per 10 dB (L_{DEN}) increase in road traffic noise. We based this estimate on studies carried out within the road traffic noise level range of approximately 20 - 85 dB (L_{DEN}). We observed increased but moderate heterogeneity among the studies. We estimated that the residual proportion of the between-study variance due to heterogeneity was $I^2_{residual} = 52.4\%$ (χ^2 test for heterogeneity: $Q = 96.69$, $Df = 46$, $p < 0.001$).

Figure 4.3 presents the results of the studies, without considering age or sex groups, resulting in 33 estimates. The value of the resulting RR per 10, using a random effects model, was somewhat higher: $RR = 1.07$ (95%CI: 1.03 – 1.12) per 10 dB (L_{DEN}). We estimated a residual proportion of the between study variance due to heterogeneity of $I^2_{residual} = 79.9\%$ (χ^2 test for heterogeneity: $Q = 159.51$, $Df = 32$, $p = 0.000$).

Also, one *cohort study* [120, 121] investigated the impact of road traffic noise (based on a 5-year average) on the incidence of hypertension and found no clear association after adjustment for several confounders. Based on the results of this study, we estimated an RR for the incidence of hypertension of 0.97 (95%CI: 0.90 – 1.05) per 10 dB increase in road traffic noise.

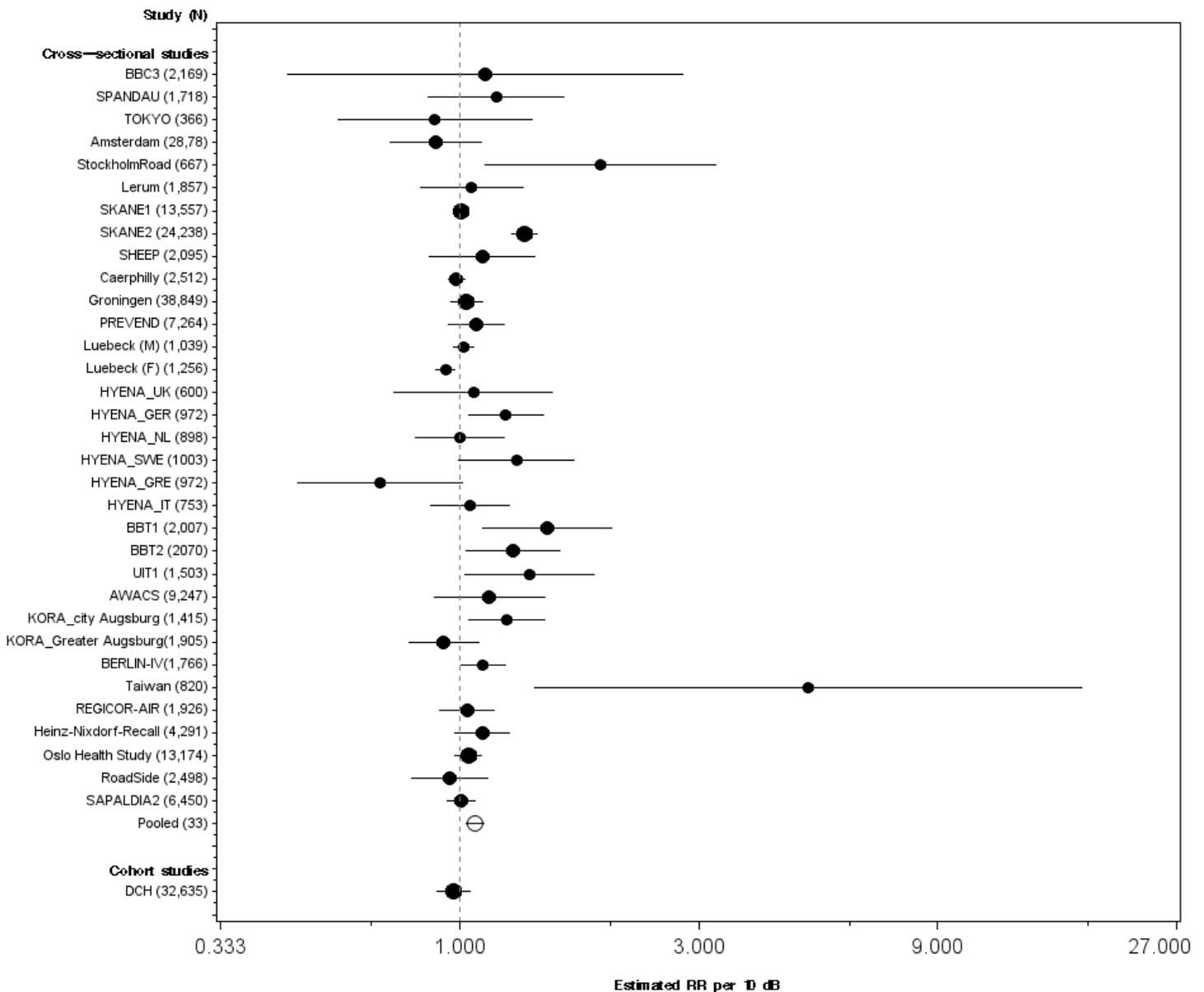


Figure 4.3: Association between road traffic noise exposure (L_{DEN} in dB) and hypertension. The black vertical line corresponds to no effect of road traffic noise exposure. The black dots correspond to the estimated RR per 10 dB and 95% CI for the different studies. The white circle represents the summary estimate and 95% CI.

4.2.4 Publication bias

To assess the extent of publication bias, we plotted the estimated RR per 10 dB against the study precision for the cross-sectional studies. Figure 4.4 presents the resulting funnel plot. The funnel appears rather asymmetric, with smaller studies (those with larger standard errors) tending to have smaller relative risks. This may suggest publication bias. The result of the Egger test (estimated bias coefficient: 0.867) provided evidence of small-study effects ($p = 0.001$). We did not assess publication bias for the cohort studies, because there was only one cohort study included.

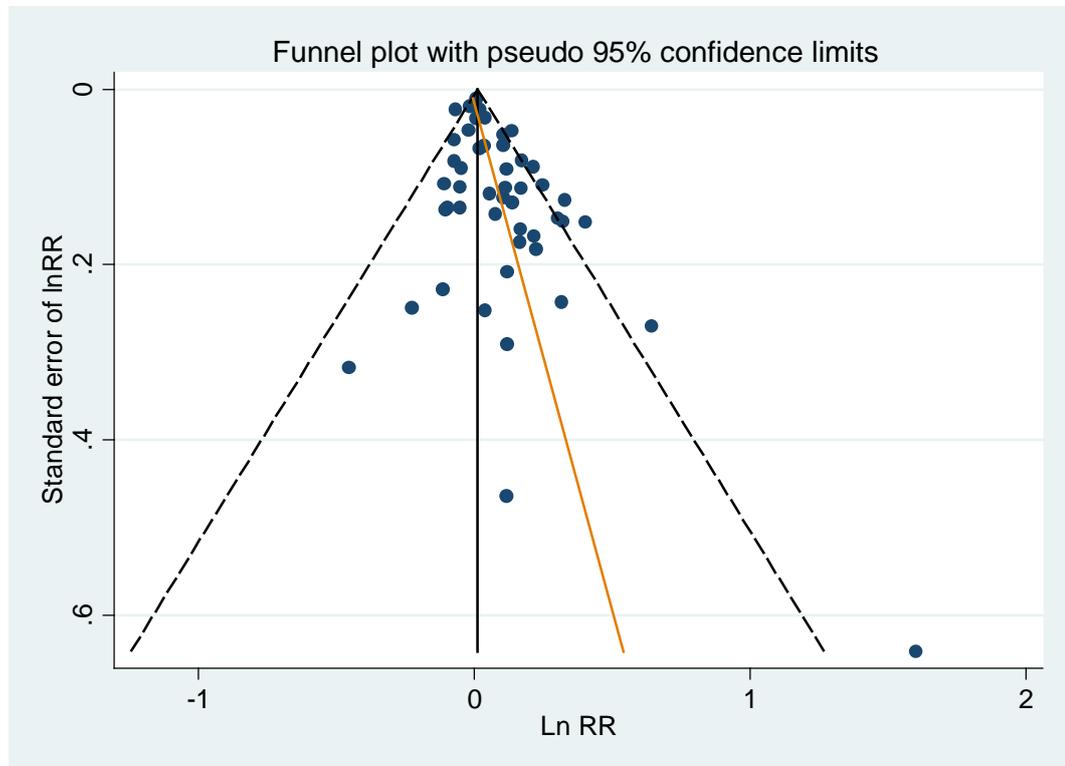


Figure 4.4: Funnel plot showing the natural logarithm of the RR per 10 dB for the relationship between road traffic noise exposure and the prevalence of hypertension of the individual cross-sectional studies plotted against the precision (standard error of lnRR), including the fitted regression line from the standard (Egger) test for small study effects.

4.2.5 Heterogeneity

To study whether the heterogeneity between the studies observed in Figure 4.3 might be due to differences in study characteristics, we carried out a meta-regression analysis, including one covariate at a time. Table 4.6 shows the results of this analysis. It shows that with the exception of risk of exposure bias, there was no clear evidence of heterogeneity due to the covariates that were tested.

Table 4.6: Results of a meta-regression analysis for the cross-sectional studies analysing the association of road traffic noise with hypertension (48 effect estimates)

Adjustment for covariate	# estimates	RR _{10dB}	95% CI	I ² _{Residual} Proportion of variation due to heterogeneity (%)	Delta I ² _{residual} Difference of residual variation (%)	P-value of variable in meta-regression
Overall considering sex categories	47	1.05	1.02 – 1.08	52.4		
Sample size				53.3	0	0.38
<1,000 participants	15	1.12	0.99 – 1.27			
1,000-2,000 participants	12	1.06	0.99 – 1.13			
>2,000 participants	20	1.03	1.00 – 1.07			
Adjustment for socio-economic status indicator				52.9	0	0.49
No	7	1.03	0.93 – 1.13			
Yes	40	1.06	1.02 – 1.09			
Adjustment for air pollution				52.3	0.1	0.99
No	34	1.05	1.01 – 1.09			
Yes	13	1.05	1.00 – 1.10			
Adjustment for other noise source				52.9	0	0.68
No	32	1.05	1.01 – 1.08			
Yes	15	1.06	0.99 – 1.14			
Gender of the population under study				50.7	1.7	0.11
Males	3	1.00	0.97 – 1.03			
Females	2	0.94	0.89 – 0.98			
Males and females	42	1.07	1.03 – 1.11			
Exposure assessment				52.7	0	0.19
Modelled	37	1.05	1.02 – 1.08			
Measured	5	0.98	0.92 – 1.04			
Modelled and measured	5	1.35	1.19 – 1.54			
Hypertension ascertainment				53.3	0	0.59
Self-report	20	1.07	1.02 – 1.13			
Blood pressure measurement	3	1.01	0.92 – 1.10			
Combination	24	1.05	1.00 – 1.10			
Response rate				53.3	0	0.79
<60%	21	1.05	1.01 – 1.10			
≥60%	21	1.05	1.00 – 1.10			
Missing	5	1.13	0.88 – 1.45			
Risk of exposure bias				47.2	5.2	0.02
High	6	0.97	0.92 – 1.03			

Adjustment for covariate	# estimates	RR _{10dB}	95% CI	I ² _{Residual} Proportion of variation due to heterogeneity (%)	Delta I ² _{residual} Difference of residual variation (%)	P-value of variable in meta-regression
Low Unclear	40 1	1.08 0.89	1.04 – 1.11 0.57 – 1.40			
Risk of confounding bias				52.35	0.05	0.43
High Low Unclear	3 44 0	1.04 1.06 -	0.87 – 1.24 1.02 – 1.09 -			
Risk of outcome bias				53.0	0	0.43
High Low	20 27	1.07 1.04	1.02 – 1.13 1.00 – 1.08			
Risk of overall bias				49.1	3.34	0.65
High Low Unclear	30 16 1	1.04 1.07 0.89	1.00 – 1.08 1.02 – 1.11 0.57 – 1.40			
Secondary analysis				53.4	0	0.43
No Yes Unclear	24 22 1	1.08 1.05 1.01	1.02 – 1.15 1.01 – 1.09 0.99 – 1.03			
Age of the population under study				53.5	0	0.32
All ages	10	1.10	1.02 – 1.19			
Early adulthood (18-35 yrs)	1	1.12	1.34 – 1.30			
Early and middle adulthood (20-74 yrs)	3	1.04	1.00 – 1.10			
Middle adulthood (30-75 yrs)	19	1.05	0.91 – 1.17			
Middle and late adulthood (>35 yrs)	1	1.04	0.94 – 1.10			
Late adulthood (>55 yrs)	11	1.02	0.44 – 9.01			
Unknown	2	1.99				

4.95 Rail traffic noise

4.95.1 Descriptive results

For the review, we identified eight studies [42, 110, 112, 114, 118, 120, 121, 198, 199, 225]. Table 4.7 gives an overview of the characteristics of these studies. All studies but one [120, 121] were cross-sectional. Sample sizes ranged from 1,653 to 9,247 persons. All studies assessed exposure by means of noise models. All studies ascertained hypertension by means of self-reporting as part of a questionnaire or interview.

Table 4.7: Overview of characteristics of the eight studies on the association between rail traffic noise and hypertension

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs.)	Exposure range and characterization ^{**)}	Ascertaining of hypertension ^{††)}
Lerum [112]	Swe	CS	1,857 (71)	MF, 18-75	45-50, 51-55, 56-60, 61-70 (1)	2
RoadSide [225]	Swe	CS	2,497 (59)	MF, 18-80	<50, 50-54, 55-59, ≥ 60 (1)	2
DCH [120, 121]	Den	CO	7,249 ^{a)}	MF, 50-64	<45, 45-50, 50-55, 55-60, 60-65, <65 (1)	2
SAPALDIA-2 [118, 198]	Swi	CS	6,450 (74)	MF, 28-72	<50, 50-55, >55 (1)	2
BBT-1 [42, 110]	Aus	CS	2,007 (80)	MF, 20-74	30 – 80 dB (1)	2
BBT-2 [42, 110]	Aus	CS	2,070 (62)	MF, 17-85	30 – 80 dB (1)	2
ALPNAP [42, 110, 114]	Aus	CS	1,653 (35)	MF, 20-74	55 – 89 dB (1)	2
AWACS [199]	NL	CS	9,247 (36)	MF, 17-65	30- 65 (1)	2

*) Aus = Austria, Den = Denmark, NL = The Netherlands, Swe = Sweden, Swi = Switzerland; †) CS = cross-sectional study, CO = cohort study; ‡) N = number of participants and the response percentage in brackets; **) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ††) The way hypertension was ascertained: 1 = measurement of blood pressure levels and/or by means of a clinical interview, 2 = by means of a question as part of a questionnaire or interview (self-reported); a) the attrition rate in the DCH study exceeds 20% in the follow-up of the cohort.

4.95.2 Study quality

We judged that all the evaluated studies have a high risk of bias (see also Table 4.8). An important reason is that all studies ascertained hypertension by means of self-reporting.

Table 4.8: Risk of bias: reviewer's judgements about each risk of bias item for each of the 8 studies on the association between rail traffic noise and hypertension that were selected for data extraction

Study	Bias due to exposure assessment	Bias due to confounding ^{*)}	Bias due to selection of participants ^{†)}	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
Lerum	Low	Low	Low	High	High	High
AWACS	Low	Low	High	High	Low	High
Roadside	Low	High	High	High	Low	High
DCH	Low	Low	High	High	Low	High
SAPALDIA-2	Unclear	Low	Low	High	Low	High
ALPNAP	Low	Low	High	High	Unclear	High
BBT-1	Low	Low	Low	High	Unclear	High
BBT-2	Low	Low	Low	High	Unclear	High

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age and sex; †) In order to score "low" participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%.

4.95.3 *Data aggregation*

We were not able to derive an effect estimate for the ALPNAP study: The ALPNAP study researchers included several interaction terms for noise exposure and other factors in their statistical model. These interaction terms were the interaction between noise exposure and age, noise exposure and health status, and noise exposure and family history of hypertension [42, 110, 114]. Since all these interaction terms were statistically significant, the effect of noise exposure differs over the different categories of these factors. For the BBT study, we were able to include the results of the phone study only. We did not include the SAPALDIA-2 [118, 198] study at all, since the exposure distribution of this study was very skewed: 99% of the participants were exposed to rail traffic noise levels below 50 dB during the day; 0.4% of the participants were exposed to rail traffic noise levels between 50 and 55 dB during the day; 0.3% were exposed to rail traffic noise levels of more than 55 dB during the day.

Figure 4.5 shows that in the *cross-sectional studies* (comprising 15,850 residents and 2,059 cases), rail traffic noise exposure tended to be positively associated with the prevalence of hypertension, although the association was not statistically significant: Using a random effects model, we estimated an RR of 1.05 (95%CI: 0.88 – 1.26) per 10 dB increase in rail traffic noise. The rail traffic noise levels in the included studies ranged from 30 - 80 dB (L_{DEN}). We observed increased but moderate heterogeneity among the studies. The residual proportion of the between-study variance due to heterogeneity was $I^2_{residual} = 57.6\%$ (χ^2 test for heterogeneity: $Q = 7.08$, $Df = 3$, $p=0.069$).

In the only available *cohort study* that investigated the impact of rail traffic noise on the incidence of hypertension, we found no clear association, after adjustment for several confounders. Based on the results of this study, we estimated an RR for the incidence of hypertension of 0.96 (95%CI: 0.88 – 1.04) per 10 dB increase in rail traffic noise.

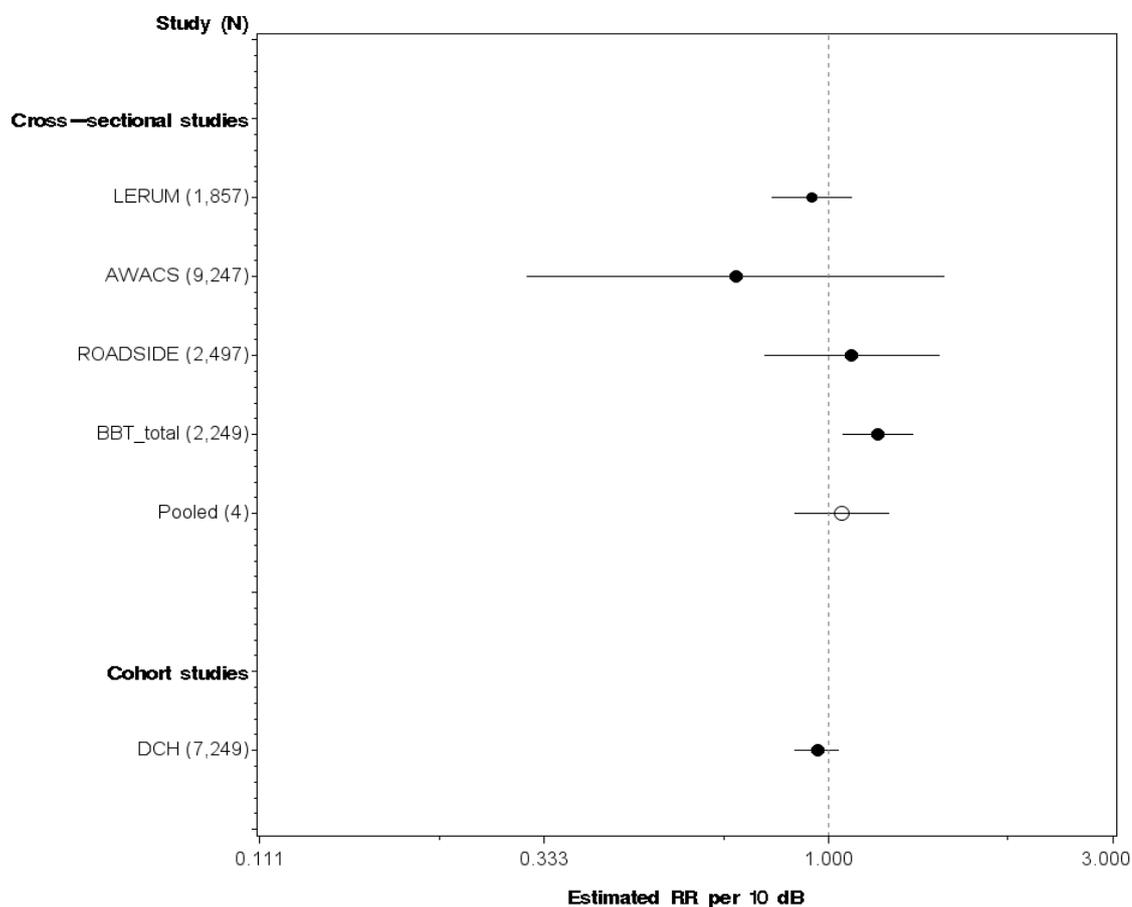


Figure 4.5: Association between rail traffic noise exposure (L_{DEN}) in dB and hypertension. The black vertical line corresponds to no effect of rail traffic noise exposure. The black dots correspond to the estimated RR per 10 dB and 95% CI for the different studies. The white circle represents the summary estimate and 95% CI.

4.95.4 Publication bias

We did not assess publication bias for cohort studies, because there was only one cohort study included. Since the number of available studies and corresponding estimates was less than 10, we were also not able to assess publication bias for the cross-sectional studies.

4.96 Wind turbine noise

4.96.1 Descriptive results

For our review, we were able to select three cross-sectional studies that investigated the association between audible noise (greater than 20 Hz) from wind turbines and hypertension [34, 174-179]: two studies were carried out in Sweden, and one was carried out in The Netherlands. Their sample sizes ranged from about 340 to 740 persons (1,830 participants in total); response rates ranged from 37% to 68%. All three studies were carried out among adults who lived close to a wind turbine.

The studies expressed exposure to wind turbine noise as A-weighted sound pressure levels (SPL) in dB(A). They estimated the level of exposure by means of noise propagation models. These models used information on the manufacturer and the type of wind turbine from the

years 2006 and 2007 as input. All the studies ascertained hypertension by means of self-reporting.

Table 4.9: Overview of the identified and selected studies on the effects of noise from wind turbines on hypertension.

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and average age (yrs.)	Exposure range and characterisation ^{**)}	Ascertaining of hypertension ^{††)}
NL-07 [34, 174-176]	NL	CS	725 (37)	MF, 51	<30, 30-45, 36-40, 41-45, >45 (1)	2
SWE-00 [34, 177, 179]	Swe	CS	351 (68)	MF, 48	<30, 30.0 – 32.5, 32.5 – 35.0, 35.0 – 37.5, 37.5 – 40.0, >40.0 (1)	2
SWE-05 [34, 178, 179]	Swe	CS	754 (58)	MF, NR	< 32.5, 32.5 – 35.0, 35.0 – 37.5, 37.5 – 40.0, ≥ 40.0 (1)	2

*) NL = The Netherlands, Swe = Sweden; †) CS = cross-sectional, ‡) n = Number of participants and response rate in brackets in %; **) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ††) The way hypertension was ascertained: 1 = measurement of blood pressure levels and/or by means of a clinical interview, 2 = by means of a question as part of a questionnaire or interview (self-reported); NR = not reported.

4.96.2 Study quality

Table 4.10 presents the results of the quality assessment of the three studies.

Table 4.10: Risk of bias: reviewer's judgements about each risk of bias item for each of the three studies on the association between noise from wind turbines and hypertension that were selected for data extraction

Study	Bias due to exposure assessment	Bias due to confounding ^{*)}	Bias due to selection of participants ^{†)}	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
NL-07	High	Low	High	High	Low	High
SWE-00	High	Low	Low	High	Low	High
SWE-05	High	Low	High	High	Low	High

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age and sex; †) In order to score "low" participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%.

Since all the studies adjusted for age and gender, we rated the item "Bias due to confounding" in all cases as "low". We rated the item "Bias due to health outcome assessment" in all cases as "high", since all studies measured hypertension by means of self-reporting. In the SWE-00 study, the response rate was higher than 60%. As a result, we rated the item "bias due to selection of participants" for this study as "low".

4.96.3 Data aggregation

We decided not to aggregate the results of the three studies on the impact of wind turbine noise, since too many parameters were unknown and/or unclear. For example, only the NL-07 study reported the prevalence of hypertension (9% in the participants of the exposure category with the lowest exposure level; 9% for the whole study population). After adjustment for a limited number of potential confounding factors (age, gender, and economic benefits), we observed that in all three studies a positive association was found between exposure to noise from wind turbines and the prevalence of self-reported hypertension. However, in none of the studies was this association statistically significant.

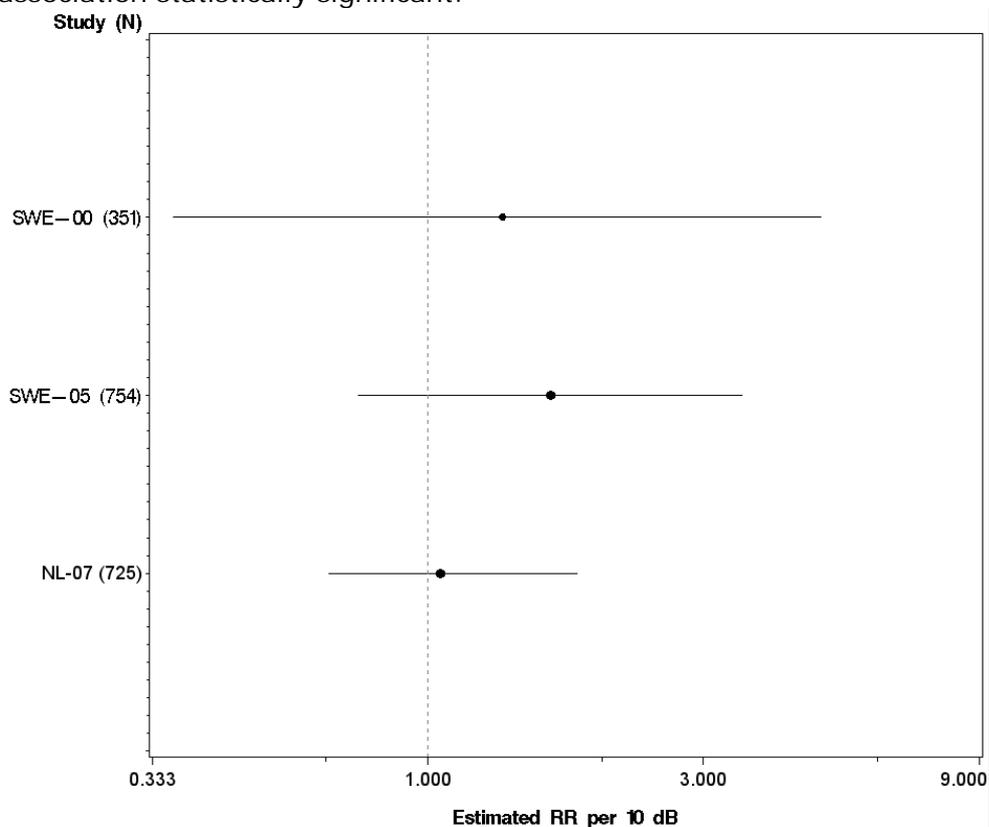


Figure 4.6: Association between exposure (SPL in dB) to wind turbine noise and hypertension. The black vertical line corresponds to no effect of wind turbine noise exposure. The black dots correspond to the estimated RR per 10 dB and 95% CI for the different studies.

5 Studies on the impact of noise on ischaemic heart disease

5.1 Aircraft noise

5.1.1 Descriptive results

We selected eight studies for data extraction [53, 54, 62, 63, 73, 75-77, 199, 212-216, 227-229, 241]. Table 5.1 presents some characteristics of these studies.

Table 5.1: Overview of characteristics of the eight studies on the association between aircraft noise and IHD

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs.)	Type ^{**)}	Exposure range and characterization ^{††)}	Ascertaining of IHD endpoint ^{‡‡)}
HYENA [65, 212-216, 227-229, 235]	Eur	CS	4,861 (24)	MF, 45-70	C	45- 70 (1)	(IHD) 2
USAairports [77]	USA	Eco	6,027,363 (NA)	MF, ≥ 65	C	≥ 45 (1)	(IHD) 3
SPANDAU [62, 63, 241]	Ger	CS	1,718 (85)	MF, 18-90	C	62 – 67, 67-75, ≥75 (1)	(MI, AP) 2
LSAS [76]	UK	Eco	3,591,719 (NA)	MF, all ages	C	≤51, 51-54, 54-57, 57-60, 60-63, ≥63 (1)	(IHD) 3
SNC [75]	Swi	CO	4,580,311 ^{a)}	MF, ≥ 30	C	<45, 45-49, 50-54, 55-59, ≥ 60 (1)	(MI) 3
AWACS-1 [199]	NL	CS	9,365 (36)	MF, 17-65	M, C	30-65 (1)	(MI) 2
AWACS-2 [199]	NL	Eco	305,926 (NA)	MF, ≥ 30	M, C	< 45, 45-59, 50-54, 55-59, ≥60 (1)	(IHD, MI) 3
IVEM [53, 54, 73]	NL	CS	432 (68)	MF, 20-55	M	<57.5, 57.5 – 60, 60.5 – 62.5, 63 – 65, 65.5 – 67.5, >67.5 (1)	(IHD) 1

*) Eur = Europe, Ger = Germany, NL = The Netherlands, UK = United Kingdom, USA = United States of America; †) CS = cross-sectional study, Eco = ecological study, CO = cohort study; ‡) N = number of participants, and the response percentage in brackets; **) Type of aircraft noise: C = civil aircraft, M = military aircraft; ††) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ‡‡) The way IHD was ascertained: 1 = measurement/clinical interview, 2 = self-reported, 3 = healthcare registration; a) the attrition rate in the SNC study did not exceed 20% in the follow-up of the cohort. Abbreviations: IHD = ischaemic heart disease, MI = myocardial infarction, AP = angina pectoris, NA = not applicable, since a targeted sample was included, NR = not reported.

Of the eight selected studies, four were cross-sectional and one was a cohort study. The three remaining studies were ecological studies, comparing the health magnitudes of different small areas (e.g. postal code areas). All studies, except one, were carried out in Europe. Sample sizes ranged from 432 to more than 6 million persons.

Most studies (n = 5) investigated the impact of civil aircraft noise exposure. One study investigated the impact of military aircraft noise exposure only, while two studies investigated the combination of civil and military aircraft noise. All the evaluated studies estimated aircraft noise levels by means of noise models incorporated in Geographic Information Systems (GIS), where they were usually linked with the home addresses of the participants. In some studies [53, 54, 73, 76, 77], estimated noise levels were linked with the area in which the participants lived (e.g. postal code area).

IHD or coronary heart disease comprises a group of diseases of which myocardial infarction and angina pectoris are probably the best known. Five studies investigated the impact of aircraft noise on IHD in general. Three studies investigated the impact on specific types of IHD: myocardial infarction or angina pectoris. Three of the evaluated studies ascertained IHD by means of self-reporting; only one study used a clinical interview. Four studies ascertained IHD by means of data derived from healthcare registrations (e.g. hospital admissions). Three studies [62, 63, 75, 199, 241] were not originally designed to investigate the effects of aircraft noise exposure.

5.1.2 *Study quality*

We judged that most of the studies have a high risk of bias (see Table 5.2). An important reason was that five of the studies did not adjust for age, sex, and smoking behaviour. For these studies, we rated the factor "Bias due to confounding" as "high". For the LSAS study, we rated the factor "Bias due to confounding" as "unclear", since the researchers used lung cancer as a proxy for smoking behaviour.

For three studies, we rated the factor "bias due to health outcome assessment" as "high", since these studies ascertained IHD by means of self-reporting only [62, 63, 65, 199, 212-216, 227-229, 235, 241].

Table 5.2: Risk of bias: reviewer's judgements about each risk of bias item for each of the eight studies on the association between aircraft noise and IHD that were selected for data extraction

Study	Bias due to exposure assessment	Bias due to confounding*)	Bias due to selection of participants†)	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
HYENA	Low	Low	High	High	High	High
USAirports	High	High	Low	Low	Low	High
SPANDAU	Low	High	Low	High	Low	High
LSAS	High	Unclear	Low	Low	Low	High
SNC	Unclear	High	Low	Low	Low	High
AWACS-1	Low	Low	High	High	Low	High
AWACS-2	Unclear	High	Low	Low	Low	High
IVEM	High	High	Low	Low	Low	High

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age, sex, and smoking; †) In order to score "low" participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. Studies with a purposeful sample also scored "low".

5.1.3 Data aggregation

We did not include the SPANDAU study for the data aggregation, since we were not able to derive an RR per 10 dB (L_{DEN}) for this study. Unfortunately, the IVEM study could not provide effect estimates that were adjusted for at least age and/or sex. Consequently, we did not include this study for the data aggregation. After aggregating the results of the remaining two cross-sectional studies (comprising 14,098 participants and 340 cases), we estimated an RR of 1.07 (95%CI: 0.94 – 1.23) per 10 dB (L_{DEN}) increase in aircraft noise for the association between aircraft noise exposure and the *prevalence* of IHD. According to the statistical test, there was no clear evidence of heterogeneity among the studies. We estimated that the residual proportion of the between study variance due to heterogeneity was $I^2_{residual} = 0.0\%$ (χ^2 test for heterogeneity: $Q = 0.26$, $Df = 1$, $p = 0.608$).

Of the eight selected studies, two studies (comprising 9,619,082 participants and 158,975 cases) investigated the association between aircraft noise exposure and the *incidence* of IHD (hospital admissions). After aggregating the results of these two ecological studies, we estimated an RR of 1.09 (95%CI: 1.04 -1.15) per 10 dB (L_{DEN}). The residual proportion of the between study variance due to heterogeneity was $I^2_{residual} = 48.4\%$ (χ^2 test for heterogeneity: $Q = 1.75$, $Df = 1$, $p = 0.164$) and can be indicated as "low".

Three studies investigated the association between aircraft noise exposure and *mortality* due to IHD: two ecological studies and one cohort study. Aggregation of the results of the two ecological studies (comprising 3,897,645 participants and 26,066 cases) revealed an RR of 1.04 (95%CI: 0.97 – 1.12) per 10 dB L_{DEN} . The residual proportion of the between study variance due to heterogeneity was $I^2_{residual} = 39.7\%$ (χ^2 test for heterogeneity: $Q = 1.66$, $Df = 1$, $p = 0.198$). In the cohort

study, we found a non-significant RR of 1.04 (95%CI: 0.98 – 1.11) per 10 dB increase of the aircraft noise level.

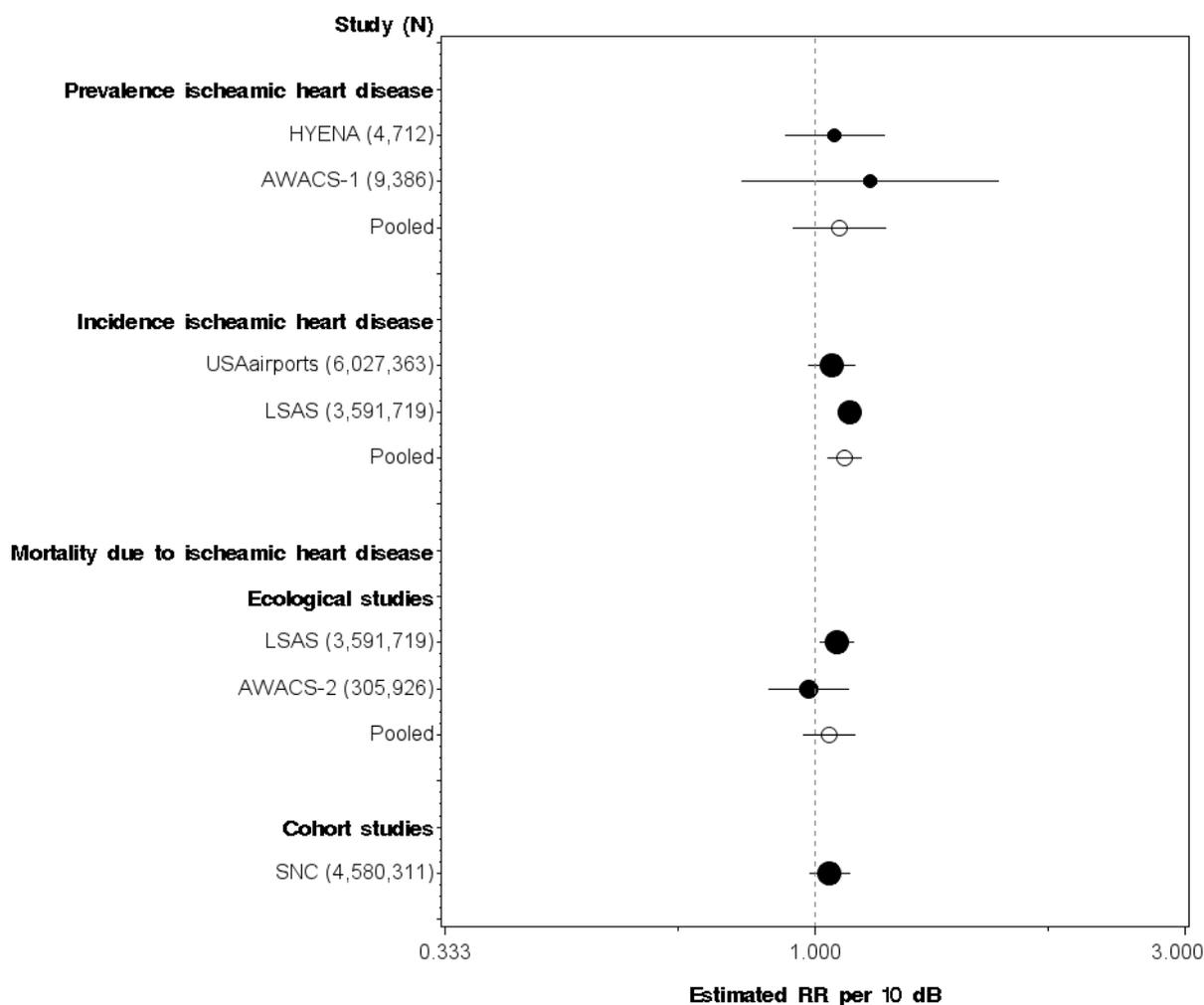


Figure 5.1: Association between aircraft noise exposure (L_{DEN}) and ischaemic heart disease. The dotted vertical line corresponds to no effect of aircraft noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI. The white circles represent the pooled random effect estimates and 95% CI.

5.1.4 Publication bias

We did not assess publication bias for any of the outcomes presented in Figure 5.1, since the number of available studies and corresponding estimates was less than 10.

5.2 Road traffic noise

5.2.1 Descriptive results

We identified and selected 18 studies for data extraction that investigated the association between road traffic noise exposure and several indicators of IHD [42, 53, 54, 62, 63, 65, 73, 86, 87, 96, 97, 102-104, 107, 110, 114, 116, 119, 122, 128-132, 134, 135, 199, 212-216, 227-229, 235, 241, 247]. Table 5.3 presents some characteristics of these 18 studies.

Table 5.3: Overview of characteristics of the 18 studies on the association between road traffic noise and IHD

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs.)	Exposure range and characterization ^{**)}	Ascertaining of IHD ^{††)}
Caerphilly-a [86, 87, 96, 97]	UK	CS	2,512 (89)	M, 45-59	51-55, 55-60, 61-65, 66-70 (2)	AP, MI (1)
Caerphilly-b [86, 87, 96, 97, 129, 130]	UK	CO	2,512 ^{a)}	M, 45-59	51-55, 55-60, 61-65, 66-70 (2)	MI (1)
Speedwell-a [86, 96, 97, 128]	UK	CS	2,348 (92)	M, 45-63	51-55, 55-60, 61-65, 66-70 (2)	AP, MI (1)
Speedwell-b [86, 96, 97, 128-130]	UK	CO	2,348 ^{a)}	M, 45-63	51-55, 55-60, 61-65, 66-70 (2)	MI (1)
SPANDAU [62, 63, 241]	Ger	CS	1,718 (85)	MF, 18-90	<55, 55-60, 61-65, >65 (1,2)	AP, MI (2)
ALPNAP [42, 110, 114]	Aus	CS	1,643 (35)	MF, 25-75	31-74 (1,2)	AP (2)
NAROMI [131, 132]	Ger	CC	4,115 (86)	MF, 20-69	≤60, 61-65, 66-70, >70 (1)	MI (1)
BCC1 [102-104]	Ger	CC	243 (90)	M, 41-70	≤60, 61-65, 66-70, 71-75, 76-80 (1)	MI (1)
BCC2 [102-104]	Ger	CC	4,035 (60)	M, 31-70	≤60, 61-65, 66-70, 71-75, 76-80 (1)	MI (1)
BCC3 [102-104]	Ger	CS	2,169 (70)	M, 31-70	≤60, 61-65, 66-70, 71-75, 76-80 (1)	MI (2)
Kaunus-1 [134, 135]	Lith	Eco	262,830 (NA)	M, 25-64	<60, 60-64, 65-69, ≥70 (2)	MI (3)
BBT-Phone [42, 110]	Aus	CS	2,002 (80)	MF, 17-85	30 – 80 (1)	MI (2)
BBT-Face [42, 110]	Aus	CS	2,070 (62)	MF, 17-85	30 – 80 (1)	MI (2)
IVEM [53, 54, 73]	NL	CS	396 (54)	MF, 18-55	<50, 50-55, 56-60, 61-65, 66-70, >70 (2)	AP, MI (1)
SHEEP [107]	Swe	CC	3,666 (75)	MF, 45-70	42-68 (1)	MI (1)
NCSDC [116]	NL	CO	117,528 ^{b)}	MF, 55-69	≤50, 50-55, 55-60, 60-65, >65 (1)	IHD (3)
Canada1 [119]	Can	CO	412,420 ^{c)}	MF, 45-85	≤55, 56-60, 61-65, 66-70, ≥70 (1)	IHD (3)
DCH [122, 247]	Den	CO	50,613 ^{d)}	MF, 50-64	<55, 55-65, >65 (1)	MI (3)
AWACS1 [199]	NL	CS	9,386 (36)	MF, 17-65	30 – 65 (1)	MI (2)
HYENA [65, 212-216, 227-229, 235]	Eur	CS	4,861 (24)	MF, 45-70	45-70 (1)	IHD (2)

*) Aus = Austria, Can = Canada, Den = Denmark, Eur = Europe, Ger = Germany, Lith = Lithuania, NL = The Netherlands, Swe = Sweden, UK = United Kingdom; †) CS = cross-sectional study, Eco = ecological study, CO = cohort study; ‡) N = number of participants and the response percentage in brackets; **) Exposure range (noise levels in L_{DEN}) and

the way exposure to noise was assessed: 1 = modelled, 2 = measured; ††) The way IHD was ascertained: 1 = measurement of blood pressure levels and/or by means of a clinical interview, 2 = by means of a question as part of a questionnaire or interview (self-reported), 3 = by means of healthcare registration; a) after 10 years follow-up the attrition rate of both the Caerphilly- and Speedwell cohorts together was 19%; b) the attrition rate in the NCSDC cohort was less than 5% (3%); c) the attrition rate of the Canada-1 cohort was less than 5%; d) the attrition rate in the DCH study could not be calculated in detail, but is expected to be much less than 20%, since the outcome data were extracted from national registers. Abbreviations: IHD = ischaemic heart disease, MI = myocardial infarction, AP = angina pectoris, M = males, F = females, NA = not applicable, since a targeted sample was included.

Of the 18 studies, one study was ecological [134, 135], eight studies were cross-sectional [42, 53, 54, 62, 63, 65, 73, 102-104, 110, 114, 199, 212-216, 227-229, 235, 241], four were case-control studies [102-104, 107, 131, 132], and five were cohort studies [86, 87, 96, 97, 116, 119, 122, 128-130, 247]. Two of the cohort studies (Caerphilly and Speedwell) also published results of cross-sectional analyses. All studies - but one [119] - were carried out in Europe. Sample sizes ranged from 243 to more than 400,000 persons.

Most studies (n = 12) estimated the road traffic noise levels of their respondents by means of noise models incorporated in Geographic Information Systems (GIS). These models were able to estimate the road traffic noise level on a very low resolution level (e.g. 25 x 25 m or even 5 x 5 m), using data on e.g. traffic intensities, traffic composition, traffic speed, distance to roads, land use, and/or location of noise barriers. Subsequently, the researchers linked the grids with the modelled noise levels to the addresses or the streets in which the participants lived.

Three studies estimated the road traffic noise levels of their participants by means of noise measurements. The location and the number of measurements varied across the studies: for example, the Caerphilly and Speedwell studies carried out noise measurements in the streets in which the respondents lived. The Kaunus-1 study carried them out in all busy streets and in a number of side streets of the city in which the study took place. From the results of their noise measurements, the researchers of these studies created a noise map and subsequently assigned a noise value to each participant. Two studies applied a noise model incorporated in GIS in combination with noise measurements.

Only three studies investigated the impact on IHD in general. The rest of the studies (n = 15) investigated the impact of specific types of IHD: myocardial infarction or angina pectoris.

Seven of the evaluated studies ascertained IHD by means of self-reporting; seven other studies used clinical interviews/measurements. Four studies ascertained IHD by means of data derived from healthcare registrations. Six studies [62, 63, 107, 116, 119, 122, 199, 241, 247] were not originally set up to investigate the impact of road traffic noise.

5.2.2 *Study quality*

Table 5.4 presents the results of the evaluation of the quality of the studies. We judged that 9 studies have a low risk of bias and 11 studies have a high risk of bias. An important reason was that eight of the studies did not adjust for age, sex, and smoking behaviour. For these studies, we rated the factor "Bias due to confounding" as "high".

Table 5.4: Risk of bias: reviewer's judgements about each risk of bias item for each of the 18 studies on the association between road traffic noise and IHD that were selected for data extraction

Study	Bias due to exposure assessment	Bias due to confounding*)	Bias due to selection of participants†)	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
Caerphilly-a	High	High	Low	Low	Low	High
Caerphilly-b	High	Low	Low	Low	Low	Low
Speedwell-a	High	High	Low	Low	Low	High
Speedwell-b	High	Low	Low	Low	Low	Low
Spandau	Low	High	Low	High	Low	High
ALPNAP	Low	Low	High	High	Unclear	High
NAROMI	Low	Low	Low	Low	Low	Low
BCC1	Low	Low	Low	Low	Low	Low
BCC2	Low	Low	Low	Low	Low	Low
BCC3	Low	Low	Low	High	High	High
Kaunus-1	High	High	Low	Low	Low	High
BBT-phone	Low	High	Low	High	Unclear	High
BBT-face	Low	High	Low	High	Unclear	High
IVEM	High	High	Low	Low	Low	High
SHEEP	Low	Low	Low	Low	Low	Low
NCSDC	Low	Low	Low	Low	Low	Low
AWACS1	Low	Low	High	High	Low	High
HYENA	Low	Low	High	High	High	High
DCH	Low	Low	Low	Low	Low	Low
Canada1	Low	High	Low	Low	Low	Low

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age, sex, and smoking; †) In order to score "low", participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. Studies with a purposeful sample also scored "low".

5.2.3 Data aggregation

Prevalence of ischaemic heart disease

The Spandau study was not included for the data aggregation, since we were not able to estimate an RR per 10 dB (L_{DEN}). We also did not include the IVEM study, as we were not able to derive effect estimates that were adjusted for at least age and/or sex.

After aggregating the results of the remaining eight cross-sectional studies (comprising 25,682 participants and 1,614 cases), we estimated an RR of 1.24 (95%CI: 1.08 – 1.42) per 10 dB (L_{DEN}) increase in road traffic noise for the association between road traffic noise exposure and the prevalence of IHD (Figure 5.2). According to the statistical test, there were indications for moderate heterogeneity among the studies. The residual proportion of the between study variance due to heterogeneity was $I^2_{residual} = 51.4\%$ (χ^2 test for heterogeneity: $Q = 12.36$, $Df = 6$, $p = 0.054$).

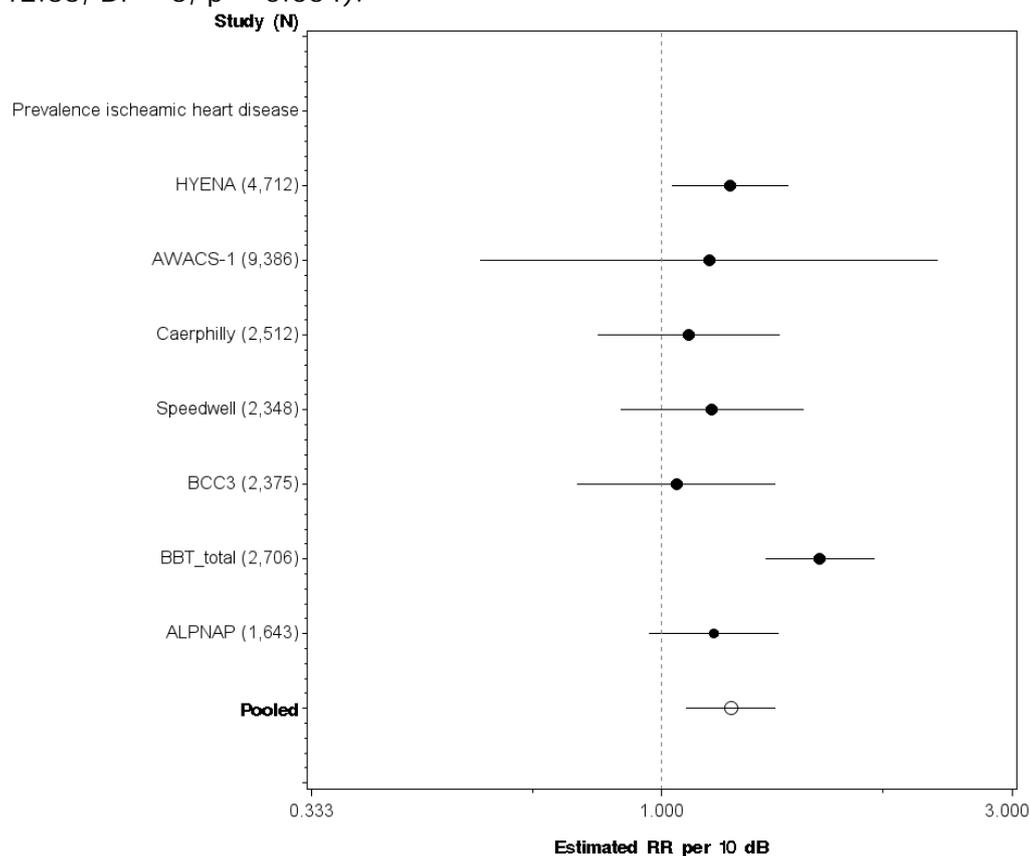


Figure 5.2: Association between road traffic noise exposure (L_{DEN}) and the prevalence of IHD. The dotted vertical line corresponds to no effect of road traffic noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI. The white circles represent the pooled random effect estimates and 95% CI.

Heterogeneity

To find out whether the observed heterogeneity between the studies (see Figure 5.2) might be due to differences in study characteristics, we carried out a meta-regression analysis, including one covariate at a time. Table 5.5 presents the results of this analysis. It shows that the

factors “whether or not a study adjusted for an indicator of smoking” and “whether or not a study adjusted for an indicator of air pollution” were important sources of heterogeneity.

Table 5.5: Results of a meta-regression (subgroup) analysis for the cross-sectional studies analysing the association between road traffic noise and the prevalence of IHD (7 effect estimates)

Adjustment for covariate	No of estimates	RR _{10dB}	95% CI	I ² _{Residual} Proportion of variation due to heterogeneity (%)	ΔI ² _{residual} Difference of residual variation*)	p-value of variable in meta-regression
Base model	7	1.24	1.08 - 1.42	51.4		
Adjustment for indicator of smoking						
No	3	1.32	1.03 - 1.69	41.9	9.5	0.31
Yes	4	1.15	1.00 - 1.33			
Adjustment for indicator of air pollution						
No	3	1.17	1.03 - 1.32	33.9	17.5	0.20
Yes	4	1.37	1.04 - 1.80			
Adjustment for indicator of socio-economic status						
No	1	1.05	0.77 - 1.43	52.6	0	0.41
Yes	6	1.27	1.10 - 1.47			
Risk of total bias						
High	5	1.28	1.07 - 1.52	52.1	0	0.46
Low	2	1.13	0.92 - 1.38			
Response rate						
<60%	3	1.21	1.06 - 1.38	54.6	0	0.78
≥60%	4	1.24	0.97 - 1.58			

*) Negative values are set to zero; negative signs are possible if the covariate explains less of the heterogeneity than expected by chance.

Incidence of ischaemic heart disease

Eight of the selected studies investigated the association between road traffic noise exposure and the *incidence* of IHD: one ecological study, three cohort studies, and four case control studies.

Although the results differed between the studies, we found that design was not a source of heterogeneity ($\Delta I^2 = 0.0\%$, $p = 0.76$). Within the ecological study, we found a positive but non-significant association: an RR of 1.12 (95%CI: 0.85 - 1.48) per 10 dB. Aggregation of the results of the three cohort studies, revealed an RR of 1.04 (95%CI: 0.93 - 1.17) per 10 dB. When combining the results of the four case-control studies, we estimated an RR of 1.09 (95%CI: 0.97 - 1.21) per 10 dB. Because the difference in study quality between the cohort and both the case-control studies, and the ecological study was too large, we decided

to combine only the results of the cohort studies and case-control studies (9 effect estimates, comprising 67,224 participants and 7,033 cases). After aggregation of the results of these studies, we estimated an RR of 1.08 (95%CI: 1.01 – 1.15) per 10 dB (L_{DEN}) increase in road traffic noise for the association between road traffic noise exposure and the *incidence* of IHD (figure 5.3). According to the statistical test, there was no clear evidence of heterogeneity among the studies. The residual proportion of the between study variance due to heterogeneity was $I^2_{residual} = 0.0\%$ (χ^2 test for heterogeneity: $Q = 7.95$, $Df = 8$, $p = 0.44$).

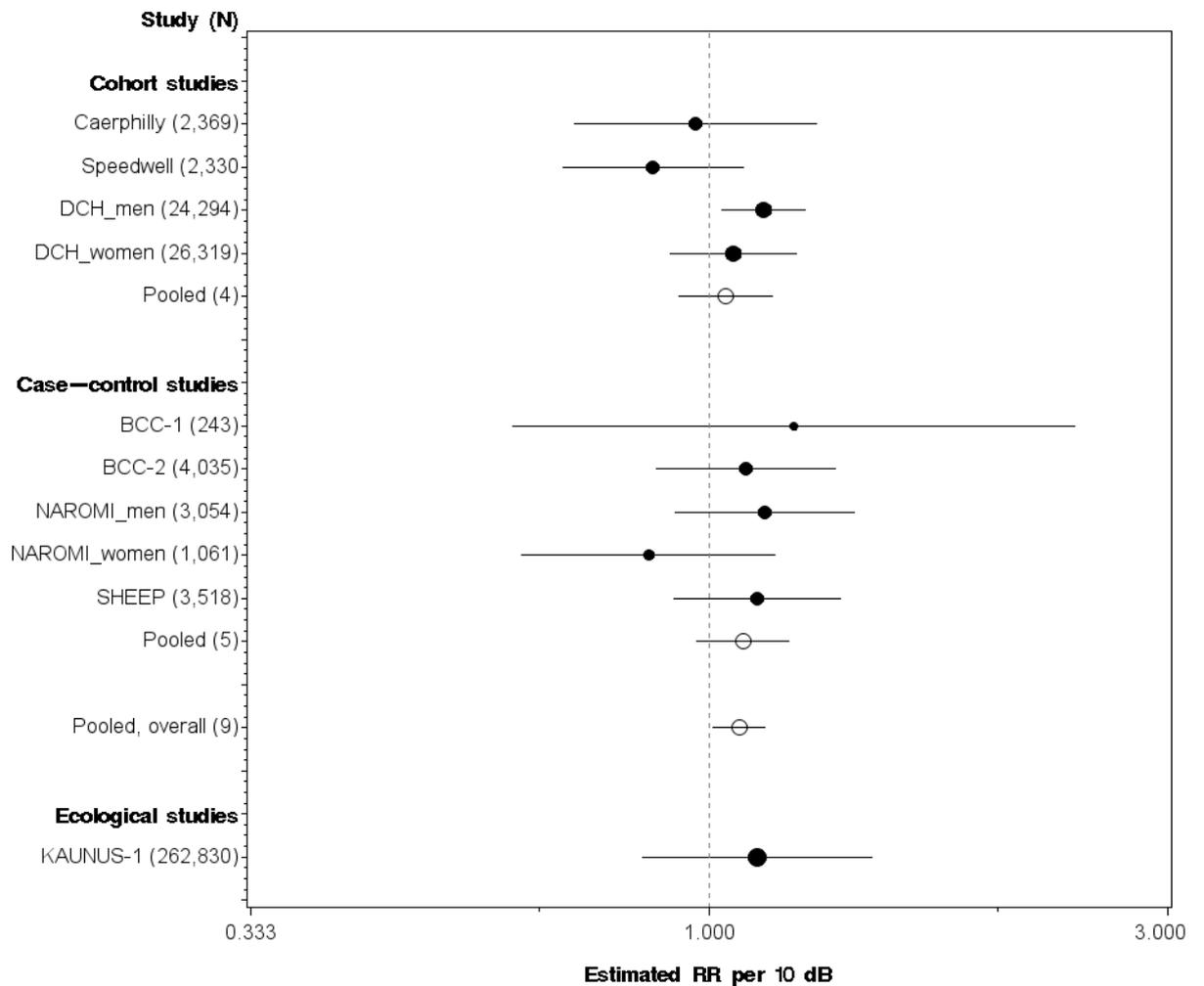


Figure 5.3: The association between road traffic noise exposure (L_{DEN}) and the incidence of IHD. The dotted vertical line corresponds to no effect of road traffic noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI. The white circles represent the pooled random effects estimates and 95% CI.

Heterogeneity

To study whether the heterogeneity between the studies observed in Figure 5.3 might be due to differences in study characteristics, we carried out a subgroup analysis. A meta-regression analysis was not possible since the residual proportion of the between study variance due to heterogeneity was 0.0%. Figure 5.4 demonstrates the results of the

subgroup analysis. It shows that the factors “whether or not a study adjusted for exposure to air pollution” or “whether or not a study adjusted for exposure to another noise source” seemed to increase the risk of IHD in relation to road traffic noise exposure. Furthermore, we observed the weakest effects in studies that were able to include at least 60% of the original study population. We found no clear effect related to the exposure duration of the population under study nor whether the study adjusted for smoking.

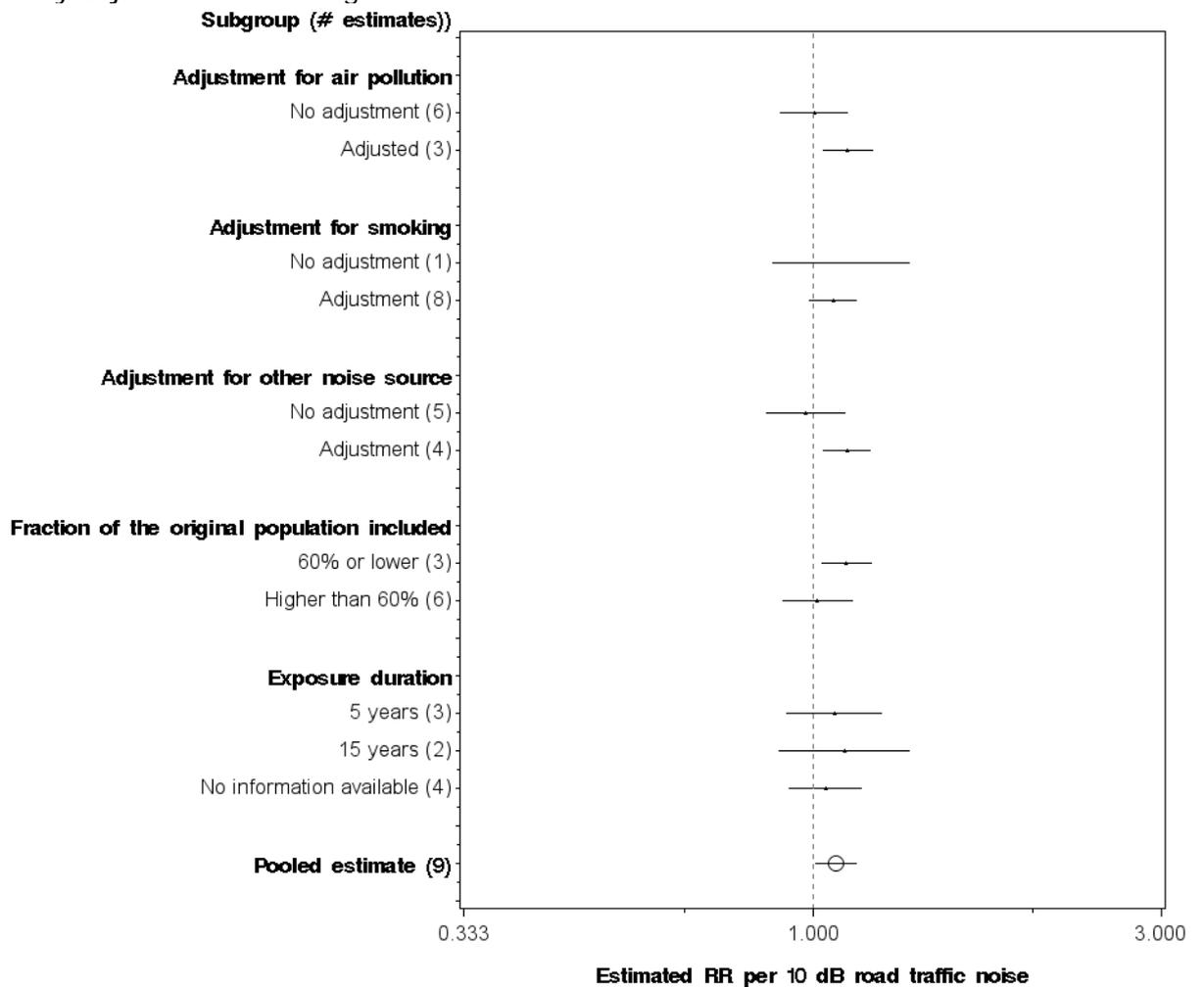


Figure 5.4: Subgroup analysis for the association between road traffic noise exposure (L_{DEN}) and the incidence of IHD. The dotted vertical line corresponds to no effect of road traffic noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI. The white circles represent the pooled random effects estimates and 95% CI.

Mortality due to ischaemic heart disease

We selected three studies (two cohort studies and one case-control study) that investigated the association between road traffic noise exposure (L_{DEN}) and mortality due to IHD for data aggregation. After aggregating the results of these studies, we estimated an RR of 1.05 (95%CI: 0.97 – 1.13) per 10 dB (L_{DEN}) increase in road traffic noise for the association between road traffic noise exposure and mortality due to IHD. According to the statistical test, there was low evidence of

heterogeneity among the studies. The residual proportion of the between study variance due to heterogeneity was $I^2_{\text{residual}} = 34.9\%$ (χ^2 test for heterogeneity: $Q = 4.61$, $Df = 3$, $p = 0.203$).

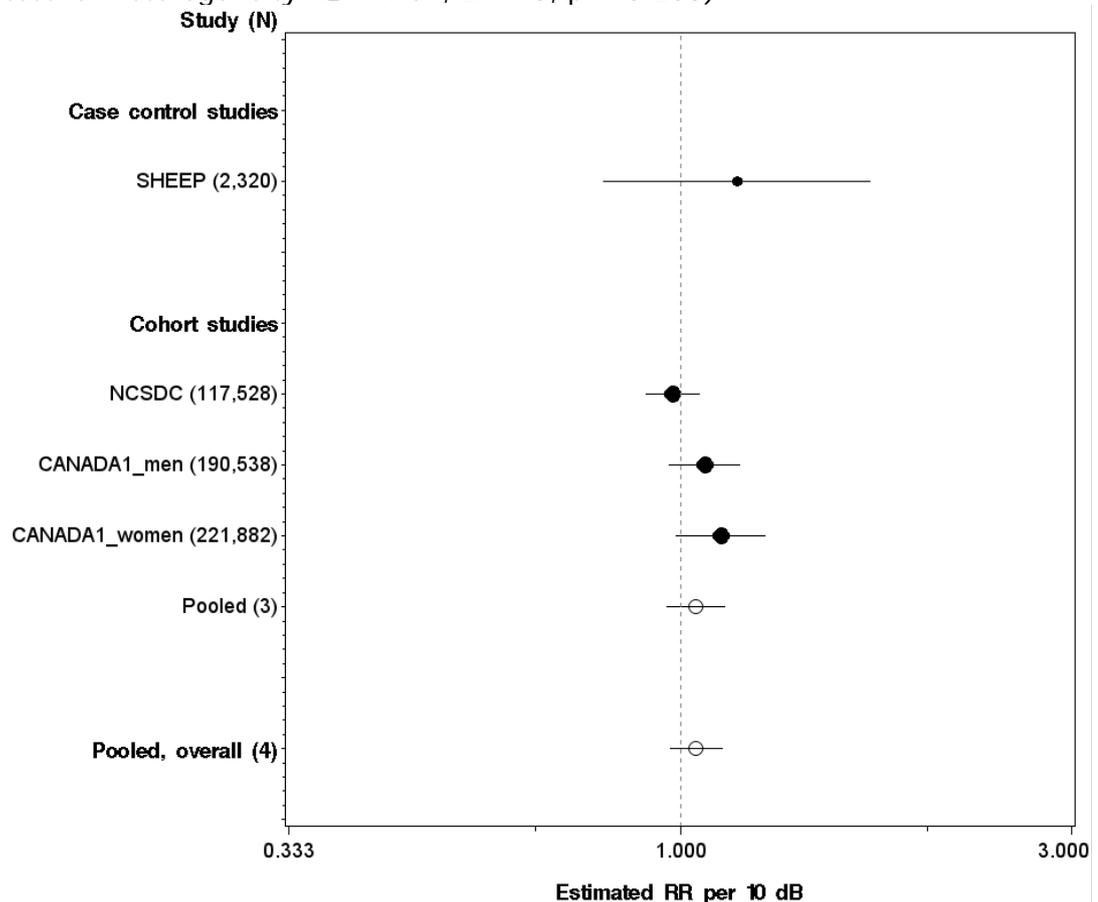


Figure 5.5: Association between road traffic noise exposure (L_{DEN}) and mortality due to IHD. The dotted vertical line corresponds to no effect of road traffic noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI. The white circles represent the pooled random effects estimates and 95% CI.

5.2.4 Publication bias

Only for the association between road traffic noise exposure and the incidence of IHD were we able to assess the extent of publication bias, by plotting the estimated RR per 10 dB against the study precision for ecological, case-control, and cohort studies together ($n = 10$ study estimates) (see Figure 5.6). The resulting funnel is somewhat asymmetric. This may suggest publication bias. The result of the Egger test ($p = 0.06$), however, provides weak evidence of small-study effects.

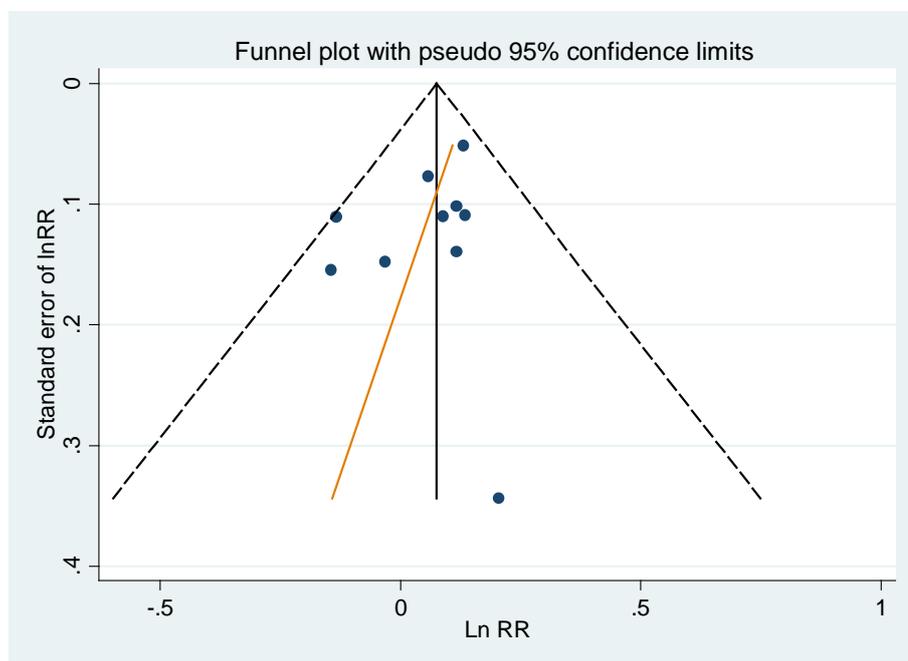


Figure 5.6: Funnel plot showing the natural logarithm of the RR per 10 dB for the relationship between road traffic noise exposure and the incidence of IHD for the individual studies plotted against the precision (standard error of LnRR) including the fitted line from the standard (Egger) test for small-study effects.

For the other outcomes presented in Figures 5.2 and 5.4, we were not able to assess publication bias, since the number of available studies and corresponding estimates was less than 10.

5.3 Rail traffic noise

5.3.1 Descriptive results

We selected four studies for data extraction that have reported on the impact of rail traffic noise on IHD [42, 110, 114, 199]. Table 5.6 presents some characteristics of these studies.

Table 5.6: Overview of characteristics of the 4 studies on the association between rail traffic noise and IHD

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs.)	Exposure range and characterization ^{**)}	Ascertaining of IHD endpoint ^{††)}
BBT-1 [42, 110]	Aus	CS	2,007 (80)	MF, 20-74	30 – 80 (1)	MI (2)
BBT-2 [42, 110]	Aus	CS	2,070 (62)	MF, 17-85	30 – 80 (1)	MI (2)
ALPNAP [42, 110, 114]	Aus	CS	1,653 (35)	MF, 20-74	31 – 74 (1)	AP (2)
AWACS [199]	NL	CS	9,247 (36)	MF, 17-65	30 -65 (1)	MI (2)

^{*)} Aus = Austria, NL = The Netherlands; ^{†)} CS = cross-sectional study, Eco = ecological study, CC = case-control study, CO = cohort study; ^{**)} Exposure range (noise levels in

L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ††) The way IHD was ascertained: 1 = measurement of blood pressure levels and/or by means of a clinical interview, 2 = by means of a question as part of a questionnaire or interview (self-reported), 3 = by means of healthcare registration. Abbreviations: IHD = ischaemic heart disease, MI = myocardial infarction, AP = angina pectoris, M = males, F = females

All studies were cross-sectional and were carried out in Europe. Sample sizes ranged from 1,653 to 9,247 persons. All studies estimated the rail traffic noise levels for the house of each participant by means of noise models incorporated in Geographic Information Systems (GIS). All studies investigated the impact of noise-specific endpoints. All studies ascertained their IHD point by means of self-reporting as part of a questionnaire.

5.3.2 Study quality

Table 5.7 presents the results of the evaluation of the quality of the studies. Largely because IHD was ascertained by means of self-reporting, we gave the quality of the studies as "poor".

Table 5.7: Overview of characteristics of the four studies investigating the association between rail traffic noise and IHD.

Study	Bias due to exposure assessment	Bias due to confounding*	Bias due to selection of participants†	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
BBT-1	Low	High	Low	High	Unclear	High
BBT-2	Low	High	Low	High	Unclear	High
ALPNAP	Low	Low	High	High	Unclear	High
AWACS	Low	Low	High	High	Low	High

*In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age, sex, and smoking; † In order to score "low", participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. Studies with a purposeful sample also scored "low".

5.3.3 Data aggregation

We included all the selected studies in the data aggregation. For the BBT studies, we had only a combined estimate at our disposal.

Combining the results of the BBT studies, the ALPNAP study, and the AWACS study (comprising 13,241 participants and 283 cases) revealed an RR of 1.18 (95%CI: 0.82 – 1.68) per 10 dB increase in rail traffic noise. According to the statistical test, there was moderate evidence of heterogeneity among the studies. The residual proportion of the between-study variance due to heterogeneity was $I^2_{\text{residual}} = 57.4\%$ (χ^2 test for heterogeneity: $Q = 4.70$, $Df = 2$, $p = 0.095$).

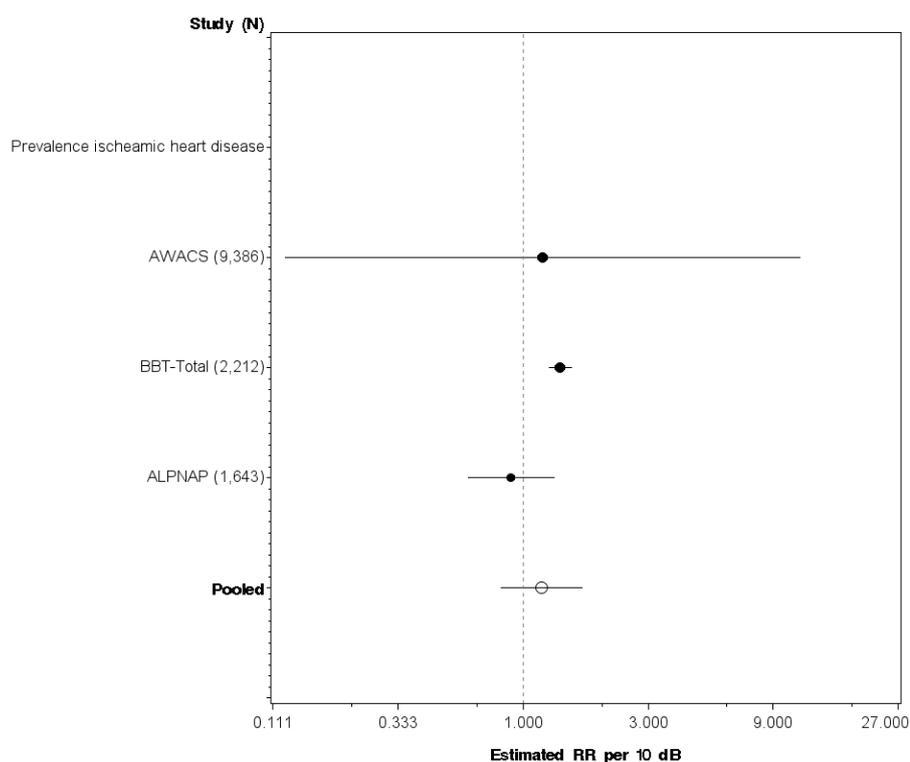


Figure 5.7: The association between rail traffic noise exposure (L_{DEN}) and the prevalence of IHD. The dotted vertical line corresponds to no effect of rail traffic noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI. The white circles represent the pooled random effects estimates and 95% CI.

5.4 Wind turbine noise

5.4.1 Descriptive results

For the review, we were not able to select any study that investigated the association between audible noise (greater than 20 Hz) from wind turbines and IHD. We identified only three cross-sectional studies that investigated the association with self-reported *cardiovascular* disease [34, 174-179]: two studies were carried out in Sweden and one in The Netherlands. Table 4.9 has already presented some characteristics of these studies.

5.4.2 Study quality

Table 4.10 presents the results of the evaluation of the quality of the studies. Since none of the studies adjusted for age, gender *and* smoking behaviour, we rated the item "Bias due to confounding" as "high". Because all studies measured cardiovascular disease by means of self-reporting, we rated the item "Bias due to health outcome assessment" as "high". Only the SWE-00 study, reported a response rate that was higher than 60%. As a result, only this study scored "low" on the item "Bias due to selection of participants".

5.4.3 Data aggregation

We decided not to aggregate the results of the three studies on the impact of wind turbine noise on self-reported cardiovascular disease, since too many parameters were unknown. For example, only the NL-07

study reported the prevalence of cardiovascular disease (6% among participants in the exposure category with the lowest exposure level; 6% for the whole study population). Figure 4.6 shows that none of the studies found an effect of wind turbine noise on the prevalence of self-reported cardiovascular disease.

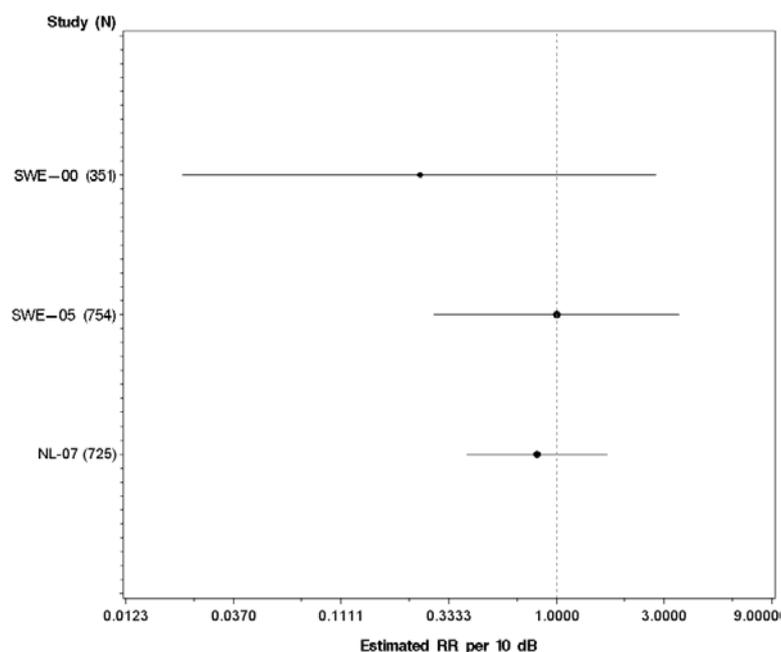


Figure 5.8: Association between wind turbine noise exposure (SPL) and self-reported cardiovascular disease. The dotted vertical line corresponds to no effect of wind turbine noise exposure. The black circles correspond to the estimated RR per 10 dB (SPL) and 95% CI.

6 Studies on the impact of noise on stroke

6.1 Aircraft noise

6.1.1 Descriptive results

Table 6.1 presents some characteristics of the six studies that were included for data extraction [65, 75-77, 199, 212-216, 227-229, 235]. All but one, were carried out in Europe. Three had an ecological design, two were cross-sectional, and only one was a cohort study. The number of participants ranged from 4,861 to 6,027,363 persons. All the evaluated studies assessed the aircraft noise exposure levels of their respondents by noise models incorporated in GIS. In GIS the modelled aircraft noise levels were in most studies linked with the addresses of the participants [65, 75, 199, 212-216, 227-229, 235]. Some studies linked the estimated noise levels with the area in which the participants lived (postcode area or output area) [76, 77].

Table 6.1: Overview of characteristics of the six studies on the association between aircraft noise and stroke.

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs)	Type [*]	Exposure range and characterization ^{††)}	Ascertaining of stroke ^{‡‡)}
HYENA [65, 212-216, 227-229, 235]	Eur	CS	4,861 (24)	MF, 45-70	C	40-75 (1)	2
LSAS [76]	UK	Eco	3,591,719 (NA)	MF, all ages	C	≤51, 51-54, 54-57, 57-60, 60-63, ≥63 (1)	3
SNC [75]	Swi	CO	4,580,311 (NA)	MF, ≥ 30	C	<45, 45-49, 50-54, 55-59, ≥ 60 (1)	3
AWACS-1 [199]	NL	CS	9,365 (36)	MF, 17-65	M,C	30-65 (1)	2
AWACS-2 [199]	NL	Eco	305,926 (NA)	MF, ≥ 30	M, C	< 45, 45-59, 50-54, 55-59, ≥60 (1)	3
USAairports [77]	USA	Eco	6,027,363 (NA)	MF, ≥ 65	C	≥ 45 (1)	3

*) Eur = Europe, Swi = Switzerland, UK = United Kingdom, USA = United States of America; †) CS = cross-sectional study, Eco = ecological study, CO = cohort study; ‡) N = number of participants and the response percentage in brackets; **) Type of aircraft noise: C = civil aircraft, M = military aircraft; ††) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ‡‡) The way stroke was ascertained: 1 = measurement/clinical interview, 2 = self-reported, 3 = healthcare registration; NA = not applicable, since a targeted sample was included.

6.1.2 Study quality

We judged that all the studies have a high risk of bias (see table 6.2). There were different reasons for this: Two of the ecological studies assessed the noise exposure levels for the *area* where the respondents lived instead of at the level of their home address. The inability to apply individual exposure estimates to the study population might have caused exposure misclassification. We rated all studies but two as “high” on the factor “Bias due to confounding” due to the fact that these studies did not adjust for age, sex, and smoking behaviour. Because in the two cross-sectional studies, stroke was ascertained by means of self-reporting, we rated these studies as “high” on the factor “Bias due to health outcome assessment”.

Table 6.2: Risk of bias: reviewer's judgements about each risk of bias item for each of the six studies on the association between aircraft noise and stroke that were selected for data extraction

Study	Bias due to exposure assessment	Bias due to confounding*)	Bias due to selection of participants†)	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
HYENA	Low	Low	High	High	High	High
LSAS	High	High	Low	Low	Low	High
SNC	Unclear	High	Low	Low	Low	High
AWACS -1	Low	Low	High	High	Low	High
AWACS -2	Unclear	High	Low	Low	Low	High
USAairports	High	High	Low	Low	Low	High

*) In order to score “low”, the study should contain information that can be used to derive effect estimates that are at least adjusted for age, sex, and smoking; †) In order to score “low”, participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. Studies with a purposeful sample also scored “low”.

6.1.3 Data aggregation

Prevalence of stroke

Figure 6.1 shows the study estimates that we derived from the studies in table 6.1. Two cross-sectional studies investigated the impact of aircraft noise on the *prevalence* of stroke. The HYENA [65, 212-216, 227-229, 235] and the AWACS-1 [199] studies found statistically non-significant positive and negative associations, respectively. Combining the results of both studies (comprising 14,098 residents and 151 cases) resulted in an RR of 1.02 (95%CI: 0.80 – 1.28) per 10 dB increase in aircraft noise (L_{DEN}). The residual proportion of the between study variance due to heterogeneity was $I^2_{residual} = 0.0\%$ (χ^2 test for heterogeneity: $Q = 0.78$, $Df = 1$, $p = 0.38$).

Incidence of stroke

After combining the results of the ecological studies (comprising 9,619,082 residents and 97,949 cases), we observed that aircraft noise exposure tended to be positively associated with the *incidence* of stroke

(hospital admissions): using a random effects model, we estimated an RR of 1.05 (95%CI: 0.96 – 1.15) per 10 dB increase in aircraft noise (L_{DEN}). We observed increased evidence of heterogeneity among the studies, which can be indicated as “high”. The residual proportion of the between-study variance due to heterogeneity was $I^2_{residual} = 82.7\%$ (χ^2 test for heterogeneity: $Q = 5.79$, $Df = 1$, $p = 0.02$): Both the USAirports study [77] and the LSAS study [76], showed positive associations between aircraft noise exposure and hospital admissions due to stroke. Only the LSAS study revealed a statistically significant association.

Mortality due to stroke

After combining the results of the ecological studies (comprising 3,897,645 residents and 12,086 cases), we observed that aircraft noise exposure was positively associated with *mortality* due to stroke: using a random effects model, we estimated an RR of 1.07 (95%CI: 0.98 – 1.17) per 10 dB increase in aircraft noise (L_{DEN}). The residual proportion of the between-study variance due to heterogeneity was $I^2_{residual} = 28.5\%$ (χ^2 test for heterogeneity: $Q = 1.40$, $Df = 1$, $p = 0.24$) and can be indicated as “low”.

In the cohort study (comprising 4,580,311 residents and 25,231 cases), we observed no association between exposure to aircraft noise (L_{DEN}) and *mortality* due to stroke; we estimated an RR of 0.99 (95%CI: 0.94 – 1.04) per 10 dB [75].

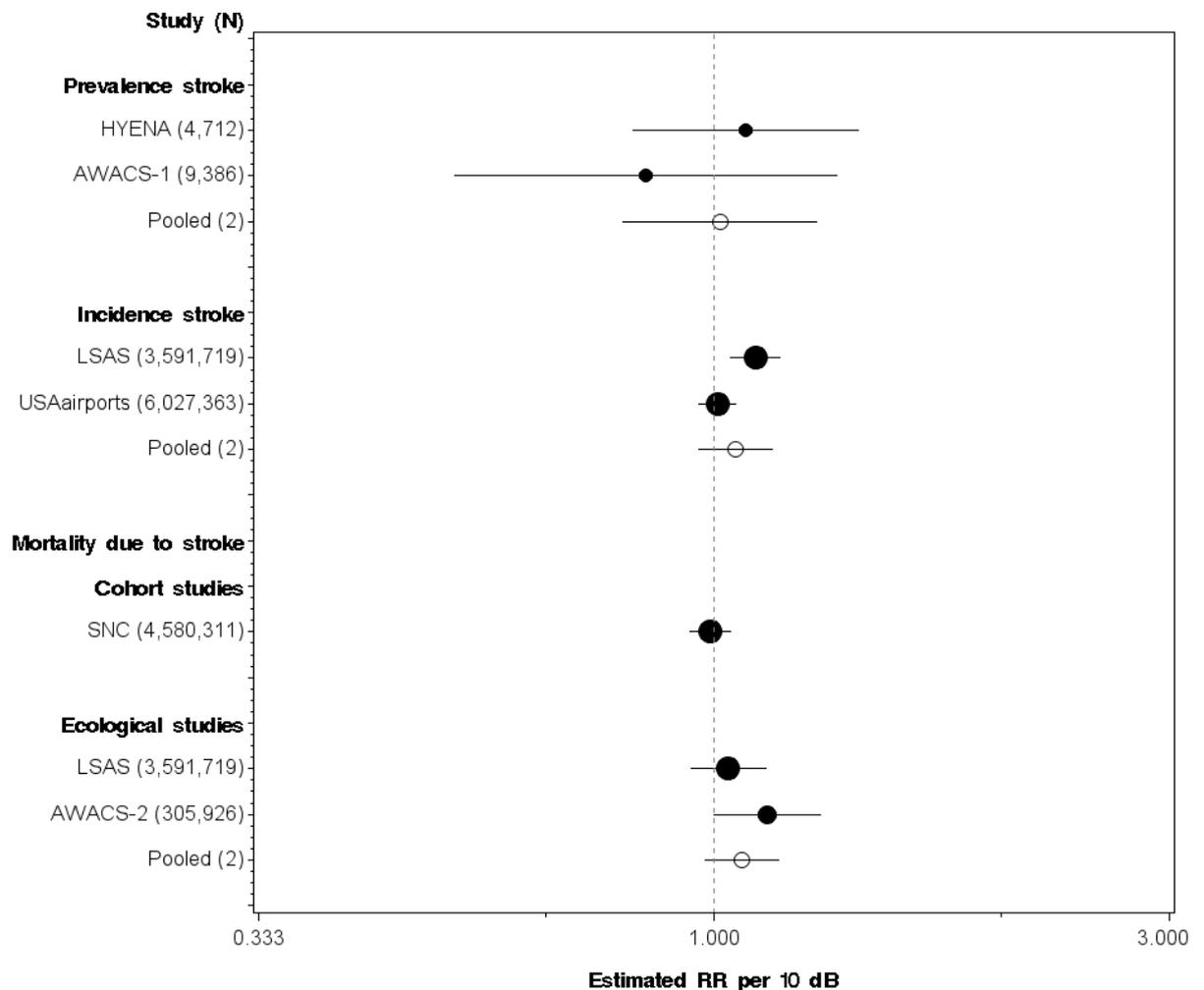


Figure 6.1: The association between aircraft noise exposure (L_{DEN}) and stroke. The dashed vertical line corresponds to no effect of aircraft noise exposure. The black dots correspond to the estimated RR per 10dB and 95% CI for the different studies. The white circle represents the summary estimate and 95% CI.

6.2 Road traffic noise

6.2.1 Descriptive results

Table 6.3 presents some characteristics of the five studies that were included for data extraction [65, 116, 119, 138, 199, 212-216, 227-229, 235, 247, 248]. All studies were carried out in Europe. Three studies were cohort studies, while the remaining two had a cross-sectional design. The number of participants ranged from 4,861 to more than 412,000 persons. The cross-sectional studies ascertained stroke by means of self-reporting. The cohort studies ascertained stroke by means of healthcare registration systems.

All the evaluated studies estimated the road traffic noise exposure levels of their participants by noise models incorporated in GIS. In GIS, the studies linked the modelled road traffic noise levels with the addresses of the participants.

Table 6.3: Overview of characteristics of the studies on the association between road traffic noise and stroke

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs.)	Exposure range and characterization ^{**)}	Ascertaining of stroke ^{††)}
HYENA [65, 212- 216, 227- 229, 235]	Eur	CS	4,861 (24)	MF, 45-70	45-70 (1)	2
NCSDC [116]	NL	CO	117,528 ^{a)}	MF, 55-69	≤50, 50-55, 55-60, 60-65, >65 (1)	3
DCH [138, 247, 248]	Den	CO	51,485 ^{c)}	MF, 50-64	<55, 55-65, >65 (1)	3
AWACS 1 [199]	NL	CS	9,365 (36)	MF, 17-65	30-65 (1)	2
Canada 1 [119]	Can	CO	412,420 ^{b)}	MF, 45-85	≤55, 56-60, 61-65, 66-70, ≥70 (1)	3

*) Can = Canada, Den = Denmark, Eur = Europe, NL = the Netherlands, †) CS = cross-sectional study, Eco = ecological study, CO = cohort study; ; ‡) N = number of participants and the response percentage in brackets; **) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ††) The way stroke was ascertained: 1 = measurement/clinical interview, 2 = self-reported, 3 = healthcare registration. a) the attrition rate in the NCSDC cohort was less than 5% (3%); b) the attrition rate of the Canada-1 cohort was less than 5%; c) the attrition rate in the DCH study could not be calculated in detail, but is expected to be much less than 20%, since the outcome data were extracted from national registers.

6.2.2 Study quality

We judged that two studies have a high risk of bias (see Table 6.4). There were different reasons for this: Two studies reported a response rate lower than 60%, and two studies ascertained stroke by means of self-reporting.

Table 6.4: Risk of bias: reviewer's judgements about each risk of bias item for each of the six studies on the association between road traffic noise and stroke that were selected for data-extraction

Study	Bias due to exposure assessment	Bias due to confounding ^{*)}	Bias due to selection of participants ^{†)}	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
HYENA	Low	Low	High	High	High	High
NCSDC	Low	Low	Low	Low	Low	Low
DCH	Low	Low	Low	Low	Low	Low
AWACS1	Low	Low	High	High	Low	High
Canada1	Low	High	Low	Low	Low	Low

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age, sex, and smoking; †) In order to score "low" participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. Studies with a purposeful sample also scored "low".

6.2.3 Data aggregation

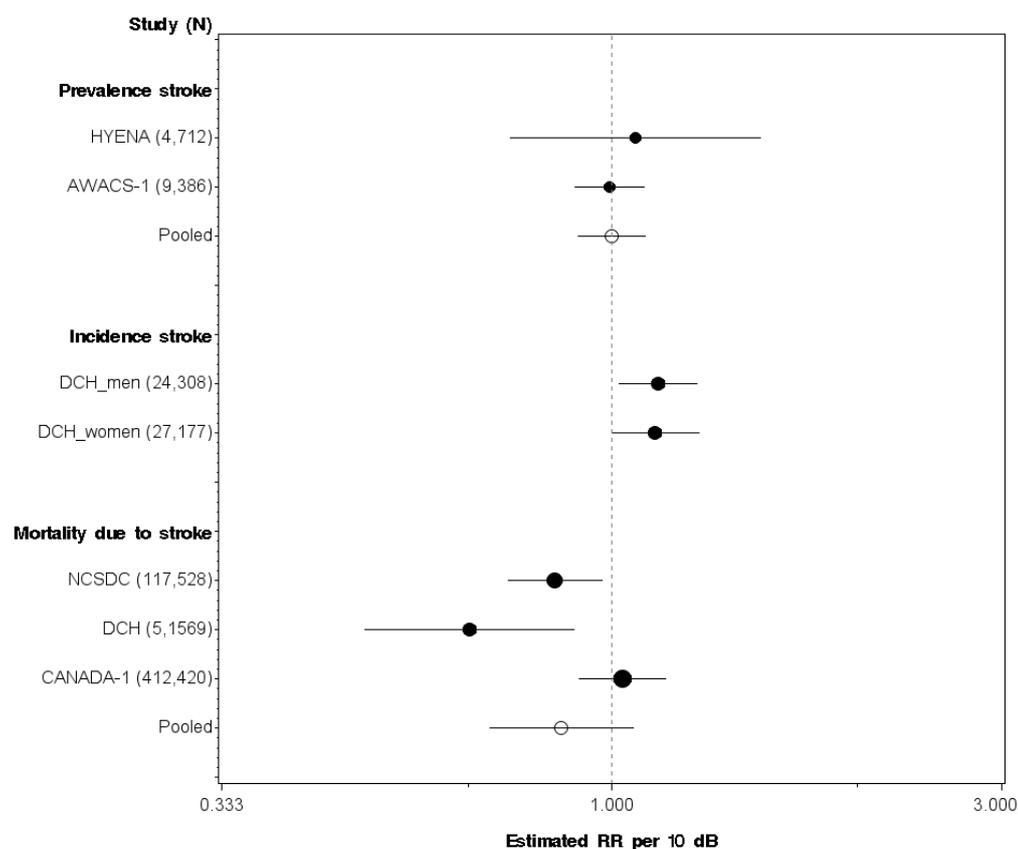


Figure 6.2: Association between road traffic noise exposure (L_{DEN}) and stroke. The dashed vertical line corresponds to no effect of road traffic noise exposure. The black dots correspond to the estimated RR per 10dB and 95% CI for the different studies. The white circle represents the summary estimate and 95% CI.

Prevalence of stroke

The cross-sectional studies on the impact of road traffic noise on self-reported stroke, did not find clear associations. Combining the results of both the AWACS1 [199] and HYENA study [65, 212-216, 227-229, 235] (comprising 14,098 residents and 151 cases) resulted in an RR of 1.00 (95%CI: 0.91 – 1.10) per 10 dB increase in road traffic noise (L_{DEN}) (see Figure 6.2). The residual proportion of the between-study variance due to heterogeneity was $I^2_{residual} = 0.0\%$ (χ^2 test for heterogeneity: $Q = 0.16$, $Df = 1$, $p = 0.691$).

Incidence of stroke

Only the DCH study (51,485 residents and 1,881 cases) investigated the association between road traffic noise and the *incidence* of stroke. For both men and women, we observed a positive association [138, 247, 248] (see Figure 6.2).

Mortality due to stroke

After combining the results of the three cohort studies [116, 119, 138, 247, 248] (comprising 581,517 residents and 2,634 deaths) investigating the association between road traffic noise and *mortality* due to stroke, we estimated an RR of 0.87 (95%CI: 0.71 – 1.06) per 10 dB (L_{DEN}). The residual proportion of the between study variance due to heterogeneity was $I^2_{residual} = 78.0\%$ (χ^2 test for heterogeneity: $Q = 9.07$, $Df = 2$, $p = 0.011$) and can be indicated as “high”.

6.3 Rail traffic noise

Only the AWACS1 study [199] investigated the impact of rail traffic noise on stroke. To this end, the researchers used data from a questionnaire, administered in 2009 by the Municipal Health Service (GGD) among 9,365 persons living in Zuid-Limburg. As part of this questionnaire, the respondents had to indicate whether they suffered from stroke. The AWACS1 study estimated rail traffic noise levels by means of a noise model incorporated in GIS. Subsequently, the researchers linked the modelled rail traffic noise levels with the addresses of the participants. After adjustment for confounders (including age, gender, and smoking), we estimated an RR of 1.07 (95%CI: 0.92 – 1.25) per 10 dB increase in rail traffic noise.

6.4 Wind turbine noise

None of the identified studies investigated the impact of wind turbine noise on stroke.

7 Studies on the impact of noise on diabetes

7.1 Aircraft noise

7.1.1 Descriptive results

Table 7.1 presents some characteristics of the two studies [141, 199] that we included for data extraction. A cohort from Stockholm, Sweden, comprising 5,156 persons of 35 - 55 years of age with a normal baseline oral glucose tolerance test at recruitment was investigated with regard to the impact of aircraft noise on the incidence of diabetes [141]. The researchers selected the population sample so that about 50% of the study participants had a family history of diabetes. They assessed time-weighted average noise levels from aircraft at the residential addresses of the participants during follow-up. Modelled aircraft noise levels ranged from 50 to 65 dB (L_{DEN}) and only 2% of the participants were classified as being exposed to aircraft noise exposure levels equal to or more than 55 dB (L_{DEN}) while 87% were exposed to aircraft noise levels of less than 50 dB (L_{DEN}). The researchers obtained information on outcomes at baseline and during follow-up from surveys and clinical examinations. They used the data from the baseline investigation to control for confounding. After a follow-up period of up to 10 years, they estimated adjusted cumulative incidence RRs of 0.87 (95%CI: 0.52 – 1.45) for prediabetes and 0.99 (95%CI: 0.47 – 2.09) for type 2 diabetes per 10 dB [495]. Stratified analyses indicated that the results were not modified by family history of diabetes. The results of sex-specific analyses, suggested an increased risk of type 2 diabetes in women (RR = 2.11, (95%CI: 0.76 – 5.88)).

Van Poll et al. [199] reported on the results of a Dutch cross-sectional study based on 9,365 participants in a questionnaire survey focusing on health effects related to aircraft noise exposure. Van Poll et al. derived aircraft noise exposure levels from actual flight tracks. After adjustment for confounders, they found an RR for self-reported diabetes of 1.01 (95%CI: 0.78 – 1.31) per 10 dB L_{DEN} .

Table 7.1: Characteristics of studies on the association between aircraft noise and diabetes

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs)	Type ^{**)}	Exposure range and characterization ^{††)}	Ascertaining of diabetes ^{‡‡)}
SDPP [141]	Swe	CO	5,111 ^{a)}	MF, 35-55	C	48 - 65 (1)	1, 2
AWACS-1 [199]	NL	CS	9,365 (36)	MF, 17-65	M,C	30 - 65 (1)	2

*) NL = The Netherlands, Swe = Sweden; †) CS = cross-sectional study, CO = cohort study; ‡) N = number of participants and the response percentage in brackets; **) Type of aircraft noise: C = civil aircraft, M = military aircraft; ††) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ‡‡) The way diabetes was ascertained: 1 = measurement/clinical interview, 2 = self-reported, 3 = healthcare registration. a) the attrition rate in the SDPP study probably exceeds 20% in the follow-up of the cohort.

7.1.2 Study quality

Table 7.2 shows the result of the evaluation of the quality of the studies. The SDPP cohort was judged as having a low risk of bias although it had an attrition rate that probably exceeded 20%. Furthermore, it included an enriched sample of study subjects with a family history of diabetes, but stratified analyses indicated that this did not modify the association between aircraft noise exposure and diabetes incidence. On the other hand, the cross-sectional AWACS study scored poorly, mainly because of a high non-response rate and subjective outcome assessment.

Table 7.2: Risk of bias: reviewer's judgements on risk of bias in studies on aircraft noise and diabetes

Study	Bias due to exposure assessment	Bias due to confounding ^{*)}	Bias due to selection of participants ^{†)}	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
SDPP	Low	Low	High	Low	Low	Low
AWACS-1	Low	Low	High	High	Low	High

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age, sex, and smoking; †) In order to score "low" participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. Studies with a purposeful sample also scored "low".

7.2 Road traffic noise

7.2.1 Descriptive results

Only three studies met the inclusion criteria and were included for data extraction [107, 142, 199]. Table 7.3 presents some characteristics of these studies. The study by Selander et al. [107] (the SHEEP study) included 1,571 cases of myocardial infarction diagnosed in 1992 - 1994 and 2,095 population-based controls from Stockholm County. Originally, the SHEEP study was investigating myocardial infarction. The analyses dealing with the impact of noise on diabetes were performed in the control group (as indicated in the text). Based on residential histories of the study participants, Selander et al. [107] estimated time-weighted average noise levels from road traffic at the residential addresses. Only around 15% of the study subjects had estimated noise levels from road traffic at the façade of 55 dB L_{Aeq24h} or more, corresponding to around 56.4 dB L_{DEN} . Selander et al. obtained information on diabetes through questionnaires and medical examinations. In a secondary cross-sectional analysis of the control group, they estimated a confounder-adjusted RR for diabetes of 1.72 (95%CI: 1.11 - 2.66) among those exposed to 55 dB L_{Aeq24h} (56.4 dB L_{DEN}) of road traffic noise or more compared with those with lower exposures [496]. The excess risk was no longer statistically significant after adjustment for exposure to air pollution, using road traffic-generated NO_2 as a marker.

Sørensen et al. [142] followed incident diabetes from a national registry in a cohort of more than 57,000 subjects from two cities in Denmark for about 10 years. Based on residential histories, they modelled time-

weighted noise levels from road traffic at residences. Noise levels ranged up to 70 dB L_{DEN} , with 64% of the cases exposed to levels of 55 dB L_{DEN} or higher. Mostly, Sørensen et al. obtained data on potential confounders from questionnaires answered at recruitment. There was an increasing trend of diabetes with road traffic noise exposure corresponding to an adjusted incidence rate ratio of 1.08 (95%CI: 1.02 - 1.14) per 10 dB L_{DEN} increase in noise level during the five years prior to diagnosis. Statistically significant excess risks for diabetes related to road traffic noise exposure persisted after adjustment for air pollution, using NO_x as a marker. Stronger associations were suggested in women than in men with rate ratios of 1.11 (95%CI: 1.03 – 1.20) and 1.05 (95%CI: 0.98 – 1.13) per 10 dB L_{DEN} , respectively.

In the Dutch cross-sectional study by van Poll et al. [199], described above in the section on aircraft noise and diabetes, there was an adjusted OR for self-reported diabetes of 1.06 (95%CI: 0.73 – 1.56) per 10 dB of increase in modelled exposure to road traffic noise at the residence.

Table 7.3: Characteristics of studies on the association between road traffic noise and diabetes

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs)	Exposure range and characterization ^{**)}	Ascertaining of diabetes ^{††)}
SHEEP [107]	Swe	CS	2,095 (72)	MF, 45-70	42-68 (1)	1, 2
DCH [142]	Den	CO	57,053 ^{a)}	MF, 50-64	<55, 55-65, >65 (1)	3
AWACS1 [199]	NL	CS	9,365 (36)	MF, 17-65	30-65 (1)	2

*) Den = Denmark, NL = The Netherlands, Swe = Sweden; †) CC = case-control study, CO = cohort study, CS = cross-sectional study; ‡) N = number of participants and the response percentage in brackets; **) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; ††) The way diabetes was ascertained: 1 = measurement/clinical interview, 2 = self-reported, 3 = healthcare registration; a) the attrition rate in the DCH study could not be calculated in detail but is expected to be much less than 20%, since the outcome data were extracted from national registers.

7.2.2 Study quality

Table 7.4 presents the results of the evaluation of the quality of the studies. We rated the Danish cohort study [142] as having a low risk of bias. The SHEEP study [107] based its results for diabetes on a secondary analysis of a control group in a case-control study of myocardial infarction. Since the outcome assessment was based on self-report, we rated the factor "Bias due to health outcome assessment" as "high". The cross-sectional AWACS1 study [199] scored poorly, mainly due to a high non-response rate and subjective outcome assessment.

Table 7.4: Risk of bias: reviewer's judgements on risk of bias in studies on road traffic noise and diabetes

Study	Bias due to exposure assessment	Bias due to confounding ^{*)}	Bias due to selection of participants ^{†)}	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
SHEEP	Low	Low	Low	High	Low	Low
DCH	Low	Low	Low	Low	Low	Low
AWACS-1	Low	Low	High	High	Low	High

*) In order to score "low", the study should contain information that can be used to derive effect estimates that are at least adjusted for age, sex, and smoking; †) In order to score "low" participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. Studies with a purposeful sample also scored "low".

7.3 Rail traffic noise

7.3.1 Descriptive results

Only two studies met the inclusion criteria and were included for data extraction [142, 199]. We have already described the design of these studies in the previous section on road traffic noise and diabetes (see Table 7.3). In the cohort study from Denmark by Sørensen et al. [142] we did not observe an association between rail traffic noise and diabetes incidence, with an incidence rate ratio of 0.97 (95%CI: 0.89 - 1.05) in those exposed to more than 60 dB L_{DEN}. In the Dutch cross-sectional study [199] an OR of 0.21 (95%CI: 0.05 - 0.82) for diabetes was reported for a 10 dB L_{DEN} increase in rail traffic noise exposure.

7.3.2 Study quality

Table 7.4 presents the results of the evaluation of the quality of the studies. The Danish cohort study had low risk of bias, while the cross-sectional AWACS study scored poorly, mainly because of a high non-response rate and subjective outcome assessment.

7.4 Wind turbine noise

7.4.1 Descriptive results

For the review, we selected three studies [34, 174-179] that investigated the association between audible noise (greater than 20 Hz) from wind turbines and self-reported diabetes. We have already presented the characteristics of these studies in Table 4.9.

7.4.2 Study quality

Table 4.10 presents the results of the evaluation of the quality of the studies. Since none of the studies adjusted for age, gender, and smoking behaviour, we scored the item "Bias due to confounding" as "high". All studies measured diabetes by means of self-reporting. Consequently, we rated the item "Bias due to health outcome assessment" as "high" for all studies. Only in the SWE-00 study was the response rate higher than 60%. As a result, we rated this study "low" on the item "Bias due to selection of participants".

7.4.3 Data aggregation

We decided not to aggregate the results of the three studies on the impact of wind turbine noise, since too many parameters were unknown

and/or unclear. For example, only the NL-07 study presented the prevalence of self-reported diabetes: 4% of the participants in the exposure category with the lowest exposure level; 4% for the whole study population.

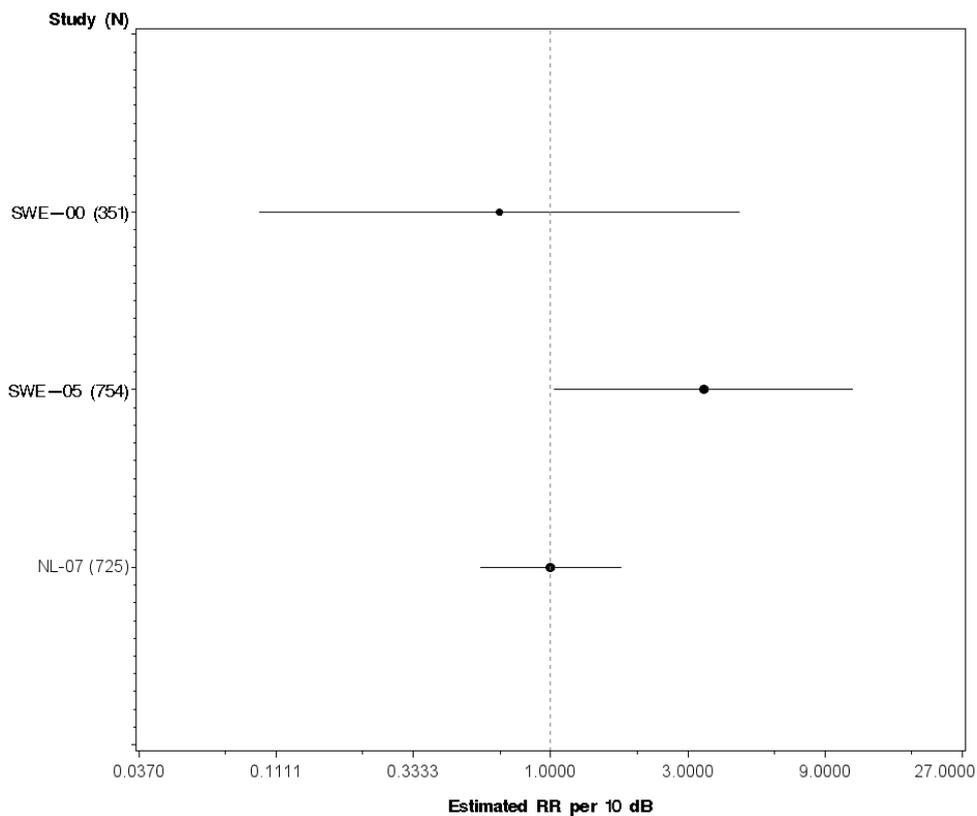


Figure 7.1: Association between wind turbine noise exposure (SPL) and self-reported diabetes. The dotted vertical line corresponds to no effect of wind turbine noise exposure. The black circles correspond to the estimated RR per 10 dB (SPL) and 95% CI.

Only the SWE-05 study reported a statistically significant association between noise from wind turbine noise and the prevalence of self-reported diabetes (see Figure 7.1). An RR of 1.13 (95%CI: 1.00 - 1.27) per 1 dB(A) increase in sound pressure level was estimated after adjustment for age and gender. In both the SWE-00 study and the NL-07 study, we observed no association with diabetes.

8 Studies investigating the impact of noise on obesity

8.1 Aircraft noise

8.1.1 *Descriptive results*

Only one study met the inclusion criteria and was included for data extraction. This is a Swedish cohort study [141] and has already been described in the previous section on aircraft noise and diabetes, with certain design characteristics summarized in Table 7.1. Briefly, it included 5,156 persons of 35 - 55 years of age with a normal baseline oral glucose tolerance test at recruitment, who were followed for up to 10 years. Eriksson et al. [141] based the assessment of exposure to aircraft noise on the residential histories of the participants and modelled levels around the Stockholm Arlanda international airport. As indicators for obesity, they used changes in BMI and waist circumference during follow-up. Overall, they found a mean increase in BMI between baseline and follow-up of $1.09 \text{ kg/m}^2 \pm 1.97$; the mean increase in waist circumference was $4.39 \text{ cm} \pm 6.39 \text{ cm}$. They found that aircraft noise exposure was associated with an increase in waist circumference of 3.46 cm (95%CI: 2.13 – 4.77) related to an increment of 10 dB in aircraft noise levels after adjustment for confounders [495]. On the other hand, they did not observe a clear increase in BMI in relation to exposure, with an increment of 0.14 (95%CI: -0.18 – 0.45) kg/m^2 per 10 dB in aircraft noise levels. No apparent effect modification occurred in relationship to gender or family history of diabetes. The association between aircraft noise and obesity markers was confirmed in a cross-sectional analysis of the same cohort [190].

8.1.2 *Study quality*

We summarized the quality features of the cohort study by Eriksson et al. [141] in Table 7.2. Overall, we judged that the total risk of bias in the study was "low".

8.2 Road traffic noise

8.2.1 *Descriptive results*

Only three studies met the inclusion criteria and were included for data extraction [190-192]. Table 8.1 presents some characteristics of these three studies. With a cross-sectional design, Oftedal et al. [191] studied the association between road traffic noise and markers of obesity in a population sample of more than 15,000 subjects living in Oslo, Norway. They assigned modelled levels of road traffic and railway noise to the home address of each participant and performed anthropometric measurements at a physical examination. Close to 30% had levels of 60 dB L_{DEN} or higher at their residence. There was no association between road traffic noise exposure and any of the obesity markers, with adjusted linear slope coefficients per 10 dB L_{DEN} of 0.01 (95%CI: -0.11 - 0.13) and -0.04 (95%CI: -0.14 - 0.06) kg/m^2 for BMI in women and men, respectively [497]. Corresponding coefficients for waist circumference were -0.12 (95%CI: -0.43 - 0.20) and -0.18 (95%CI: -0.47 - 0.12) cm. Statistically significant positive associations between traffic noise exposure and these markers were seen in the subgroups of highly noise-sensitive women.

Pyko et al. [190] performed cross-sectional analyses among 5,075 participants in the SDPP cohort from suburban and rural areas in Stockholm County, Sweden, at a follow-up up to 10 years after recruitment. They assigned modelled levels of noise from road traffic, railways and aircraft to the home address of each participant and performed anthropometric measurements at a physical examination. Only 5% of the participants were exposed to levels above 60 dB at their residence. Adjusted slope coefficients per 10 dB L_{DEN} for BMI were -0.17 (95%CI: -0.38 - 0.04) and -0.19 (95%CI: -0.42 - 0.04) kg/m^2 in women and men, respectively [498]. Corresponding estimates for waist circumference were 0.56 (95%CI: 0.05 - 1.07) and 0.12 (95%CI: -0.47 - 0.71) cm. A particularly high risk of central obesity (determined by increased waist circumference) was seen in those with combined exposure to road, rail, and air traffic noise at a level of >45 dB L_{DEN} from each noise source (OR = 1.95 (95%CI: 1.24 - 3.05)).

In a cross-sectional analysis using data at recruitment to the DCH cohort, Christensen et al. [192] studied 57,053 subjects from Copenhagen and Aarhus, Denmark. They assigned modelled levels of noise from road and rail traffic to the home address of each participant and performed anthropometric measurements at a physical examination. A third of the participants were exposed to noise levels higher than 60 dB L_{DEN} at their residence. A five-year mean road traffic noise exposure increment of 10 dB L_{DEN} preceding enrolment was associated with 0.20 (95%CI: 0.12 - 0.28) and 0.19 (95%CI: 0.10 - 0.27) kg/m^2 increase in BMI in women and men, respectively, adjusted for potential confounders. Corresponding estimates for waist circumference were 0.30 (95%CI: 0.08 - 0.52) cm and 0.40 (95%CI: 0.18 - 0.63) cm. The slope coefficients for the obesity markers related to road traffic noise were particularly raised in those with concomitant exposure to rail traffic noise.

Table 8.1: Characteristics of studies on the association between road traffic noise and obesity

Study	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs.)	Exposure range and characterization ^{*)}	Ascertaining of obesity markers ^{**)}
HUBRO [191, 243]	Nor	CS	13,900 (36)	MF, 30-76	<50, 50-60, \geq 60 (1)	1
SDPP [190]	Swe	CS	5,075 (37)	MF, 43-66	<45, 45-54, \geq 55 (1)	1
DCH [192]	Den	CS	52,456 (33)	MF, 50-64	<54, 54-60, >60 (1)	1

*) Den = Denmark, Nor = Norway, Swe = Sweden; †) CS = cross-sectional study; ‡) N = number of participants and the response percentage in brackets; *) Exposure range (noise levels in L_{DEN}) and the way exposure to noise was assessed: 1 = modelled, 2 = measured; **) The way obesity markers were ascertained: 1 = measurement/clinical interview, 2 = self-reported, 3 = healthcare registration.

8.2.2 *Study quality*

Table 8.2 presents the results of our evaluation of the quality of the studies. The analyses in all three studies were based on a cross-sectional design. We considered all three studies to have a low risk of bias, in spite of low participation rates.

Table 8.2: Risk of bias: reviewer's judgements on risk of bias in studies on road traffic noise and obesity

Study	Bias due to exposure assessment	Bias due to confounding	Bias due to selection of participants	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
HUBRO	Low	Low	High	Low	Low	Low
SDPP	Low	Low	High	Low	Low	Low
DCH	Low	Low	High	Low	Low	Low

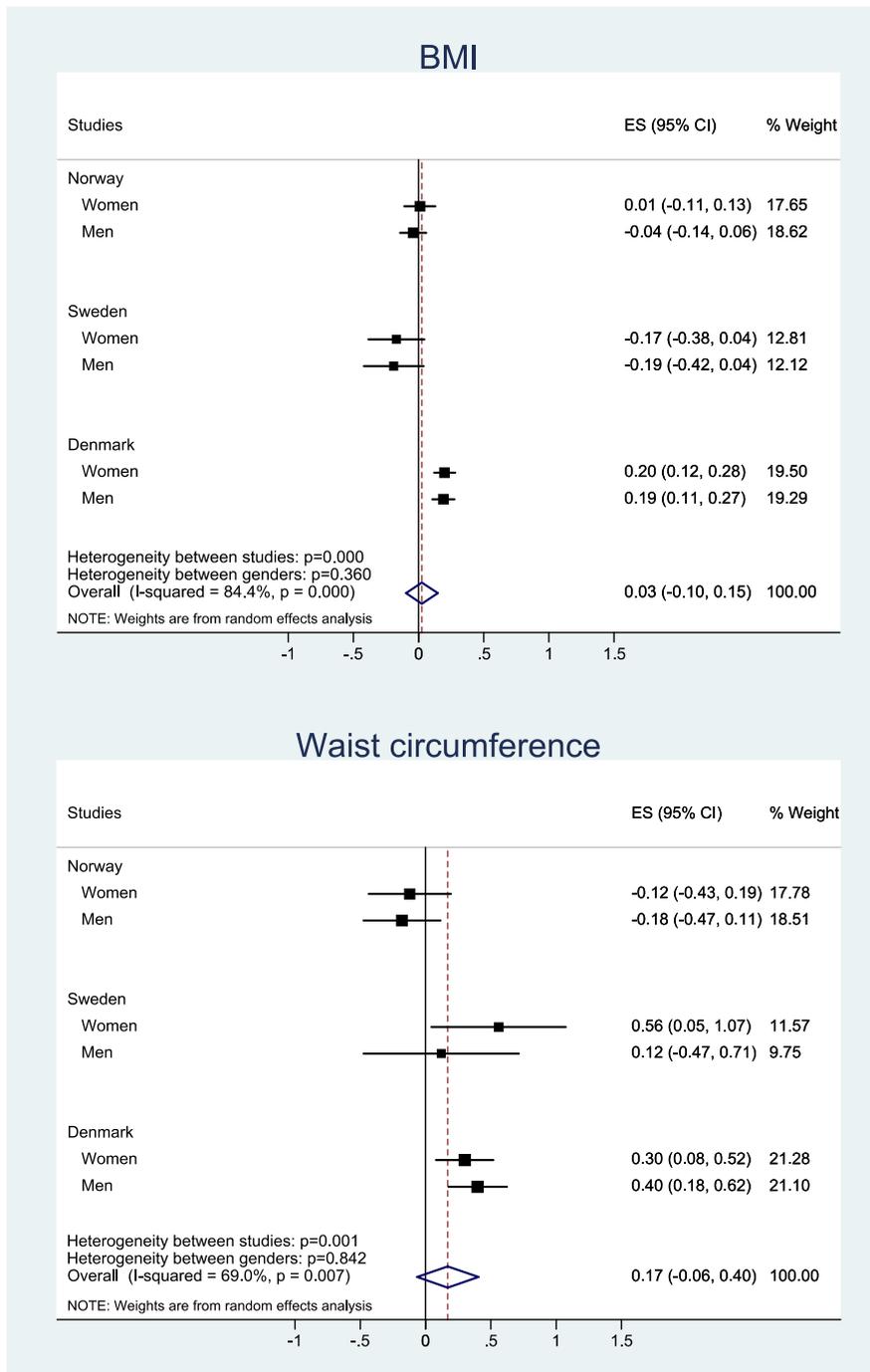


Figure 8.1: Association between road traffic noise exposure (L_{DEN}) and BMI (expressed as kg/m^2 per 10 dB) as well as waist circumference (expressed in cm per 10 dB) in three Nordic studies. The vertical line corresponds to no effect of noise exposure. The black dots correspond to the estimated slope coefficients per 10 dB for each sex in each study with 95% CI. The diamonds designate summary estimates and 95% CI based on random effects models.

8.2.3 Data aggregation

Figure 8.1 shows the slope estimates for the three studies on traffic noise and obesity markers as well as combined estimates. There appeared to be a heterogeneity in the estimates between the three

studies for both BMI and waist circumference, but not between men and women. The combined slope estimates were 0.03 (95%CI: -0.10 - 0.15) kg/m² and 0.17 (95%CI: -0.06 - 0.40) cm per 10 dB L_{DEN} for BMI and waist circumference, respectively, based on random effects models. It should be noted that the effect estimates in the three studies are not fully comparable, since the HUBRO study measured only the “direct” effect of road traffic noise on the obesity markers, *i. e.* not mediated by annoyance or sleep disturbance, while the other two measured the “total” effect, including these pathways.

8.3 Rail traffic noise

8.3.1 *Descriptive results*

Only two studies met the inclusion criteria and were included for data extraction [190, 192]. We have already described the design of these studies in the previous section on road traffic noise and obesity (see Table 8.1). Both studies used cross-sectional methodology and modelled noise exposure at the residential addresses. In their study, Christensen et al. [192] observed statistically significant slope estimates of 0.18 (95%CI: 0.00 - 0.36) kg/m² for BMI and 0.62 (95%CI: 0.14 -1.09) cm for waist circumference in those exposed to rail traffic noise at levels above 60 dB L_{DEN}. In the study by Pyko et al. [190] significant associations were seen only for waist circumference, with a slope estimate of 0.92 cm per 10 dB L_{DEN} (95%CI: 0.06 - 1.78). The corresponding estimate for BMI was 0.06 (95%CI: -0.02 - 0.16).

8.3.2 *Study quality*

Table 8.2 presents the results of our evaluation of the quality of the studies. The table shows that we considered both studies to have a high risk of bias.

8.4 Wind turbine noise

We did not identify any studies that investigated the impact of wind turbine noise on obesity.

9 Studies estimating the impact of noise on children's blood pressure

9.1 **Descriptive results**

We selected eight studies for data extraction [117, 158, 159, 162, 166, 220-222, 239, 240, 245]. Table 9.1 presents some characteristics of these studies.

Table 9.1: Overview of characteristics of the studies on the association between transportation noise and blood pressure in children

Study	Country*)	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs)	Noise source ^{**)}	Setting ^{††)}	Exposure range and characterization ^{§)}	Measurement of blood pressure (mmHg) ^{§§)}
RANCH [117, 166]	NL, UK	CS	853 (40)	BG, 9-11	A, R	S, H	34-68, 34-73 (L _{Aeq16hr}) 34-67, 28-67 (L _{Aeq16hr}) (1)	1
ICCBP-a [158, 159]	Aus	CS	1230 (38)	BG, 6-7	A	S, H	15-45 ANEI (1)	1
ICCBP-b [159]	Aus	CO	628 ^{a)}	BG, 6-7	A	S, H	15-45 (ANEI) (1)	1
PIAMA [222]	NL	CS ^{b)}	1,400 (53)	BG, 12-14	R	S, H	45 – 70 (L _{DEN}) (1)	1
GINIplus [239, 240]	Ger	CS ^{b)}	405 (55)	BG, 10	R	H	35-78 (L _{DEN}) (1)	1
LISAplus [239, 240]	Ger	CS ^{b)}	200 (57)	BG, 10	R	H	35-78 (L _{DEN}) (1)	1
BELGRADE1 [245]	Cro	CS	825 (41)	BG, 7-11	T	S, H	49-72 (L _{day}) (2)	2
REGECOVA [162]	SR	CS	1,542 (76)	BG, 3-7	T	S, H	≤ 60, 61-69, 70-81 (L _{Aeq24hr}) (2)	2
USA1 [220, 221]	USA	CS	250 (89)	BG, 6-14	T	S, H	NR (L _{Eq}) (2)	1

*) Aus = Australia, Cro = Croatia, Ger = Germany, NL = The Netherlands, SR = Slovak Republic, UK = United Kingdom, USA = United States of America, †) CS = cross-sectional study, CO = cohort study; ‡) N = number of participants and the response percentage in brackets; **) Source: A = air traffic, R = road traffic, T = transport (no specific source is indicated); ††) Setting: S = school, H = home; §) Exposure range and the way exposure to noise was assessed: 1 = modelled, 2 = measured; §§) Measurement of blood pressure: 1 = automatic blood pressure meter, 2 = mercury Sphygmomanometer; a) the attrition rate in the AICBB study was 49%; b) this is a cross-sectional analysis performed in a cohort study.

9.1.1 *Aircraft noise*

Two studies investigated the association between aircraft noise and blood pressure in children. The European RANCH study [117, 166] included 1,283 children (aged 9 - 11 yrs) attending 62 primary schools around Schiphol Amsterdam airport and London Heathrow airport. The RANCH study researchers assessed noise exposure for each child by linking home and/or school addresses to modelled equivalent aircraft noise levels (expressed in $L_{Aeq7-23 \text{ hrs.}}$). They obtained aircraft noise levels from nationally available noise contours. They took blood pressure measurements in the afternoon in a quiet room in the school building using automatic (oscillometric) blood pressure meters. In the statistical analyses, they used the average of three blood pressure measurements (with 1 - 2 minutes between the measurements) as the outcome measure. In addition to blood pressure, they measured the height and the weight of the children. They obtained information about other potential confounders by means of a questionnaire that was given to the children to take home for a parent or other carer to fill in. Eventually, 853 (40%) children were eligible for data analysis.

The Inner City Child Blood pressure study (ICCBP) studied the impact of aircraft noise both at school and at home [158, 159] in the context of the reconstruction of a new north - south runway at Sydney (Kingsford-Smith) airport. In 1994 / 95, they carried out a baseline study. The follow-up was conducted in 1997. They measured and re-measured the same individuals over changing conditions of exposure to aircraft noise. In the first phase of the study (1994 / 95), they investigated a sample of 75 primary schools within a 20 km radius of Sydney airport, under various noise exposure conditions, both existing and those projected with the advent of the new runway participated in the study. During this first phase, they included 1,230 children (40.2%) in the study. At follow-up (1997), 628 children participated in the study, representing 51% of the original participants. The main reason for loss to follow-up was that children moved from one school to another.

The ICCBP study researchers took blood pressure measurements in small groups of children at school, using automatic (oscillometric) blood pressure meters. In the statistical analyses, they used the average of the second and third blood pressure measurements as the outcome measure. They obtained information on potential confounders from a parental questionnaire, among other sources. The ICCBP study researchers assessed aircraft noise exposure by means of aircraft noise contours provided by the National Acoustics Laboratories (NAL). To this end, NAL carried out 3,000 aircraft noise measurements from 90 locations around the airport. Subsequently, NAL stored these noise data in a database called the Integrated Noise Model (INM). In the INM, they combined the noise data with historical flight tracking data, resulting in monthly mean aircraft noise levels. Subsequently, they linked these aircraft noise levels to the home and school addresses of the participating children. In contrast with most studies on the impact of noise on the cardiovascular system, the ICCBP study researchers did not express the noise exposure levels in decibels, but by means of the Australian Noise Energy Index (ANEI). As opposed to A-weighted noise pressure levels (commonly used in studies on the impact of noise on health), an index as the ANEI is based on the noisiness concept that was

developed by Kryter [499-501]. A-weighted noise pressure levels are based on the equal energy (L_{eqT}) concept.

9.1.2 *Road traffic noise*

We selected six studies that investigated the association between road traffic noise exposure and blood pressure in children: Bilenko et al. [222] linked the blood pressure of 1,432 children (aged 12 -14 yrs) from the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study [502] to road traffic noise exposure levels. The PIAMA birth cohort started with 3,963 participants. These were the children of women who had been recruited during their second trimester of pregnancy in 1996 / 97 from a series of communities in the north, west, and centre of the Netherlands. Follow-up occurred at several ages (3 months, 1 year, and yearly thereafter up to 8 years, 11 year). During these follow-ups, the mothers of the children had to fill in questionnaires. At the age of about 12 years, the children were invited the children to undergo a medical examination during a home visit. As part of this medical examination, Bilenko et al. measured the children's blood pressure using an automatic (oscillometric) blood pressure meter. They took at least two measurements and used the average of these measurements as the outcome measure. The PIAMA birth cohort researchers assessed road traffic noise exposure for each child by linking home and/or school addresses to modelled equivalent road traffic noise levels (expressed in L_{DEN}). For the calculation of road traffic noise levels, they adopted national standard methods to obtain grids with resolutions of 25 x 25 m. As this was one of the first studies on the impact of noise on children's blood pressure, they also took the possible impact of air pollution into account.

Liu et al. [239, 240] linked the blood pressure levels of 10-year old children from the GINIplus and LISApplus birth cohorts [503, 504] to road traffic noise exposure levels. The GINIplus birth cohort was originally set up to investigate the impact of several risk factors on allergy development. In 1995 – 1998, 5,991 new-borns were recruited from obstetric clinics in Munich. Follow-up occurred at the ages of 1 - 4, 6, and 10 years. In their study on the effects of road traffic noise, Liu et al. [239, 240] used the data of the children at 10 years of age (55% of the children originally recruited at birth). The LISApplus cohort was originally set up to investigate the impact of lifestyle factors. The cohort was formed from 14 obstetric clinics in Munich, Leipzig, Wesel, and Bad Bonnen; 3,095 healthy, full-term neonates were recruited in the period 1997 - 1999. Follow-up occurred at the ages of 0.5, 1, 1.5, 2, 4, 6, and 10 years. In their study Liu et al. [239, 240] used the data of the children at 10 years of age (75% of the children originally recruited). They restricted their data analysis to those children living in Munich and whose home address was known. In both the GINIplus and LISApplus cohorts, the researchers measured the blood pressure of the children at the age of 10. This was done by a physician, twice on the right arm, with the child in a sitting position after 5 minutes of rest, using an automatic (oscillometric) blood pressure meter. In the statistical analyses, Liu et al. used the average of the two measurements. For each child, the researchers assessed road traffic noise exposure by linking home addresses to modelled equivalent road traffic noise levels (expressed in L_{DEN}). For the calculation of road traffic noise levels, they

adopted national standard methods to obtain grids with resolutions of 5 x 5 m. They obtained information on potential confounders from a questionnaire for parents to fill in.

In addition to the impact of aircraft noise exposure, the European RANCH study [166] also investigated the impact of road traffic noise exposure on children's blood pressure levels. To this end, they assessed noise exposure for each child by linking the school addresses to modelled equivalent road traffic noise levels (expressed in $L_{Aeq7-23 \text{ hrs}}$). Unfortunately, road traffic noise levels for the child's *home address* were available only for the Dutch children. In order to obtain grids of modelled road traffic noise level (resolution of 25 x 25 m), the RANCH study researchers adopted national standard methods [505]. For the UK sample, they calculated road traffic noise levels for the school situation by means of the UK standard CRTN noise prediction method [506].

Three other cross-sectional studies have reported on the impact of road traffic noise levels on children's blood pressure level for both the school and home setting [162, 220, 221, 245]. In contrast to the studies using the PIAMA, GINIplus, and LISAPLUS birth cohorts, and the RANCH study, these studies made use of measured noise levels. The BELGRADE-1 study [245] investigated children aged 7 - 11 years attending eight primary schools in Stari Grad, Belgrade. Of the 2,000 children that were invited, 1,113 participated. Their blood pressure was measured by a physician in school, using a mercury sphygmomanometer. In the statistical analyses, the researchers used the average of two measurements. If there was more than 5 mmHg difference between these two readings, they obtained additional readings. They ascertained noise exposure by means of sound level meters that were situated in front of the eight schools that the participating children were attending and in all 115 streets of Stari Grad. By means of the noise measurements, they calculated composite daytime equivalent noise levels for each school and each street where noise measurements were carried out. Subsequently, the researchers assessed the individual noise exposure level by linking the home and school addresses of each child to the obtained composite noise levels at home and school. They obtained information on potential confounders from a questionnaire that had to be filled in by the parents. Unfortunately, the researchers were not able to measure the noise levels in the streets of 288 children. For 24 other children, the home address was unknown. This meant that 825 children were included in the final analyses.

Regecova and Kellerova investigated 1,542 children aged 3 - 7 years attending 30 kindergartens in Bratislava [162]. They carried out blood pressure measurements in the kindergartens using a Doppler phenomenon-based ultrasound device (sphygmomanometric meter). They used the average of two measurements in the statistical analyses. If there was more than 5 mmHg difference between these two readings, they obtained additional readings. As in the BELGRADE-1 study [245], Regecova and Kellerova [162] created a noise map with mean 24-hour equivalent traffic noise emissions on the basis of noise measurements carried out on busy roads and on side streets at 275 locations in the city. Subsequently, they linked the noise map that they created with both the school and home addresses of the participating children. For

the statistical analysis, they grouped the children into three traffic noise categories: ≤ 60 dB(A), 61 - 69 dB(A), and ≥ 71 dB(A). They obtained information about potential confounders from a questionnaire that was filled in by the parents.

In the USA-1 study [220, 221] Belojevic and Evans investigated 250 children aged 6 - 14 years attending 20 elementary schools in a city in the United States. They measured the blood pressure of the children by means of a Dinamap PRO 100 (oscillometric) monitor. For their statistical analyses, they used the average of two measurements. Prior to the blood pressure measurements, they interviewed each child. They assessed exposure to noise by means of noise measurements in front of children's schools and on the street where the children lived, from which they obtained equivalent noise levels (L_{Eq}). From the obtained L_{Eq} values, they calculated composite L_{EqS} for each address and each school.

9.1.3 Rail traffic noise and wind turbine noise

We did not identify any studies that investigated the impact of rail traffic noise or wind turbine noise on children's blood pressure.

9.2 Study quality

Table 9.2 presents the results of our evaluation of the quality of the studies. All studies were judged as having a high risk of bias. The main reasons were inadequate exposure assessment, and low response rates (lower than 60%).

Table 9.2: Risk of bias: reviewer's judgements on risk of bias in studies on noise and children's blood pressure

Study	Bias due to exposure assessment	Bias due to confounding ^{*)}	Bias due to selection of participants ^{†)}	Bias due to health outcome assessment	Bias due to not blinded outcome assessment	Total risk of bias
RANCH	Unclear	Low	High	Unclear	Unclear	High
ICCBP-a	Low	Low	High	Unclear	Unclear	High
ICCBP-b	Low	Low	High	Unclear	Unclear	High
PIAMA	Unclear	Low	High	Unclear	Low	High
GINIplus	Unclear	Low	High	Unclear	Low	High
LISAplus	Unclear	Low	High	Unclear	Low	High
BELGRADE1	High	Low	High	Unclear	Unclear	High
REGECOVA	High	High	Low	Unclear	Unclear	High
USA1	High	High	Low	Unclear	Unclear	High

^{*)} In order to score "low" the study should contain information that can be used to derive effect estimates that are at least adjusted for age and sex. ^{†)} In order to score "low", participants had to be randomly sampled from a known population and the response rate of the study had to be higher than 60%. An additional condition for cohort studies was that the attrition rate had to be at least 20%.

Three studies [162, 220, 221, 245] were unable to apply individual exposure estimates; the researchers measured noise levels for an area

(e.g. a street) using sound level meters. Subsequently, they assigned these noise levels to everybody who lived in that street or attended a school in that street. The measurement of noise levels has the advantage over modelled noise levels that it can provide more precise noise levels and account for any unexpected variables or unpredicted exposures. However, the disadvantage is that noise measurements over a short period might not be representative of the exposure of a location over a longer period, depending on the measuring protocols and site characteristics. In addition, it is difficult to isolate exposures of interest, such as road traffic, from other noise sources, such as neighbour noise, depending on the site characteristics (specificity is limited). Furthermore, this method is not cost-effective for large study samples.

All studies, except REGECOVA and USA-1, adjusted their results for at least age and gender. Although REGECOVA and USA-1 collected information on age and gender, the researchers did not report the adjusted results. As a consequence, these studies scored "high" on the factor "Bias due to confounding".

As was the case in many of the adult studies on the impacts of noise on the cardiovascular system, the response rate in studies on the impact on children's blood pressure was also often lower than 60%. Consequently, most studies scored "high" on the factor "bias due to selection of participants".

It is very difficult to say whether the blood pressure measurements suffered from high or low bias due to health outcome assessment. The majority of the studies ascertained the blood pressure with an automatic oscillometric meter. Only two studies ascertained blood pressure by means of a sphygmomanometer [162, 245]. From the literature, several factors are known to complicate the assessment of blood pressure in children [18]. An important factor relates to the device that is used to measure the blood pressure. The standard device for blood pressure measurements has been the mercury manometer (sphygmomanometer). However, automated oscillometric devices are now used increasingly often. These electronic devices have several advantages: they are precise, very simple and convenient to use, and have almost no observer-bias. When used according to the instructions, these devices are as reliable as a sphygmomanometer [18, 507].

Together with the device used, the selection of the appropriate cuff size is very important. Arafat and Mattoo [508] (in: [18]) recommended using child/paediatric cuffs (median width 8.25 cm) in children up to 10 years of age, small-adult cuffs (median width 11 cm) in adolescents up to 16 years, and large cuffs (median width 17 cm) in adolescents over 16. Apart from two studies, all studies specified the size of the cuffs they used (2 – 19 cm, 7.5 – 19.5 cm, 15 – 22 cm, 22 – 32 cm, 11-27 cm, 17 – 25 cm). Like Paunovic et al. [18] in their review, we matched the criteria of Arafat and Mattoo [508] with the children's ages and the reported cuffs used. We were not able to notice any obvious errors in the studies.

The number of measurements on which the blood pressure is based is also important: more measurements and/or repetition of measurements

on several consecutive days increases the validity of the measurements [18]. In the evaluated studies, the range of the total number of blood pressure measurements was narrow (2 – 3 measurements). Only the ICCBP study excluded the results of the first measurement. All studies carried out the measurements on the same day and most studies took the blood pressure measurements in the morning. Only the PIAMA study and the USA-1 study did not specify at what time of the day the measurements were taken. However, the number of blood pressure measurements taken, and the number included in the statistical analysis, was not always the same. Four studies [162, 220, 221, 239, 240, 245] followed more or less the guidelines for blood pressure measurement: they measured blood pressure twice, but if the difference between the readings exceeded 5 mmHg, they performed additional measurements. According to the literature, the first measurement usually tends to be the highest, due to e.g. anxiety and/or discomfort. Only one study [158, 159, 167] excluded the first blood pressure measurement from the statistical analysis. Most studies took blood pressure measurements at a location that was familiar to the children: school, home, kindergarten, boys' /girls' club. This reduced the risk of bias due to fear of the examination.

The PIAMA birth cohort and both the GINIplus and LISApplus birth cohorts were not originally developed for investigating the impact of noise. So it is not likely that the results were biased because the participants (or their) parents were aware of the fact that they participated in a study on the impact of noise. For the other studies, this is less clear.

9.3 Data aggregation

9.3.1 *Systolic blood pressure* *Aircraft noise*

The results of the evaluated studies on the impact on *systolic* blood pressure are presented in Figure 9.1. For both the school and the home situation, we were not able to aggregate the data of the studies on the association between aircraft noise and systolic blood pressure. The reason was that we were not able to express the results of the ICCBP study as a change in blood pressure per 10 dB change in noise level. Pooling the results of only the two study groups investigated in the RANCH study revealed a non-significant increase in systolic blood pressure of 0.80 mmHg per 10 dB(A) increase in aircraft noise level for the school situation; for the home situation, a non-significant increase of 1.00 mmHg per 10 dB(A) was estimated.

Road traffic noise

For both the school and the home situation, we were able to aggregate the data of the studies on the association between road traffic noise and systolic blood pressure.

For the *school* situation, we estimated a decrease in systolic blood pressure of 0.60 (95%CI: -1.51 – 0.30) mmHg per 10 dB increase in road traffic noise. To this end, we combined the results of six studies (including 4,520 children), using a random effects model. According to the statistical tests, there was no clear evidence of heterogeneity among

the studies. The residual proportion of the between-study variance due to heterogeneity was $I^2_{\text{residual}} = 16.0\%$ (χ^2 test for heterogeneity: $Q = 5.96$, $Df = 5$, $p = 0.311$).

For the *home* situation, we estimated an increase in systolic blood pressure of 0.08 (95%CI: -0.48 – 0.64) mmHg per 10 dB increase in road traffic noise. To this end, we combined the results of six studies (including 4,197 children), using a random effects model. According to the statistical tests, there was no clear evidence of heterogeneity among the studies. The residual proportion of the between study variance due to heterogeneity was $I^2_{\text{residual}} = 8.9\%$ (χ^2 test for heterogeneity: $Q = 5.49$, $Df = 5$, $p = 0.359$). These results should, however, be interpreted with caution, because for three studies (BELGRADE-1, REGECOVA and USA-1), we were not able to derive estimates that were adjusted for at least age and sex. An extra concern in these studies was that we were not able to isolate the impact of road traffic noise from the impact of other noise sources.

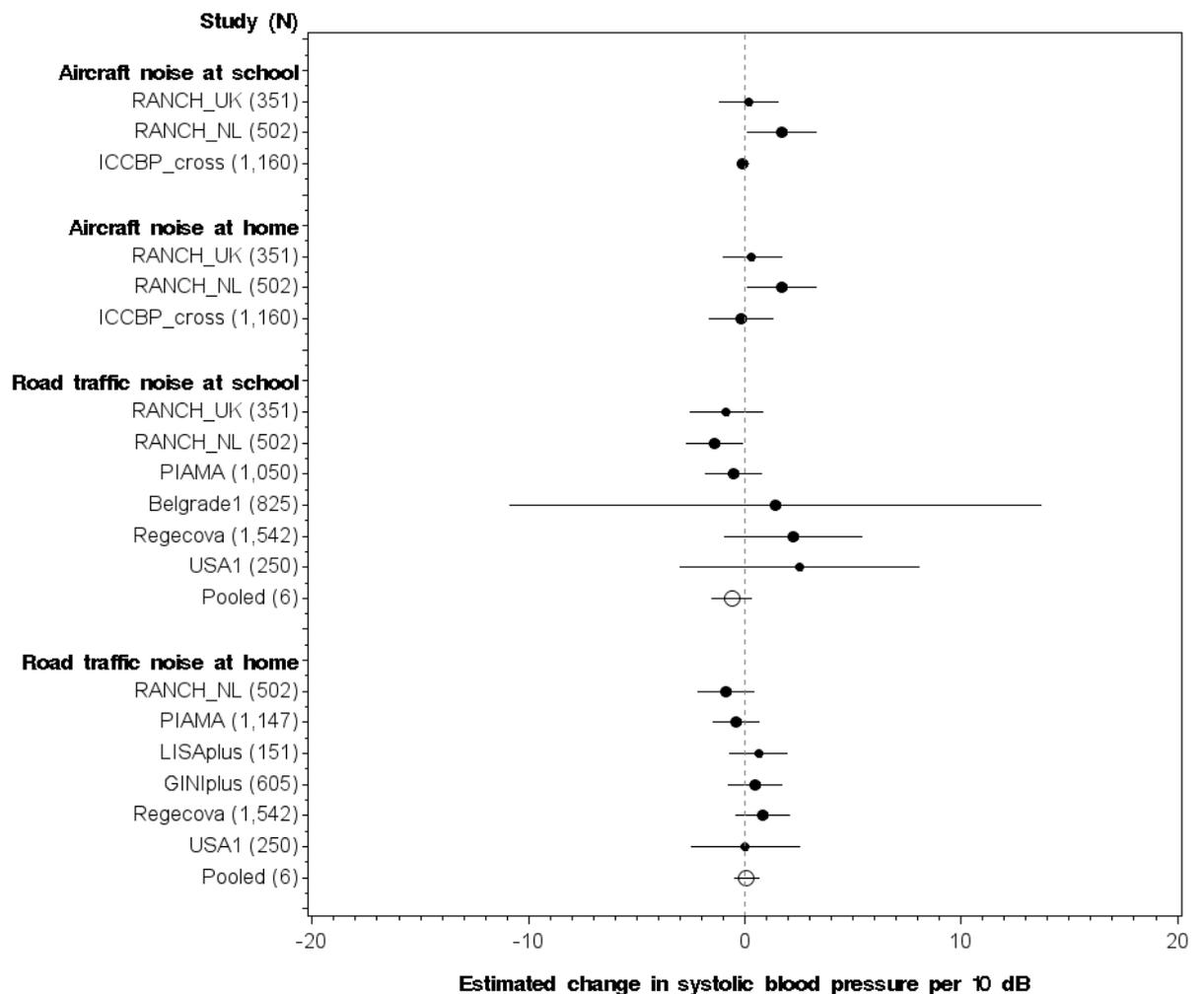


Figure 9.1: Association between noise exposure and systolic blood pressure in children. The dotted vertical line corresponds to no effect of noise exposure; with the exception of ICCBP_cross [159, 167] the circles and horizontal lines correspond to the estimated change in systolic blood pressure per 10 dB in noise

and their 95% CI. For the ICCBP_Cross the circles and horizontal lines correspond to the estimated change in systolic blood pressure per 10 ANEI increase and 95% CI.

9.3.2 Diastolic blood pressure Aircraft noise

Figure 9.2 shows the results of the studies for the association between noise and *diastolic* blood pressure. For both the school and the home situations, we did not aggregate the data of the studies on the association between aircraft noise and systolic blood pressure. The reason was that we were not able to express the results of the ICCBP study as a change in blood pressure per 10 dB change in noise level. After pooling the results of only the two study groups investigated in the RANCH study, we found a non-significant increase in systolic blood pressure of 0.50 mmHg per 10 dB(A) increase in aircraft noise level for the school situation; for the home situation, we estimated a non-significant increase of 0.80 mmHg per 10 dB(A).

Road traffic noise

For both the school and the home situations, we aggregated the data of the studies on the association between road traffic noise and diastolic blood pressure. For the *school* situation, we estimated an increase in diastolic blood pressure of 0.46 (95%CI: -0.60 – 1.53) mmHg per 10 dB increase in road traffic noise. To this end, we combined the results of six studies (including 4,520 children), using a random effects model. According to the statistical tests, there was evidence of heterogeneity among the studies. The residual proportion of the between-study variance due to heterogeneity was $I^2_{\text{residual}} = 61.6\%$ (χ^2 test for heterogeneity: $Q = 13.04$, $Df = 5$, $p = 0.023$).

For the home situation, we estimated an increase in diastolic blood pressure of 0.47 (95%CI: -0.30 – 1.24) mmHg per 10 dB increase in road traffic noise. To this end, we combined the results of six studies (including 4,197 children), using a random effects model. According to the statistical tests, there was clear evidence of heterogeneity among the studies. The residual proportion of the between study variance due to heterogeneity was $I^2_{\text{residual}} = 76.0\%$ (χ^2 test for heterogeneity: $Q = 20.83$, $Df = 5$, $p = 0.001$). These results should, however, be interpreted with caution, because for three studies (BELGRADE-1, REGECOVA and USA-1), we were not able to derive estimates that were adjusted for at least age and sex. An extra concern in these studies was that it was not possible to isolate the impact of road traffic noise from the impact of other noise sources.

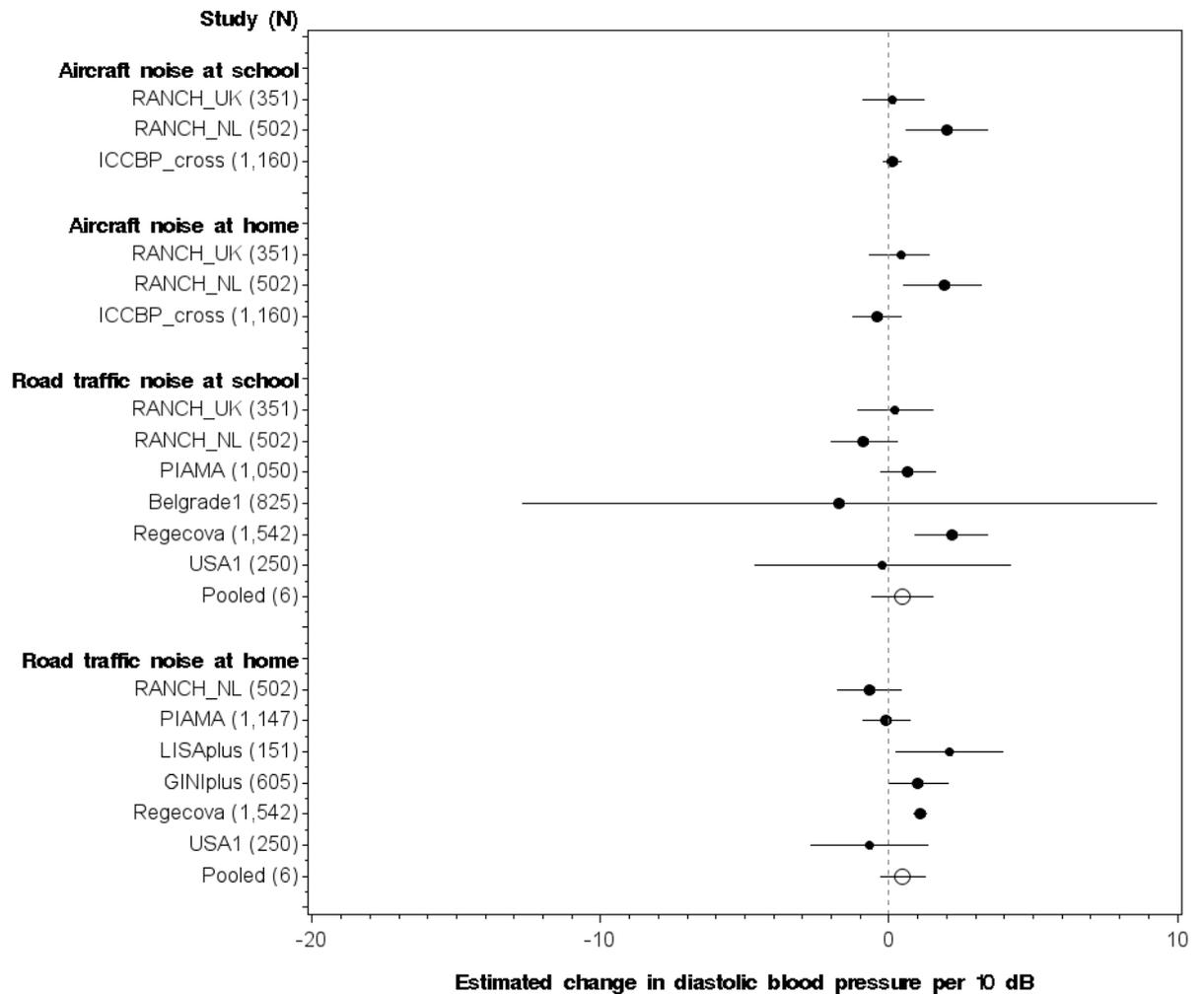


Figure 9.2: Association between noise exposure and diastolic blood pressure in children. The dotted vertical line corresponds to no effect of noise exposure; with the exception of ICCBP_cross [159, 167] the circles and horizontal lines correspond to the estimated change in diastolic blood pressure per 10 dB in noise and their 95% CI. For the ICCBP_Cross the circles and horizontal lines correspond to the estimated change in diastolic blood pressure per 10 ANEI increase and 95% CI.

10 Assessment of the quality of evidence

10.1 GRADE

In this section, we assess the quality of the evidence that has been retrieved in this review. In other words, we assess to what extent we are confident that an estimate of an effect or association is likely or unlikely to be changed by further research. For the WHO, the outcome of such an assessment is of importance, because the level of quality of the evidence will be linked with the guideline values and recommendations that will be included in the environmental noise guidelines [200]. To assess the quality of the body of evidence, we applied a modified version of the GRADE considerations [509, 510]. GRADE is a systematic and explicit approach making judgements about quality of evidence. For every *outcome*, we assessed the quality of evidence according to several elements (e.g. study design, study quality, consistency, directness of evidence).

The assessment contained the following three steps: In the first step, we determined the initial level of certainty, based on the designs of the studies on a specific (clinical) outcome. Subsequently, we lowered or raised the level after considering a range of elements, leading to the final level of certainty.

GRADE has four levels for the quality of evidence, ranging from “very low” to “high” (see Table 10.1).

Table 10.1: The levels of quality of evidence of the GRADE system (source: [509, 510]).

Quality of evidence	Definition	Examples of when this is the case
High	Further research is very unlikely to change our confidence in the estimate of effect	Several high-quality studies with consistent results
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	One high-quality study Several studies with some limitations
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	One or more studies with severe limitations
Very low	Any estimate of effect is very uncertain	No direct research evidence One or more studies with very severe limitations

When the level of the quality of evidence was rated as “High” this means that further research is very unlikely to change our confidence in the estimate of effect. This is usually the case if for a specific outcome we have at our disposal several high quality studies with consistent results.

In case that, for a specific outcome, we have only at our disposal studies with very severe limitations, it is likely that the level of the quality of evidence was rated as “Very low”. This means nothing more than that any estimate of effect is uncertain.

10.2 Adaptation of GRADE for this review

10.2.1 *Initial level of the quality of evidence*

Up to now, GRADE has been predominantly used to answer questions on interventions in healthcare (e.g. “Should intervention A or B be used for X?” or “What is the impact of an intervention compared with an alternative on patient or population important outcomes?”). However, in the setting of environmental health, and in the setting of noise and health specifically, this kind of question sounds rather strange [510-513]. In addition, because questions assessing environmental exposures (noise) as risk factors or causative agents are used in risk assessments, several other sub-questions are asked. For example:

- Hazard identification: what health problems are caused by long-term exposure to noise?
- Exposure response assessment: What are the health problems at different noise levels?
- Exposure assessment: What is the extent and nature of noise in the target population?

While GRADE originally considers randomized clinical trials as the highest level of quality of evidence, in the area of noise and its impact on the cardiovascular system, observational human studies are often the highest quality evidence available to understand whether there is an association between long-term noise exposure and a health outcome. This is apart from the question how ethical it is to carry out a random clinical trial, where volunteers are exposed to noise, in order to investigate the impact of an environmental risk factor such as noise on health [510, 514].

Table 10.2: Adaptation of the initial level of the quality of the evidence

Study design	Initial level of the quality of the evidence in an estimate of effect	
	Original score	Adapted score
Randomized (clinical) trial	High certainty	-
Cohort study	Low certainty	High certainty
Case-control study	Low certainty	High certainty
Cross-sectional study	Low certainty	Low certainty
Ecological study	Low certainty	Very low certainty

As a consequence, we decided to adjust the initial level of certainty for the GRADE score as follows:

- Where we evaluated a group of studies that investigated the impact of noise exposure on a specific cardiovascular outcome by means of cohort and/or case control studies, we rated the initial level of certainty as “high”.
- Where we evaluated a group of studies that investigated the impact of noise exposure on a specific cardiovascular outcome by

means of cross-sectional studies, we rated the initial level of certainty as “low”.

- Where we evaluated a group of studies that investigated the impact of noise exposure on a specific cardiovascular outcome by means of ecological studies, we rated the initial level of certainty as “very low”.
- We decided *not* to combine the results of studies with different inherent quality. For example, we did not combine the results of cohort and case control studies, which are “high” quality, with the results of ecological studies, which are “very low” quality.

After we had determined the initial level of the quality of evidence, we considered several factors that could lower or increase the certainty level. The following paragraphs describe the reasoning behind these considerations.

10.2.2 *Limitations in the study design (risk of bias)*

Limitations in the study design may bias the results of a study. The quality of the evidence decreases if studies suffer from major limitations. The more serious these limitations are, the more likely it is that the quality of evidence is downgraded [510, 512]. For this criterion, we took into account, per outcome, the results of the quality assessments of the individual studies that were available. Where we judged that more than half of the available studies was rated as “poor” (having a high risk of bias), we downgraded the quality of the evidence.

10.2.3 *Inconsistency*

Widely differing estimates of the impact of noise on health across studies are not only related to bias. Instead, this variability may also reflect true variation in the underlying relative risk between locations [512]. In order to find out whether there was inconsistency, we visually inspected the forest plots presenting the estimates of the separate studies. Where possible, we supported our observations with the results of the test for heterogeneity (see also method section). Subsequently, we applied the following rules:

- When we observed heterogeneity (i.e. widely differing estimates of the RR per 10 dB), we downgraded the quality of the evidence.
- When only one study contributed to the evidence base, we decided *not* to downgrade the quality of the evidence.

10.2.4 *Indirectness*

The term “indirectness” refers to the extent to which the characteristics of those who will be exposed to noise in the real-world, match with the characteristics of those who were in the evaluated studies exposed to noise [506]. In other words: “Did the study design address the topic of the evaluation?” To determine whether to downgrade the quality of the evidence based on indirectness, several factors have to be considered: the relevance (directness) of the end points to the primary health outcomes, the nature of the exposure, and the length of time between exposure and outcome. However, human studies are not usually downgraded for indirectness, since they usually investigate persons directly exposed to the relevant risk factor. This was also the case for the studies that were evaluated in the current review. Because all the studies assessed population, exposure, and outcome of interest, we

found it unnecessary for all the evaluated outcomes to downgrade the quality of the evidence for indirectness. Consequently, we did not address this factor, when assessing the level of the quality of evidence for the separate outcomes; the result was the same every time: no downgrading.

10.2.5 *Imprecision*

Precision is defined as the degree of certainty for an estimate of effect with respect to a specific outcome [515]. Results are *imprecise* when studies include relatively few participants and cases and thus have wide confidence intervals around the estimate of the effect. To evaluate whether the evidence base should be downgraded or not, we took into account the total number of participants, the total number of cases (events) and the 95% CI of the estimated RR per 10 dB [515]. In accordance with GRADE [515], we downgraded the quality:

- Where the sample size was fewer than 200 cases, *and*
- Where the 95% CI included an important effect. This is the case when $RR > 1.25$ or $RR < 0.75$.

In our review, we have also included several continuous outcomes: change in BMI, change in waist circumference, and change in blood pressure. For these outcomes we applied the following rule: Downgrade for imprecision in cases where the 95% CI includes no effect *and* the lower and upper confidence intervals cross the minimal important difference (MID) for harm or benefit. The MID is defined as the smallest change in an outcome that is considered important by patients or healthcare professionals [516]. However, what is the MID for BMI, waist circumference, or blood pressure in children? For the current review, we decided to keep it simple: For continuous outcomes, such as a change in BMI, we applied the rules that are being developed by OHAT [512]. For example, according to OHAT, the result of the available evidence with regard to the change in BMI is considered to be very imprecise in cases where the standard deviation of the estimate is large: i.e. standard deviation > mean.

10.2.6 *Publication bias*

Reporting bias or publication bias occurs when the publication of studies depends on the nature and direction of the results, so that the results in published studies may be systematically different from those in unpublished studies. This will result in misleading estimates of treatment effects and associations between study variables [517]. In other words, publication bias can lead to under- or overestimation of the effect of noise due to selective publication of studies.

Where enough studies were available ($n \geq 10$), we were able to (visually) test whether we suspected publication bias (see also the Method section). We decided to downgrade the quality:

- Where we suspected publication bias on the basis of the test for publication bias, *but*
- Where fewer than 10 study estimates contributed to the evidence base, we decided *not* to downgrade the quality of the evidence.

10.2.7 *Exposure response gradient*

If a dose response association was present, we upgraded the level of the quality of the evidence. The presence of a dose response gradient may increase the confidence in the findings of the observational studies. In order to determine whether we should up- or downgrade the quality of the evidence we took into account the following:

- We visually inspected the effect size data (RR per 10 dB) of the different studies in order to assess the consistency of a dose response association across studies.
- We counted the number of studies that (statistically significantly) increased the risk of a certain health end point with an increasing noise level (10 dB).
- We checked the size and direction of the effect estimate that was found after aggregating the results of the evaluated studies.
- Where sufficient effect estimates were available, we tested the role of exposure-related factors such as the duration of exposure: did the studies find a greater impact of noise as the duration of exposure increased?

We decided to upgrade the level of evidence in cases where (i) most studies found an association between increased noise level and an increased risk of a certain health endpoint, and (ii) we were able to derive a statistically significant positive effect size after aggregating the results of the evaluated studies, or (iii) there were strong indications for an effect over the duration of the exposure.

10.2.8 *Magnitude of effect*

The magnitude of effect is defined as the likelihood that the observed effect is large enough that it cannot have occurred solely as a result of potential confounding factors. In GRADE it is assumed that confounding alone is unlikely to explain associations with a relative risk (RR) greater than 2 (or less than 0.5), and very unlikely to explain associations with an RR greater than 5 (or less than 0.2) [509]. Thus, these are the definitions that GRADE applies to upgrade the certainty score by one or two levels due to a "large magnitude of effect". However, applying the GRADE definition of "large magnitude of effect", i.e. RR greater than 2 or even 5 is problematic in environmental health because for dichotomous outcomes (which is also the case in this review) an RR is a function of the exposure comparator [512]. At present, however, an empirically defined "large magnitude of effect" is not available. Therefore, for the purpose of the current review, we decided to upgrade the level of evidence in cases where the RR was at least 1.5. This is in line with other reviews in which the quality of evidence of studies on the association between a certain environmental risk factor and health has been evaluated. In those reviews, the decision whether an effect is of large magnitude was made on a project-specific basis [512]. Furthermore, we believe that it is highly unlikely that an RR of 1.5 or higher can be explained by residual confounding in environmental epidemiology after adjustment for other major risk factors. Where available, we included information with regard to what is considered to be a clinically relevant effect.

10.2.9 *Plausible confounding*

Plausible confounding or residual confounding refers to consideration of all unmeasured determinants of an outcome unaccounted for in an adjusted analysis that are likely to be distributed unequally across groups [512, 518]. According to GRADE, upgrading of the evidence should be considered when there are indications that residual confounding or bias would underestimate an apparent association (i.e. bias towards the null), or suggest a spurious effect when results suggest no effect.

10.2.10 *Number of studies*

The GRADE system takes into account the number of studies only indirectly in the "imprecision"-criterion. However, if the evidence is provided by only one study, several criteria cannot be taken into account: the result of one study cannot be inconsistent with its own results. It is also very difficult to test for publication bias. As a consequence, we decided to downgrade the overall level of the quality of evidence in cases where the evidence was based on only one study.

11 Assessment of the quality of evidence of studies on the impact on the cardiovascular system

In this chapter, we assess the quality of the evidence of the evaluated studies on the impact of noise on the different cardiovascular endpoints by applying the adapted GRADE system (as explained in the previous chapter). We explain as fully as possible the reasoning behind our judgement. The scores for the different GRADE criteria, can be found in the Appendices III - VIII.

11.1 Hypertension

We evaluated 40 studies that investigated the impact of noise from air, road, and rail traffic and wind turbine noise on the risk of hypertension. Two studies had a cohort design; the other 38 studies were cross-sectional. All studies were carried out in residential settings. Table 11.1 provides a summary of the findings; more detailed information, including the scores on each GRADE criterion can be found in Appendix III.

Table 11.1: Noise exposure and the risk of hypertension: summary of findings

Noise source	Outcome ^{§)}	Number of study design(s) [*]	RR per 10 dB (95%CI) ^{†)}	Number of participants (cases)	Quality of evidence ^{‡)}
Air traffic	Prev	9 CS	1.05 (0.95 – 1.17)	60,121 (9,487)	⊕⊕
	Inc	1 CO	1.00 (0.77 – 1.30)	4,721 (1,346)	⊕⊕
Road traffic	Prev	26 CS	1.05 (1.02 – 1.08)**	154,398 (18,957)	⊕
	Inc	1 CO	0.97 (0.90 - 1.05)	32,635 (3,145)	⊕⊕
Rail traffic	Prev	5 CS	1.05 (0.88 – 1.26)	15,850 (2,059)	⊕
	Inc	1 CO	0.96 (0.88 – 1.04)	7,249 (3,145)	⊕⊕
Wind turbine	Prev	3 CS	***	1,830 (NR)	⊕

§) Outcome: Prev = prevalence of hypertension, Inc = incidence of hypertension; *) CS = cross-sectional study, CO = cohort study; †) RR = Relative risk per 10 decibel (dB) change in noise level and its 95% Confidence Interval (CI) after aggregating the results of the evaluated studies. For air, road –and, rail traffic noise, levels are expressed in L_{DEN}; for wind turbines, noise levels are expressed in Sound Pressure Levels (SPL); ‡) GRADE Working Group Grades of Evidence: High quality (⊕⊕⊕⊕): Further research is very unlikely to change our confidence in the estimate of effect, Moderate Quality (⊕⊕⊕): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, Low Quality (⊕⊕): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, Very low quality (⊕): We are very uncertain about the estimate. **) The estimate for the association between road traffic noise and the prevalence of hypertension is based on 47 estimates derived from 26 studies. ***) We decided not to aggregate the results of the three studies on the impact of wind turbine noise, since too many parameters were unknown and/or unclear. NR = Not Reported

11.1.1 Prevalence of hypertension

Applying a modified version of the GRADE system to the cross-sectional studies on the association between noise exposure and the prevalence of hypertension, we started with a grading of “low”. This is because we think a study with a cross-sectional design has important limitations: In cross-sectional studies, for each participant, noise exposure, the ascertainment of the outcome (in this case hypertension), and any other

factors are measured together, at the same time. As a consequence, it is not clear when and how fast the effects of noise develop, or even whether exposure preceded the outcome. Since cross-sectional studies are based on *prevalence*, the association between exposure and outcome is affected not only by the relationship between exposure and *incidence*, but also by the influence by exposure on the *duration* of the outcome. The main reason there are so many studies on noise and hypertension is probably efficiency. Cross-sectional studies are cost-effective because of the long duration of hypertension, resulting in a comparatively high prevalence.

11.1.1.1 Risk of bias

The studies that investigated the impact of noise on the *prevalence* of hypertension have some other study limitations: The evaluated cross-sectional studies on the impact on hypertension had response rates that were often below 60%. From the literature [519], we know that a high response rate is necessary for a reliable estimation of the prevalence of the outcome. When the response rate is low, we can only *assume* that the respondents are representative of the total sample, which is a selection of the population of the research area, and that this representativeness would not be much affected if the (non)-response were random. It has to be kept in mind that, even in case of a high response rate, selective non-response is possible. From cross-sectional studies on the impact of aircraft noise on the prevalence of annoyance, we know that the prevalence can differ substantially between responders and non-responders [57, 74]. For the studies that were evaluated in this review, we cannot say whether there is selective (non)-response and how this might have affected the results.

Another important limitation of most of the evaluated studies is that hypertension was ascertained by means of questionnaires only. The reliability of such a method is questionable. For example, since a person does not always notice whether he or she is suffering from hypertension, it is possible that some hypertensive persons may have classified themselves as having a normal blood pressure. Consequently, ascertaining hypertension by means of questionnaires can lead to underreporting of the outcome. A comparison between blood pressure measurements and self-reported data from Statistics Netherlands (CBS) among participants in the REGENBOOG project showed that for every 10 participants who suffered from hypertension according to the blood pressure measurements, more than one had not reported in the questionnaire that he or she suffered from hypertension. This was especially the case among participants older than 40 years [520]. In the studies on the impact of noise on hypertension we see a similar phenomenon: in the study by Schulte and Otten [55], it appeared that the prevalence of hypertension ascertained by means of clinical measurements was higher than the prevalence of self-reported hypertension. Biased reporting is also possible. Studies on adults' health have suggested that persons with poorer perceived health, often attribute the cause of their symptoms to external conditions, such as their living environment [234]; subjects might be more prone to blame their environment for their health problems, or may even tend to exaggerate adverse effects of exposure in order to influence noise policy.

The heterogeneity analyses, presented in Chapter 4 of this review, showed, however, that the way hypertension was ascertained was not a significant source of heterogeneity. We observed small differences in RR per 10 dB between studies in which hypertension was ascertained by means of self-reporting and studies in which hypertension was ascertained by means of clinical measurements (see Tables 4.3 and 4.6). Because many of the evaluated studies suffer from a low response rate and because, in a substantial number of the evaluated studies, hypertension was assessed by means of questionnaires only, we decided to downgrade the quality of the evidence of the studies on the impact of noise on the prevalence of hypertension.

11.1.1.2 Inconsistency

Figures 4.1, 4.3, 4.5, and 4.6 showed that results across studies differed in the magnitude and direction of effect estimates. This was confirmed by the results of the heterogeneity analyses, presented in Chapter 4, which demonstrated moderate heterogeneity for studies on the association between air traffic noise, road traffic noise, and rail traffic noise, and the prevalence of hypertension. The three studies on the association between the exposure to noise from wind turbines and the prevalence of hypertension all found a positive but non-significant association between noise exposure and hypertension. Although we were not able to test for heterogeneity, we considered the results of these studies to be consistent. We decided to downgrade the quality of the evidence only of the studies on the impact of air, road, and rail traffic noise; the quality of the evidence of the studies on the impact of wind turbine noise, was not downgraded.

11.1.1.3 Imprecision

We considered the results of the two meta-analyses dealing with impact of noise from air and road traffic on the prevalence of hypertension to be precise: the total number of cases was 9,487 and 18,957 persons, respectively; the 95% CIs were sufficiently narrow, since they did not contain values below 0.75 or above 1.25.

Although the aggregated result of the studies on the impact of rail traffic noise did contain values above 1.25, we considered the results of the meta-analyses to be precise, since we judged the total number of cases as high ($n = 2,059$). We therefore did not downgrade the quality of the evidence further for studies on the impact of air, road, and rail traffic noise.

For the studies on the impact of wind turbine noise, we were not able to carry out a meta-analysis because too many parameters (e.g. the number of cases) were unclear. Given the number of cases in one of the three evaluated studies (67 cases and 725 participants in the NL-07 study), it is the question whether the total number of cases for all three studies together will be larger than 200. Looking at Figure 4.6, presenting the separate results of the different studies, we see that the confidence intervals included values below 0.75 and 1.25. As a consequence, we decided to downgrade the quality of the evidence of the studies on the impact of wind turbine noise further.

11.1.1.4 Publication bias

For the studies evaluating the impact of air traffic noise, we had little reason to believe that there is major publication bias. This is also visible when looking at the funnel plot (Figure 4.2). In addition, the Egger test did not provide evidence of small-study bias. This was different for the studies on the impact of road traffic noise: although the funnel plot (Figure 4.4) did not show clear publication bias, the Egger test did provide evidence of small-study bias. For both the studies that investigated the impact of rail traffic noise and wind turbine noise, the number of available effect estimates was too small, to test for publication bias or small-study bias. As a result, we further downgraded the quality of the evidence only for the studies on the impact of road traffic noise.

11.1.1.5 Exposure-response gradient

We found several indications for the existence of an exposure response gradient between exposure to noise from air, road or rail traffic and the prevalence of hypertension: Although results differed across studies, Figures 4.1, 4.3, 4.5, and 4.6 show that most studies found that the risk of hypertension increased when the noise level increased (RR per 10 dB > 1). For all evaluated noise sources, except for noise from wind turbines, we were able to derive a dose response gradient by means of a meta-analysis. Only for the association with road traffic noise exposure did we find a significant effect size of 1.05 per 10 dB across a noise range of 20 - 80 dB (L_{DEN}).

Several of the evaluated studies also took into account the duration of residence or exposure duration. After looking at the results of these studies, we found several indications for an effect of exposure duration. Figure 11.1 shows the association between traffic noise exposure and the prevalence of hypertension for subgroups differing in duration of residence. In several cases, the effect estimates turned out to be largest for the sample that had lived for a longer period in the same house.

For the association between air traffic noise and the prevalence of hypertension, we were able to test the effect of the exposure duration of the population under investigation in the meta-regression analysis (see Table 4.3). After we aggregated the results of studies on populations that were exposed for at least five years, we found a non-significant effect size of 1.06 per 10 dB for the association between aircraft noise and the prevalence of hypertension. After aggregating the results of studies including populations that were exposed for a maximum of three years, we found a non-significant effect size of 1.00 per 10 dB. Although it should be noted that the strongest association between aircraft noise exposure and the prevalence of hypertension was found in the group of studies on persons where information regarding duration of residence was unclear or even lacking, we think that these findings make the existence of an exposure response more likely. Consequently, we decided to upgrade the quality of the evidence.

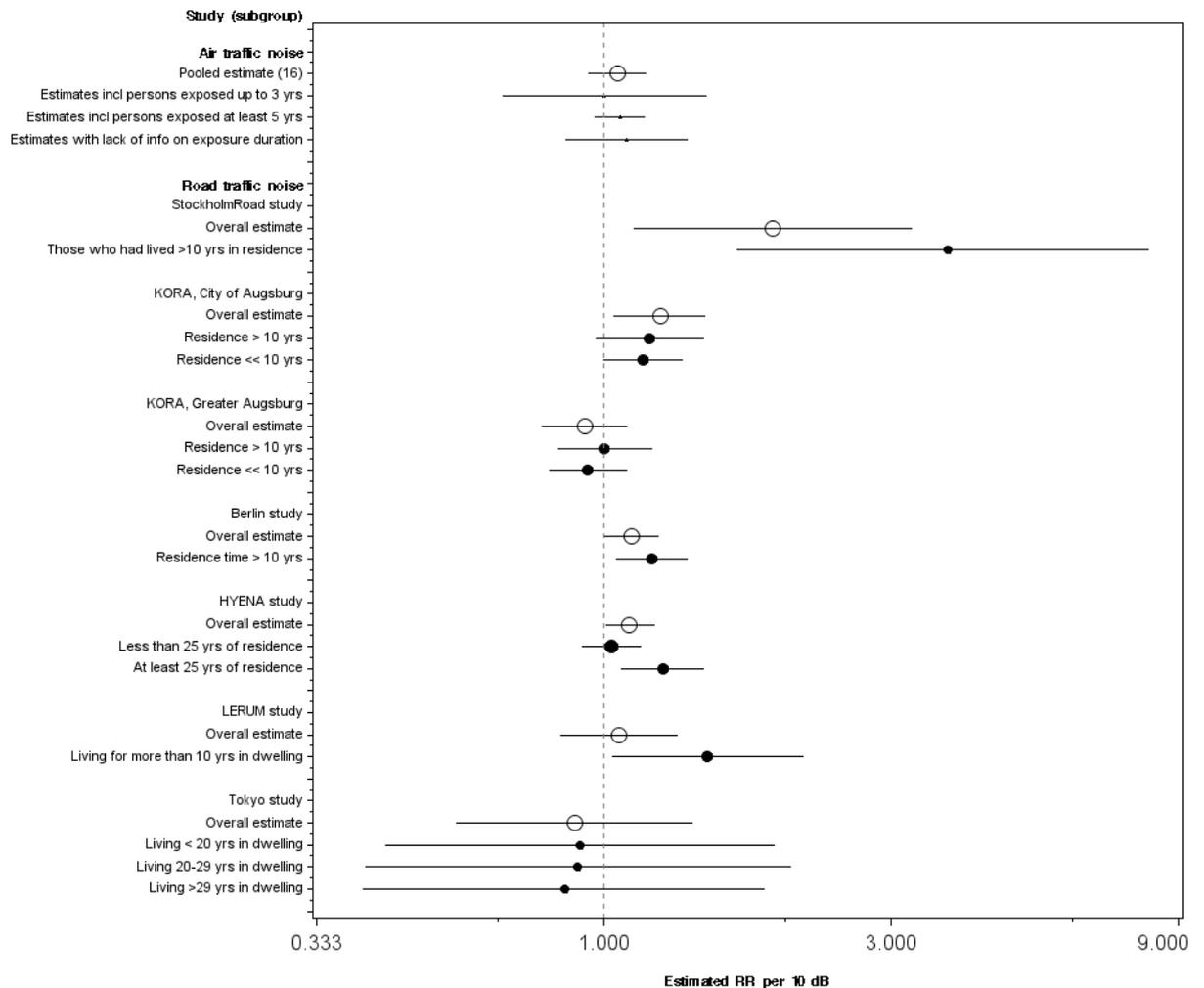


Figure 11.1: Association between noise exposure (L_{DEN}) and the prevalence of hypertension for different subgroups differing in duration of residence. The dotted vertical line corresponds to no effect of road or air traffic noise exposure. The black circles correspond to the estimated RR per 10 dB and 95% CI for the different subgroups within a study. The white circles represent the overall estimate of a study and 95% CI.

11.1.1.6 Magnitude of effect

As already indicated, only for the association between road traffic noise exposure and the prevalence of hypertension did we find a significant effect size of 1.05 per 10 dB across a noise range of 20 - 80 dB (L_{DEN}). This means that where the road traffic noise exposure level increases from 20 to 80 dB (L_{DEN}), the $RR = 1.34$. In the area of environment and health, we consider this to be a small effect (since the RR is less than 1.5). Consequently, we decided not to upgrade the quality of the evidence of studies on the impact of noise on the prevalence of hypertension for magnitude of effect.

11.1.1.7 Mitigated bias and confounding

We have already addressed the possible effect of selective non-response on the results of the evaluated studies. However, other factors might also have caused residual confounding: The observed impact of noise

exposure on the prevalence of hypertension might not only be a direct effect of the exposure to noise, but also be the effect of a decrease in sleep quality caused by noise exposure during the night. Some of the evaluated studies [62, 63, 65, 214, 216, 224, 234-236, 241] investigated (in addition to L_{DEN}) the impact of noise during the night (expressed as L_{night}). Figure 11.2 shows that the associations between 24-hour noise exposure (expressed as L_{DEN}) and the prevalence of hypertension were comparable with the associations between night-time noise exposure (expressed as L_{night}) and the prevalence of hypertension.

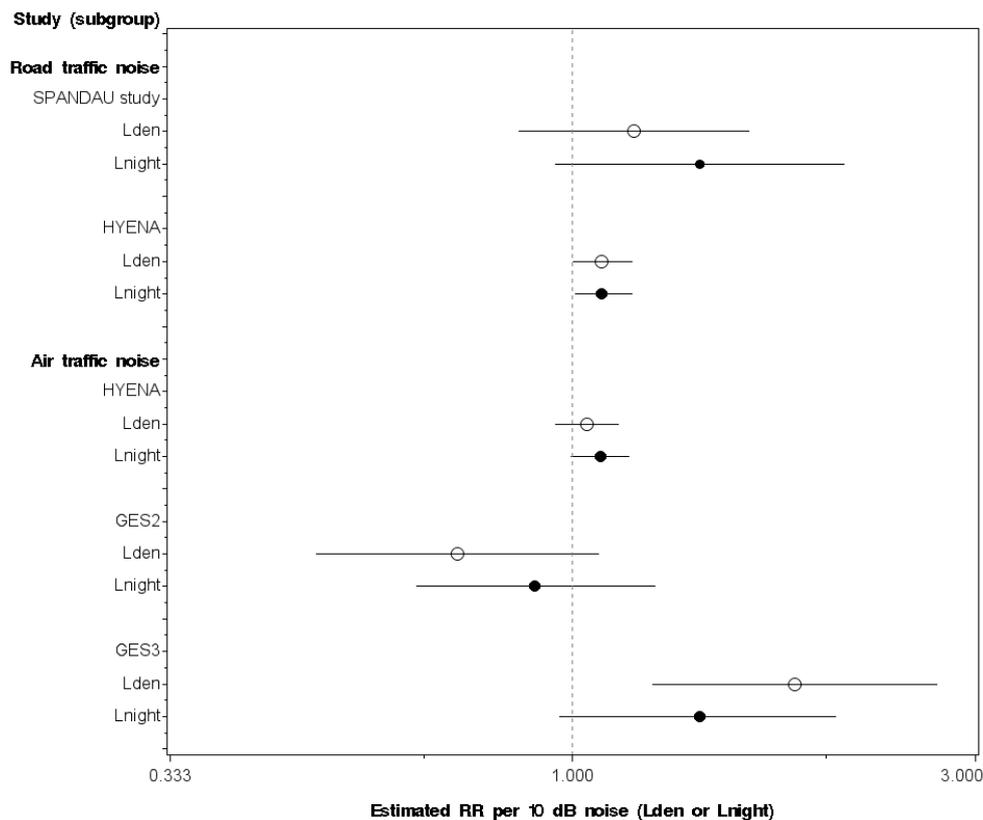


Figure 11.2: Association between traffic noise exposure (expressed as L_{DEN} and L_{night}) and the prevalence of hypertension. The dotted vertical line corresponds to no effect of road traffic or aircraft noise exposure. The black circles correspond to the estimated RR_{10dB} and 95% CI representing the effects exposure during the night period. The white circles correspond to the estimated RR_{10dB} and 95% CI representing the effects exposure during the day, evening and night period.

As indicated in the introduction to this review, it is evident that people living in a city or close to roads are exposed not only to traffic noise, but also to air pollution generated by traffic. Several studies indicate that exposure to air pollution may affect the cardiovascular system. Air pollution and noise from road traffic share the same source, so the effects could be attributed to both exposure types. This may give rise to confounding, where it is difficult to ascribe observed effects to a specific exposure. In our heterogeneity analyses, we were able to test whether this was the case. Table 4.6 shows that there was generally not a big difference between the results of studies on the impact of road traffic

noise on hypertension that adjusted for air pollution and studies that did not adjust for air pollution. However, it should be noted that whether or not a study adjusted for air pollution was a factor that only marginally explained heterogeneity between the studies. A possible explanation for this might be that the studies adjusted for different air pollutants, differing in composition.

Since air pollution and noise from road traffic share the same source, and their effects could be attributed to both exposure types, this also may give rise to effect modification, where the two exposures interact in causing cardiovascular effects. However, none of the evaluated studies investigated the interaction effect of noise exposure and air pollution for the association between noise exposure and the prevalence of hypertension.

In general, the literature reports negative associations between SES and health. Diseases such as cardiovascular disease, stroke, and diabetes are more prevalent in people with a lower SES. In many situations people with a lower SES tend to live in unhealthy environments. Unfortunately, the evaluated studies were not always able to adjust for SES. Looking at the results of the meta-regression analyses in Tables 4.3 and 4.6, we see that with regard to hypertension, there are only small differences between the results of studies on the impact of aircraft or road traffic noise on hypertension that adjusted for SES and those that did not adjust for SES.

An issue that also could have played a role in the studies on the effects of noise on hypertension is the problem of self-selection: Individuals may select their living area (or the neighbourhood in which they live) according to unobservable factors that are correlated with their health. This may give rise to bias [521]. With regard to noise and health, the place where people live is typically based on preferences for quietness, pre-existing health conditions, and their ability to afford to live in a quiet neighbourhood [522]. If this selection is not accounted for, then there are serious concerns about the internal validity of the stated causal relationship [521, 522]. One could argue both for a negative and for a positive selection: Several studies have found indications that wealthy people with high educational levels tend to settle in quiet regions ([75, 523] in: [522]). Since noise-sensitive individuals experience more stress and annoyance when exposed to noise than noise-insensitive individuals, the assumption is that noise-sensitive people tend to live in quiet areas, whereas noise insensitive people tend to self-select into noisier and often cheaper regions. Such residential sorting will bias the effect of noise on health if noise sensitivity is related to both factors [522]. In the literature, indications were found that noise sensitivity is associated with, among other things, components of a pre-morbid personality, psychiatric disorders, heart problems, and sleeping problems ([477] in: [522]). Several authors [37, 522] have argued that a cross-sectional study design may act conservatively on the results. For the studies that were evaluated in this review, it is unclear whether there is self-selection and how this might have affected the results.

Since no clear sources of residual confounding could be detected – and because most of the studies that were included in the evaluation

adjusted for a range of important confounders -, we decided to upgrade the quality of the evidence of the studies on the impact of air and road traffic. Of course, we also attempted to find out in what way the results for rail traffic noise were affected by adjustment for factors such as SES and air pollution. However, on the basis of the available data, we were not able to draw any conclusions about the possible role of these factors. We therefore decided not to upgrade the levels of evidence for rail traffic noise.

Adjustment for potential confounders was limited in the studies on the impacts of wind turbine noise. Therefore, we decided not to upgrade the quality of the evidence of these studies.

11.1.1.8 Conclusion

As a result of the above considerations, we rated the quality of the evidence of an impact from noise from air, road, and rail traffic on the prevalence of hypertension as "very low" or "low". We rated the quality of the evidence of an impact from noise from wind turbine noise on the prevalence of hypertension as "very low".

11.1.2 *Incidence of hypertension*

We evaluated two cohort studies that investigated the impact of noise from air, road, and rail traffic on the *incidence* of hypertension. In a cohort study one tries to follow the course of events over time. For a group of people (a cohort) who are still free of disease (in this case hypertension), the exposure of each person is determined, and is awaited which person gets the disease. Therefore, we started our GRADE assessment for all noise sources with a grading of "high".

11.1.2.1 Risk of bias

A disadvantage of a prospective cohort study is that the observation period can sometimes span many years. Therefore, it can be difficult to track subjects for the entire study period. Because of death, relocation, or loss of interest in the study, subjects may disappear. Losses to follow-up can introduce bias if there are differences in likelihood of loss to follow-up that are related to exposure status and outcome. In some cohort studies on the impact of noise on the cardiovascular and/or metabolic system, the attrition rate was relatively high: In the cohort of the Stockholm Diabetes Preventive Program (SDPP) [66, 71, 223], investigating the impact of aircraft noise exposure on self-reported hypertension, the final baseline study group comprised 3,128 men and 4,821 women. After 8 - 10 years, the SDPP study researchers invited the participants to a follow-up survey. We estimate that the attrition rate exceeded 20%. Due to this loss of follow-up and because hypertension was ascertained by means of self-reporting, we decided to downgrade the quality of the evidence of an association between aircraft noise exposure and the incidence of hypertension.

In the other cohort study that investigated the impact of road and rail traffic noise, we estimated that the losses to follow-up were less than 20%: The original study group of the Diet, Cancer and Health (DCH) cohort comprised 57,053 subjects who were enrolled in the cohort between 1993 and 1997 [120-122, 138, 142, 247, 248]. In the period 2000 – 2002, the cohort comprised 54,379 participants (95% of the original study group). In the end, 45,271 of them (79% of the original

study group) agreed to participate in the study on the impact of road traffic noise.

For both cohort studies (SDPP and DCH), however, it is unknown whether there are systematic differences related to the health outcome under investigation or noise exposure between those who dropped out, and those who stayed in the study.

We decided to downgrade the quality of the evidence of an association between road or rail traffic noise and the incidence of hypertension, because hypertension in the DCH cohort was ascertained by means of questionnaires. We discussed the limitations of this measurement method in the previous section already.

11.1.2.2 Inconsistency

Because for each noise source, one cohort study was available that investigated the impacts on the incidence of hypertension, it did not make sense to include this criterion in our judgement with regard to the quality of the evidence. However, within the SDPP study, investigating the impact of aircraft noise, there was some inconsistency visible, when comparing the results of men and women: in the SDPP study, for men an RR of 1.17 (95% CI: 0.90 – 1.15) per 10 dB was found; for women an RR of 0.85 (95% CI: 0.62 – 1.15) per 10 dB was found. Nevertheless, this may correspond to biological differences between men and women. Therefore, we did not further downgrade the quality of the evidence for any of the three noise sources.

11.1.2.3 Imprecision

The sample size of the two cohort studies was very large, since the number of cases ranged from 1,346 to 3,145. In addition, the 95% CIs were considered to be sufficiently narrow, since they did not contain values below 0.75 or above 1.25. Consequently, we did not downgrade the quality of the evidence of studies on the impact of air, road and rail traffic noise for imprecision.

11.1.2.4 Publication bias

The number of available effect estimates was too small, to test for publication bias or small-study bias. As a result, we did not downgrade the quality of the evidence.

11.1.2.5 Exposure response gradient

The results of the evaluated cohort studies reporting on the effect of noise from different transportation noise sources on the incidence of hypertension did not provide any evidence of an association (see Figures 4.1, 4.3, 4.5, and 4.6). We therefore decided not to upgrade the quality of the evidence in relation to this factor.

11.1.2.6 Magnitude of effect

As already indicated, we found a small and non-significant effect size of 1.00 per 10 dB (L_{DEN}) for the association between air traffic noise exposure and the incidence of hypertension. In relation to both road and rail traffic noise exposure, we observed no effects. As a result, we decided not to upgrade for magnitude of effect.

11.1.2.7 Mitigated bias and confounding

As was the case in the cross-sectional studies, we checked several factors that might have caused residual confounding. First, we looked at the role of the SES of the study participants. Looking at the results of the SDPP study on the impact of aircraft noise, we see that there is no difference between the groups of participants with different SES with regard to the association between aircraft noise and the incidence of hypertension. The DCH study, which investigated the impact of road and rail traffic noise, was able to adjust for a number of confounders including SES. At the time of writing this review, no information was available from the DCH study that demonstrated whether there was an effect of SES on the association between road or rail traffic noise and the incidence of hypertension.

In the SDPP study, misclassification of disease may have occurred due not only to the subjective assessment of hypertension, but also to the fact that a large number of the subjects smoked prior to the blood pressure measurements. The SDPP study researcher also presented results after the exclusion of those who had smoked before the blood pressure measurement. This resulted in stronger associations. According to the researchers, this might suggest that the results were affected by non-differential misclassification of disease. In the DCH study, hypertension was based on subjective assessment from the participants (self-report). The limitations of such a way of ascertaining hypertension have already been addressed.

The DCH study was able to adjust for exposure to air pollution; the SDPP study was not. At the time of writing of this review, no information was available from the DCH study (as was the case in most evaluated studies) that demonstrated whether there was an effect of exposure to air pollution (separately) on the association between road or rail traffic noise and the incidence of hypertension.

In the end, we decided not to upgrade the quality of the evidence of the study on the impact of air, road, or rail traffic noise.

11.1.2.8 Conclusion

We rated the quality of the evidence of the studies on the impact of air, road, and rail traffic noise on the incidence of hypertension as "moderate". However, since only one study was available for each noise source, we decided to downgrade the overall quality to "low".

11.2 Ischaemic heart disease

In total, we evaluated the results of twenty-two studies that investigated the effect of noise on the risk of IHD. The studies investigated the impact of air, road, and rail traffic noise. Of the evaluated studies, four had an ecological design and eight were of cross-sectional design. Four studies were case-control studies and six studies were cohort studies. All studies were carried out in residential settings. The three studies on the impact of noise from wind turbines are not evaluated here, since they investigated the impact on cardiovascular disease and not specifically on IHD. Table 11.2 provides a summary of

the findings; more detailed information, including the scores on each GRADE criterion, can be found in Appendix IV.

Table 11.2: Noise exposure and the risk of IHD: summary of findings

Noise source	Outcome ^{§)}	Number of study design(s) *	RR† per 10 dB (95%CI)	Participants (cases)	Quality of evidence‡)
Air traffic	Prev	2 CS	1.07 (0.94 – 1.23)	14,098 (340)	⊕
	Inc	2 ECO	1.09 (1.04 – 1.15)**	9,619,082 (158,977)	⊕
	Mort	2 ECO	1.04 (0.97 – 1.12)	3,897,645 (26,066)	⊕
1 CO		1.04 (0.98 – 1.11)	4,580,311 (15,532)	⊕⊕	
Road traffic	Prev	8 CS	1.24 (1.08 – 1.42)**	25,682 (1,614)	⊕⊕
	Inc	1 ECO	1.12 (0.85 – 1.48)	262,830 (418)	⊕
		3 CO, 4CC	1.08 (1.01 – 1.15)**	67,224 (7,033)	⊕⊕⊕⊕
	Mort	1 CC, 2 CO	1.05 (0.97 – 1.13)	532,268 (6,884)	⊕⊕⊕
Rail traffic	Prev	4 CS	1.18 (0.82 – 1.68)	13,241 (283)	⊕

§) Outcome: Prev = prevalence of IHD, Inc = incidence of IHD, Mort = mortality due to IHD; *) ECO = ecological study, CS = cross-sectional study, CC = case control study, CO = cohort study; †): RR = Relative Risk per 10 decibel change in noise level, 95%CI = 95% Confidence Interval. For air, road, – and rail noise, levels are expressed in L_{DEN} ; ‡) GRADE Working Group Grades of Evidence: High quality (⊕⊕⊕⊕): Further research is very unlikely to change our confidence in the estimate of effect, Moderate Quality (⊕⊕⊕): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, Low Quality (⊕⊕): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, Very low quality (⊕): We are very uncertain about the estimate.

11.2.1 Prevalence of IHD

Applying the GRADE system to the association between noise exposure from air, road and rail traffic and the prevalence of IHD investigated in cross-sectional studies, we started with a grading of "low". We addressed the limitations of a cross-sectional design in Section 11.1.1.

11.2.1.1 Risk of bias

Apart from their cross-sectional design, the studies that investigated the impact of noise on the prevalence of IHD have some other study limitations. For the same reasons as the studies on the association between noise and the prevalence of hypertension, we decided to downgrade the quality of the studies on the impact of noise on the prevalence of IHD: Response rates in most studies were below 60%. In most of the evaluated studies, IHD was ascertained by means of questionnaires only.

11.2.1.2 Inconsistency

Figures 5.1, 5.2 and 5.6 show that the results across studies differed not only in magnitude of effect, but sometimes also in direction of the effect. This was confirmed by the results of the different tests for heterogeneity, which demonstrated moderate heterogeneity for studies on the association between road ($I^2 = 51.4\%$) and rail traffic noise ($I^2 = 57.4\%$) and the prevalence of IHD. The two studies on the association between exposure to noise from air traffic and the prevalence of IHD, both found a positive but non-significant association between noise exposure and IHD. We decided to further downgrade the quality of the evidence only of the studies on the impact of road and rail traffic; for

the studies on the impact of aircraft noise exposure, we decided not to downgrade.

11.2.1.3 Imprecision

The meta-analyses dealing with the impact of noise from air, road or rail traffic on the prevalence of IHD included a total number of cases that ranged from 283 to 1,614, which was large.

For studies on the impact of noise from air traffic, we considered the 95% CIs to be sufficiently narrow, since they did not contain values below 0.75 or above 1.25; for studies on the impact of noise from road or rail traffic the 95% CIs contained values above 1.25. Nevertheless, since the aggregated result of the studies on the impact of both road - and rail traffic noise did not contain values below 0.75, we considered the results of the meta-analyses to be precise and did not further downgrade the quality of the evidence of studies on the impact of air, road and rail traffic noise for imprecision.

11.2.1.4 Publication bias

The number of available effect estimates was too small to test for publication bias or small-study bias. As a result, we did not further downgrade the quality of the evidence.

11.2.1.5 Exposure-response gradient

We found several indications for the existence of an exposure-response gradient: Although results differed across studies, Figures 5.1, 5.2, and 5.6 show that most studies found that the risk of IHD increased when the noise level increased ($RR \text{ per } 10 \text{ dB} > 1$). For road, rail and air traffic we were able to derive an exposure-response gradient in the meta-analysis. Only for the association between road traffic noise exposure and the prevalence of IHD did we estimate a significant effect size of 1.24 per 10 dB across a noise range of 30 - 80 dB (L_{DEN}). None of the evaluated studies took into account the duration of residence. We decided to upgrade the quality of the evidence only of studies on the impact of road traffic noise.

11.2.1.6 Magnitude of effect

As already indicated, only for the association between road traffic noise exposure and the prevalence of IHD did we find a significant effect size of 1.24 per 10 dB across a noise range of 30 - 80 dB (L_{DEN}). This means that where the road traffic noise exposure level increases from 30 to 80 dB (L_{DEN}), the $RR = 2.93$. In the area of environment and health, we consider this to be large effect (since the RR is more than 1.5). Consequently, we decided to upgrade the quality of the evidence of an association between road traffic noise and the prevalence of IHD. Although not statistically significant, we also consider the effect size found after aggregating the results of the studies on the impact of rail traffic noise to be large: for example, after aggregating the results of these studies, we found a non-significant effect size of 1.18 per 10 dB across a noise range of 30-80 dB (L_{DEN}). This means that where the rail traffic noise exposure level increases from 30 to 80 dB (L_{DEN}), the $RR = 2.29$. Despite this large magnitude of effect, we decided not to upgrade the quality of the evidence of the studies on the impact of rail nor air

traffic noise, since the reported RR per 10 dB was statistically not significant.

11.2.1.7 Mitigated bias and confounding

We considered several possible sources of residual confounding. For the studies that were evaluated in this review, it is unclear whether there is self-selection and how this might have affected the results. Also, it is not clear whether the observed impact of noise exposure on the prevalence of IHD might not only be a direct effect of the exposure to noise, but also be the effect of a decrease in sleep quality, caused by noise exposure during the night. Only the HYENA study investigated the impact of noise exposure during the night. For exposure to aircraft noise both during the day and during the night, the HYENA study researcher found a non-significant increase in the risk of IHD. For aircraft noise exposure during the day they found an RR of 1.06 (95%CI: 0.91 – 1.22) per 10 dB L_{day} ; for aircraft noise during the night they reported an RR of 1.11 (95%CI: 0.96 – 1.29) per 10 dB L_{night} [228].

Unfortunately, not all the evaluated studies were able to adjust for smoking. Smoking is considered to be an important risk factor for IHD [524]. At the same time, psychosocial stressors have been implicated as risk factors for tobacco use, and may influence smoking behaviour in a number of ways: for example, smoking may function as coping behaviour; exposure to stress may result in a diminished self-regulation to control the urge to smoke ([525-527] in: [528]). The results of our heterogeneity analyses presented in table 5.5, show that adjusting or not for smoking, can be considered to be an important source of heterogeneity for the association between road traffic noise and the prevalence of IHD. Furthermore, the table shows that adjusting for smoking seems to diminish the impact of noise: the effect of road traffic noise in the group of studies *not* adjusting for smoking was larger (RR = 1.32 (95%CI: 1.03 – 1.69) per 10 dB) than in the group of studies that did adjust for smoking (RR = 1.15 (95%CI: 1.00 – 1.33) per 10 dB). For studies on the impact of *aircraft* noise, we found the opposite: The HYENA study, where the researchers were not able to adjust for smoking, found a non-significant RR of 1.06 per 10 dB, while the AWACS-1 study found a non-significant RR of 1.18 per 10 dB after adjusting for smoking.

Table 5.5 also shows that adjusting or not for an indicator of air pollution, can be considered to be an important source of heterogeneity. The table shows that adjusting for air pollution seemed to increase the impact of road traffic noise. The effect of road traffic noise in the group of studies *not* adjusting for air pollution tended to be smaller (RR = 1.17 (95%CI: 1.03 – 1.32) per 10 dB) than in the group of studies that did adjust for air pollution (RR = 1.37 (95%CI: 1.04 – 1.80) per 10 dB).

Since adjustment for indicators of air pollution and smoking might have affected the results of our meta-analysis of the association between road traffic noise and the prevalence of IHD, we decided not to further upgrade the level of evidence. For the studies on the impact of air or rail traffic noise, we were not able to test whether the results were affected by sources of residual confounding. We cannot, however, properly rule out the possibility that the results of the studies on these sources were

affected by residual confounding. Consequently, we also decided not to upgrade the level of evidence.

11.2.1.8 Conclusion

As a result of the above considerations, we rated the quality of the evidence of an impact of noise from air and rail traffic on the prevalence of IHD as “very low”. The quality of the evidence of an impact of noise from road traffic was rated as “low”.

11.2.2 *Incidence of IHD*

We selected two studies that investigated the association between *air* traffic noise and the *incidence* of IHD. The design of the studies was ecological. In these studies, the number of hospital admissions due to IHD in local areas (output areas, postcode areas) was correlated with the average noise exposure level of these areas. This generated the hypothesis that IHD results from exposure to noise. Applying the GRADE system to the association between aircraft noise exposure and the *incidence* of IHD investigated in ecological studies, we started with a grading of “very low”.

We selected eight studies that investigated the association *road* traffic noise and the *incidence* of IHD: three cohort studies, four case-control studies, and one ecological study. We addressed the limitations of ecological studies in the previous paragraph; we addressed the advantages and limitations of cohort studies in Section 11.1.2. Both cohort studies and case-control studies offer good possibilities to investigate the true impact of noise on the cardiovascular system: A case-control study is a retrospective investigation in which a diseased group (cases) and a disease-free group (controls) are compared with the aim of uncovering risk factors that differ between the groups. The controls are in principle a sample of the population from which the cases were derived. In other words: the control group are persons who, if they had the disease, would be in the case group. The big advantage of a case-control study over a cohort study is that it can be carried out relatively quickly and efficiently. Persons suffering from the disease under investigation can be found relatively easily in (healthcare) registration systems. On the other hand, because of the fact that the data collection is mainly retrospective, a case-control study is subject to several types of bias.

As was indicated in the previous section, we decided *not* to combine the results of studies with different inherent quality. This means that we will not combine the results of cohort and case-control studies with the results of ecological studies. For the group of cohort and case-control studies on the association between road traffic noise and the incidence of IHD, we started our GRADE assessment with “high”. For the ecological study on the association between road traffic noise exposure and the *incidence* of IHD we started our assessment with a grading of “very low”.

11.2.2.1 Risk of bias

An important omission from the ecological studies [76, 77, 134, 135] is the lack of information about lifestyle factors that are important risk factors for IHD (e.g. smoking, diet, alcohol use, physical activity, high

cholesterol level). Despite the fact that some of the studies attempted to (partly) adjust for the differences in non-measured risk factors between areas, we cannot rule out the possibility that the results of these studies are biased due to a lack of adjustment to these factors [199].

Looking at the quality of the studies, we also have some worries with regard to the exposure assessment. Unfortunately, not all studies were able to apply individual exposure estimates: for example, in order to ascertain noise exposure, the researchers for the ecological studies that investigated the association between aircraft noise and the incidence of IHD [76, 77] used modelled noise levels for a local area. Subsequently, they assigned these noise levels to everybody who was a member of that group. Three of the studies that investigated the association between road traffic noise and the incidence of IHD [129, 134, 135] made use of noise measurements to ascertain road traffic noise exposure. Based on the results of these noise measurements, they created a noise map and assigned a noise value to each participant. The inability to apply individual exposure estimates to larger study populations might have caused exposure misclassification. As a consequence, we decided to downgrade the quality of the evidence of all the ecological studies on the association between air or road traffic noise exposure and the incidence of IHD. We did not further downgrade the quality of the evidence of the case-control and cohort studies on the association between road traffic noise and the incidence of IHD.

11.2.2.2 Inconsistency

The results of the two ecological studies on the impact of aircraft noise (see Figure 5.1) were quite consistent: Both studies found a positive association between air traffic noise exposure and the incidence of IHD. Only the association reported in the LSAS study was statistically significant. The test for heterogeneity ($I^2_{\text{residual}} = 48.4\%$) indicated low to moderate heterogeneity.

Looking at the case-control and cohort studies on the impact of road traffic noise (see Figure 5.3), we observed that their results were quite consistent. Of the nine effect sizes, six were larger than one; three effect sizes were smaller than one. However, none of the effect sizes were statistically significant. The test for heterogeneity indicated no heterogeneity. As a consequence we decided not to downgrade the quality of the level of evidence due to inconsistency for either air or road traffic noise exposure.

11.2.2.3 Imprecision

The sample size of the *meta-analyses* dealing with the impact of air and road traffic noise on the incidence of IHD was very large, since the number of cases ranged from 7,033 to 158,977. For the results of the meta-analyses investigating the impact of road traffic noise, we considered the 95% CIs to be sufficiently narrow, since they did not contain values below 0.75 or above 1.25. Consequently, we did not further downgrade the quality of the evidence for imprecision.

We also did not further downgrade the quality of the evidence from the ecological study on the association between road traffic noise and the incidence of IHD, despite the fact that the result of this ecological study

contained values above 1.25. We considered the number of cases in this ecological study to be large enough ($n = 418$).

11.2.2.4 Publication bias

The number of available effect estimates for the association between air traffic noise and the incidence of IHD was too small to test for publication bias. As a result, we did not further downgrade the quality of the evidence of the studies on the impact of aircraft noise. For the studies on the impact of road traffic noise, 10 effect estimates were available. Consequently, we were able to test for publication bias. Figure 5.5 presents the result and suggests some publication bias. Despite the fact that the result of the Egger test provided weak evidence of publication bias, we decided to downgrade the quality of the evidence of the studies on the impact of road traffic noise.

11.2.2.5 Exposure-response gradient

For the association between aircraft noise and the incidence of IHD, we derived a significant exposure-response gradient: after aggregating the results of the two ecological studies, we found an effect size of 1.09 per 10 dB across a noise range of approximately 45 to approximately 65 dB (L_{DEN}). We also found a significant exposure-response gradient for road traffic noise: after aggregating the results of the cohort and case-control studies, we found an effect size of 1.08 per 10 dB across a noise range of approximately 40 - 80 dB (L_{DEN}).

The existence of an exposure-response gradient for the association between road traffic noise and the incidence of IHD is more likely, since we found indications for an effect of exposure duration. Figure 11.3 shows for three of the evaluated studies [103, 104, 129] the association between road traffic noise exposure and the incidence of IHD for subgroups differing in duration of residence. The figure demonstrates that in two of the three studies, the effect estimates turned out to be largest for the sample that had lived for a longer period in the same house. Figure 5.4 shows similar results: Studies on persons who were exposed for 15 years found a somewhat stronger association than studies on persons who were exposed for 5 years. We decided to upgrade the quality of the evidence of studies on the impact of road and aircraft noise for this factor.

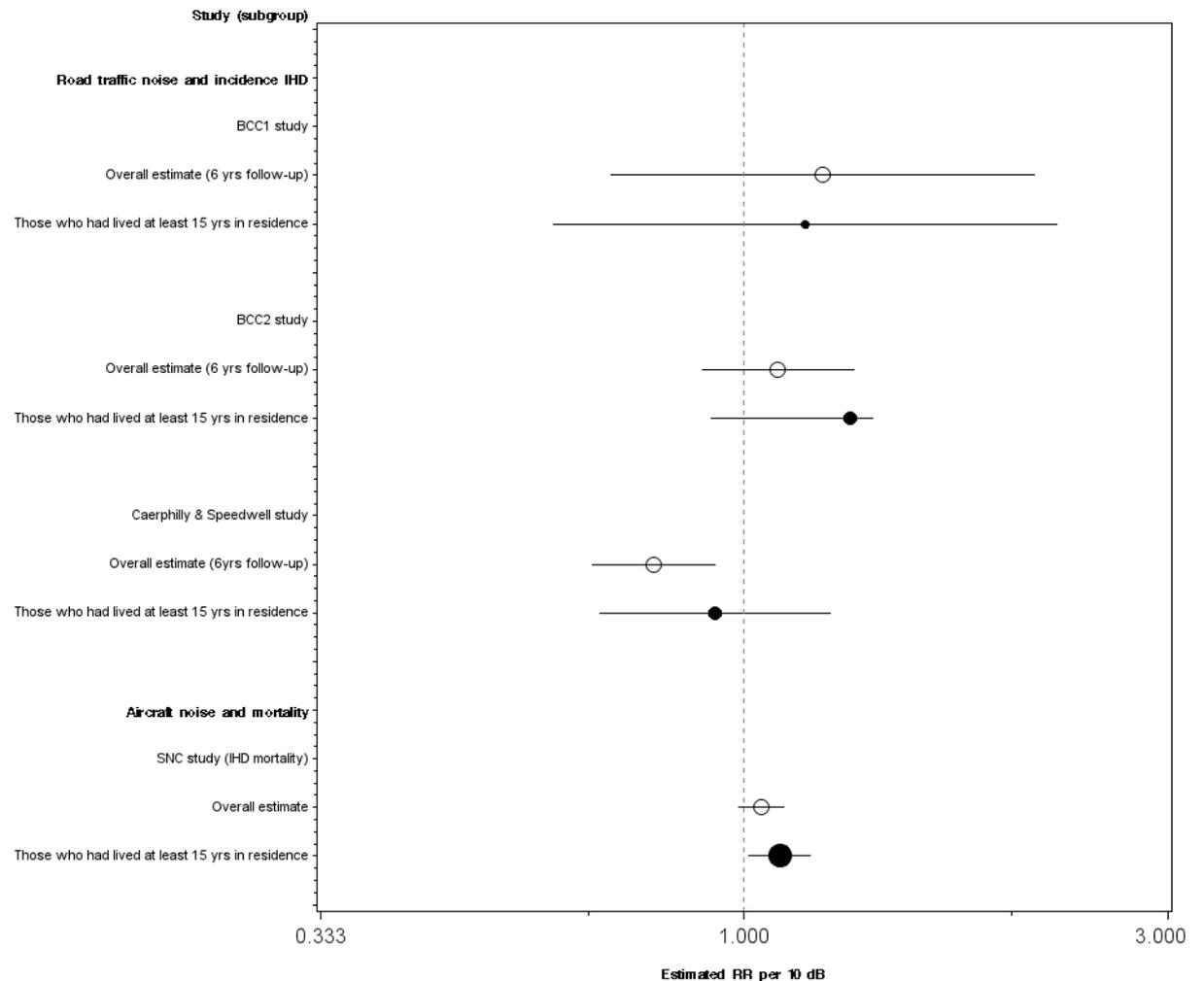


Figure 11.3: Association between noise exposure (L_{DEN}) and the incidence of IHD or mortality due to IHD for different subgroups differing in duration of residence. The dotted vertical line corresponds to no effect of road traffic or aircraft noise. The white circles represent the estimates and 95% CIs that were derived for the total population of the respective study; the black circles represent the estimates that were derived for a subgroup with a certain exposure duration for the respective study.

11.2.2.6 Magnitude of effect

As already indicated, we found a significant effect size of 1.09 per 10 dB across a noise range of approximately 45 - 65 dB for the association between aircraft noise and the incidence of IHD. This means that where the aircraft noise exposure level increases from 45 to 65 dB, the $RR = 1.19$. We consider this to be a rather small effect.

For the association between road traffic noise and the incidence of IHD, we found a significant effect size of 1.08 per 10 dB only after aggregating the results of the case-control and cohort studies. The noise range was approximately 40 - 80 dB (L_{DEN}). This means that if the road traffic noise exposure level increases from 40 to 80 dB, the $RR = 1.36$. We considered this to be a small effect.

We decided not to upgrade the quality of the evidence of an impact of road traffic noise on the incidence of IHD on this basis.

11.2.2.7 Mitigated bias and confounding

We considered several sources of potential residual confounding.

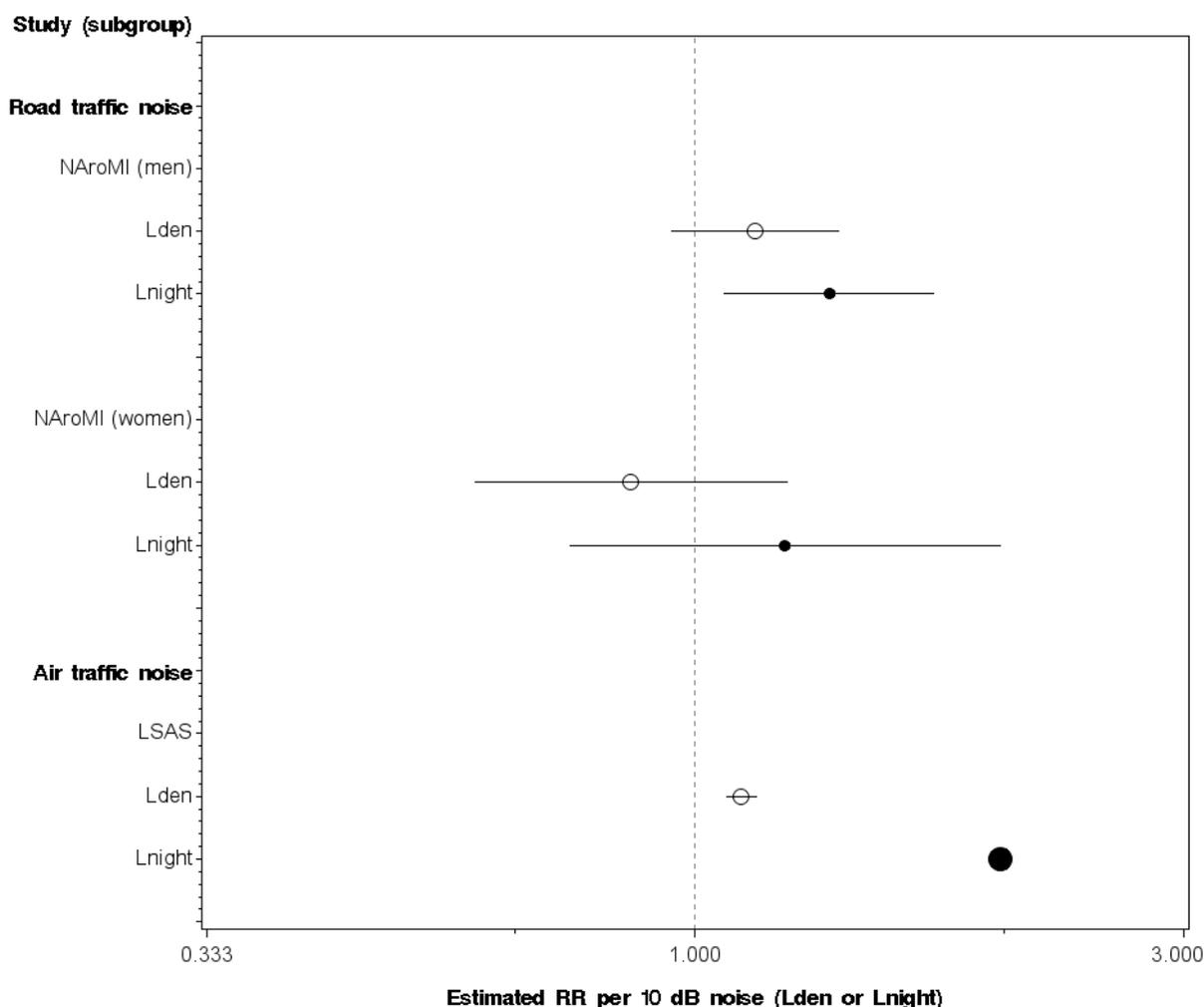


Figure 11.4: Association between traffic noise exposure (L_{DEN} or L_{night}) and the incidence of ischemic heart disease. The dotted vertical line corresponds to no effect of road traffic or aircraft noise exposure. The black circles correspond to the estimated RR_{10dB} and 95% CI representing the effects exposure during the night period. The white circles correspond to the estimated RR_{10dB} and 95% CI representing the effects exposure during the day, evening and night periods.

The observed impact of noise exposure on the incidence of IHD may also be the effect of a decrease in sleep quality, caused by noise exposure during the night. Only the NARoMI and the LSAS study investigated the impact of noise exposure during the night [76, 131, 132]. They did this in addition to L_{DEN} . Figure 11.4 shows the association between traffic noise exposure and the incidence of IHD derived from the NARoMI and the LSAS studies. The figure shows the results for both L_{DEN} and L_{night} . Looking at the figure, we can observe that the L_{night} seemed to be more strongly associated with the incidence of IHD than the L_{DEN} . Despite

these observed differences, however, we cannot say whether the observed effects are indeed due to exposure to noise during the night, since the correlation between the different noise metrics was high in both the NAroMI and LSAS studies.

As explained in the previous section, several studies indicate that air pollution may affect the cardiovascular system. Noise and air pollution share the same source. Therefore, the effects found in the studies on the association between traffic noise and the incidence of IHD could be attributed to both noise and air pollution. Figure 5.4 shows that adjusting for exposure to air pollution seems to *increase* the risk of IHD in relation to road traffic noise exposure. We were not able to test whether this increase was statistically significant. For the association between air traffic noise and the incidence of IHD, the USAirports study also found a stronger association after adjustment for air pollution indicators [77].

Instead of confounding, exposure to air pollution can modify the association between noise exposure and the incidence of IHD. Unfortunately, the evaluated studies hardly investigated the possible effect modification of the association between noise and the incidence of IHD by air pollution. Only the SHEEP study [107] investigated the possible effect modification of air pollution. Figure 11.5 presents the results of this analysis. It shows the association between road traffic noise ($L_{Aeq24hr}$) and myocardial infarction for subcategories of traffic-related air pollution (NO_2 expressed in $\mu g/m^3$). The reference category consists of persons exposed to low levels of road traffic noise ($L_{Aeq24hr} < 50$ dB) and low levels of traffic-related air pollution ($NO_2 < 17 \mu g/m^3$). The figure does not show an interaction effect between the two exposures. Furthermore, it should be noted that none of the presented ORs were statistically significant; all 95% CIs contained OR = 1.

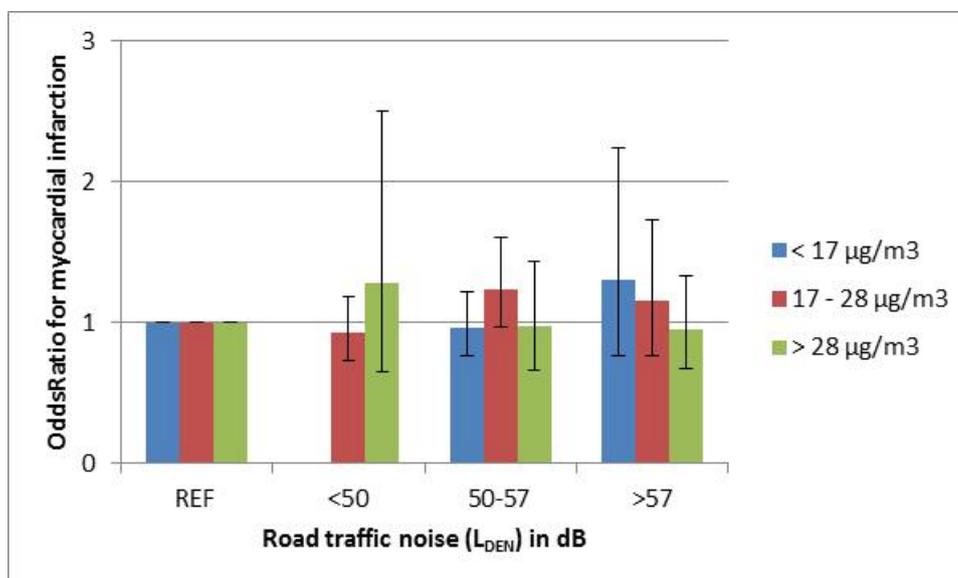


Figure 11.5: Exposure to road traffic noise and air pollution due to road traffic in relation to myocardial infarction. The Odds Ratios (OR) were adjusted for sex, catchment area, age, smoking, physical inactivity, diabetes, and occupational noise exposure. Source: [107].

We have already indicated that due to death, relocation, or loss of interest in the study, subjects can disappear from an existing cohort or leave a case-control study. This can introduce bias. Figure 5.4 demonstrated that the weakest associations between road traffic noise and the incidence of IHD were found in studies that were able to include at least 60% of their original study population in the analyses. We were not able to test whether this difference was statistically significant.

Only the BCC2 study [103, 104] was not able to adjust for smoking. Figure 5.4 demonstrates that the results of this study did not differ from the results of the other studies. We therefore consider an impact of smoking on our results not to be very likely.

Figure 5.4 shows that there is a difference between the results of the studies that were able to adjust for other noise sources and the results of the studies that were not able to adjust for other noise sources. After aggregating the results of the studies that were able to adjust for other noise sources, we found that an increase in road traffic noise was associated with a statistically significant increase in the risk of IHD. We found no association in the group of studies that were not able to adjust for other noise sources. We were not able to test whether this difference was significant.

Given the results of the subgroup analyses and the results of the SHEEP study, no definite conclusions can be drawn with regard to a confounding or interaction effect of air pollution on the association between road traffic noise and the incidence of IHD. The results of the subgroup analyses demonstrated no clear effects from study characteristics such as "whether or not the study adjusted for exposure to another noise sources", "response rate" or "the duration of exposure of the population under investigation". Although we cannot rule it out,

we think it is unlikely that residual confounding explained the results of the cohort and case-control studies on the impact of road traffic noise on the incidence of IHD.

For the ecological studies on the impact of air or road traffic noise exposure, we were not able to draw any conclusions with regard to the possible impact of residual confounding.

Consequently, we decided only to upgrade the quality of the evidence of the case-control and cohort studies on the impact of road traffic noise.

11.2.2.8 Conclusion

As a result of the above considerations, we rated the quality of the evidence from ecological studies on the impact of noise from air traffic on the incidence of IHD as "very low". We rated the quality of the evidence from the cohort and case-control studies on the impact of noise from road traffic as "high". We rated the quality of the evidence from the ecological study on the association between road traffic noise and the incidence of IHD as "very low". Because the evidence was based on only one (ecological) study, we should downgrade the quality by one level. This, however, would make no sense.

11.2.3 *Mortality due to ischaemic heart disease*

We based the evidence on the impact of air traffic noise on mortality due to IHD on two ecological studies and one cohort study. Applying the GRADE system to the two ecological studies on the association between air traffic noise exposure and mortality due to IHD, we started with a grading of "very low". We rated the starting level of the evidence derived from the cohort study on the impact of aircraft noise on mortality due to IHD as "high".

We based the evidence on the impact of road traffic noise on mortality due to IHD on one case control study and two cohort studies. Applying the GRADE system to the results of these three studies, we started our GRADE assessment with a grading of "high".

11.2.3.1 Risk of bias

Looking at the quality of the two ecological studies on the impact of aircraft noise, we had our worries concerning the exposure assessment. At least one of the evaluated studies used noise levels that were modelled for a local area [76]. Subsequently, the researchers assigned these noise levels to everybody who was a member of that group.

For both ecological studies, we worried that the way of adjustment for confounders might give rise to bias. An important omission from both ecological studies is that they were not always able to adjust for confounders at the individual level. Therefore, we decided to downgrade the quality of these studies further.

We also decided to downgrade the quality of the cohort study on the impact of aircraft noise on mortality due to IHD. We decided this for two reasons: (i) the study linked the addresses of the participants with aircraft noise maps, for which noise levels were assessed on grids of 100 x 100 m, which is quite rough; (ii) the study suffered from a lack of

information about lifestyle factors at the individual level that are important risk factors for IHD (e.g. smoking, diet, alcohol use, physical activity, increased cholesterol level).

Unfortunately, the largest of the three studies on the association between road traffic noise and mortality due to IHD, the CANADA-1 study [119] did not adjust for smoking. Furthermore, there was an issue with regard to exposure assessment: it appeared that the results were not available for road traffic noise specifically. Instead, the researchers combined the modelled noise exposure levels due to road, rail, and air traffic. Consequently, we decided to further downgrade the quality of the level of evidence for a road traffic noise effect.

11.2.3.2 Inconsistency

The results of the two ecological studies on the impact of aircraft noise were not quite consistent. The LSAS study found a positive but statistically non-significant effect of road traffic noise, while the AWACS-2 study found a negative and statistically non-significant association. The result of the heterogeneity test indicated low to moderate heterogeneity.

We found similar results for the studies on the impact of road traffic noise: all three studies found a non-statistical effect of road traffic noise. Both the SHEEP and CANADA1 study found a positive effect while the Dutch NCSDC study found a negative effect. The result of the heterogeneity test indicated low to moderate heterogeneity. We decided not to further downgrade the level of evidence of all studies on the association with mortality due to IHD.

11.2.3.3 Imprecision

We judged that it was not necessary to downgrade the quality of the evidence for imprecision. The results of the meta-analysis dealing with road traffic noise included a large number of cases (6,884 cases). The cohort study on the impact of aircraft noise was large enough, as was the case with the combined result of the two ecological studies on the effects of aircraft noise. We found the 95% CIs of the different (pooled) effect estimates as sufficiently narrow, since they did not contain values below 0.75 or above 1.25.

11.2.3.4 Publication bias

The number of available effect estimates for the association between noise from road or air traffic and mortality due to IHD was too small to test for publication bias. As a result, we did not downgrade the quality of the evidence any further.

11.2.3.5 Exposure-response gradient

The results of the SNC study (Figure 11.3) showed that the impact of aircraft noise increases and becomes statistically significant when the analyses are restricted to participants who remain for at least 15 years in the affected residence. Despite this result, we did not upgrade the level of evidence, since for the impact of both aircraft and road traffic noise on mortality due to IHD, we found only non-significant exposure-responses gradients.

11.2.3.6 Magnitude of effect

For the impact of aircraft noise on mortality due to IHD that was investigated in the two ecological studies, we found a non-significant RR of 1.04 per 10 dB across a noise range of ~40 – 65 dB (L_{DEN}). This means if case the aircraft noise exposure level increases from 40 to 65 dB, the RR = 1.10. We consider this to be a small effect.

The magnitude of effect that was found in the cohort study on the impact of aircraft noise was even somewhat smaller: the SNC study reported a non-significant RR of 1.04 per 10 dB within a somewhat narrower noise range: ~40 – 60 dB. This means that if the aircraft noise exposure level increases from 40 to 60 dB, the RR = 1.08.

We also consider the results found in the two cohort studies and case-control study that investigated the association between road traffic noise and mortality due to IHD to be small. After aggregating the results of these studies, we found a non-significant RR of 1.05 per 10 dB within a noise range of ~42 - 75 dB. This means that if the road traffic noise exposure level increases from 42 to 75 dB, the RR = 1.17

Since all exposure-response gradients were statistically non-significant, and were considered to be small, we decided not to upgrade the level of evidence.

11.2.3.7 Mitigated bias and confounding

We considered several potential sources of residual confounding. First, we attempted to find out whether the observed effects might also be the effect of exposure during the night. Unfortunately, none of the evaluated studies investigated the association with both night-time noise exposure and 24-hour exposure (L_{DEN}) separately. Consequently, we cannot say whether the observed effects are exclusively the effect of 24-hour exposure to noise.

Second, we attempted to find out whether the observed effects might not be caused by air pollution. For only three studies, were we able to show how the effect estimate changes after additional adjustment for an indicator of air pollution. Figure 11.6 shows the result. It shows that for two studies, the effect estimates decreased somewhat after adjustment for exposure to air pollution. We were not able to test whether these observed decreases were statistically significant. None of the evaluated studies investigated a possible effect modification of air pollution on the association between traffic noise exposure and mortality due to IHD. We therefore cannot draw definite conclusions with regard to either a confounding or an interaction effect of air pollution.

Third, we tested whether the observed effects can be explained by the SES of the populations that were studied. For two of the three studies that investigated the association between aircraft noise and mortality due to IHD we were able to show how the effect estimate changes after additional adjustment for an indicator of SES. Figure 11.6 shows that the results were not consistent: The LSAS study found that the effect estimate decreased a little bit after additional adjustment for SES. The SNC study researchers found that the effect estimate increased slightly after additional adjustment for SES. We were not able to test whether

these observed decreases were statistically significant. For road traffic noise, we were only able to make a comparison across the studies: We compared the results of the two studies that adjusted for SES (NCSDC and CANADA1) with the results of the SHEEP study, which did not adjust for SES. In the SHEEP study, we found a non-significant RR of 1.17 per 10 dB; after combining the results of the NCSDC and CANADA1-study, we found a non-significant RR of 1.04 per 10 dB. We were not able to test whether this difference was statistically significant. We therefore cannot draw definite conclusions with regard to a possible confounding effect of SES.

Fourth, in order to find out whether the observed association between road traffic noise and mortality due to IHD could be explained by smoking, we compared the results of the two studies that adjusted for smoking (SHEEP, NCSDC) with results of the study that did not adjust for smoking (CANADA1). Unfortunately, we were not able to test the impact of smoking on the association between aircraft noise exposure and mortality due to IHD. We therefore cannot draw definite conclusions with regard to a possible confounding effect of smoking.

In sum, we were not able to draw any conclusions with regard to the possible impact of residual confounding. We therefore decided not to upgrade the quality of the evidence.

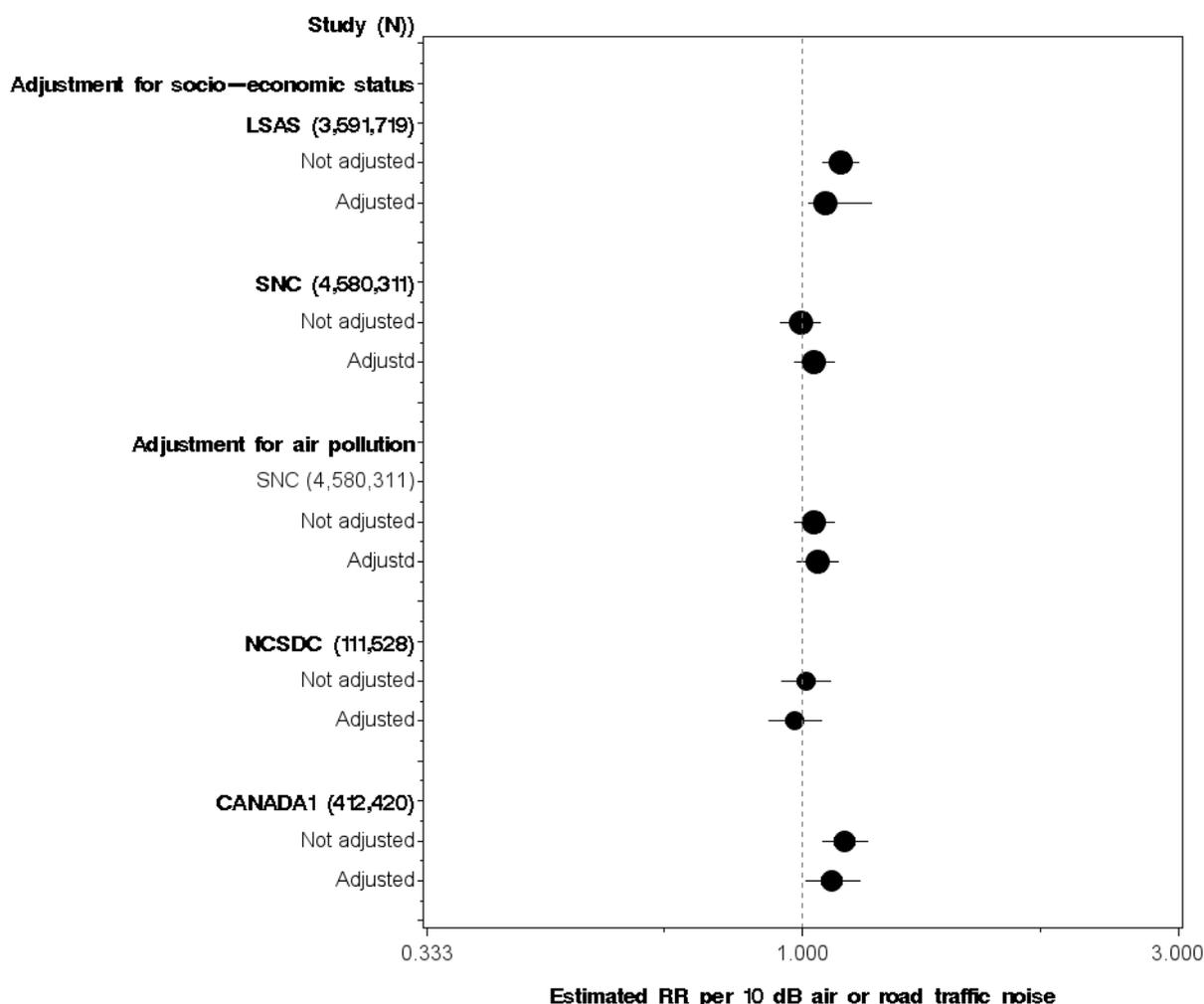


Figure 11.6 Association between air or road traffic noise and mortality due to IHD: the impact of adjustment for indicators of SES, and indicators of air pollution. The dotted vertical line corresponds to no effect of road traffic or aircraft noise exposure. The black circles correspond to the estimated RR_{10dB} and 95% CIs with or without adjustment for SES or air pollution for a certain study.

11.2.3.8 Conclusion

As a result of the above considerations, we rated the quality of the evidence from ecological studies on the association between exposure to noise from air traffic and mortality of IHD as “very low”. The quality of the evidence from the cohort study on the impact of noise from air traffic was rated as “moderate”. However, since only one study was available, we downgraded the overall quality to “low”.

The quality of the evidence from the one case-control and two cohort studies on the association between noise from road traffic and mortality due to IHD was rated as “moderate”.

11.3 Stroke

We evaluated nine studies that investigated the risk of stroke. These studies investigated the impact of exposure to air, road, and rail traffic noise. Of the evaluated studies, three had an ecological design, two

were cross-sectional, and four were cohort studies. All studies were carried out in residential setting. Table 11.3 provides a summary of the findings; more detailed information, including the score on each GRADE criterion, can be found in Appendix V.

Table 11.3: Noise exposure and the risk of stroke: summary of findings

Noise source	Outcome ^{§)}	Number of study design(s)*)	RR† per 10 dB (95%CI)	Participants (cases)	Quality of evidence‡)
Air traffic	Prev	2 CS	1.02 (0.80 – 1.28)	14,098 (151)	⊕
	Inc	2 ECO	1.05 (0.96 – 1.15)	9,619,082 (97,949)	⊕
	Mort	2 ECO	1.07 (0.98 – 1.17)	3,897,645 (12,086)	⊕
		1 CO	0.99 (0.94-1.04)	4,580,311 (25,231)	⊕⊕⊕
Road traffic	Prev	2 CS	1.00 (0.91 – 1.10)	14,098 (151)	⊕
	Inc	1 CO	1.14 (1.03 - 1.25)**	51,485 (1,881)	⊕⊕⊕
	Mort	3 CO	0.87 (0.71 – 1.06)	581,517 (2,634)	⊕⊕⊕
Rail traffic	Prev	1 CS	1.07 (0.92 – 1.25)	9,365 (89)	⊕

§) Outcome: Prev = prevalence of stroke, Inc = incidence of stroke, Mort = mortality due to stroke; *) ECO = ecological study, CS = cross-sectional study, CO = cohort study; †) : RR = Relative Risk per 10 decibel change in noise level, 95%CI = 95% Confidence Interval. The noise levels are expressed in L_{DEN}; ‡) GRADE Working Group Grades of Evidence: High quality (⊕⊕⊕⊕): Further research is very unlikely to change our confidence in the estimate of effect, Moderate Quality (⊕⊕⊕): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, Low Quality (⊕⊕): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, Very low quality (⊕): We are very uncertain about the estimate.

11.3.1 Prevalence of stroke

We based the evidence of an association between noise exposure and the *prevalence* of stroke on two cross-sectional studies and we started our GRADE assessment with a grading of “low”. Both studies (HYENA and AWACS-1) [199, 227, 228] investigated the impact of both road and air traffic noise exposure. The AWACS-1 study also investigated the impact of rail traffic noise exposure.

11.3.1.1 Risk of bias

We further downgraded the quality due to serious limitations in the study design: The response rates of both studies were below 60%, and the HYENA study was not able to adjust for smoking.

11.3.1.2 Inconsistency

Although the tests for heterogeneity did not give any indication of heterogeneity, we judged the findings of the studies as rather inconsistent. The HYENA study reported positive associations for both air and road traffic noise. The AWACS-1 study found negative associations for both air and road traffic noise. However, none of the observed associations was statistically significant.

The AWACS-1 study also investigated the impact of rail traffic noise and reported a non-significant positive association between rail traffic noise and the prevalence of stroke.

For none of the noise sources, did we downgrade the level of evidence further.

11.3.1.3 Imprecision

The results of the meta-analyses were based on only a small number of cases (151). The confidence intervals did not contain values below 0.75; only the confidence interval for the association with aircraft noise contained values above 1.25. Therefore, we rated the results as rather imprecise, and decided to downgrade the quality of the evidence further for all noise sources.

11.3.1.4 Publication bias

Since the number of available effect estimates was too small, we were not able to test for publication bias or small-study bias. As a result, we did not downgrade the quality of the evidence further.

11.3.1.5 Exposure-response gradient

The findings of the studies did not provide any clear evidence of an association between noise exposure from different noise sources and the prevalence of stroke. Only for the effects of aircraft and rail traffic noise were we able to assess an exposure-response gradient. However, none of these gradients was statistically significant. As a result, we did not upgrade the quality of the evidence.

11.3.1.6 Magnitude of effect

We did not upgrade the quality of the evidence for magnitude of effect, since we considered the effect sizes to be rather small. As already indicated, we were able to derive an exposure-response gradient only for the effects of aircraft and rail traffic noise. In relation to aircraft noise exposure, we assessed a non-significant RR of 1.02 per 10 dB across a noise range of 30 - 75 dB (L_{DEN}). This means that in case the aircraft noise exposure level increases from 30 to 75 dB, the RR = 1.09. We consider this to be a small effect. For rail traffic noise we found a non-significant RR of 1.07 across a noise range of 30 - 65 dB (L_{DEN}). This means that if the rail traffic noise exposure level increases from 30 to 65 dB, the RR = 1.27. We consider this to be a small effect.

11.3.1.7 Mitigated bias and confounding

We considered several possible sources of residual confounding. First, we attempted to find out whether the observed effects might also be the effect of exposure during the night. With regard to the effects of aircraft noise, the HYENA study presented results for both L_{day} and L_{night} . Although the effects of night-time noise exposure seemed to be stronger, both daytime and night-time aircraft noise exposure were not statistically significantly associated with the prevalence of stroke. After adjustment for sex, age, BMI, education and ethnicity, the HYENA study reported an RR of 1.08 (95%CI: 0.82 – 1.41) per 10 dB in relation to daytime noise exposure; in relation to night-time noise exposure, the researchers reported an RR of 1.18 (95%CI: 0.89 – 1.56) per 10 dB. The HYENA study did not present results for night-time noise exposure to road traffic noise.

The AWACS-1 study was able to investigate the impact of other aircraft noise indicators in addition to the L_{DEN} . It appeared that none of the other noise indicators gave a better prediction than the L_{DEN} . Unfortunately, the AWACS-1 study researchers were not able to

investigate the impact of night-time noise exposure for any of the noise sources specifically. Based on the findings of the HYENA and AWACS-1 studies, we cannot say whether the observed effects are exclusively the effect of 24-hour exposure to noise.

Of course, we also attempted to find out in what way the results were affected by air pollution, adjustment for factors such as smoking and SES, and selective (non-)response. However, from the available data we were not able to draw any conclusions about the possible role of these factors. We therefore decided not to upgrade the level of evidence for any noise source.

11.3.1.8 Conclusions

Overall, we rated the quality of the evidence of an impact of noise from air, road, and rail traffic on the prevalence of stroke as “very low”.

11.3.2 *Incidence of stroke*

We based the evidence of an association between aircraft noise exposure and the *incidence* of stroke on two ecological studies only. For the association between road traffic noise exposure and the incidence of stroke, we based our evidence on the results of one cohort study. We found no studies on the impact of rail traffic noise.

Therefore, we started our GRADE assessment for aircraft noise with a grading of “very low”. For road traffic noise, we started our assessment with a grading of ‘high”.

11.3.2.1 Risk of bias

We downgraded the quality of the evidence for aircraft noise further, because both available ecological studies were not able to apply individual exposure estimates and were not able to adjust for smoking. We did not downgrade the quality of the evidence for road traffic noise, since we judged that the available evidence was of good quality; i.e. there was no risk of bias.

11.3.2.2 Inconsistency

The results of the two ecological studies were rather inconsistent: the LSAS study found a positive and statistically significant association with aircraft noise, while the USAirports study reported a positive but non-significant association with aircraft noise. This was confirmed by the results of the test for heterogeneity. The residual proportion of the between-study variance due to heterogeneity was $I^2 = 82.7\%$. For aircraft noise, we decided to downgrade the level of evidence further.

Since we based our evidence of an association between road traffic noise exposure and the incidence of stroke on only one study, the criterion of “inconsistency” was not applicable. We therefore did not change the level of evidence.

11.3.2.3 Imprecision

We regarded the result of the aggregation of the results of the two studies reporting on the effects of aircraft noise as precise: the number of cases was large enough (greater than 200), and the 95%CI did not contain values below 0.75 or above 1.25. For the same reasons, we also

regarded the results of the cohort study reporting on the effects of road traffic noise as precise. We therefore did not downgrade the level of evidence for this criterion.

11.3.2.4 Publication bias

Because the number of available effect estimates was too small, we were not able to test for publication bias or small-study bias. As a result, we did not downgrade the level of the quality of the evidence further.

11.3.2.5 Exposure-response gradient

For both aircraft noise and road traffic noise, we found a positive association with the incidence of stroke. This association was statistically significant for road traffic only: we found an RR of 1.14 (95%CI: 1.03 – 1.25) per 10 dB. In cases exposed to road traffic noise for at least 10 years, we observed an RR of 1.11 (95%CI: 1.04 – 1.19) per 10 dB. We decided to upgrade the quality of evidence for road traffic noise, but not for aircraft noise.

11.3.2.6 Magnitude of effect

As already indicated, we observed a significant effect size only for the association between road traffic noise exposure and the incidence of stroke. We observed a significant effect size of 1.14 per 10 dB across a road traffic noise range of approximately 50 – 70 dB. This means that if the road traffic noise level increases from 50 to 70 dB, the RR = 1.30. We do not regard this as a large effect; consequently, we decided not to upgrade the quality of the evidence for road traffic noise.

11.3.2.7 Mitigated bias and confounding

We considered several potential sources of residual confounding. First, we attempted to find out whether the observed effects were caused by air pollution. For only two studies, were we able to show how the effect estimate changes after adjustment for an indicator of air pollution. Figure 11.7 shows the result. It shows that for the USAirports study (investigating the effects of aircraft noise), the effect estimate increased slightly after adjustment for exposure to air pollution. The figure also shows that for the DCH study (investigating the effects of road traffic noise), the effect estimate decreased slightly after adjustment for air pollution. It is unlikely that the difference was statistically significant. None of the evaluated studies investigated possible effect modification of air pollution on the association between traffic noise exposure and mortality due to stroke. We therefore cannot draw definite conclusions with regard to a possible confounding nor interaction effect of air pollution.

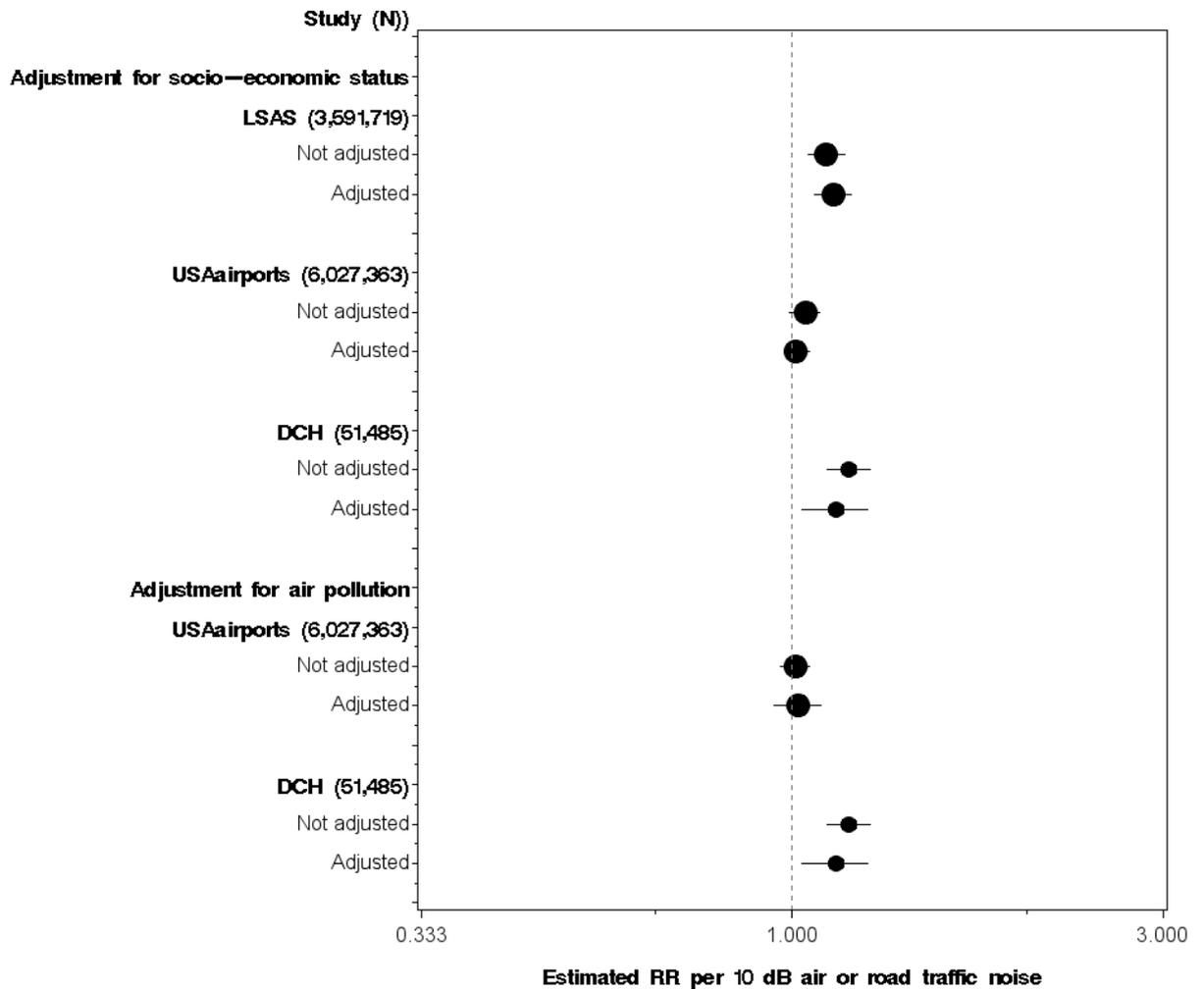


Figure 11.7: Subgroup analyses for the association between air or road traffic noise and the incidence of stroke. The dotted vertical line corresponds to no effect of road traffic or aircraft noise exposure. The black circles correspond to the estimated RR_{10dB} and 95% CIs with or without adjustment for SES or air pollution for a certain study.

Second, we tested whether the observed effects could be explained by the SES of the populations that were studied. For three studies, we were able to show how the effect estimate changed after adjustment for an indicator of SES. Figure 11.7 shows, however, that the results were not consistent: The LSAS study (investigating the effects of aircraft noise) found that the effect estimate increased slightly after adjustment for SES. The USAairports and the DCH study researchers found that the effect estimate decreased slightly after adjustment for SES. It is unlikely that the difference was statistically significant. From the available data, we were not able to draw any conclusions about the possible role of SES.

We also attempted to find out in what way the results were affected by adjustment for factors such as smoking, and selective (non-)response as well as whether the observed effects might also be the effect of exposure during the night. However, from the available data we were not able to draw any conclusions about the possible role of these

factors. We therefore decided not to upgrade the level of evidence for any noise sources.

11.3.2.8 Conclusions

Overall, we rated the quality of the evidence of an impact of noise from air traffic on the incidence of stroke as “very low”; the overall quality of the evidence of an impact of road traffic noise was rated as “high”. However, since only one study was available, we downgraded the quality of the evidence of an impact of noise from road traffic on the incidence of stroke to “moderate”.

11.3.3 *Mortality due to stroke*

We based the evidence of an association between air traffic noise and mortality due to stroke on the results of two ecological studies and one cohort study. For the ecological studies, we started our GRADE assessment with a grading of “very low”; for the cohort study, we started with a grading of “high”.

We based the evidence of an association between road traffic noise and mortality due to stroke on the results of three cohort studies. Consequently, we started our GRADE assessment with a grading of “high”.

11.3.3.1 Risk of bias

Neither ecological studies was able to adjust for important confounders at individual level. In addition, the assessment of exposure was a problem in these studies. For example, the LSAS study was not able to apply individual exposure estimates. Therefore, we further downgraded the level of evidence from these two studies.

Unfortunately, we were not sure whether the cohort study on the association between aircraft noise exposure and mortality due to stroke had applied individual exposure estimates. Furthermore, this study did not adjust for smoking. Therefore, we downgraded the level of evidence from this study.

For the studies on the impact of road traffic noise, we judged that the risk of bias was limited (the CANADA-1 study did not adjust for smoking). We did not downgrade the level of evidence from these studies.

11.3.3.2 Inconsistency

The results of the two ecological studies were quite consistent: both found a positive association between aircraft noise and mortality due to stroke. This was confirmed by the result of the test for heterogeneity: $I^2_{\text{residual}} = 28.5\%$.

The results of the cohort studies on the impact of road traffic noise were inconsistent: two of the three studies found a statistically significant negative association (see Figure 6.2). Inconsistency was also demonstrated by the outcome of the heterogeneity test ($I^2_{\text{residual}} = 78.0\%$). Therefore, we downgraded the level of evidence from the three cohort studies on the impact of road traffic noise.

11.3.3.3 Imprecision

We considered the evidence of an impact of aircraft noise to be precise: both the number of participants and the number of cases were large, and the 95% CIs did not contain values below 0.75 or above 1.25.

We considered the total number of participants and the total number of cases in the three studies on the impact of road traffic noise to be large. We regarded the 95% CI as rather broad, since it contained values below 0.71. On the other hand, it did not contain values above 1.25. Consequently, we decided not to downgrade the level of evidence from the three cohort studies on the impact of road traffic noise.

11.3.3.4 Publication bias

Because the number of available effect estimates was too small, we were not able to test for publication bias or small-study bias. As a result, we did not downgrade the quality of the evidence.

11.3.3.5 Exposure-response gradient

We did not upgrade the level of the quality of evidence, since only the ecological studies found a positive association between aircraft noise and mortality due to stroke. This association (RR = 1.07 per 10 dB within a noise range of ~40 – 65 dB (L_{DEN})) was, however, not statistically significant.

Figure 11.8 shows that for the SNC study, the effect estimate hardly changed after restricting the analyses to persons that had spent at least 15 years in the same residence. This is supportive for the existence of an exposure-response gradient.

After combining the results of the three cohort studies on the impact of road traffic noise, we found a statistically non-significant RR of 0.87 per 10 dB.

11.3.3.6 Magnitude of effect

As we have already indicated, only the ecological studies found a positive association between aircraft noise and mortality due to stroke. This association (RR = 1.07 per 10 dB within a noise range of ~40 – 65 dB (L_{DEN})) was however, not statistically significant and can be regarded as small. Therefore, we did not upgrade the level of the quality of evidence for this effect.

11.3.3.7 Mitigated bias and confounding

We considered the following potential sources of residual confounding: First, we attempted to find out whether the observed effects were caused by air pollution. For five studies, we were able to show how the effect estimate changes after adjustment for an indicator of air pollution. Figure 11.8 shows the results. It shows that for two studies (both investigating the impact of road traffic noise), the effect estimates decreased slightly after adjustment for exposure to air pollution. We were not able to test whether these observed decreases were statistically significant. None of the evaluated studies investigated possible effect modification of air pollution on the association between traffic noise exposure and mortality due to stroke. We cannot draw

definite conclusions with regard to a possible confounding or interaction effect of air pollution.

For two studies (both investigating the impact of aircraft noise) we were able to show how the effect estimate changed after adjustment for an indicator of SES. Figure 11.8 shows that the results were not consistent: The LSAS study (investigating the effects of aircraft noise) found that the effect estimate decreased slightly after adjustment for SES. The SNC study researchers found that the effect estimate increased slightly after adjustment for SES. It is unlikely that the differences in estimates were statistically significant. From the available data, we were not able to draw any conclusions about the possible role of SES.

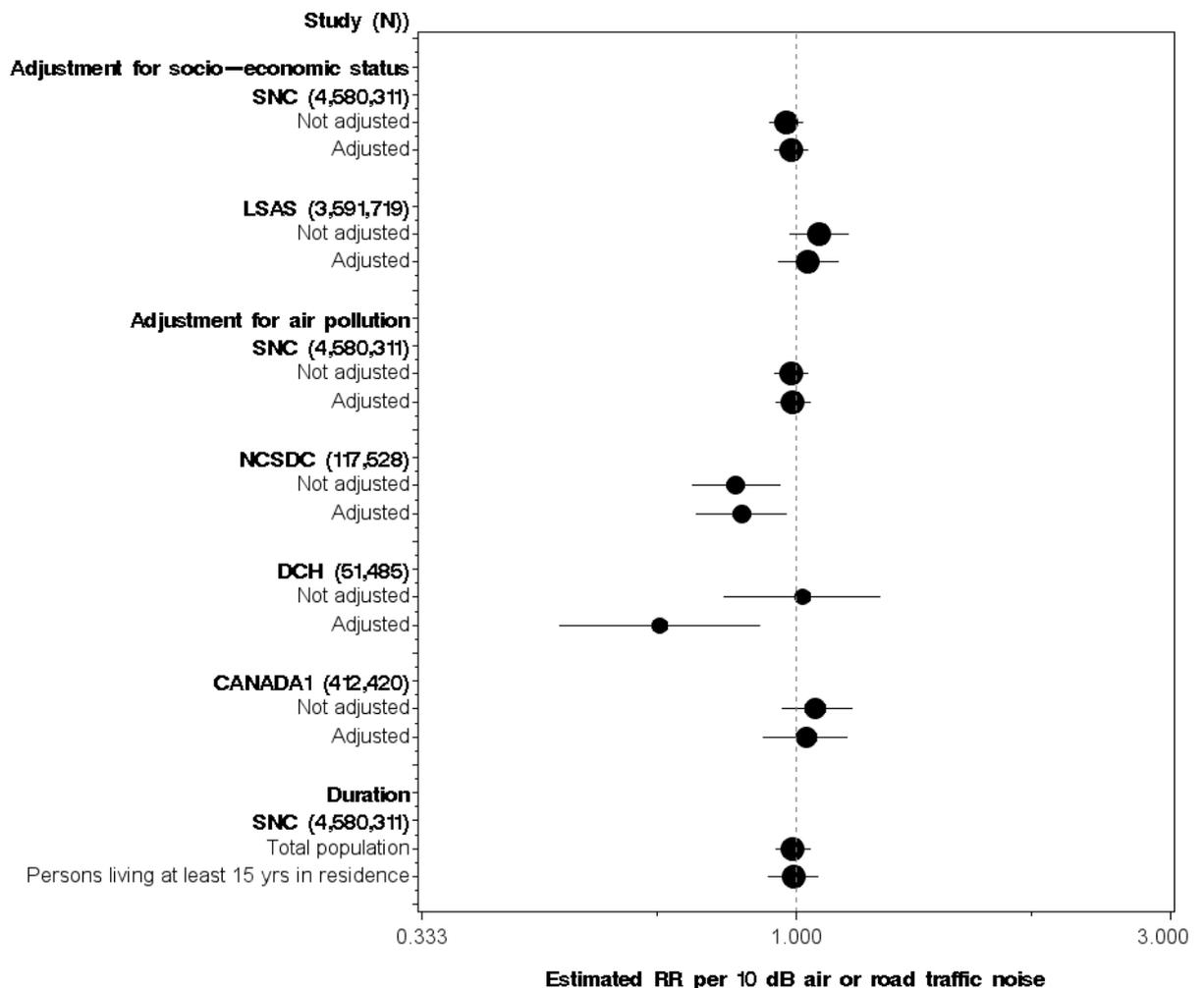


Figure 11.8: Subgroup analyses for the association between air or road traffic noise and mortality due to stroke. The dotted vertical line corresponds to no effect of road traffic or aircraft noise exposure. The black circles correspond to the estimated RR_{10dB} and 95% CIs with or without adjustment for SES or air pollution for a certain study.

We also attempted to find out in what way the results might be affected by adjustment for factors such as smoking, and selective (non-)response, and whether the observed effects might be the effect of exposure during the night. However, from the available data we were

not able to draw any conclusions about the possible role of these factors. We therefore decided not to further upgrade the level of evidence for any noise sources.

11.3.3.8 Conclusions

We rated the overall quality of the evidence of an association between aircraft noise and mortality due to stroke, as derived from two ecological studies, as “very low”. The evidence derived from the available cohort study was rated as “high”. However, since the evidence was based on only one study, the overall level of the quality of the evidence was downgraded to “moderate”.

We rated the quality of the evidence of an association between road traffic noise and mortality due to stroke as “moderate”.

11.4 Diabetes

We have evaluated seven studies that investigated the risk of diabetes. These studies investigated the possible impact of noise from air, road, and rail traffic and wind turbine noise. Of the evaluated studies, four studies were cross-sectional, one was a case-control study and two were cohort studies. Table 11.4 provides a summary of the findings; more detailed information, including the scores on each GRADE criterion, can be found in Appendix VI.

Table 11.4: Noise exposure and the risk of diabetes: summary of findings

Noise source	Outcome ^{§)}	Number of study design(s) *	RR† per 10 dB (95%CI)	Participants (cases)	Quality of evidence‡)
Air traffic	Prev	1 CS	1.01 (0.78 – 1.31)	9,365 (89)	⊕
	Inc	1 CO	0.99 (0.47 – 2.09)	5,156 (1,346)	⊕⊕
Road traffic	Prev	2 CS	#	11,460 (242)	⊕
	Inc	1 CO	1.08 (1.02 – 1.14) **	57,053 (2,752)	⊕⊕⊕
Rail traffic	Prev	1 CS	0.21 (0.05 – 0.82)	9,365 (89)	⊕
	Inc	1 CO	0.97 (0.89 – 1.05)	57,053 (2,752)	⊕⊕⊕
Wind turbine	Prev	3 CS	***	1,830 (NR)	⊕

§) Outcome: Prev = prevalence of diabetes, Inc = incidence of diabetes; *) CS = cross-sectional study, CO = cohort study; †) RR = Relative risk per 10 decibel change in noise level, 95%CI = 95% Confidence Interval. For air, road –, and rail traffic, noise levels are expressed in L_{DEN}. For wind turbines, noise levels are expressed in Sound Pressure Level (SPL); ‡) GRADE Working Group Grades of Evidence: High quality (⊕⊕⊕): Further research is very unlikely to change our confidence in the estimate of effect, Moderate Quality (⊕⊕⊕): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, Low Quality (⊕⊕): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, Very low quality (⊕): We are very uncertain about the #) The data from one cross-sectional study were not included in the table since they were based on a secondary analysis with important information lacking; ***) We decided not to aggregate the results of the three studies on the impact of wind turbine noise, since too many parameters were unknown/unclear; NR = Not Reported.

11.4.1 Prevalence of diabetes

Five studies investigated the association between air, road, and rail traffic noise, and wind turbine noise, and the *prevalence* of diabetes: four cross-sectional studies and one case-control study, presenting the

results of a cross-sectional analysis. Consequently, we started our GRADE assessment with a grading of "low".

11.4.1.1 Risk of bias

Most of the evaluated studies had a response rate lower than 60%. Furthermore, all studies ascertained diabetes by means of questionnaires. These aspects constituted serious limitations to the studies, and consequently we decided to downgrade quality of the evidence further.

11.4.1.2 Inconsistency

Only one of the five studies investigated the impact of air and rail traffic noise.

The two studies that investigated road traffic noise both found a harmful effect of road traffic noise, but the effect was statistically significant only in the SHEEP study. Whether the effect sizes differed between the studies, was difficult to say, because the results of the SHEEP study could not be expressed in an RR per 10 dB. Consequently, we decided not to further downgrade the level of evidence of the studies on the effects of road traffic.

The results of the three studies on the impact of wind turbine noise were inconsistent: two of the three studies did not find a statistically significant association. Consequently, we decided to further downgrade the evidence from studies reporting on the impact of wind turbine noise.

11.4.1.3 Imprecision

We considered the results of the AWACS-1 study, investigating the impact of air and rail traffic noise, to be imprecise. The results of this study were based on only 89 cases, which is a small number. Furthermore, the confidence intervals for the different noise sources contained values below 0.75 and/or above 1.25. Consequently, we decided to further downgrade the quality for the impact of air and rail traffic noise.

For the studies on the impact of road traffic noise, we decided not to combine the results of the two available studies. The total number of cases in both studies together, is somewhat greater than 200, but, looking at the separate results of both studies, we see that the confidence intervals included values below 0.75 and above 1.25. Therefore, we decided to further downgrade the quality of the evidence for the studies on the impact of road traffic noise.

For the studies on the impact of wind turbine noise, we were also not able to carry out a meta-analysis because too many parameters (e.g. the number of cases) were unclear. Given the number of cases in the Dutch study (29 cases, 725 participants) [34, 175, 176], it is the question whether the total number of cases for all three studies together will be larger than 200. Looking at Figure 7.1, presenting the separate results of the different studies, we see that the confidence intervals included values below 0.75 and 1.25. Therefore, we decided to further downgrade the quality of the evidence of the studies on the impact of wind turbine noise.

- 11.4.1.4 **Publication bias**
The number of available effect estimates was too small to test for publication bias or small-study bias. As a result, we did not further downgrade the quality of the evidence.
- 11.4.1.5 **Exposure-response gradient**
For the association between air traffic noise and the prevalence of diabetes, we found a non-significant effect size of 1.01 per 10 dB across a noise range of 30 - 65 dB (L_{DEN}). For the association with rail traffic noise, we found a significant effect size of 0.21 per 10 dB across a noise range of 30 - 65 dB (L_{DEN}). The latter is an unexpected finding. We were not able to assess the role of duration. As a result, we did not upgrade the quality of the evidence.
- 11.4.1.6 **Magnitude of effect**
We did not upgrade the level of the quality of evidence for this criterion, since no increased prevalence of diabetes was observed in relation noise exposure.
- 11.4.1.7 **Mitigated bias and confounding**
We attempted to find out in what way the results were affected by adjustment for factors such as smoking, air pollution, and SES, and by selective (non-)response. We also attempted to find out whether the observed effects might be the result of exposure during the night. However, from the available data we were not able to draw any conclusions about the possible role of these factors. We therefore decided not to upgrade the level of evidence for any noise sources.
- 11.4.1.8 **Conclusion**
Overall, we rated the quality of evidence of an impact of noise from air, road, and rail traffic noise, and noise from wind turbines on the prevalence of diabetes to be "very low".
- 11.4.2 *Incidence of diabetes*
The association between exposure to air traffic noise and the incidence of diabetes was investigated in only one cohort study: the SDPP study [141]. For the impact of road traffic and rail traffic noise only the DCH study [142] was available. Therefore, we started our GRADE assessment with a grading of "high".
- 11.4.2.1 **Risk of bias**
As we have already indicated in the section describing the results for the association between aircraft noise and the incidence of hypertension, the number lost to follow-up in the SDPP study was probably higher than 20%. Furthermore, we could ascertain no serious limitations to this study. We also regarded the DCH study as of high quality. For both noise sources, therefore, we did not downgrade the level of evidence.
- 11.4.2.2 **Inconsistency**
Since for all noise sources only one study was available, we were not able to score this criterion. Consequently, we did not downgrade the level of evidence for this criterion.

11.4.2.3 Imprecision

The number of cases included in both studies was large (>200). Because the confidence interval of the results for air traffic was rather broad and contained values below 0.75 and above 1.25, we decided to downgrade the level of evidence of an association between aircraft noise and the incidence of diabetes further.

We considered the confidence intervals of the findings for road and rail traffic noise to be narrow, as they did not contain values below 0.75 or above 1.25. Therefore, we did not downgrade the level of evidence of a road and rail traffic noise effect.

11.4.2.4 Publication bias

The number of available effect estimates was too small to test for publication bias or small-study bias. As a result, we did not downgrade the quality of the evidence.

11.4.2.5 Exposure-response gradient

Only for road traffic noise did we find a harmful effect of noise: The DCH study researchers reported a statistically significant RR of 1.08 per 10 dB increase. They also showed that the associations were slightly stronger with long-term exposure (5 years) than with short-term exposure (1 year). We did not find any effects of air and rail traffic noise. We therefore decided to upgrade the level of evidence of an association between road traffic noise and the incidence of diabetes only.

11.4.2.6 Magnitude of effect

We considered the significant effect size found in the DCH study for the association between road traffic noise and the incidence of diabetes to be small: the DCH study found an RR of 1.08 per 10 dB across a noise range of ~ 50 - 70 dB. This means that if the road traffic noise level increases from 50 to 70 dB, the RR = 1.17.

11.4.2.7 Mitigated bias and confounding

We attempted to find out in what way the results were affected by adjustment for factors such as smoking, air pollution, and SES, and by selective (non-)response. We also attempted to find out whether the observed effects might be the result of exposure during the night. However, from the available data we were not able to draw any conclusions about the possible role of these factors. We therefore decided not to upgrade the level of evidence for any noise sources.

11.4.2.8 Conclusion

We rated the overall quality of the evidence of an association between aircraft noise and the incidence of diabetes as "moderate". However, since we based this evidence on only one study, we rated the overall level of the quality of the evidence as "low".

We rated the quality of the evidence of an association between road and rail traffic noise and the incidence of diabetes as "high". As with aircraft noise, the evidence was based on the results of only one study. Consequently, we downgraded the overall level of the quality of the evidence to "moderate".

11.5 Obesity

We evaluated four studies that investigated the impact of noise on change in BMI and change in waist circumference: one cohort study and three cross-sectional studies. Table 11.5 provides a summary of the findings; more detailed information, including the scores on each GRADE criterion, can be found in Appendix VII.

Table 11.5: Noise exposure and the risk of obesity: summary of findings

Noise source	Outcome	Number of study design(s) *	Change per 10 dB (95%CI) †	Participants	Quality of evidence ‡
Air traffic	Change in BMI (kg/m ²)	1 CO	0.14 (-0.18 – 0.45)	5,156	⊕⊕
	Change in waist circumference (cm)	1 CO	3.46 (2.13 – 4.77)	5,156	⊕⊕⊕
Road traffic	Change in BMI (kg/m ²)	3 CS	0.03 (-0.10 – 0.15)	71,431	⊕
	Change in waist circumference (cm)	3 CS	0.17 (-0.06 – 0.40)	71,431	⊕
Rail traffic	Change in BMI (kg/m ²)	2 CS	**	57,531	⊕
	Change in waist circumference (cm)	2 CS	**	57,531	⊕⊕

*) CS = cross-sectional study, CO = cohort study; † ⊕ 95%CI = 95% Confidence Interval. Noise levels are expressed in L_{DEN}; ‡) GRADE Working Group Grades of Evidence: High quality (⊕⊕⊕⊕): Further research is very unlikely to change our confidence in the estimate of effect, Moderate Quality (⊕⊕⊕): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, Low Quality (⊕⊕): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, Very low quality (⊕): We are very uncertain about the estimate. **) We decided not to aggregate the results of the studies on the impact of rail traffic noise, since not all parameters were available to assess a change in BMI or waist circumference per 10 dB; dB = decibel, BMI = Body Mass Index.

11.5.1 Change in BMI

In total, we evaluated three studies that investigated the harmful impact of air, road, and rail traffic noise on BMI. For aircraft noise, we used the results of the SDPP study. Consequently, we started our GRADE rating for aircraft noise with a grading of "high".

For the impact of road traffic noise, we combined cross-sectional results of both the SDPP and DCH cohorts with the result of the cross-sectional HUBRO study. As a consequence, we started our GRADE rating for road traffic noise with a grading of "low".

For the impact of rail traffic noise, we also started with a grading of "low", since the evidence consisted of the cross-sectional results of the DCH study and the HUBRO study.

11.5.1.1 Risk of bias

We did not downgrade the quality of the evidence due to risk of bias, as we judged the SDPP cohort as having a low risk of bias although it had an attrition rate that probably exceeded 20%. In spite of the low participation rates (36% and 33%), we considered both the HUBRO -and DCH studies to have a low risk of bias.

11.5.1.2 Inconsistency

For aircraft noise, we had evidence from only one study. Consequently, we were not able to score this criterion and we did not downgrade the level of evidence.

We regarded the results of the studies on the impact of road traffic noise as rather inconsistent: only one study found a positive and significant effect. The test for heterogeneity ($I^2_{\text{residual}} = 84.4\%$) indicated strong heterogeneity. We regarded the results of the two studies on the impact of rail traffic noise as inconsistent: We found a positive and (borderline) statistically significant impact of rail traffic noise in the DCH study; the HUBRO study did not find an effect of rail traffic noise. Consequently, we downgraded the level of evidence from the studies dealing with road and rail traffic noise.

11.5.1.3 Imprecision

For both aircraft and road traffic noise, we considered the results to be rather imprecise: The estimated standard deviations of the summary estimate were larger than the estimated summary estimate (or the mean difference in BMI). As a result, we decided not to downgrade the quality of the evidence for both noise sources.

We did not downgrade the quality of the evidence of a rail traffic noise effect, since we were not able to derive a summary estimate.

11.5.1.4 Publication bias

The number of available effect estimates was too small to test for publication bias or small-study bias. As a result, we did not downgrade the quality of the evidence.

11.5.1.5 Exposure-response gradient

For both road and air traffic noise, we found a positive but statistically non-significant association between noise exposure and change in BMI. For rail traffic noise, we were not able to derive a summary estimate. As a result, we did not upgrade the quality of the evidence.

11.5.1.6 Magnitude of effect

The changes in BMI that we observed probably fall within the normal homeostasis. At individual level the reported effects are clinically not significant: In 2006, Stevens et al. [529] recommended, on the basis of a thorough evaluation of the literature, that a reduction of 5% in BMI may be considered a clinically relevant change for individual subjects in the short term, and a reduction of 3% may be considered clinically relevant for individual subjects in the long term. The average BMI for men and women participating in the SDPP study was 25.7 and 25.1 kg/m², respectively [530]. We found a non-significant effect size of 0.14 kg/m² per 10 dB within a noise range of ~48 - 65 dB. This means that if the air traffic noise level increases from 48 to 65 dB, the BMI will increase by 0.24 kg/m². Given the average BMI values for men and women, this means a reduction of 0.9 – 1.0% in BMI, which, according to the recommendations of Stevens et al. [529], is not clinically significant. We can follow a similar reasoning for the association between road traffic noise and BMI.

However, given a certain population distribution of BMI, even a small shift due to noise exposure may yield a substantial increase in the prevalence of other diseases. An example of the impact of a small BMI change on the chronic disease burden (in Ireland) is given by Kearns et al. [531]. In their study, they found that a 1 kg/m² decrease in BMI resulted in 26 - 28 fewer cases of chronic diseases per 1,000 persons. However, since we were not able to find any statistically significant effects of noise exposure on BMI, we did not upgrade the quality of the evidence for either an aircraft or a road traffic noise effect.

11.5.1.7 Mitigated bias and confounding

According to the SDPP study researchers, the results of their study on aircraft noise could have been affected by residual confounding due to a lack of data on exposure to noise from other noise sources. To overcome this, the researchers [141] adjusted for annoyance due to other noise sources. However, residual confounding cannot be ruled out.

Furthermore, the cohort oversampled persons with a family history of diabetes. It appeared that the association between aircraft noise and BMI was stronger among those without a family history of diabetes, although the effect modification was not statistically significant. According to the researchers, the results may also have been affected by regional differences in SES.

The results of the DCH study changed after adjustment for SES. According to the researchers, residual confounding cannot be ruled out [192]. In the other two studies on the impact of road traffic noise, the results were not/hardly affected after additional adjustment for SES. In all three studies, no effects of air pollution were found.

We attempted to find out in what way the results were affected by adjustment for factors such as smoking, and by selective (non-)response. We also attempted to find out whether the observed effects might be the result of exposure during the night. However, from the available data we were not able to draw any conclusions about the possible role of these factors, and we decided not to upgrade the level of evidence for any noise sources.

11.5.1.8 Conclusion

We rated the overall quality of the evidence of an association between aircraft noise and BMI as "moderate". However, since we based our evidence on one study only, the overall level of the quality of the evidence was downgraded to "low".

We rated the quality of the evidence of an associations between road or rail traffic noise and BMI as "very low".

11.5.2 *Change in waist circumference*

We evaluated three studies that investigated the harmful impact of air, road, and rail traffic noise on waist circumference. For aircraft noise, we used the results of the SDPP study. Therefore, we started our GRADE rating for aircraft noise with a grading of "high".

For the impact of road traffic noise, we combined the cross-sectional results of both the SDPP and DCH studies with the result of the cross-

sectional HUBRO study. As a consequence, we started our GRADE rating for road traffic noise with a grading of "low".

For the impact of rail traffic noise, we also started our GRADE rating with a grading of "low", since the evidence consisted of the cross-sectional results of the DCH and the HUBRO studies.

11.5.2.1 Risk of bias

We did not downgrade the quality of the evidence due to risk of bias: We judged the SDPP cohort as having a low risk of bias, although it had an attrition rate that probably exceeded 20%. In spite of the low participation rates, we considered both the HUBRO and DCH studies to have a low risk of bias.

11.5.2.2 Inconsistency

This criterion was not relevant for aircraft noise, since we could use the results of only one study.

We regarded the results of the studies on the impact of road traffic noise as inconsistent: Figure 8.1 shows that only the DCH study found a positive and significant effect. The result of the test for heterogeneity ($I^2_{\text{residual}} = 69.0\%$) indicated moderate heterogeneity. Consequently, we downgraded the level of evidence from studies on road traffic noise.

We considered the results of the two studies on the impact of rail traffic noise to be consistent: Both studies found statistically significant associations between exposure to rail traffic noise and change in waist circumference. We therefore did not downgrade the level of evidence.

11.5.2.3 Imprecision

We considered the results of the studies on air or road traffic noise to be precise enough, since the estimated standard deviations of the summary estimate were smaller than the mean difference in waist circumference. As a result, we decided not to downgrade the quality of the evidence for either noise source.

Since we were not able to derive a summary estimate, we did not downgrade the quality of the evidence of a rail traffic noise effect.

11.5.2.4 Publication bias

The number of available effect estimates was too small to test for publication bias or small-study bias. As a result, we did not downgrade the quality of the evidence.

11.5.2.5 Exposure-response gradient

For both aircraft and road traffic noise exposure, we found a positive association with waist circumference. Only in relation to aircraft noise exposure, however, was this association statistically significant. An increase in the aircraft noise level of 10 dB (L_{DEN}) is associated with an increase of 3.46 cm in waist circumference. Consequently, we decided to upgrade the level of evidence only of an association between aircraft noise and waist circumference.

11.5.2.6 Magnitude of effect

For the association between air traffic noise and change in waist circumference, we found a significant effect size of 3.46 cm per 10 dB across a noise range of 48 - 65 dB (L_{DEN}). This means that if the air traffic noise level increases from 48 to 65 dB, waist circumference increases by more than 5.8 cm. Even after taking into account possible measurement variability (0.7 – 12 cm), we consider this to be a large effect: As long ago as 1998, the National Institutes of Health stated that a sustained reduction of 4 cm may be clinically relevant ([532]in: [533]). Later, Stevens recommended that, as with BMI, a reduction in waist circumference of >5% may be considered a clinically relevant change for individual subjects in the short term and a maintained waist circumference of >3% from initial waist circumference may be considered clinically relevant for individual subjects in the long term [529]. For a woman, a change of 2.4 – 4 cm is considered to be clinically relevant.

For the association between road traffic noise and change in waist circumference, we found a non-significant effect size of 0.17 cm per 10 dB across a noise range of ~40 - 65 dB (L_{DEN}). This means that if the road traffic noise level increases from 40 to 65 dB, waist circumference will increase by 0.43 cm. We consider this to be a small effect.

11.5.2.7 Mitigated bias and confounding

For the same reasons as described in the section “mitigated bias and confounding” with regard to the evidence for BMI, we decided not to upgrade the level of evidence.

11.5.2.8 Conclusion

We rated the overall quality of the evidence of an association between aircraft noise and waist circumference as “high”. However, since we based the evidence on one study only, we downgraded the overall level of the quality of the evidence to “moderate”.

We rated the quality of the evidence of an association between road traffic noise and waist circumference as “very low”; for rail traffic noise, we rated the level of evidence as “low”.

11.6 Blood pressure in children

We evaluated eight studies on the impact of noise on children’s systolic and diastolic blood pressure. The studies specifically investigated the impact of air and transportation noise (including road traffic noise). All studies were cross-sectional. The ICCBP-study reported results from cross-sectional and follow-up analyses. Only two studies investigated the impact of noise in a residential setting; the remaining seven studies investigated the impact of noise in both the home and the school environment. Table 11.6 gives a summary of the findings; further information, including the scores on each GRADE criterion, can be found in Appendix VIII.

Table 11.6: Noise exposure and the impact on children's blood pressure: summary of findings

Noise source	Setting	Outcome	Number of study design(s) *	Change in blood pressure (mmHg) per 10 dB (95%CI) †	Participants	Quality of evidence ‡
Air traffic	School	Systolic blood pressure (mmHg)	2 CS	-	2,013	⊕
		Diastolic blood pressure (mmHg)	2 CS	-	2,013	⊕
	Home	Systolic blood pressure (mmHg)	2 CS	-	2,013	⊕
		Diastolic blood pressure (mmHg)	2 CS	-	2,013	⊕
Road traffic	School	Systolic blood pressure (mmHg)	5 CS	-0.60 (-1.51 – 0.30)	4,520	⊕
		Diastolic blood pressure (mmHg)	5 CS	0.46 (-0.60 – 1.53)	4,520	⊕
	Home	Systolic blood pressure (mmHg)	6 CS	0.08 (-0.48 – 0.64)	4,197	⊕
		Diastolic blood pressure (mmHg)	6 CS	0.47 (-0.30 – 1.24)	4,197	⊕

*) CS = cross-sectional study; †) 95%CI: 95% confidence interval. Blood pressure is expressed in millimeter mercury (mmHg). Noise levels are expressed in L_{DEN} ; ‡) GRADE Working Group Grades of Evidence: High quality (⊕⊕⊕): Further research is very unlikely to change our confidence in the estimate of effect, Moderate Quality (⊕⊕⊕): Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, Low Quality (⊕⊕): Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, Very low quality (⊕): We are very uncertain about the estimate; mmHg: millimetre mercury.

Two studies investigated the impact of aircraft noise on children's blood pressure: one cross-sectional study and a longitudinal study presenting results of a cross-sectional analysis. Both investigated the impact of exposure at home and at school. Therefore, we started our GRADE assessment with a grading of "low".

Seven studies investigated the impact of road traffic noise at home and in school on children's blood pressure. All were cross-sectional or presented the results of cross-sectional analyses. Therefore, we started our GRADE assessment with a grading of "low".

11.6.1.1 Risk of bias

We further downgraded the quality of the evidence from the studies on the impact of aircraft noise. An important reason for this was that the response rates of the studies were lower than 60%. Furthermore, we

found it very difficult to judge whether the blood pressure measurements suffered from bias.

We also downgraded the quality of the evidence from the studies on the impact of road traffic noise. We observed that a number of studies were unable to apply individual exposure estimates, and that not all studies were able to adjust for important confounders. Furthermore, the response rates of several studies were lower than 60%.

11.6.1.2 Inconsistency

Figures 9.1 and 9.2 show that the results of the studies on the impact of aircraft noise differed: The RANCH study found positive associations for both the home and the school situations; the ICCBP study found negative associations. We decided to downgrade the quality for aircraft noise.

Although figure 9.1 shows that the study estimates for the association between road traffic noise and systolic blood pressure vary in size and direction, this is not confirmed by the results of the test for heterogeneity: we estimated an I^2_{residual} of 16% for the school situation and an I^2_{residual} of 8.9% for the home situation.

Figure 9.2 shows that the study estimates for the association between road traffic noise and diastolic blood pressure, vary in size and direction. This is also confirmed by the results of the tests of heterogeneity: we estimated an I^2_{residual} of 61.6% for the school situation and an I^2_{residual} of 76% for the home situation. We therefore decided to further downgrade the quality of the evidence for studies on the impact of road traffic noise.

11.6.1.3 Imprecision

We considered the results of the studies on the association with air traffic noise to be precise enough, since the standard deviations of the study estimates were smaller than the mean differences in blood pressure. As a result, we decided not to further downgrade the quality of the evidence of an aircraft noise effect.

We considered the results for road traffic noise to be less precise: the standard deviations of the pooled effect estimates were larger than the estimated mean changes in systolic blood pressure. As a result, we decided to further downgrade the quality of the evidence from the studies on the impact of road traffic noise.

11.6.1.4 Publication bias

The number of available effect estimates was too small to test for publication bias or small-study bias. As a result, we did not further downgrade the quality of the evidence.

11.6.1.5 Exposure-response gradient

Because we were not able to express the exposure levels reported by the ICCBP study in L_{DEN} , it was not possible to combine them with the results of the RANCH study. Consequently, there was no exposure-response gradient available for the association between air traffic noise and blood pressure in children.

It was possible to combine the results of the studies on the impact of road traffic noise. We observed, however, no exposure-response gradient. As a result, we did not upgrade the quality of the evidence of either an aircraft or a road traffic noise effect.

11.6.1.6 Magnitude of effect

As already indicated, we were not able to combine the results of the ICCBP study with the results of the RANCH study. Pooling the data from two RANCH study groups revealed a non-significant increase in systolic blood pressure of 0.80 – 1.00 mmHg per 10 dB increase in aircraft noise across a noise range of ~35 - 70 dB. This means that if the noise level increases from 35 to 70 dB, systolic blood pressure will increase by 2.8 to 3.5 mmHg. Whether this is a clinically relevant effect is difficult to say, since it depends on the child's age and sex.

11.6.1.7 Mitigated bias and confounding

The results from the RANCH study with regard to the association between aircraft noise and blood pressure did not change after adjustment for air pollution [117]. Whether this was also the case for the ICCBP study is not clear.

In studies on the impact of road traffic noise exposure at school, road traffic noise levels measured or modelled at the façade of the children's school might not reflect the average level of exposure during the children's time at the school. In the evaluated studies, the noise level was estimated only at the façade of the school building, which might have led to an over- or underestimation of the noise level affecting other parts of the school building. In reality, children move in and out of settings daily and change classrooms during their time at school. For studies estimating the impact of aircraft noise exposure, this is less of a problem, since in comparison with road traffic, aircraft noise affects an area in a relatively uniform way. Road traffic noise is more difficult to predict: it is a ground-based noise source with a complex propagation path from source to receptor and variations due to traffic flow throughout the day [235].

The results of the PIAMA, GINIPLUS, and LISAPLUS studies all showed that the effect of noise on children's blood pressure was hardly affected after adjustment for air pollution.

We attempted to find out in what way the results might be affected by adjustment for factors such as SES, and by selective (non-)response. However, from the available data we were not able to draw any conclusions about the possible role of these factors. We therefore decided not to upgrade the level of evidence for any of the noise sources.

11.6.1.8 Conclusion

We rated the overall quality of the evidence of an association between noise and children's blood pressure as "very low".

12 Discussion

In this report, we systematically reviewed evidence dealing with the impact of noise from air traffic, road traffic, and rail traffic and from wind turbines on the cardiovascular and metabolic systems. To this end, we selected 61 observational studies. From these studies, we systematically extracted data related to both the characteristics and the results of the studies; subsequently, we evaluated all the studies for quality. The studies included the following end-points: hypertension, ischaemic heart disease, stroke, diabetes and obesity in adult populations, and blood pressure in children. Where possible, we combined the results of the evaluated studies, using meta-analysis techniques.

In this chapter we discuss not only how our findings compare with the results of other meta-analyses, but also with the results of recent studies. Since we carried out the search for this systematic review, new studies have been published (November 2014 – March 2017) that investigate the associations between transportation noise exposure and metabolic and cardiovascular disease. Unfortunately, owing to time constraints, we were not able to carry out a structured and extensive additional search for new studies. However, in order to identify at least some of the new studies we were missing, we carried out a search on SCOPUS in March 2017. For this we applied the same SCOPUS search profile as was used to identify studies for the current review (see Appendix I).

In an “ideal” systematic review we should have included the results of these newly identified studies in the results of the current review, and where necessary updated our results. However, due to time constraints, we have not yet been able to systematically evaluate the newly identified studies. Nevertheless, we have decided to present their results in this chapter in a narrative way, and attempted to assess how they affect the results of the current review.

12.1 Main findings and comparison with the results of other meta-analyses and recent studies

12.1.1 Hypertension

12.1.1.1 Comparison with the results of other meta-analyses

We selected 40 studies that investigated the association between noise from air, road, rail traffic and wind turbine noise and hypertension. Two studies had a cohort design; the other 38 studies were cross-sectional. For all the evaluated noise sources, except for noise from wind turbines, we found an exposure-response gradient related to the *prevalence* of hypertension.

For *air traffic* noise, we estimated a statistically non-significant association: RR = 1.05 (95%CI: 0.95 – 1.17) per 10 dB (L_{DEN}). This effect size appeared lower than the estimated effect sizes found in earlier meta-analyses by Babisch and Van Kamp [22] and Di Huang [47]. Babisch and Van Kamp [22] found a statistically significant effect of 1.13 (95%CI: 1.00 – 1.28) per 10 dB increase in aircraft noise level.

Di Huang [47] also found a positive and statistically significant association between aircraft noise and hypertension: after combining the results of four cross-sectional studies, an OR of 1.63 (95%CI: 1.14 – 2.33) was estimated for a contrast between exposed persons and the reference group, meaning that persons exposed to aircraft noise have a higher risk of hypertension than those who are not exposed.

We found the association between exposure to *road traffic* noise and the *prevalence* of hypertension to be statistically significant: using a random effects model (47 estimates), we estimated an RR of 1.05 (95%CI: 1.02 – 1.08) per 10 dB (L_{DEN}) increase in road traffic noise (comprising 154,398 residents and 18,957 cases). This was similar to the results of the meta-analysis by Van Kempen and Babisch [41], who also found a positive and statistically significant association between road traffic noise and the prevalence of hypertension. They estimated an OR of 1.03 (95%CI: 1.01 – 1.06) per 5 dB increase in a 16-hour average road traffic noise level.

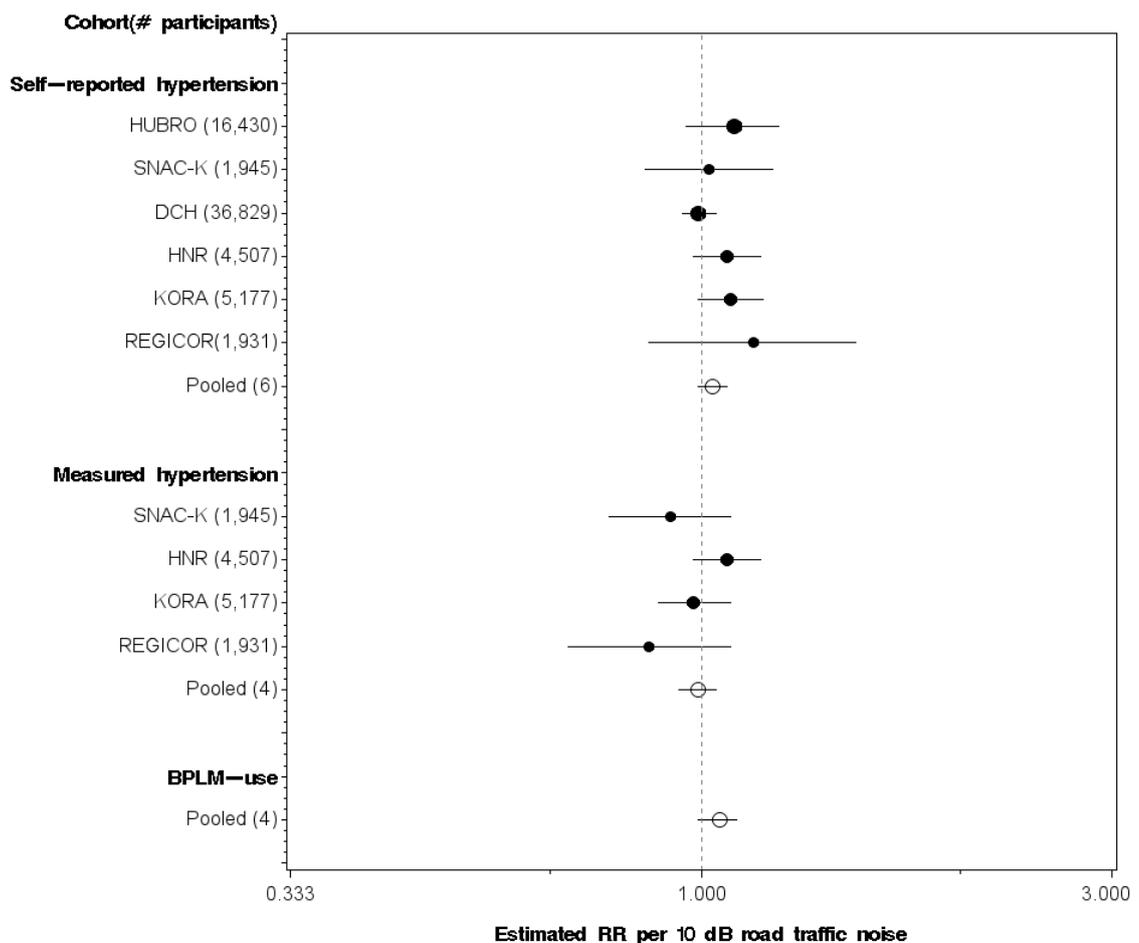


Figure 12.1: Association between road traffic noise (L_{DEN}) and the incidence of hypertension, derived from Fuks et al. [534]. The dotted vertical line refers to no effect of road traffic noise exposure. The black and white circles correspond to the estimated RR per 10 dB and its 95%CI. Abbreviations: BPLM-use = Use of blood pressure lowering-medication; HUBRO = Oslo Health Study; SNAC-K = the Swedish national study of aging and care in Kungsholmen; DCH = Diet Cancer and Health Cohort; HNR = Heinz-Nixdorf risk factors, evaluation of coronary

calcification, and lifestyle study; KORA = the Cooperative Health Research in the Region of Augsburg; REGICOR = Registre Gironi del Cor (Girona's heart registry).

In the two evaluated cohort studies that investigated the impact on hypertension, we found no excess risk of hypertension related to traffic noise. This is consistent with the results of a recent meta-analysis dealing with the association between road traffic noise and the incidence of hypertension [534]. This meta-analysis, carried out in the framework of the European ESCAPE project, included seven European cohorts. The meta-analysis comprised three endpoints: the incidence of self-reported hypertension, the incidence of measured hypertension, and the incidence of blood pressure-lowering medication. After aggregating the results of six cohorts (including 41,072 participants and 6,207 cases), an RR of 1.03 (95%CI: 0.99 – 1.07) per 10 dB (L_{DEN}) was estimated for the association between road traffic noise and the incidence of self-reported hypertension. The residual proportion of the between-study variance due to heterogeneity was I^2 : 6.08%. Because the researchers that carried out this meta-analysis had at their disposal individual data, they were able to adjust each of the included estimates for age, sex, education, economic activity, BMI, smoking status, pack-years of smoking, passive smoking, total alcohol consumption, wine consumption, physical activity, family history of hypertension, and area-level SES. After aggregation of the results of four cohort studies, an RR of 0.99 (95%CI: 0.94 – 1.04) per 10 dB (L_{DEN}) was estimated for the association between road traffic noise and the incidence of measured hypertension. The residual proportion of the between-study variance due to heterogeneity was I^2 : 0.15%. After aggregation of the results of four cohort studies, an RR of 1.05 (95%CI: 0.99 – 1.10) per 10 dB (L_{DEN}) was estimated for the association between road traffic noise and the incidence of blood pressure-lowering medication.

For both the impact of rail traffic noise and wind turbine noise on hypertension, this was the first attempt to carry out a meta-analysis. Consequently, we were not able to make a comparison.

12.1.1.2 Comparison with the results of new studies

Our SCOPUS search revealed seven new studies [535-541] published between November 2014 and March 2017. A report on recent results from the SNC study was also identified [542]. Table 12.1 presents some characteristics of these studies. It shows that four studies had a cross-sectional design, three had a cohort design, and one a case-control design. The sample sizes of the studies ranged from 627 persons to almost 4.5 million persons. With the exception of the Danish National Birth Cohort (DNBC) [536] and the study carried out by Barceló et al. [539], all studies investigated healthy living men and women; the DNBC study included only pregnant women; Barceló et al. investigated dead persons. Four studies reported on the impact of exposure to road traffic noise and one study reported on the impact of exposure to aircraft noise. Several studies reported on exposure to combinations of noise sources: one study reported on the impact of both road and rail traffic noise, and two studies additionally investigated the impact of aircraft noise.

Table 12.1: Overview of characteristics of new studies investigating the association between noise and hypertension

Study [Ref]	Country ^{*)}	Design ^{†)}	N and resp. rate (%) ^{‡)}	Sex and age (yrs)	Noise source ^{**)}	Exposure range (noise metric) ^{††)}	Ascertaining of hypertension ^{‡‡)}
WHII [535]	UK	CS	1,965 (28.4%)	MF, 50-75	Road	56 – 79 (L _{night})	1a, 2
SABRE [535]	UK	CS	627 (> 60%)	MF, 57-90	Road	56 – 79 (L _{night})	1a, 2
DNBC [536]	Den	CO	72,745 (72%)	F, 23-38	Road, Rail	38-80 (L _{DEN}), 21-81 (L _{DEN})	3
CPRD [537]	UK	CO	211,016 (5.5%)	MF, 40-79	Road	< 55, 55-60, > 60 (L _{night})	3
NoraH [538]	Ger	CS	844 (46.3%)	MF	Road, Rail, Air	<40, 40-45, 45-50, 50-55, 55-60, >60 (L _{pA,eq,18-06h})	1b
Barceló [539]	Sp	CC	10,972 (NA)	MF	Road	55-60, 60-65, 65-70, 70-75, >75 (L _{DEN})	3
Narita [540, 541]	Jp	CS	3,659 (46%)	MF, 20-79	Air	Control area, 52-57, 57-62, 62-67, >67 (L _{DEN})	Unclear
SNC [542]	Swi	CO	4,415,206	MF, > 30	Air, Road, Rail	~30 – 65 (L _{DEN})	3

^{*)} UK = United Kingdom, Den = Denmark, Ger = Germany, Sp = Spain, Jp = Japan, Swi = Switzerland; ^{†)} CS = cross-sectional study, CC = case-control study CO = cohort study; ^{‡)} N = number of participants and response rate (for cross-sectional studies) or attrition rates (for cohort studies); ^{**)} Road = road traffic noise, Rail = rail traffic noise, Air = air traffic noise; ^{††)} Exposure range (in dB) and the way exposure to noise was expressed; ^{‡‡)} The way hypertension was ascertained: 1a= measurement of blood pressure levels and/or by means of a clinical interview, 1b = measurement of blood pressure levels by the respondent; 2 = by means of a question as part of a questionnaire or interview (self-reported), 3 = from registration data;

Three studies specifically reported on the impact of night- time noise exposure. The NORAH study [538] estimated the exposure of participants over the 12 months prior to participation in the study, and expressed exposure to aircraft noise by means of L_{pA,eq,18-06h}. In addition to L_{DEN}, Héritier et al. [542] also evaluated the effects temporal noise exposure characteristics, expressed by means of the Intermittency Ratio (IR). The IR refers to events above the background noise level. The cohort studies ascertained hypertension by means of registrations (e.g. national patient registry). Three of the five cross-sectional studies ascertained hypertension by means of blood pressure measurements, supplemented by information on the use of anti-hypertensives from a questionnaire. Where studies made use of blood pressure measurements, these were carried out by clinicians and/or trained professionals. In the NORAH study, the participants measured their own blood pressure.

After adjustment for age, gender, ethnicity, marital status, smoking status, deprivation and NO_x , both the Whithall II (WHII) and SABRE studies found no effect of exposure to road traffic noise during the night. The WHII study found an OR of 1.06 (95%CI: 0.82 – 1.37) per 10 dB increase in road traffic noise (L_{night}). The SABRE study found an OR of 0.74 (95%CI: 0.48 – 1.16) per 10 dB increase in road traffic noise (L_{night}). Furthermore, both studies [535] reported that (i) the correlation between daytime and night-time road noise was 0.99, and (ii) that the results using night-time noise were comparable to the results using daytime noise. Unfortunately, both studies suffer from several limitations: Halonen et al. [535] were not able to estimate noise exposure at the individual level: instead of noise exposure estimates at address level, they applied noise exposure estimates at postcode level. Although the difference between noise levels at address level and postcode level is supposed to be small (< 1 dB), we cannot rule out exposure misclassification. Another problem is that the response rate of the WHII study was lower than 30%. Furthermore, Halonen et al. [535] were not able to adjust for important confounders such as BMI. Like the WHII and SABRE researchers [535], Carey et al. [537] reported on the association between road traffic noise exposure during the night and the incidence of hypertension. To this end, they used data from the Clinical Practice Research Datalink (CPRD), including 211,016 persons aged 40 - 79 years. Carey et al. [537] found no evidence of an association between night-time noise and hypertension (Hazard Ratio: 0.99 (95%CI: 0.94 – 1.05) for ≥ 60 dB vs < 55 dB) after adjustment for age, gender, smoking, BMI, and SES. This remained true after they restricted the analyses to participants residing in areas not subject to high levels of aircraft or rail traffic noise. Like the WHII and SABRE researchers, Carey et al. [537] were not able to estimate noise exposure at the individual level; instead of noise exposure estimates at address level, they applied noise exposure estimates at postcode level.

Pedersen et al. [536] reported on seven different hypertensive outcomes in relation to road traffic noise. To this end, they used data from the Danish National Birth Cohort [543]. After adjustment for maternal age, parity, pre-pregnancy BMI, height, disposable income, education and season of conception, Pedersen et al. [536] found a positive association between exposure to road traffic noise and the incidence of pre-eclampsia (for all subtypes in total and for each separate subtype), pre-eclampsia onset, gestational hypertension, and hypertensive disorders in pregnancy. They found the strongest associations and statistically significant associations for mild pre-eclampsia and pre-eclampsia with early onset. However, after additional adjustment for NO_2 , the reported associations were no longer statistically significant.

The NORAH study [538] also found no associations with transportation noise: After adjustment for age, gender, SES, pack-years, physical activity, and waist-hip-ratio, they found no systematic elevations in the fraction of hypertensive people with increasing noise levels from any of the traffic noise sources (air, road, and rail) under investigation.

The only available case-control study [539] investigated the association between exposure to road traffic noise and mortality due to hypertension. To this end, the researchers compared a group of persons

who died from hypertension (ICD-10: I10-I15) in the period 2004 - 2007 in Barcelona, with a group of control persons who died from other (non-cardiovascular) causes. They retrieved data from the mortality registration. It appeared that in the period 2004 – 2007, 4,412 persons died from hypertension. The total number of controls (people who died from other causes) was 6,560. The controls were matched with the cases by sex and age. To assess noise exposure, the researchers made use of the strategic noise maps that were made in 2007 in the framework of the END. The data from these maps were supplemented by noise measurements. After adjustment for (among other things) age, sex, land use, population density, altitude, and distance to (i) streets with high-density traffic, (ii) petrol stations, (iii) green areas, and (iv) industrial estates, mortality due to hypertension was found to be associated with noise levels (day, evening and night), but only for women was a statistically significant association found: OR = 1.013 (95%CI: 1.004 - 1.023) per 1 dB $L_{Aeq7-21}$.

This study suffered from several limitations: (i) Information with regard to noise exposure was available only for the year 2007; (ii) exposure levels for 2007 were linked with the (former) location of the dwellings of persons who had died in 2004 – 2007; (iii) no information on the cases' exposure history before 2004 was included; (iv) the researchers were not able to adjust for important confounders at individual level, such as BMI or SES; (v) some of the causes of death taken as controls may be (in)directly related to noise exposure.

Recently, Héritier et al. [542] published the results of an analysis on the association between noise exposure from air, road and rail traffic and mortality due to hypertension (ICD-10: I10-I15). To this end, they made use of data from the SNC study [544]. Traffic noise exposure from three sources was estimated by means of noise models. These models estimated the noise levels at the most exposed side of the dwelling of the participant. The study population comprised 4,415,206 observations during the period December 2000 – December 2008. The cohort contained 13,549 deaths from hypertension. After adjustment for sex, neighbourhood index of socio-economic position, civil status, education level, mother tongue, nationality, exposure to aircraft and rail traffic noise, and NO₂ exposure, road traffic noise exposure was found to be statistically significantly associated with an increase in mortality due to hypertension. Héritier et al. [542] estimated a Hazard Ratio of 1.053 (95%CI: 1.030 – 1.075) per 10 dB (L_{DEN}). Both rail and air traffic noise exposure were found to be non-significantly associated with an increase in mortality due to hypertension. For rail traffic noise, an HR of 1.011 (95%CI: 0.995 – 1.027) per 10 dB (L_{DEN}) was estimated; for air traffic noise an HR of 1.012 (95%CI: 0.985 – 1.039) per 10 dB (L_{DEN}) was estimated. In their paper, Héritier et al acknowledge that their study suffers from several limitations. An important limitation is the fact that information about individual lifestyle factors is lacking. Consequently, residual confounding of lifestyle cannot be ruled out.

In a Japanese study [540, 541], a questionnaire was administered to 3,659 adults aged 20-79 years, living in the vicinity of Narita International Airport. After adjustment for sex, age, noise-sensitivity, and BMI, no association was found between exposure to aircraft noise and the prevalence of hypertension. It was, however, not described how

aircraft noise exposure and hypertension were ascertained. In addition, the response rate was low.

Four studies [535, 536, 539] found an association between noise exposure and hypertension. Statistically significant effects were found by Barceló et al. [539] and Héritier et al. [542] only. Since these studies focus on mortality due to hypertension, we think that it is not very likely that the results of the newly published studies will change the size of our estimates of the RR per 10 dB for the association between noise and the prevalence of incidence of hypertension considerably. Furthermore, we rated the quality of the evidence from most of the newly reported studies as “low”.

12.1.2 *Ischaemic Heart Disease*

12.1.2.1 Comparison with the results of other meta-analyses

We evaluated the results of 22 studies that investigated the effect of noise on the risk of IHD. The studies investigated several sources of noise: air, road, and, rail traffic. In addition, there were three studies on the impact of noise from wind turbines on cardiovascular disease. For several sources and types of IHD indicators, we found exposure-response relations. Table 11.2 presents an overview of these exposure-response relations (RR per 10 dB). The table shows statistically significant associations for i) the association between aircraft noise and the *incidence* of IHD, ii) the association between road traffic noise and the *prevalence* of IHD, and iii) the association between road traffic noise and the *incidence* of IHD. In relation to rail traffic noise exposure, no significant exposure-response relation was found.

In this review, we include the results of three other reviews, that included meta-analyses of the relationship between traffic noise and IHD [28, 37, 38, 44]. All three reviews focused on the effects of road traffic noise.

In 2006, Babisch [37] aggregated the results of three case-control studies and a cohort study, investigating the association between road traffic noise and the incidence of myocardial infarction. As a result, he estimated an OR of 1.17 (95%CI: 0.87 – 1.57) per 10 dB ($L_{Aeq, 6-22hr}$). Later, in 2014, Babisch [28] supplemented this meta-analysis with the results of new studies. As part of his new meta-analysis, he combined the results of five cross-sectional studies and found an RR of 1.11 (95%CI: 0.94 – 1.31) per 10 dB (L_{DEN}). He also found a positive but non-significant association between road traffic noise exposure and mortality due to IHD: After aggregating the results of three cohort studies, Babisch found an RR of 1.08 (95%CI: 0.99 – 1.18) per 10 dB (L_{DEN}). Within his meta-analysis, Babisch also combined the results of *both* the cross-sectional studies ($n = 2$) (prevalence of IHD) *and* the case-control ($n = 4$) and cohort studies ($n = 3$) (incidence of IHD). As a result, he found an RR of 1.09 (95%CI: 1.03 – 1.16) per 10 dB for the impact of road traffic noise on clinical heart disease. He justified his analysis by the argument that prevalence can be regarded as cumulative incidence, if the length of exposure is taken into account.

In 2014, Vienneau et al. [44] also reported the results of a meta-analysis of the association between road, rail, or aircraft noise and myocardial infarction or coronary heart disease. After pooling the results of three case-control studies, four cohort studies, and two ecological

studies on the impact of road or air traffic noise on non-fatal IHD, the authors estimated an RR of 1.07 (95%CI: 1.05 – 1.09) per 10 dB (L_{DEN}). Aggregating the results of one case-control study, four cohort studies, and one ecological study revealed an RR of 1.05 (95: %CI 1.01 – 1.09) per 10 dB (L_{DEN}) for *mortality* due to IHD.

Figure 12.2 shows how the results of the current meta-analysis correspond with the results of the earlier meta-analyses of Babisch [28, 37] and Vienneau et al. [38, 44]. Like the current meta-analyses, all three earlier meta-analyses found a slight increase in IHD risk in populations exposed to air and/or road traffic noise. Furthermore, the quantitative exposure-response estimates seem to overlap largely between the different meta-analyses.

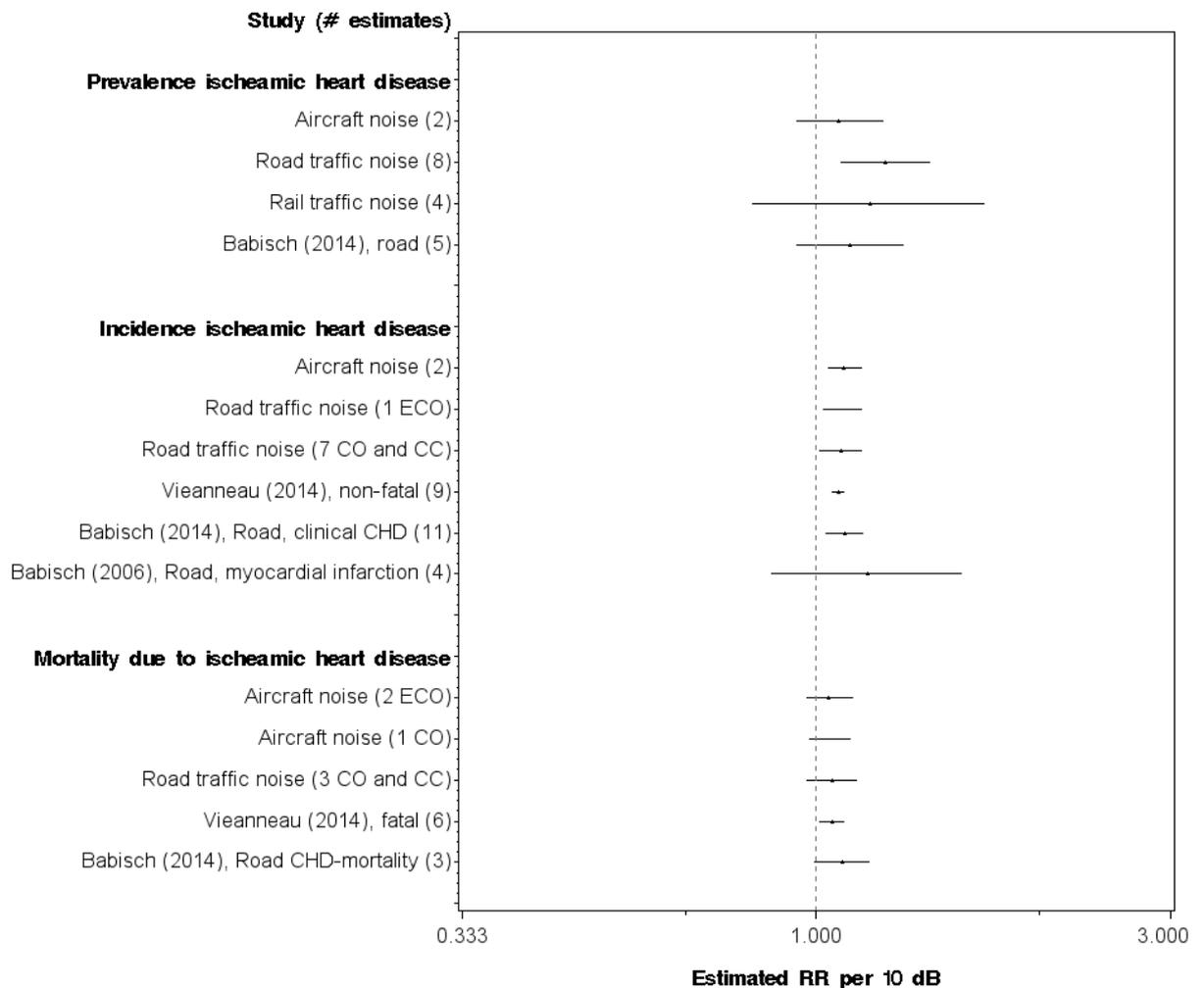


Figure 12.2: Association between aircraft, road and rail traffic noise exposure (L_{DEN}) and IHD, reported by the current meta-analysis and meta-analyses performed by Babisch [37], Babisch [28] and Vienneau et al. [38, 44]. The dotted vertical line corresponds to no effect of noise exposure. The circles correspond to the estimated RR per 10 dB and its 95%CI. Abbreviations: CHD = Cardiovascular Heart Disease.

12.1.2.2 Comparison with the results of new studies

Since we carried out the search for the current review, new studies have been published that investigate the impact of noise on IHD. As a result of our SCOPUS search, we found eight new studies reporting on the association between noise from transportation and IHD [537, 539, 542, 545-549]: one ecological study, two case-control studies, and five cohort studies. All published in the period November 2014 – March 2017 (see Table 12.2).

All the studies were carried out in Europe. Sample sizes ranged from 4,443 to 8.16 million. All the studies investigated the impact of road traffic noise. Two studies also investigated the impact of rail and aircraft noise. Four studies specifically reported on the impact of exposure during the night [537, 545, 548-550]. One of the new studies was an update of the SNC study [542] included in the current meta-analysis.

Table 12.2: mOverview of characteristics of new studies on the association between noise and IHD

Study [Ref]	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs)	Noise source ^{**)}	Exposure range (noise metric) ^{††)}	Ascertaining of IHD (outcome) ^{‡‡)}
CPRD [537]	UK	CO	211,016 (5.5)	MF, 40-79	Road	< 55, 55-60, > 60 (L _{night})	3 (IHD, MI)
NoraH [545]	Ger	CC	1,026,658 (NA)	MF, ≥ 40	Road, Rail, Air	<40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, ≥70 (L _{pAeq,24h})	3 (MI)
SPHC [546]	Swe	CO	13,510 (0.6)	MF, 18-80	Road	41-66 (L _{DEN})	3 (MI, IHD)
Halonen [550]	UK	ECO	8.16 million (NA)	MF, ≥25 and ≥75	Road	<55, 55-60, >60 (L _{Aeq16hr} , L _{night})	3 (IHD)
Heinz-Nixdorf Recall study [548]	Ger	CO	4,433 (7.9)	MF, 45-74	Road	NR (L _{night})	1 (IHD)
MINAP [549]	UK	CO	18,038 (0.6)	MF, >25	Road	NR (L _{Aeq,16hr})	3 (MI)
SNC [542]	Swi	CO	4,415,206	MF, > 30	Air, Road, Rail	~30 – 65 (L _{DEN})	3 (IHD, MI)
Barceló [539]	Sp	CC	10,972 (NA)	MF	Road	55-60, 60-65, 65-70, 70-75, > 75 (L _{DEN})	3 (MI)

^{*)} UK = United Kingdom, Den = Denmark, Ger = Germany, Swi = Switzerland, Sp = Spain; ^{†)} CS = cross-sectional study, CC = case-control study, CO = cohort study; ^{‡)} N = number of participants and response rate for cross-sectional studies, or attrition rate for cohort or case-control studies (where applicable); ^{**)} Road = road traffic noise, Rail = rail traffic noise, Air = air traffic noise; ^{††)} Exposure range (noise levels (dB) and the way exposure to noise was expressed; ^{‡‡)} The way IHD was ascertained: 1 = by means of a clinical interview/examination, 2 = by means of a question as part of a questionnaire or interview

(self-reported), 3 = from registration data; IHD = ischaemic heart disease; MI = myocardial infarction.

In the current review, we derived a positive and statistically significant association between aircraft noise and the *incidence* of IHD. From the results of two ecological studies, we estimated an RR of 1.09 (95%CI: 1.04 – 1.15) per 10 dB. This was not consistent with the results of the NORAH study [545]. The NORAH study was a case-control study on a population that consisted of persons aged 40 years and older that were insured by three statutory health insurance funds. The researchers identified incident cases of cardiovascular diseases between 2006 and 2010, using claims and prescription data from the participating health funds. In total, they identified 19,632 incident cases of myocardial infarction. The control group consisted of individuals that had no diagnosis of the respective disease in the particular period. After adjustment for confounders (age, sex, education, work status, and SES), the NORAH study reported no association between exposure to *aircraft* noise ($L_{pAeq, 24hr}$) and the *incidence* of myocardial infarction (OR = 0.99 (95%CI: 0.97 – 1.02) per 10 dB).

In the current review, we derived two positive associations between aircraft noise and mortality due to IHD. Both associations were statistically non-significant. One association (RR: 1.04 (95%CI: 0.97 – 1.12) per 10 dB) was based on the results of two ecological studies. The other association was based on the results of the SNC study. Recently, Héritier et al. [542] presented new results from the SNC study. In their paper, they reported on (among other things) the association between exposure to aircraft noise and (i) mortality due to IHD (ICD-10: I20-I25), and (ii) mortality due to myocardial infarction (ICD-10: I21-I22). They based their analyses on 4,415,206 participants. During the follow-up period, 60,261 people died of IHD; 19,313 from myocardial infarction. After adjustment for a range of confounders, Héritier et al. [542] found that an increase in mortality due to myocardial infarction was associated with an increase in aircraft noise exposure. An HR of 1.027 (95%CI: 1.006 – 1.049) per 10 dB was estimated.

The NORAH study [545] also presented the results of an analysis of the association between aircraft noise and mortality due to myocardial infarction. After adjustment for confounders, an OR of 1.03 (95%CI: 0.94 – 1.07) per 10 dB was estimated. It is expected that the new results of both the NORAH and SNC studies, strengthen the evidence base for a positive association between aircraft noise and mortality due to IHD.

In the current review, we derived positive and statistically significant associations between road traffic noise and the incidence of IHD. One association (RR = 1.08 (95%CI: 1.02 – 1.15) per 10 dB) was based on the results of an ecological study. The results were quite consistent with the results of an ecological study recently published by Halonen et al. [547]. The aim of the study was to quantify small-area effects of long-term exposure to road traffic noise on all-cause and cardiovascular mortality as well on cardiovascular hospital admissions in adult and elderly populations. In their study, they applied Census Output Areas

(COAs) for hospital admission analysis and Lower Layer Super Output Areas (LSOAs) for mortality analysis as the smallest units for investigation. These are areas with a mean population of 300 and 1,500 persons, respectively. In total, they included 27,686 COAs and 5,358 LSOAs. After adjustment for age, sex, area-level deprivation, ethnicity, smoking, and PM_{2.5}, they found an RR of 1.00 (95%CI: 0.99 – 1.01) per 5 dB increase in day-evening road traffic noise levels for the association between road traffic noise and *hospital admissions* due to IHD in the group of adults (n = 133,688). They found a similar result among elderly persons.

Based on the results of three cohort studies and four case-control studies, we derived an RR of 1.08 (95%CI: 1.01 – 1.15) per 10 dB for the association between road traffic noise and the incidence of IHD. This was confirmed by the results of the NORAH study [545]. After adjustment for confounders, the authors reported a positive and statistically significant association between exposure to *road traffic* noise exposure and the *incidence* of myocardial infarction (OR = 1.03 (95%CI: 1.01 – 1.05) per 10 dB).

However, more studies have come available, that investigated the impact of road traffic noise on the incidence of IHD. Recently, Hoffmann et al. [548] reported on the impact of road traffic noise during the *night*. To this end, they used data from the Heinz-Nixdorf Recall study, a prospective population-based cohort study in the Ruhr Region of Germany. For their analyses, they evaluated 4,433 subjects, representing 90% of the total population of the Heinz-Nixdorf Recall study. Over an average observation period of almost 8 years, they observed 135 coronary events in 34,909 person years. After adjustment for sex, recruitment year, marital status, education, employment status, smoking status, smoking duration and intensity, unemployment rate in the residential district, BMI, physical activity, and alcohol consumption, they found a positive but non-significant association between road traffic noise exposure during the *night* and the *incidence* of IHD. They reported an HR of 1.25 (95%CI: 0.70 – 2.23) per 26 dB increase of road traffic noise during the night. Assuming that a difference of 26 dB L_{night} is about the same as a difference of 26 dB L_{DEN}, this is effect size is comparable with the results of our meta-analysis.

There were also studies on the association between road traffic noise and the incidence of IHD that did *not* find an effect: Carey et al. [537] not only reported on the association between road traffic noise exposure during the night and the incidence of hypertension. They also reported on the association between road traffic noise and IHD and myocardial infarction. They found no evidence of an association between night noise and either IHD (HR: 1.00 (95%CI: 0.93 – 1.09) for ≥ 60 dB vs < 55 dB) or myocardial infarction (Hazard Ratio: 0.99 (95%CI: 0.86-1.14) after adjustment for age, gender, smoking, BMI, and SES.

Another study on the association between road traffic noise and the incidence of IHD that did not find an effect has been published by Bodin et al. [546]. For their study, they made use of data from the Scania Public Health Cohort (SPHC), following persons between 2000 and 2010. For each participant, they obtained hospital admission and/or cause of death data from national registries. Between 2000 and 2010, they

observed 664 cases of incident first-time myocardial infarction and 137 deaths. Regarding IHD, there were 904 incident cases, and 100 deaths. After adjustment for confounders (age, sex, BMI, smoking, education, alcohol consumption, civil status, year, country of birth, physical activity, and NOx), Bodin et al. [546] did not find an increased incidence rate ratio (IRR) for either myocardial infarction or IHD. The IRR for myocardial infarction in relation to a 10 dB (L_{DEN}) increase in average road traffic noise was 0.99 (95%CI: 0.86 – 1.14).

Based on the results of one case-control study and two cohort studies, the current review derived an RR of 1.05 (95%CI: 0.97 – 1.13) per 10 dB for the association between road traffic noise and mortality due to IHD. This result was confirmed by the results of the NORAH study [545], Héritier et al. [542], and the analyses reported by Barceló et al. [539]: after adjustment for confounders, the NORAH study found a positive association between road traffic noise exposure and *mortality* due to myocardial infarction. An OR of 1.04 (95%CI: 1.02 – 1.06) per 10 dB was estimated. After adjustment for a range of confounders, Héritier et al. [542] found that an increase in both mortality due to IHD and mortality due to myocardial infarction were associated with an increase in road traffic noise exposure. HRs of 1.023 (95%CI: 1.012 – 1.034) and 1.040 (95%CI: 1.021 – 1.059) per 10 dB (L_{DEN}) were estimated for mortality due to IHD and myocardial infarction, respectively. They based their analyses on 4,415,206 participants. During the follow-up period, 60,261 people died of IHD; 19,313 persons from myocardial infarction. Barceló et al. [539] not only investigated the association between exposure to road traffic noise and mortality due to hypertension. They also investigated the association with mortality due to myocardial infarction (ICD-10: I21-I22). It appeared that during the study period, 2004 - 2007, 6,439 persons died from myocardial infarction. The total number of controls (people who died from other causes other than hypertension) was 6,560. After adjustment for confounders, mortality due to myocardial infarction was found to be associated with road traffic noise, but a statistically significant association was found only for men.

The results of the MINAP cohort [549] were more difficult to compare: the researchers followed 18,138 myocardial infarction survivors older than 25 years, living in London over four years for death or readmission for myocardial infarction. After adjustment for year of follow-up, age, reperfusion, type of myocardial infarction survivor, area-level income deprivation, and $PM_{2.5}$, they found an HR of 1.02 (95%CI: 0.99 – 1.06) per 5 dB for the association between road traffic noise ($L_{Aeq16hr}$) and all-cause mortality. Furthermore, they found a non-significant association between road traffic noise and all-cause mortality or readmission for myocardial infarction (HR = 1.02 (95%CI: 0.99 – 1.05)).

As part of the current review, no studies were evaluated that investigated the associations between rail traffic noise and the incidence of IHD or rail traffic noise and mortality due to IHD. Both the NORAH study [545] and Héritier et al. [542] have since reported on the association between rail traffic noise and mortality due to IHD. The NORAH study found a positive and statistically significant association for the association between rail traffic noise and mortality due to myocardial infarction. After adjustment for confounders they estimated an OR of

1.04 (95%CI: 1.01 – 1.06). Héritier et al. [542] also found significant positive associations: for mortality due to IHD an HR of 1.012 (95%CI: 1.005 – 1.020) per 10 dB was estimated; for myocardial infarction an HR of 1.020 (95%CI: 1.007 – 1.033) per 10 dB. It is estimated that combining the results of the NORAH and Héritier et al. studies would result in a positive and probably significant association between rail traffic noise exposure and mortality due to IHD. The quality of the evidence that results from these studies will probably be rated as “high”, despite some limitations as both studies have a design that can be rated as “high”, the results can be rated as consistent and precise.

12.1.3 Stroke

12.1.3.1 Comparison with the results of other meta-analyses

For our review, we evaluated nine studies that investigated the impact of noise on the likelihood of stroke. The findings of the studies did not provide any clear evidence of an association between noise exposure from different sources and the *prevalence* of stroke (see Table 11.3). For the association between air traffic noise and the *incidence* of stroke, we found a non-significant effect size of 1.02 per 10 dB across a noise range of 30 - 75 dB. We based the results for the association between road traffic noise and the *incidence* of stroke, on the results of only one cohort study. Within this study, we observed a statistically significant effect size of 1.14 per 10 dB.

The results of the current meta-analysis did not correspond fully with the results of the meta-analysis by Dzhambov and Dimitrova [551, 552]. More recently, they published the results of a meta-analysis investigating the relationship between traffic noise and stroke. As can be seen in Figure 10.9, they found a slightly increased risk of stroke associated with both road and air traffic noise. For road traffic noise, after combining the results of six studies, they derived an effect size of 1.03 (95%CI: 0.87 – 1.22) per 10 dB (L_{DEN}); for aircraft noise, they derived an effect size of 1.05 (95%CI: 1.00 – 1.10) per 10 dB (L_{DEN}) after combining the results of five studies.

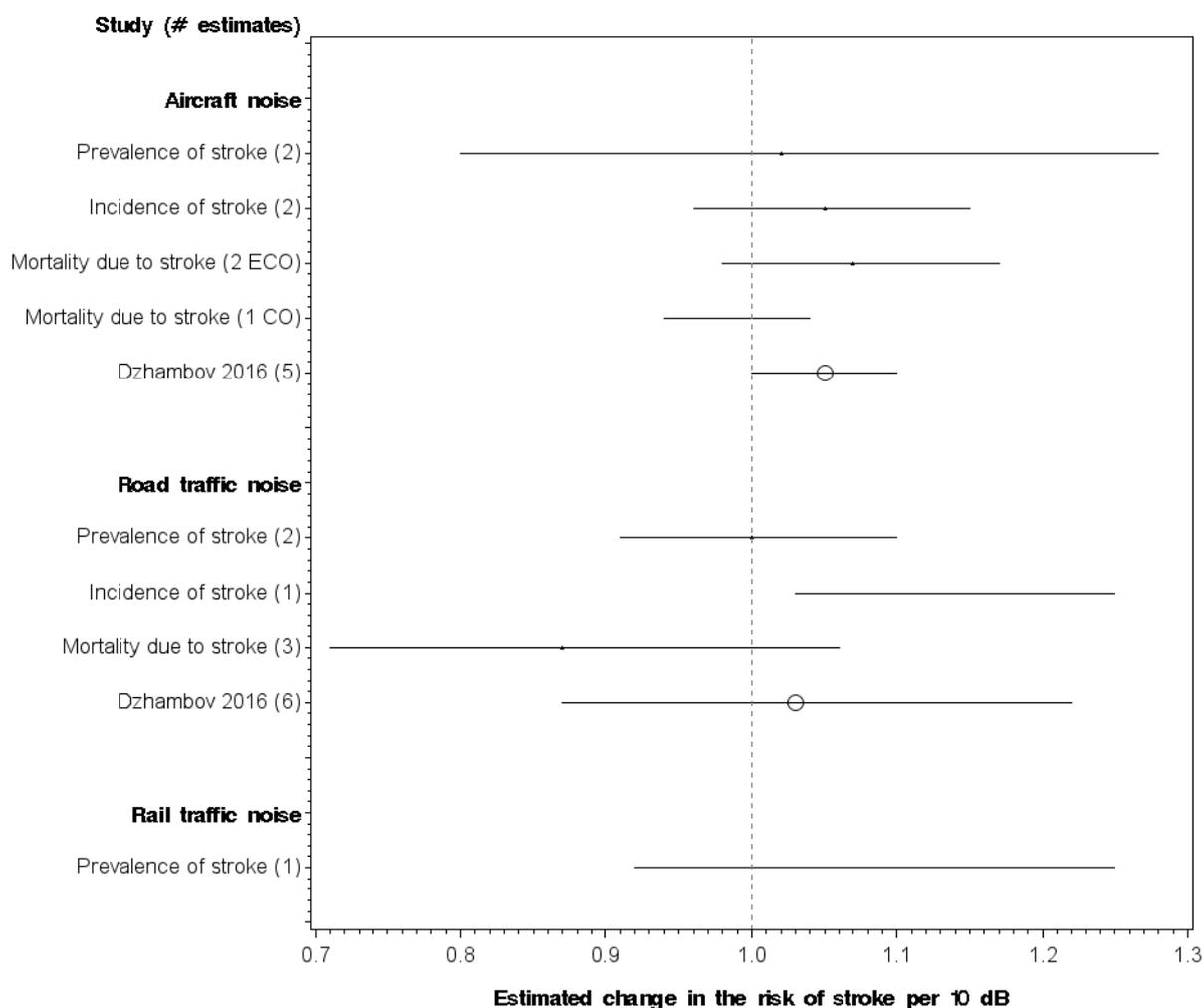


Figure 12.3: Association between aircraft and road traffic noise exposure (L_{DEN}) and stroke, reported by the current meta-analysis and a meta-analysis performed by Dzhambov and Dimitrova [551, 552]. The dotted vertical line corresponds to no effect of noise exposure. The circles correspond to the estimated RR per 10 dB and its 95%CI.

Reasons for the differences between the results of the meta-analyses in this report and the results of the meta-analyses of Dzhambov and Dimitrova [551, 552], might be the fact that the latter combined the results of studies with different designs. For example, Dzhambov and Dimitrova combined the results of the HYENA study [227, 228] (a cross-sectional study, measuring the *prevalence* of stroke) with the results of the LSAS study [76] (an ecological study, measuring the *incidence* of stroke). In the current systematic review, we limited ourselves to studies that were published up to September 2015. Dzhambov and Dimitrova also included studies [550, 553, 554] that were published after this date.

12.1.3.2 Comparison with the results of new studies

As a result of our SCOPUS search, we identified five new studies [537, 542, 545, 547, 548] on the association between noise and stroke (see Table 12.3).

Table 12.3: Overview of characteristics of new studies investigating the association between noise and stroke

Study [Ref]	Country ^{*)}	Design ^{†)}	N and response rate (%) ^{‡)}	Sex and age (yrs)	Noise source ^{**)}	Exposure range (noise metric) ^{††)}	Ascertaining of stroke ^{‡‡)}
CPRD [537]	UK	CO	211,016 (5.5)	MF, 40-79	Road	< 55, 55-60, > 60 (L _{night})	3
NoraH [545]	Ger	CC	1,026,658 (NA)	MF, ≥ 40	Road, Rail, Air	<40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, ≥70 (L _{pAeq,24h})	3
Halonen [547]	UK	ECO	8.16 million (NA)	MF, ≥25 and ≥75	Road	<55, 55-60, >60 (L _{Aeq,16h} , L _{night})	3
Heinz-Nixdorf Recall study [548]	Ger	CO	4,433 (7.9)	MF, 45-74	Road	NR (L _{night})	1
SNC [542]	Swi	CO	4,415,206	MF, > 30	Air, Road, Rail	~30 – 65 (L _{DEN})	3

^{*)} UK = United Kingdom, Den = Denmark, Ger = Germany, Swi = Switzerland; ^{†)} CS = cross-sectional study, CC = case-control study, CO = cohort study; ^{‡)} N = number of participants and response rate for cross-sectional studies, or attrition rate for cohort or case-control studies (where applicable); ^{**)} Road = Road traffic noise, Rail = rail traffic noise, Air = air traffic noise; ^{††)} Exposure range of noise levels (in dB) and the way exposure to noise was expressed; ^{‡‡)} The way stroke was ascertained: 1 = by means of a clinical interview/examination, 2 = by means of a question as part of a questionnaire or interview (self-reported), 3 = from registration data.

In the current review, we derived a positive association between aircraft noise and the *incidence* of stroke. On the basis of the results of two ecological studies, we estimated an RR of 1.05 (95%CI: 0.96 – 1.15) per 10 dB. Of the newly identified studies, only the NORAH study [545] investigated the association between aircraft noise and the incidence of stroke. The results were not consistent with the current review, since the researchers of the NORAH study found a negative association between aircraft noise and the incidence of stroke: After adjustment for confounders, they reported an OR of 0.976 (95%CI: 0.953 – 1.000) per 10 dB.

For the association between aircraft noise and mortality due to stroke, two exposure-response gradients were derived in the current review. One gradient was based on the results of two ecological studies (RR = 1.07 (95%CI: 0.98 – 1.17) per 10 dB), and another gradient was based on the results of the SNC-study. Recently, Héritier et al. [542] presented new results from the SNC study. During the follow-up period, 22,377 people died from stroke. After adjustment for a range of confounders, Héritier et al. [542] found that an increase in mortality due to stroke was associated with an increase in air traffic noise exposure. An HR of 1.013 (95%CI: 0.993 – 1.033) per 10 dB was estimated. This was not confirmed by the results of the NORAH study, since they found a

negative association between aircraft noise and mortality due to stroke: After adjustment for confounders, they reported an OR of 0.991 (95%CI: 0.9595 – 1.024) per 10 dB.

In the current review, we derived a statistically significant RR of 1.14 (95%CI: 1.03 – 1.25) per 10 dB for the association between road traffic noise and the incidence of stroke. This was based on the results of the DCH cohort. Our quick search revealed four studies that have recently reported on the association between road traffic noise and the incidence of stroke [537, 545, 547, 548]. Their results were not consistent. The CPRD study [537] did not find an association between road traffic noise exposure during the night and the incidence of stroke. After adjustment for age, gender, smoking, BMI, and SES, the CPRD study researchers estimated an HR of 0.92 (95%CI: 0.82 – 1.04) when comparing persons exposed to more than 60 dB (L_{night}) with persons exposed to less than 55 dB (L_{night}).

The Heinz-Nixdorf Recall study also did not find an association between exposure to road traffic noise during the night and the incidence of stroke [548]. Like the DCH study, the NORAH study [545] also found a positive and statistically significant association between exposure to road traffic noise and the incidence of stroke: an OR of 1.02 (95%CI: 1.00 – 1.03) per 10 dB was estimated.

In their ecological study, Halonen et al. [547] found that daytime road traffic noise was significantly associated with hospital admissions for stroke in adults with an RR of 1.05 (95%CI: 1.02 – 1.09) in areas exposed to > 60 vs < 55 dB. They found no effects of night-time noise exposure. They found similar results for elderly: they estimated a RR of 1.09 (95%CI 1.04 – 1.14) in areas exposed to > 60 vs < 55 dB L_{day} . For exposure during the night, they found a statistically significant RR of 1.05 (95%CI: 1.01 – 1.09) in areas exposed to 55-60 vs <55 dB.

Overall, it is not expected that the results of the newly reported studies affect the findings and the strength of the evidence of the current review as regards the association between road traffic noise and the incidence of stroke.

In the current review, no association was found between road traffic noise exposure and mortality due to stroke. After aggregating the results of three cohort studies, we estimated an RR of 0.87 (95%CI: 0.71 – 1.06) per 10 dB. This is not consistent with the results of the NORAH [545] and H eritier et al. [542] studies. For the association between road traffic noise exposure and mortality due to stroke, the NORAH study researchers estimated an OR of 1.03 (95%CI: 1.01 – 1.05) per 10 dB. After adjustment for a range of confounders, H eritier et al. [542] found that an increase in mortality due to stroke was associated with an increase in road traffic noise exposure. An HR of 1.011 (95%CI: 0.993 – 1.028) per 10 dB (L_{DEN}) was estimated. During the follow-up period, 22,377 people died from stroke.

It is expected that the results of the NORAH and H eritier et al. studies will change the effect estimate of the current review towards an RR of 1 per 10 dB. This is more in accordance with our effect estimate for the association between road traffic noise and the incidence of stroke.

We also identified an ecological study that investigated the association between road traffic noise and mortality due to stroke: Halonen et al.

[547] found positive, but statistically non-significant increases in mortality due to stroke among adults and the elderly.

As part of the current review, no studies were evaluated that investigated the associations between rail traffic noise and the incidence of stroke or rail traffic noise and mortality due to stroke. Both the NORAH and H eritier et al. studies reported on the association between rail traffic noise and mortality due to stroke.

The NORAH study found a positive and statistically significant association between rail traffic noise and mortality due to stroke. After adjustment for confounders they estimated an OR of 1.03 (95%CI: 1.01 – 1.05). In the H eritier et al. study, no positive association was seen: for mortality due to stroke an HR of 0.995 (95%CI: 0.983 – 1.008) per 10 dB was estimated.

It is estimated that combining the results of the NORAH H eritier et al. studies and would result in a positive but non-significant association between rail traffic noise exposure and mortality due to stroke. The quality of the evidence that results from these studies will probably be rated as “high”, despite some limitations, since both studies have a design that can be rated as “high” and the results can be rated as consistent and precise.

12.1.4 *Diabetes and obesity*

12.1.4.1 Comparison with the results of other meta-analyses

We evaluated seven studies that investigated the impact of noise on type 2 diabetes. Most of the studies were of cross-sectional design, which generally did not show significant associations. One cohort study showed a statistically significant association between road traffic noise and type 2 diabetes, which was not supported for railway noise. Another cohort study on aircraft noise, suggested an increased risk related to exposure primarily in women.

More recently, Dzhambov [45, 139] reported the results of a meta-analysis on the association between noise and the risk of type 2 diabetes. Although Dzhambov [45, 139] found very clear associations between the impact of environmental noise type 2 diabetes in the studies he evaluated, the results of his meta-analysis were difficult to compare with the results of the current meta-analysis. After combining the results of two case-control studies and three cohort studies carried out in residential setting, Dzhambov found an RR of 1.22, meaning that people exposed at their homes to L_{DEN} values of more than 60 dB had a 22% higher risk of diabetes than to those exposed to L_{DEN} values of less than 64 dB. Another difference from the current meta-analysis is that the estimate presented by Dzhambov was not source specific: two of the five studies that were included in his review investigated the impact of aircraft noise exposure; the remaining three investigated the impact of road traffic noise exposure.

Since this is the first known review that systematically evaluates the results of studies on the impact of noise on obesity, we were not able to make a comparison with the results of existing reviews and/or meta-analyses.

12.1.4.2 Comparison with the results of new studies

Our SCOPUS search resulted in the identification of two studies [539, 555] that linked long-term exposure to transportation noise with diabetes. One is a cross-sectional study that was carried out in the city of Plovdiv in Bulgaria. The participants were 513 persons (response rate 23.8%) aged 18 years or older. Whether a person had suffered from diabetes was ascertained by means of a questionnaire. Exposure to road traffic noise (expressed as L_{DEN}) was assessed by linking the respondents' home address or the street in which the home of the respondent was situated with strategic noise maps of the city of Plovdiv. After adjustment for a range of confounders (exposure to $PM_{2.5}$, exposure to Benzo-a-Pyrene, age, gender, ethnicity, BMI, family history of diabetes, noise sensitivity, annoyance due to air pollution, annoyance due to noise, location of the bedroom, sleep disturbance, and pack-years of smoking), Dzhambov and Dimitrova [555] reported an OR of 4.49 (95%CI: 1.38 – 14.68) in the group of respondents exposed to 71 - 80 dB (L_{DEN}) vs 51-70 dB (L_{DEN}).

The other study on the impact of noise on diabetes was that of Barceló et al. [539]. In addition to hypertension and IHD, they investigated the association with mortality due to diabetes mellitus (ICD-10: E10-E14). It appeared that during the study period, 2004 - 2007, 2,670 persons died from diabetes mellitus. The total number of controls (people who died from causes other than diabetes) was 6,560. After adjustment for confounders, mortality due to diabetes mellitus was found to be associated with exposure to road traffic noise during the evening and night in men.

As a result of our quick search, we also identified two longitudinal studies on traffic noise and markers of obesity. One study was based on the same DCH cohort that has been used in several publications cited above on noise and cardiovascular outcomes and diabetes, as well as the cross-sectional analysis on noise and obesity markers [192]. This study found a statistically significant increase in weight of 15.4 gr per year (95%CI: 2.14 – 27.8) for a 10 dB increase in road traffic noise during five years prior to an average of 5.4 years of follow-up [556]. The same held true for waist circumference, with a yearly increase of 0.22 mm (95%CI: 0.018 – 0.43) per 10 dB. Exposure to rail noise was associated with a weight gain of 39.9 gr per year (95%CI: 10.2 – 69.6) per 10 dB, but not with a significant change in waist circumference. Baseline BMI and waist circumference were significant effect modifiers of the associations between noise and adiposity outcomes, which were observed primarily in those with obesity and a large waist circumference. Unfortunately, the information on weight and waist circumference at follow-up were self-reported, and such data are susceptible to bias.

The other study included 40,974 children from the Danish National Birth Cohort, who were followed from birth to 7 years of age [557]. Exposure to noise from road and rail traffic was estimated in the same way as in the studies based on the DCH cohort. Pregnancy and childhood exposure to road traffic noise were related to overweight in childhood with ORs of 1.06 (95%CI 1.00 – 1.12) and 1.06 (95%CI 0.99 – 1.12) per 10 dB, respectively. There were no associations for rail traffic noise. The anthropometric data were obtained from parental questionnaires.

The limited evidence on road traffic noise and obesity presented in the current review is strengthened by these two longitudinal studies from Denmark, although both studies suffer from the potentially serious flaw of self-reported anthropometric data at follow-up. In the current review, the evidence for an association between road traffic noise and obesity was based on cross-sectional studies only and was rated as “very low”. After taking into account possible downgrading for the of risk of bias due to the self-reported outcome information, and upgrading because of positive exposure-response relationships, a more relevant overall grading would be “moderate”. The same reasoning could be relevant for railway noise and obesity markers.

12.1.5 *Blood pressure in children*

We evaluated eight studies on the impact of noise on children’s systolic and diastolic blood pressure. Within the studies the impact of transportation noise (the impact of air- and road traffic noise specifically) were investigated. After combining the results of studies on the impact of an increase in road traffic noise, we found small, but non-significant associations with elevated of the blood pressure. Unfortunately, we were not able to combine the results of the studies that have investigated the impact of aircraft noise.

12.1.5.1 Comparison with the results of other meta-analyses

More recently, Dzhambov and Dimitrova [558] presented the results of a systematic review dealing with the association between road traffic noise exposure and children’s blood pressure. In their review, they evaluated 13 studies, including the individual study quality. From the 13 studies that were under review, 37 effect estimates were derived, and combined in a meta-analysis. As in the current meta-analysis, Dzhambov and Dimitrova [558] found small but non-significant elevations of blood pressure in relation to road traffic noise exposure. The blood pressure elevations reported in relation to road traffic noise by Dzhambov and Dimitrova [558], differed from those reported in the current review. This is probably explained by the fact that Dzhambov and Dimitrova [558] included the results of several studies [559-561] that were not considered nor included in the current meta-analysis for different reasons.

Sughis et al. [559] (one of the studies also included by Dzhambov and Dimitrova) investigated the association between particulate air pollution and blood pressure in children, by comparing two groups of children, consisting of 73 children attending a school in a high-polluted area, and 93 children attending a school in a low-polluted area. They also made also noise measurements at both schools. Unfortunately, the noise meters that were used by Sughis et al. [559], did allow them to assess time-weighted average noise levels; the authors were only able to present minimum and maximum noise values.

The same is more or less true of the study by Lepore et al. [560], who measured the blood pressure of 95 children attending a school in a noisy area, and 94 children attending a school in a relatively quiet area in the city of Pune (India). They ascertained the level of noise exposure by means of noise measurements at both the schools. Unfortunately, for each school they were only able to report a peak level.

The results of a study carried out by Belojević et al. [561] became available after we have carried out the search for the current systematic review; as a consequence they were not included.

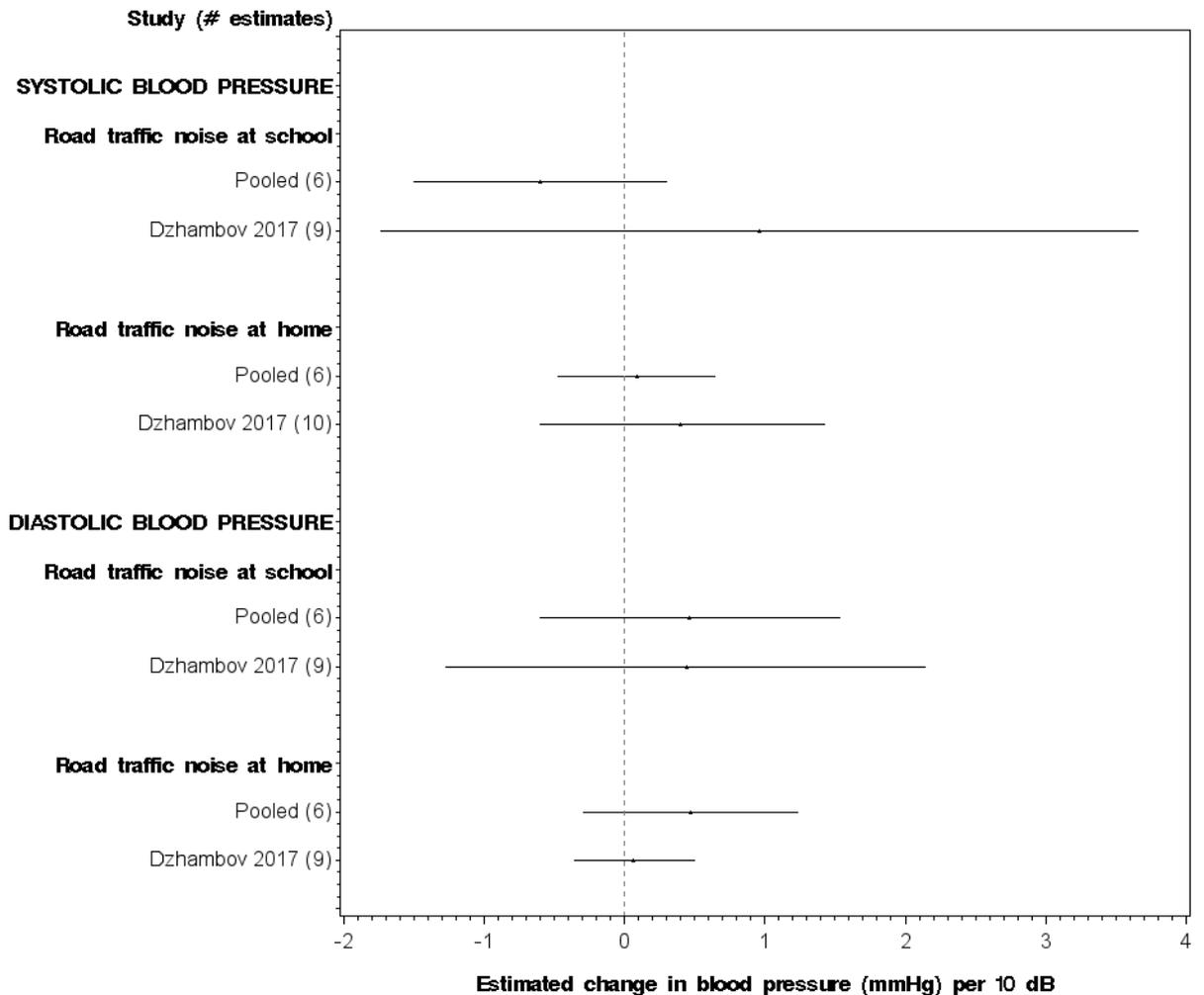


Figure 12.4: Association between road traffic noise and blood pressure in children, reported by the current meta-analysis and a meta-analysis carried out by Dzhambov and Dimitrova [558]. The dotted vertical line corresponds to no effect of road traffic noise exposure. The dots correspond to the estimated change in systolic or diastolic blood pressure (mmHg) per 10 dB and its 95%CI.

12.1.5.2 Comparison with results of new studies

Our SCOPUS search revealed only one study, carried out by Belojević et al. [561], who cross-sectionally measured the blood pressure of 467 children and adolescents (response rate 49%) aged 11 - 15 years, attending six schools in Belgrade. They ascertained exposure to noise by means of noise measurements carried out in the middle of the street where the participating children lived, and in front of the school they attended. From the acquired noise data, the researchers derived a composite evening-night L_{eq} value for each street and a composite daytime L_{eq} for each school. Noise levels at school ranged from 55 to 72 dB (L_{eq} value for the day-period); the noise levels in the streets where the children lived, ranged from 52 to 84 dB (L_{eq} value for the day-night period). After adjustment for age, gender, and BMI, it appeared that

noise exposure at school was significantly associated with an increase in systolic blood pressure: an increase of 0.45 (95%CI: 0.26 – 0.63) mmHg per 1 dB was found. This is a large effect in comparison with the results of the current meta-analysis. The current review found that noise exposure at home was related to non-significant decreases in both systolic and diastolic blood pressure.

12.2 Threshold and shape of a possible exposure-response relationship

It is unclear from the evidence assessed in the current review whether thresholds exist for the effect of environmental noise exposure on cardiovascular and/or metabolic outcomes. The meta-analyses that were presented in the current systematic review were confined to the estimation of RRs per 10 dB increase in noise level, assuming a constant RR per unit of noise. This suggests an exponential relationship between noise exposure and the prevalence (or incidence) of the effect concerned. A major reason for the use of an RR per 10 dB is that participating studies in our review used different “reference” groups. For example, some studies considered persons exposed to noise levels of less than 60 dB as the reference group, others persons exposed to noise levels of less than 55 dB as reference group, and still others persons exposed to noise levels of less than 45 dB. In setting these levels, researchers implicitly assumed that no effects of noise would occur below these levels.

However, we realize that the choice of a certain reference category may be the result of the difficulty of assessing low noise levels. Because more recent studies have been able to assess noise levels down to 55 dB or lower, Babisch [28] noted in his recent meta-analysis that the starting point for the relationship between traffic noise exposure and IHD is decreasing. For example, in his meta-analysis of the impact of road traffic noise exposure on myocardial infarction, Babisch [37, 133] implicitly assumed that no effects of road traffic noise exposure would occur below levels of 60 dB(A) ($L_{Aeq\ 6-22hrs}$), whereas in his recent meta-analysis reported in 2014, Babisch [28] found a linear relationship between transportation noise and IHD and suggested a starting point (not a threshold) of approximately 52 dB (L_{DEN}). In their meta-analysis, Vienneau et al. [44] found a starting point for their relationship between traffic noise exposure and IHD that was even lower: 50 dB (L_{DEN}).

Of all the associations that were investigated in the current review, we think that the relationship between road traffic noise and the incidence of IHD is the most robust. After combining the results of three cohort studies and four case-control studies, we found an RR of 1.08 (95%CI: 1.01 – 1.15) per 10 dB for the association between road traffic noise and the incidence of IHD within the range of approximately 42 – 80 dB L_{DEN} . Because the quality of the evidence from the relevant studies was rated as “high”, we decided it was valid to explore the shape of this relationship. Figure 12.5 shows the result. Through the eyelashes one can see that the risk of IHD seems to increase continuously for road traffic noise levels from about 50 dB (L_{DEN}). This is consistent with the findings of Vienneau et al. [44]. In 1999, the WHO guidelines stated: “epidemiological studies show that cardiovascular effects occur after

long-term exposure to noise with $L_{Aeq24hr}$ values of 65-70 dB". In the WHO Night-noise guidelines, published in 2009, a general threshold of 55 dB (L_{night}) was recommended for protection of cardiovascular disease."

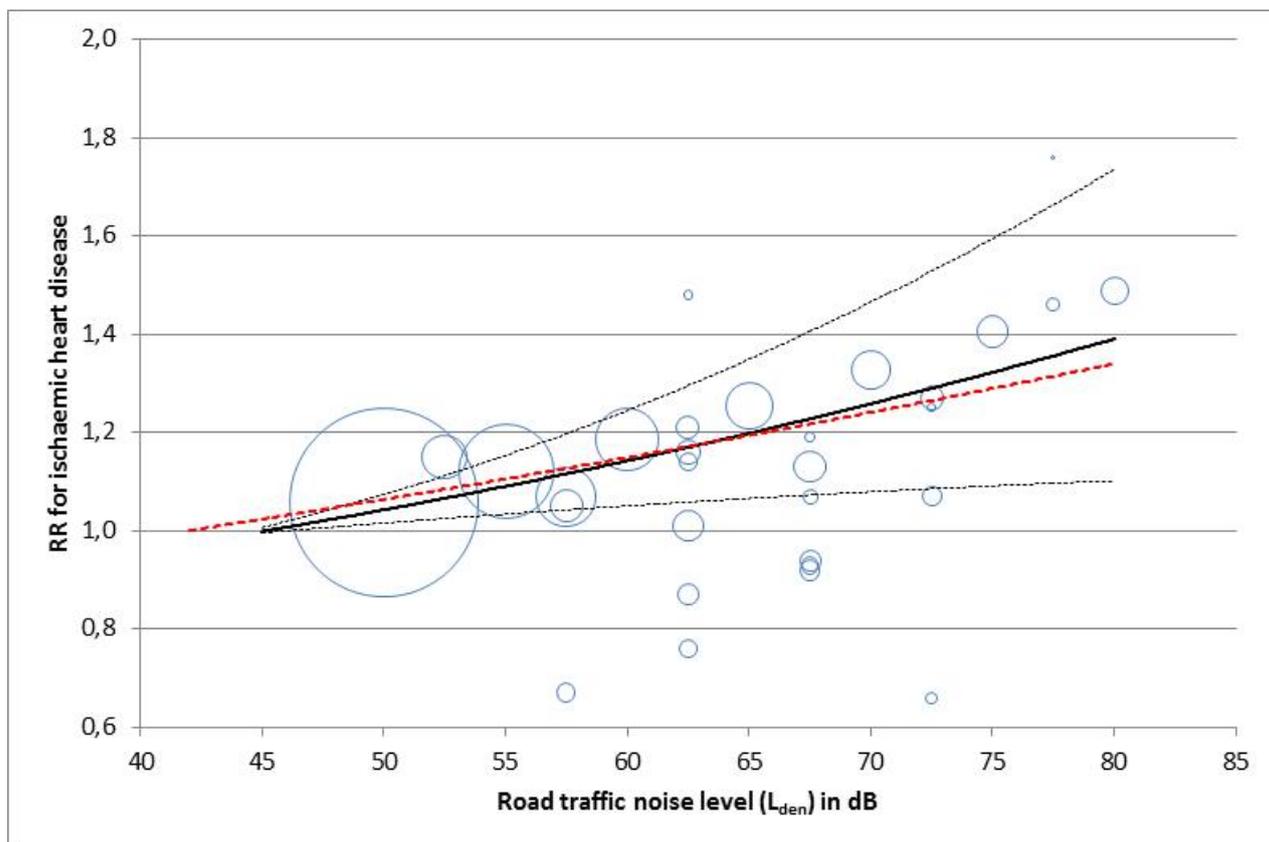


Figure 12.5: Pooled exposure-response association between road traffic noise exposure (L_{DEN}) and RR of IHD (p for non-linearity = 0.85). Road traffic noise was modelled with restricted cubic splines with 3 knots at fixed percentiles (10th, 50th, and 90th percentile) of the aggregated exposure in a random model, applying Orsini [562, 563]. The dashed black lines represent the 95% CIs for the spline model. Persons exposed to road traffic noise levels of 45 dB (L_{DEN}) served as the reference group. The open circles indicate the observed RR of IHD in the individual studies at different levels of exposure; the size of the bubbles is proportional to the precision (inverse of variance) of the RR for IHD. The red dashed line represents the linear relationship ($RR = 1.08$ per 10 dB) derived by combining the RR per 10 dB for the different studies; for this line, a level of 42 dB (L_{DEN}) was used as starting point.

12.3 Source-specific estimates of the RR per 10 dB vs overall estimates of the RR per 10 dB

The current review presented, for every health outcome, source-specific estimates of the RR per 10 dB. This was specifically done at the request of WHO for deriving their guidelines. However, Tables 11.1 (the prevalence of hypertension) and 11.2 (the incidence of IHD) showed that there was not a lot of difference between the source-specific estimates (RR per 10 dB). In other words, the reported effect size for the association between e.g. road traffic noise and the prevalence of

hypertension did not differ substantially from the reported effect size for the association between aircraft noise exposure and the prevalence of hypertension, or the reported effect size for the association between rail traffic noise exposure and the prevalence of hypertension. This implies that we could present one RR per 10 dB for the impact of noise in general on the prevalence of hypertension. The advantage is that the power of such an "overall" estimate of the RR per 10 dB is higher. Furthermore, an "overall" estimate of the RR per 10 dB can be more easily applied in health impact assessments, in order to estimate the number of people that are affected by noise.

Until now, we have not often, for example estimated the number of people that suffers from hypertension due to rail traffic noise because a source-specific exposure-response relationship was not available. As an alternative, we sometimes applied the relationship that described the association between road traffic noise and hypertension. As a result of the current review, we could now use the RR per 10 dB derived specifically for the association between rail traffic noise and hypertension. However, this association is based on the results of only five cross-sectional studies, and is statistically not significant (RR = 1.05 (95%CI: 0.88 – 1.26) per 10 dB) if we would have one "overall" relationship for the association between transportation noise exposure and the prevalence of hypertension based on the results of 32 studies, this would constitute a far more robust measure.

The problem is that some studies investigate the impact of several noise sources and it is not clear which of these sources is the main object of investigation. For example the HYENA study aimed to investigate the impact of both air and road traffic noise, and the study population was selected accordingly (taking into account noise from both air –and road traffic). The AWACS-1 study researchers used data from a questionnaire administered in 2009 by the Municipal Health Service (GGD) among 9365 persons living in Zuid-Limburg. To investigate the impact of noise on several self-reported cardiovascular end-points they linked modelled noise levels from air, road, and rail traffic with the addresses of the participants. The RoadSide, BBT, and Lerum studies all aimed to investigate the impact of both road and rail traffic noise. If we regard exposure to noise from air traffic as the main source of exposure in the HYENA and the AWACS studies, and if we regard road traffic as the main source of exposure in the Lerum and RoadSide studies, and the BBT-study, we would estimate an overall RR of 1.06 (95%CI: 1.02 – 1.10) per 10 dB for the association between transportation noise exposure and the prevalence of hypertension.

The same reasoning can be followed for IHD. In case the results of all seven studies investigating the association between aircraft, road or rail traffic noise and the prevalence of IHD are combined, an RR of 1.20 (95%CI: 1.03 – 1.39) per 10 dB is estimated.

13 Conclusions and recommendations

13.1 Conclusions

As indicated in Section 1.1 dealing with “possible ways in which noise exposure affects the cardiovascular system” (which is a summary of the background document “Biological plausibility”), it is very plausible that noise exposure has an effect on our cardiovascular and metabolic systems. The main mechanism explaining the fact that noise affects human health is the hypothesis that noise can act as a stressor. In addition, it is assumed that the effects of noise exposure on the cardiovascular and metabolic systems might be the consequence of a decrease in sleep quality due to noise exposure during the night, or the effect of co-exposure to air pollution.

13.1.1 Hypertension

For the purpose of this review, we evaluated 37 studies that investigated the impact of noise from air, road, and rail traffic on the risk of hypertension. We found indications that noise from air, road, and rail traffic increases the risk of hypertension.

We observed the strongest associations in the cross-sectional studies, which formed the largest part ($n = 38$) of the available evidence. Only in relation to road traffic noise did we find a statistically significant increase in the risk of hypertension: after aggregating the results of 26 cross-sectional studies (comprising 154,398 residents, including 18,957 cases), we derived an RR of 1.05 (95%CI: 1.02 – 1.08) per 10 dB (L_{DEN}) for the association between road traffic noise and the *prevalence* of hypertension. The results of the current meta-analysis on the association between noise from road and aircraft noise were similar to the results of other recent meta-analyses.

Despite the fact that most studies were able to adjust for important confounders, and were able to ascertain individual exposure levels, we rated the quality of the evidence from the cross-sectional studies mainly as “very low”. This is among other reasons, because the response rate in many of the evaluated studies was less than 60%. Furthermore, most studies ascertained hypertension as part of a questionnaire or interview.

In the two evaluated cohort studies that investigated the impact of traffic noise on hypertension, we found no increased risks of hypertension related to traffic noise exposure. This is confirmed by a recent meta-analysis, including the individual data from six cohort studies on the association between road traffic noise and the incidence of hypertension. The reason for the apparent discrepancy in the findings between the cross-sectional and cohort studies, is unclear.

Overall, we consider the quality of the evidence *supporting an association between traffic noise exposure and hypertension* as “very low”, indicating that any estimate of effect is very uncertain.

13.1.2 *Ischaemic heart disease*

We evaluated 22 studies that investigated the impact of noise from air, road, and rail traffic on the risk of IHD. The majority (n = 11) were of cross-sectional design.

The studies that investigated the impact of *air traffic* found indications of an increased risk of IHD. Aircraft noise was associated with the prevalence of IHD, the incidence of IHD, and mortality due to IHD. Only the association between aircraft noise and the *incidence* of IHD was statistically significant. We estimated an RR of 1.09 (95%CI: 1.04 – 1.15) per 10 dB after aggregating the results of two studies comprising of 9,619,082 participants, including 158,977 *incident* cases of IHD. Since most studies on the impact of aircraft noise were of ecological and cross-sectional design, the quality of the evidence from these studies, was mostly rated as “very low”. However, the results of the current review are consistent with the results of new longitudinal studies that were not yet included, which reported positive associations between aircraft noise and mortality due to IHD.

Overall, we consider the quality of the evidence supporting an association between *air traffic* noise and IHD as “low”, indicating that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

We found evidence that noise from road traffic is associated with an increased risk of IHD. An increase in road traffic noise was associated with significant increases in the prevalence of IHD, and the incidence of IHD. The relationship between noise from road traffic noise and the *incidence* of IHD was the most robust: After combining the results of three cohort studies and four case-control studies (comprising 67,224 participants, including 7,033 *incident* cases of IHD), we found an RR of 1.08 (95%CI: 1.01 – 1.15) per 10 dB (L_{DEN}) for the association between road traffic noise and the *incidence* of IHD within the range of approximately 40 – 80 dB L_{DEN} . This means that if road traffic noise levels increase from 40 to 80 dB (L_{DEN}), the RR = 1.36. We rated the quality of the evidence that comes from these studies as “high”. Supporting evidence came from studies on the association between road traffic noise and the prevalence of IHD. However, we rated the quality of the evidence from these studies as “low”. The results of the current review are strengthened by the results of several recently published longitudinal studies. A visualization of the shape of this association indicated that the risk of IHD increases continuously for road traffic noise levels from about 50 dB (L_{DEN}). This is consistent with the findings of another recent meta-analysis on the association between road traffic noise and IHD.

Overall, taking into account all the evidence from road traffic noise on IHD, we rate the quality of the evidence supporting an association between road traffic noise and IHD to be “moderate”, indicating that further research is likely to have an impact on our confidence in the estimate of effect and may change the estimate. However, for road traffic noise and the incidence of IHD, we rated the quality of the evidence as “high”.

Compared with noise from road and air traffic, we found only a few studies that investigated the impact of noise from *rail traffic*. These had a cross-sectional design. After aggregating the results of the studies on the association between *rail traffic* noise and the *prevalence* of IHD, we found a non-significant RR of 1.18 per 10 dB (L_{DEN}).

Overall, we consider the quality of the evidence *supporting an association between rail traffic noise exposure and IHD as “very low”, indicating that any estimate of effect is very uncertain.*

13.1.3 *Stroke*

Compared with the number of studies on the impact of noise on hypertension and IHD, relatively few studies were available that investigated the impact on stroke (n = 9).

According to the results of the ecological and cross-sectional studies an increase in aircraft noise was associated with an increase in the prevalence and the incidence of stroke. Neither of these associations was statistically significant.

The observations found for the prevalence and incidence of stroke were supported by the ecological studies on the association between air traffic noise and *mortality* due to stroke.

No association between air traffic noise exposure and mortality due to stroke was observed in the evaluated cohort study. This is consistent with the results of new longitudinal studies, which showed no clear indications of an association between aircraft noise and mortality due to stroke.

The results of the studies that investigated the impact of road traffic were not consistent. Only for the association between road traffic noise and the *incidence* of stroke did we find a statistically significant RR of 1.14 (95%CI: 1.03 – 1.25) per 10 dB (L_{DEN}). This result was based on one cohort study, comprising 51,485 participants, including 1,881 incident cases of stroke.

In the evaluated cross-sectional and ecological studies on the association between road traffic noise and the *prevalence* of stroke or mortality due to stroke, no increased risks of stroke due to road traffic noise were observed. This was not consistent with the results of recently published longitudinal studies, which showed that an increase in road traffic noise was statistically significantly associated with an increase in mortality due to stroke.

As part of the current review, only one cross-sectional study was evaluated, which investigated the association between rail traffic noise and the prevalence of stroke.

Overall, we consider the quality of the evidence *supporting an association between traffic noise and stroke as “low”. This indicates that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.*

13.1.4 *Diabetes*

For the current review, we were able to evaluate seven studies that investigated the association between environmental noise and the risk of diabetes. Four studies investigated the possible impact of transportation (air, road, rail traffic) noise.

We found two studies that investigated the impact of *air* traffic noise on diabetes occurrence. In a cross-sectional study, investigating the association between air traffic noise and the *prevalence* of diabetes, there was a non-significant RR of 1.01 per 10 dB (L_{DEN}). In the evaluated cohort study on the association between air traffic noise and the *incidence* of diabetes, no increased risk of diabetes due to air traffic noise was observed.

We found indications that noise from *road traffic* increases the risk of diabetes. The two evaluated cross-sectional studies showed an increasing but positive non-significant trend of the *prevalence* of diabetes with road traffic noise exposure. In the evaluated cohort study, an increase in road traffic noise was associated with a statistically significant increase in the incidence of diabetes. We estimated an RR of 1.08 (95%CI: 1.02 – 1.14) per 10 dB (L_{DEN}) across a noise range of approximately 50 – 70 dB.

Remarkably, an increase in *rail* traffic noise was associated with a decrease in the risk of diabetes in one cross-sectional study while a cohort study found no statistically significant association.

Overall, we consider the quality of the evidence *supporting an association between traffic noise and diabetes as “low”*. This indicates that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

13.1.5 *Obesity*

The number of evaluated studies that investigated the impact of noise on markers of obesity was limited to four: one cohort study and three cross-sectional studies. All the studies showed that an increase in traffic noise was associated with an increase in the risk of obesity, although, according to one study, this was present only in certain subgroups. An increase in aircraft noise of 10 dB (L_{DEN}) was associated with a significant increase in waist circumference of 3.46 (95%CI: 2.13-4.77) cm during 8 to 10 years of follow-up. The evidence of traffic noise affecting obesity markers is strengthened by the results of two recent longitudinal studies. Unfortunately, we were not able to include the results of these studies in the current review

Overall, we consider the quality of the evidence *supporting an association between traffic noise and markers of obesity, respectively, as “low”*. This indicates that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

13.1.6 *Children's blood pressure*

We evaluated eight studies on the impact of noise on children's blood pressure. Seven studies were cross-sectional. One study reported both the results of cross-sectional and follow-up analyses. With the exception of the association between road traffic noise at school and systolic blood

pressure, we observed positive but non-significant associations between exposure to road traffic noise and blood pressure. No combined exposure-response estimate could be computed from the studies on the impact of aircraft noise since, no quantitative results were provided in one of the studies.

Overall, we consider the quality of the evidence *supporting an association between traffic noise and blood pressure in children, as “very low”, indicating that any estimate of effect is very uncertain.*

13.1.7 *Wind turbine noise*

Overall, we evaluated only three cross-sectional studies that investigated the impact of noise from wind turbines on the cardiovascular and metabolic systems. Important limitations of these studies were the low response rates (two studies had a response rate of less than 60%) and, the fact that in most studies the cardiovascular or metabolic endpoint was ascertained by a questionnaire or interview.

In these studies, we observed that an increase in wind turbine noise was associated with non-significant increases in self-reported hypertension, and non-significant decreases in self-reported cardiovascular disease. For self-reported diabetes, the results were inconsistent.

Overall, we consider the quality of the evidence *supporting an association between exposure from wind turbine noise and deteriorations of the cardiovascular or metabolic system as “very low”, indicating that any estimate of effect is very uncertain.*

13.1.8 *Overall conclusions*

The current review shows that, despite the fact that a large number of studies have investigated the impact of noise on the cardiovascular system applying the GRADE, the quality of the evidence is often rated as relatively low. This does not mean that exposure to noise has no effect on the cardiovascular system, but encourages further research to improve the quality of the evidence. After all, there is a strong biological plausibility that noise affects human health. Furthermore, in a large number of the studies that were evaluated in the current review, we observed statistically significant effects of noise on the cardiovascular system. The most robust were the effects of road traffic noise on IHD. On the basis of the results of cohort and case-control studies, we found high quality evidence that exposure to road traffic noise associated with increased incidence of IHD.

This review also addressed the possible impact of noise on the metabolic system. In comparison with the studies on the impact of noise on the cardiovascular system, the number of available studies was rather limited. The results of these studies were not always consistent. In addition, the quality of the evidence was rather low. It is therefore, at this moment, too early to draw definite conclusions with regard to the impact of noise on the metabolic system.

13.2 Identification of knowledge gaps: research needs

On the basis of the results of the current review, we identified several gaps in research. The most urgent are mentioned below.

13.2.1 *More high-quality studies are needed*

In order to improve the quality of the existing evidence, we recommend that more studies with a cohort or case-control design, specifically designed to investigate the impacts of transportation noise exposure, should be set up and carried out.

The current review shows that, despite the fact that a large number of studies are available that have investigated the impact of noise on the cardiovascular system, the quality of the evidence is relatively low. This does *not* mean that exposure to noise has no effect on the cardiovascular system; it means that, at this moment, not enough studies of good quality are available that investigate the impact of noise on the cardiovascular system. The plausibility of an association calls for further efforts with improved research. In order to improve the quality of the existing evidence, more studies with a cohort or case-control design are needed.

A good start to reach this goal, has now been made by groups of researchers that are using data gathered mostly in cohort studies that were not originally designed to investigate the impact of noise. This enables them to answer their research question(s) relatively rapidly and inexpensively. However, a problem is that the researchers have little or no control over the data have been collected, and how: the selection of the population to study, which data to collect, the quality of data gathered, and how variables were measured and recorded were all predetermined. The data are sometimes collected from a population that is not ideal for investigating the impact of noise on health. To overcome the limitations of secondary analyses on cohort data, we recommend that more studies with a cohort or case-control design, specifically designed to investigate the impacts of transportation noise exposure, should be set up and carried out.

13.2.2 *More research on wind turbines and rail traffic is needed*

In accordance with the recommendations of the Ministerial Conference of Parma in 2010, this review also included studies investigating the impacts of noise from rail traffic noise and noise from wind turbines. Especially for wind turbine noise, the number of studies is very limited. In order to improve the quality of the existing evidence, we recommend that more well-designed studies on health effects in relation to exposure to noise from wind turbines and/or rail traffic are set up and carried out.

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Appendix I. Applied search profiles

In order to identify "Observational studies such as ecological studies, cross-sectional studies, case control studies, cohort studies involving the association between aircraft and/or rail traffic noise exposure and hypertension and/or high blood pressure, and/or ischemic heart disease (including angina pectoris and/or myocardial infarction) in adults published from 2000 until October 2014 with no language restriction", the following search profiles were applied:

Database:

MEDLINE 1950 to present, MEDLINE In-Process & Other Non-Indexed Citations 20141021

-
- 0 ((rail* or aircraft or airport* or air traffic*) adj5 noise).tw. (504)
 - 1 Aircraft/ or Airports/ or Railroads/ (9486)
 - 2 *Transportation/ (3419)
 - 3 (rail* or aircraft or airport* or air traffic).tw. (11558)
 - 4 *Noise/ (10029)
 - 5 Noise, transportation/ (1017)
 - 6 exp Blood pressure/ (254113)
 - 7 exp Hypertension/ (217361)
 - 8 Myocardial ischemia/ (33403)
 - 9 exp Cardiovascular diseases/ or exp Vascular diseases/ or exp Heart diseases/ (1944605)
 - 10 (hypertension or blood pressure).tw. (445550)
 - 11 (isch?emic heart disease* or coronary heart disease* or angina pectoris or myocard* infarct* or cardiovascular disease* or heart disease*).tw. (368878)
 - 12 (1 or 2 or (3 and 4)) and (1 or 5 or 6) (860)
 - 13 and (7 or 8 or 9 or 10 or 11 or 12) (119)
 - 14 not child*.ti. (112)
 - 15 limit 15 to yr=2000-current (83)

Scopus, 20141022

((TITLE-ABS-KEY((rail* OR aircraft OR airport* OR air-traffic*) W/5 noise)) AND (TITLE-ABS-KEY(hypertension OR blood-pressure OR ischemic-heart-disease* OR coronary-heart-disease* OR angina-pectoris OR myocard*-infarct* OR cardiovascular-disease* OR heart-disease*))) AND PUBYEAR > 1999) AND NOT (TITLE(child*))

In order to identify "Observational studies such as ecological studies, cross-sectional studies, case-control studies, cohort studies involving the association between aircraft and/or rail traffic and/or road traffic noise exposure and stroke and/or diabetes type II, and/or obesity in adults, published until October 2014 with no language restriction", the following search profiles were applied:

Database:

Medline 20141023 MEDLINE 1950 to present, MEDLINE In-Process & Other Non-Indexed Citations

Search Strategy:

-
- 1 ((rail* or aircraft or airport* or road* or traffic* or automobile* or vehicle*) adj5 noise).tw. (1188)
 - 2 exp *Transportation/ (35715)
 - 3 Aircraft/ or Airports/ or Railroads/ or Motor Vehicles/ (12387)
 - 4 *Noise/ (10039)
 - 5 Noise, transportation/ (1023)
 - 6 (1 or 2 or 3) and (1 or 4 or 5) (1774)
 - 7 exp Cerebrovascular disorders/ (290152)
 - 8 exp Diabetes Mellitus/ (328383)
 - 9 exp Obesity/ or exp Overweight/ or exp Body Mass Index/ (208810)
 - 10 (stroke or cerebrovascular* or cva or brain vascular accident* or brain vascular disorder*).tw. (187910)
 - 11 (diabetes or obesit* or overweight or bmi or body mass index).tw. (556663)
 - 12 7 or 8 or 9 or 10 or 11 (1065975)
 - 13 6 and 12 (54)
 - 14 13 not child*.ti. (51)
 - 15 limit 14 to yr=2000-current (47)

Scopus 20141023

((TITLE-ABS-KEY((rail* OR aircraft OR airport* OR road* OR traffic* OR automobile* OR vehicle*) W/1 noise)) AND (TITLE-ABS-KEY(stroke OR cerebrovascular OR cva OR brain-vascular OR diabetes OR obesit* OR overweight OR bmi OR body-mass-index)) AND PUBYEAR > 1999) AND NOT (TITLE(child*))

In order to identify "Observational studies such as ecological studies, cross-sectional studies, case control studies, cohort studies involving the association between road traffic noise exposure and hypertension and/or high blood pressure published from 2010 until October 2014 with no language restriction", the following search profiles were applied:

Database:

Medline 20141017 MEDLINE 1950 to present, MEDLINE In-Process & Other Non-Indexed Citations

Search Strategy:

-
- 1 ((road* or traffic* or automobile* or vehicle* or motor cycle* or motorcycle* or transport*) adj5 noise).tw. (993)
 - 2 exp *Transportation/ (35698)
 - 3 Motor Vehicles/ (2962)
 - 4 *Noise/ (10029)
 - 5 Noise, transportation/ (1017)
 - 6 (1 or 2 or 3) and (1 or 4 or 5) (1714)
 - 7 exp Blood pressure/ (254113)
 - 8 exp Hypertension/ (217361)
 - 9 (blood pressure or hypertension).tw. (445404)
 - 10 6 and (7 or 8 or 9) (134)
 - 11 10 not child*.ti. (120)
 - 12 limit 11 to yr=2010-current (46)

PubMed 20141024

((traffic*[ti] OR road*[ti] OR automobile*[ti] OR vehicle*[ti] OR motorcycle*[ti] OR transport*[ti]) AND noise[ti])

Scopus 20141024

(TITLE-ABS-KEY((rail* OR aircraft OR airport* OR road* OR traffic* OR automobile* OR vehicle*) W/1 noise)) AND (TITLE-ABS-KEY(hypertension OR blood-pressure)) AND PUBYEAR > 2009 AND NOT TITLE(child*)

In order to identify "Observational studies such as ecological studies, cross-sectional studies, case-control studies, cohort studies involving the association between road, rail and air traffic noise exposure and blood pressure in children published until October 2014 without any language restriction", the following search profiles were applied:

Database:

Medline 20141017 MEDLINE 1950 to present, MEDLINE In-Process & Other Non-Indexed Citations

Search Strategy:

-
- 1 ((rail* or aircraft or airport* or road* or traffic or automobile* or vehicle*) adj5 noise).tw. (1185)
 - 2 exp *Transportation/ (35698)
 - 3 Aircraft/ or Airports/ or Railroads/ or Motor Vehicles/ (12379)
 - 4 *Noise/ (10029)
 - 5 Noise, transportation/ (1017)
 - 6 (1 or 2 or 3) and (1 or 4 or 5) (1770)
 - 7 exp Blood pressure/ (254113)
 - 8 exp Hypertension/ (217361)
 - 9 (blood pressure or hypertension).tw. (445404)
 - 10 6 and (7 or 8 or 9) (144)
 - 11 10 and (child* or infant* or adolescent*).mp. (43)

Scopus 20141024

TITLE-ABS-KEY((rail* OR aircraft OR airport* OR road* OR traffic* OR automobile* OR vehicle*) W/1 noise) AND TITLE-ABS-KEY(blood-pressure OR hypertension) AND TITLE-ABS-KEY(child* OR infant* OR adolescent*)

In order to identify "Observational studies such as ecological studies, cross-sectional studies, case-control studies, cohort studies involving the association between audible noise (greater than 20 Hz) and infrasound and low-frequency noise (less than 20 Hz) from wind turbines or wind farms and blood pressure and/or cardiovascular disease published from October 2012 until October 2014 without any language restriction", the following search profiles were applied:

Database:

PubMed 20141024

(((((wind turbine* OR wind farm*[Title/Abstract]))) AND ((noise[MeSH Terms] OR noise[Title/Abstract]))) AND (((health*[Title/Abstract] OR blood pressure OR cardiovascular))
2012-current

Medline 20141027 MEDLINE 1950 to present, MEDLINE In-Process & Other Non-Indexed Citations

Search Strategy:

-
- 1 ((wind adj3 turbine*) or (wind adj3 farm*) or windturbine* or windfarm*).tw. (271)
 - 2 Wind/ (2794)
 - 3 Renewable energy/ (273)
 - 4 Power Plants/ (5234)
 - 5 Electric Power Supplies/ (4979)
 - 6 Energy-Generating Resources/ (1684)
 - 7 2 and (3 or 4 or 5 or 6) (183)
 - 8 1 or 7 (362)
 - 9 Noise/ or Sound/ (26842)
 - 10 (infrasound* or noise or low frequenc*).tw. (131959)
 - 11 (blood pressure or cardiovascular).tw. (474959)
 - 12 Blood Pressure/ (243394)
 - 13 Cardiovascular Physiological Phenomena/ or Cardiovascular Diseases/ or Cardiovascular System/ (129880)
 - 14 health*.ti. (532337)
 - 15 8 and (9 or 10) and (11 or 12 or 13 or 14) (19)
 - 16 limit 15 to yr=2012-current (14)

Scopus 20141027

TITLE-ABS-KEY((wind W/3 turbine*) OR windturbine* OR (wind W/3 farm*) OR windfarm*) AND TITLE-ABS-KEY(noise OR infrasound* OR low-frequenc*) AND (TITLE-ABS-KEY(blood-pressure OR cardiovascular*) OR TITLE(health*) OR KEY(health*)) AND PUBYEAR > 2011

Embase and SciSearch:

same search profile used as in Medline.

Appendix II. The conversion of different noise indicators to

L_{DEN}

Definitions

D = Day period

E = Evening period

N = Night period

L_D = Equivalent noise level during the day period

L_E = Equivalent noise level during the evening period

$L_{E, allowance} = L_E + 5 \text{ dB(A)}$

L_N = Equivalent noise level during the night period

$L_{N, allowance} = L_N + 5 \text{ dB(A)}$

$L_{DEN} = 10 \cdot \log(8/24 \cdot 10^{(L_D/10)} + 4/24 \cdot (L_{E, allowance}/10) + 8/24 \cdot 10^{(L_{N, allowance}/10)})$

$L_{24hrs} = 10 \cdot \log(8/24 \cdot 10^{(L_D/10)} + 4/24 \cdot (L_E/10) + 8/24 \cdot 10^{(L_N/10)})$

Formulas

Situation: road traffic noise

$L_{DEN} = L_{24hrs} + 1.4$

$L_{DEN} = L_{day} + 1.1$

Situation: air traffic noise

$L_{DEN} \sim L_{eq(4)}$

$L_{DEN} \sim L_{A24hrs}$

$L_{DEN} \sim \text{FBN}$

Appendix III. Summary of findings tables dealing with studies on the impact of noise on hypertension

Table III.1

Question	Does exposure to aircraft noise increase the risk of hypertension			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities (general population) located around airports in Europe and Japan			
Outcome	The prevalence of hypertension			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.05 (95%CI: 0.95 – 1.17) per 10 dB		
	Number of participants (# evaluated studies)	60,121 (9)		
	Number of cases	9,487		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	9 cross-sectional studies ^a	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^b	Downgrading
		Inconsistency	Serious ^c	Downgrading
		Indirectness	None ^d	No downgrading
		Imprecision	None ^e	No downgrading
		Publication bias	None ^f	No downgrading
	Factors increasing confidence	Strength of association	Small ^g	No upgrading
		Exposure-response gradient	Non-significant exposure-response gradient ^g	Upgrading
		Possible confounding	No serious bias ^h	Upgrading
Overall judgement of quality of evidence			16 (low)	

a) Since only cross-sectional studies were available, we started with a grading of "low" (2);

b) Methods used to select the population: In six studies, the participants were randomly selected, taking into account aircraft noise exposure; three studies were originally not designed to investigate the impact of aircraft noise exposure, but still participants were randomly selected. In six studies, participants were probably not aware of the fact that they participated in a study investigating the impact of noise; for three studies, this was unclear. For one study, it was likely that participants were aware of the fact that they participated in a study investigating the impact of noise. In six studies, response rates were below 60%; for two studies, the response rate was unclear and only in one study response rate was higher than 60%. c) Results across studies differed in magnitude and direction of effect estimates (see Figure 4.1). This was confirmed by the results of the heterogeneity analyses, demonstrating moderate heterogeneity ($I^2_{residual} = 72.1\%$); d) The studies assessed population, exposure, and outcome of interest; e) We considered the results to be precise, since the number of participants and the number of cases was large enough. The 95% confidence interval was sufficiently narrow; f) There was little reason to believe that there is major publication bias or small study bias (see also Figure 4.2). The Egger test did not provide evidence for small-study effects; g) Most studies found that the risk of hypertension increased when aircraft noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the

results of the evaluated studies, we found a non-significant effect size of 1.05 per 10 dB. The noise range of the studies under evaluation was 35-75 dB. This means that if air traffic noise level increases from 35 to 75 dB, the RR = 1.22. We found indications for an effect of exposure duration: The effect estimates turned out to be larger for the sample that lived for a longer period in the same house; h) We did not find evidence that suggests that possible residual confounders or biases would reduce our effect estimate.

Table III.2

Question	Does exposure to road traffic noise increase the risk of hypertension			
People	Adult population (men and women)			
Setting	Residential setting: people living several cities in Europe			
Outcome	The prevalence of hypertension			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	1.05 (95%CI: 1.02 – 1.08) per 10 dB*		
	Number of participants (# evaluated studies)	154,398 (26)		
	Number of cases	18,957		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	26 cross-sectional studies ^a	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^b	Downgrading
		Inconsistency	Serious ^c	Downgrading
		Indirectness	None ^d	No downgrading
		Imprecision	None ^e	No downgrading
		Publication bias	Small probability of publication bias ^f	Downgrading
	Factors increasing confidence	Strength of association	Small ^g	No upgrading
		Exposure-response gradient	Evidence of an exposure-response gradient ^g	Upgrading
		Possible confounding	No serious bias ^h	Upgrading
	Overall judgement of quality of evidence			1 (very low)

*) The estimate was based on 47 effect estimates; a) Since only cross-sectional studies were available, we started with a grading of "low" (2); b) In 12 studies, the participants were randomly selected taking into account exposure to road traffic noise; although the participants of these studies were randomly selected, 14 studies were originally not designed to investigate the impact of road traffic noise exposure; In 2 studies it was likely that participants were aware of the fact that they participated in a study investigating the impact of noise. In 8 studies, the participation rate was below 60%; for 16 studies, the participation rate was larger than 60%; c) Results across studies differed in magnitude and direction of effect estimates (see Figure 4.3). This was confirmed by the results of the heterogeneity analyses, demonstrating "moderate" heterogeneity ($I^2_{residual} = 52.4\%$); d) The evaluated studies assessed population, exposure, and outcome of interest; e) We considered the results to be precise: the number of participants and the number of cases

was large enough, and the 95%CI was sufficiently narrow; f) There was reason to believe that there is some publication bias or small study bias (result of the Egger test provided evidence for small-study effects) (see also Figure 4.4); g) Most studies found that the risk of hypertension increased when road traffic noise level increased (RR per 10 dB > 1). There was evidence of a significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a significant effect size of 1.05 per 10 dB. The noise range of the studies under evaluation was 20-85 dB. This means that if road traffic noise level increases from 20 to 85 dB, the RR = 1.34. We found indications for an effect of exposure duration: The effect estimates turned out to be larger for the sample that lived for a longer period in the same house
h) We did not find evidence to suggest that possible residual confounders or biases would reduce our effect estimate.

Table III.3

Question	Does exposure to rail traffic noise increase the risk of hypertension			
People	Adult population (men and women)			
Setting	Residential setting: people living in several cities in Europe			
Outcome	The prevalence of hypertension			
Summary of findings	RR per 10 dB increase in rail traffic noise level (L_{DEN})	1.05 (95%CI: 0.88 – 1.26) per 10 dB		
	Number of participants (# evaluated studies)	15,850 (5)		
	Number of cases	2,059		
			Rating	
			Adjustment to rating	
Quality assessment		Starting rating	5 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
	Factors increasing confidence	Publication bias	NA ^{e)}	No downgrading
		Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
		Overall judgement of quality of evidence		0 (Very low)

[#] Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) In three studies, the participants were randomly selected taking into account road- and/or rail traffic noise exposure; although the participants of these studies were randomly selected, two other studies were originally not designed to investigate the impact of (rail) traffic noise exposure; In one study there is a chance that the participants were aware that they took part in a study investigating the impact of noise; in two other

studies it is not very likely that participants were aware that they took part in a study investigating the impact of noise, since they were not originally set up to investigate the impact of noise. For one study, it was unclear whether participants were aware of taking part in a noise study. In two studies, response rates were below 60%; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 4.5). This was confirmed by the results of the heterogeneity analyses, demonstrating “moderate” heterogeneity ($I^2_{\text{residual}} = 57.6\%$); c) The evaluated studies assessed population, exposure, and outcome of interest; d) We considered the results to be precise: the number of cases was large enough, and the 95%CI was sufficiently narrow; e) Due to the low number of available effect estimates it was not possible to test for publication bias or small study bias; f) Most studies found that the risk of hypertension increased when rail traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.05 per 10 dB. The noise range of the studies under evaluation was 30-80 dB (L_{DEN}). This means that if rail traffic noise level increases from 30 to 80 dB, the RR = 1.28. g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table III.4

Question	Does exposure to noise from wind turbines increase the risk of hypertension			
People	Adult population (men and women)			
Setting	Residential setting: people in the neighbourhood of wind turbines in the Netherlands and Sweden			
Outcome	The prevalence of hypertension			
Summary of findings	RR per 10 dB increase in wind turbine noise level (SPL)	-		
	Number of participants (# evaluated studies)	1,830 (3)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	3 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Very serious ^{a)}	Downgrading
		Inconsistency	None ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Limited ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	Serious bias cannot be ruled out ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

[#] Since only cross-sectional studies were available, we started with a grading of “low” (2);

a) Methods used to select the population: response rates were in two of the three studies below 60%. The participants were randomly selected taking into account the distance between their house and a wind turbine (park); hypertension was in all cases measured by means of a questionnaire; b) Although results across studies differed in the magnitude of effect estimates (see Figure 4.6), all studies found a positive association between exposure to wind turbine noise and the prevalence of hypertension; c) The evaluated studies assessed population, exposure, and outcome of interest; d) We considered the

results to be imprecise: we assessed that the number of cases was less than 200, which is small. The 95% CIs of the separate studies contained values below 0.5 and above 2.0; e) Due to the low number of available effect estimates it was not possible to test for publication bias or small study bias; f) We decided not to carry out a meta-analysis; g) Although we did not find evidence to suggest that possible residual confounders or biases would reduce our effect estimate, the studies were unable to adjust for important confounders.

Table III.5

Question	Does exposure to aircraft noise increase the risk of hypertension			
People	Adult population (men and women, 35-56 yrs)			
Setting	Residential setting: people living around Stockholm Arlanda airport in Sweden			
Outcome	The incidence of hypertension			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.00 (0.77 – 1.30) per 10 dB		
	Number of participants (# studies)	4,712 (1)		
	Number of cases	1,346		
			Rating	Adjustment to rating
Quality assessment		Starting rating	1 cohort study [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Serious limitations ^{a)}	Downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	Non-residual misclassification of disease	No upgrading
	Overall judgement of quality of evidence			2 (Low) ^{g)}

#) Since a cohort study was available, we started with a grading of "high" (4); a) Participants were a (partly) random selection from people participating in the Stockholm Preventive Programm. Hypertension was ascertained by both a clinical examination and a questionnaire; although it was not possible to exactly assess the attrition rate, it was probably > 20%; b) Since only one study was evaluated, this criterion was not applied. c) The study assessed population, exposure, and outcome of interest; d) We considered the results to be precise: the sample was sufficiently large, and the 95%CI was sufficiently narrow; e) Since only one study was evaluated, we were not able to test for publication bias; f) We found a non-significant effect size of 1.00 per 10 dB. The noise range of the evaluated study was 45-65 dB (L_{DEN}); g) The overall judgement of the quality of evidence was graded as "moderate" (3). Since only one study was available, we downgraded the overall level of evidence to "low" (2).

Table III.6

Question	Does exposure to road traffic noise increase the risk of hypertension			
People	Adult population (men and women, 50-64 yrs)			
Setting	Residential setting: people living in Aarhus or Copenhagen (Denmark)			
Outcome	The incidence of hypertension			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	0.97 (0.90 – 1.05) per 10 dB		
	Number of participants (# studies)	43,635 (1)		
	Number of cases	3,145		
			Rating	Adjustment to rating
Quality assessment		Starting rating	1 cohort study [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Serious limitations ^{a)}	Downgrading
		Inconsistency	Na ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of exposure-response gradient ^{f)}	No upgrading
		Possible confounding	None	No upgrading
Overall judgement of quality of evidence			2 (low) ^{g)}	

#) Since a cohort study was available, we started with a grading of "high" (4); a) Participants were people participating in the DCH cohort. For this cohort, people living in Aarhus or Copenhagen, aged 50-64 years, and who were cancer-free, were randomly selected and invited. Attrition rate was > 20% after three years of follow-up time. Hypertension was ascertained by a questionnaire; b) Since only one study was evaluated, this criterion was not applied; c) The study assessed population, exposure, and outcome of interest; d) We considered the results to be precise: the sample was sufficiently large, and the 95%CI was sufficiently narrow; e) Since only one study was evaluated, we were not able to test for publication bias; f) We found a non-significant effect size of less than 1.00 per 10 dB; g) The overall judgement of the quality of evidence was graded "moderate" (3). Since only one study was available, we downgraded the overall level of evidence to "low" (2).

Table III.7

Question	Does exposure to rail traffic noise increase the risk of hypertension			
People	Adult population (men and women, 50-64 yrs)			
Setting	Residential setting: people living in Aarhus or Copenhagen (Denmark)			
Outcome	The incidence of hypertension			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	0.96 (0.88 – 1.04) per 10 dB		
	Number of participants (# studies)	7,249 (1)		
	Number of cases	3,145		
			Rating	Adjustment to rating
Quality assessment		Starting rating	1 cohort study [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Serious limitations ^{a)}	Downgrading
		Inconsistency	Na ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	None	No upgrading
Overall judgement of quality of evidence			2 (low) ^{g)}	

^{#)} Since a cohort study was available, we started with a grading of "high" (4); a) Participants were people participating in the DCH cohort. For this cohort, people living in Aarhus or Copenhagen, aged 50-64 years, and who were cancer-free, were randomly selected and invited. Attrition rate was > 20% after three years of follow-up time. Hypertension was ascertained by a questionnaire; b) Since only one study was evaluated, this criterion was not applied. c) The study assessed population, exposure, and outcome of interest; d) We considered the results to be precise: the sample was sufficiently large, and the 95%CI was sufficiently narrow; e) Since only one study was evaluated, we were not able to test for publication bias; f) We found a non-significant effect size of less than 1.00 per 10 dB; g) The overall judgement of the quality of evidence was graded as "moderate" (3). Since only one study was available, we downgraded the overall level of evidence to "low" (2).

Appendix IV. Summary of findings tables dealing with studies on the impact of noise on ischaemic heart disease

Table IV.1

Question	Does exposure to aircraft noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in Europe			
Outcome	The prevalence of IHD			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.07 (95%CI: 0.94 – 1.23)		
	Number of participants (# studies)	14,098 (2)		
	Number of cases	340		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	None ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
	Factors increasing confidence	Publication bias	NA ^{e)}	No downgrading
		Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
		Overall judgement of quality of evidence		

[#] Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) In both studies, the population was selected randomly. Response rates were in both studies below 60%. In the studies, IHD was ascertained by means of a questionnaire only; one of the studies was not able to adjust for smoking; b) Although results across studies differed in the magnitude of effect estimates, both studies found a positive association between exposure to aircraft noise and the prevalence of IHD (see Figure 5.1); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be precise: the number of cases was large enough, and the 95%CI was sufficiently narrow; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) Both studies found that the risk of IHD increased when air traffic noise level increased (RR per 10 dB > 1). There was

evidence of a non-significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.07 per 10 dB. The noise range of the studies under evaluation was 30-70 dB (L_{DEN}); g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table IV.2

Question	Does exposure to road traffic noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living several cities in Europe			
Outcome	The prevalence of IHD			
Summary of findings	RR per 10 dB increase in road traffic noise level (L _{DEN})	1.24 (95%CI: 1.08 – 1.42) per 10 dB		
	Number of participants (# studies)	25,682 (8)		
	Number of cases	1,614		
			Rating	Adjustment to rating
Quality assessment		Starting rating	8 cross-sectional studies [#]	2 (low) [#]
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Minor ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Large ^{f)}	Upgrading
		Exposure-response gradient	Evidence of an exposure-response gradient ^{f)}	Upgrading
		Possible confounding	Possible bias ^{g)}	No upgrading
	Overall judgement of quality of evidence			2 (low)

[#] Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) Methods used to select the population: In 6 studies, the participants were randomly selected taking into account road traffic noise exposure. The response rates were below 60%. In four of the eight studies. In three of the included studies, exposure was assessed by noise models incorporated in GIS. The noise models used were able to estimate the noise levels at individual level. In four of the studies, IHD was ascertained by means of a questionnaire only; b) Results across studies differed only in the magnitude of effect estimates (see Figure 5.2). This was confirmed by the results of the heterogeneity analyses, indicating "moderate" heterogeneity ($I^2_{\text{residual}} = 51.4\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be less

precise: the number of cases was large enough, and although the 95%CI contained values > 1.25, we considered the sample size as sufficiently large; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) All studies found that the risk of IHD increased when road traffic noise level increased (RR per 10 dB > 1). There was evidence of a significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a significant effect size of 1.24 per 10 dB. The noise range of the studies under evaluation was 30-80 dB. This means that if road traffic noise level increases from 30 to 80 dB, the RR = 2.93; g) Adjustment for smoking and indicators of air pollution were found to be important sources of heterogeneity.

Table IV.3

Question	Does exposure to rail traffic noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living several cities in Europe			
Outcome	The prevalence of IHD			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	1.18 (95%CI: 0.82 – 1.68) per 10 dB		
	Number of participants (# studies)	13,241 (4)		
	Number of cases	283		
			Rating	Adjustment to rating
Quality assessment		Starting rating	4 cross-sectional studies	2 (low) [#]
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Minor ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Large, but non-significant ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

[#] Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) Response rates were in two of the four studies below 60%. In all studies, IHD was

ascertained by means of a questionnaire only; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 5.7). This was confirmed by the results of the heterogeneity analyses, indicating “moderate” heterogeneity ($I^2_{\text{residual}} = 57.4\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be less precise: the 95%CI contained values > 1.25 ; however, we considered the sample size to be sufficiently large; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) Most studies found that the risk of IHD increased when rail traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.18 per 10 dB. The noise range of the studies under evaluation was 30-80 dB. This means that if rail traffic noise level increases from 30 to 80 dB, the RR = 2.29; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table IV.4

Question	Does exposure to aircraft noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in the UK and USA			
Outcome	The incidence (hospital admissions) of IHD			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.09 (95%CI: 1.04 – 1.15)		
	Number of participants (# studies)	9,619,082 (2)		
	Number of cases	158,977		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 ecological studies	1 (very low) [#]
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a significant exposure-response gradient ^{f)}	Upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			1 (very low)	

[#] Since only ecological studies were available, we started with a grading of “very low” (1);

a) Both ecological studies worked with a purposeful sample; so randomization and response rate is not an issue. Studies were not able to adjust for important confounders at individual level. Studies were unable to apply individual exposure estimates; b) Although

results across studies differed in the magnitude of effect estimates, both found a positive association between exposure to aircraft noise and the incidence of IHD (see Figure 5.1). This was confirmed by the results of the heterogeneity analyses, indicating “low” heterogeneity ($I^2_{\text{residual}} = 48.4\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be precise: the number of participants, as well as the number of cases were much larger than 200, and the 95%CI did not contain values below 0.75 or above 1.25; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) There was evidence of a significant exposure-response gradient: We found a significant effect size of 1.09 per 10 dB across a noise range of 45 to ~65 dB, this means that if the aircraft noise level increases from 45 to 65 dB, the RR = 1.19; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table IV.5

Question	Does exposure to road traffic noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living in Kaunas (Lithuania)			
Outcome	The incidence of IHD			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	1.12 (95%CI: 0.85 – 1.48) per 10 dB		
	Number of participants (# studies)	262,830 (1)		
	Number of cases	418		
			Rating	Adjustment to rating
Quality assessment		Starting rating	1 ecological study	1 (very low) [#]
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Na ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	Downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	Evidence of non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low) ^{h)}	

Since only one ecological study was available, we started with a grading of “very low” (1); a) Ecological studies worked with a purposeful sample; so randomization and response rate is not an issue. The study was not able to adjust for important confounders

at individual level, and was unable to apply individual exposure estimates; b) Only one study was evaluated, so inconsistency was not an issue; c) The study assessed population, exposure and outcome of interest; d) Although the 95%CI contained values above 1.25, we considered the results to be precise: the number of participants, as well as the number of cases were much larger than 200; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias. However, when combining this study with the other case-control and cohort studies that investigated the association between road traffic noise and the incidence of IHD, the number of estimates became large enough to test for publication bias. The funnel plot (Figure 5.6) was somewhat a-symmetric, but the Egger test provided only weak evidence for small-study effects; f) There was evidence of a non-significant exposure-response gradient: We found a non-significant effect size of 1.12 per 10 dB across a noise range of 55 - 75 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) The overall judgement of the quality of the evidence was "very low" (0). Downgrading of the overall level of evidence, because only one study was available, made no sense.

Table IV.6

Question	Does exposure to road traffic noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living several cities in Europe			
Outcome	The incidence of IHD			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	1.08 (95%CI: 1.01 – 1.15) per 10 dB		
	Number of participants (# studies)	67,224 (7)		
	Number of cases	7,033		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	3 cohort studies, 4 case-control studies	4 (high) [#]
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	Small probability of publication bias ^{e)}	Downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of an exposure-response gradient ^{f)}	Upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			4 (high)	

[#] Since cohort and case-control studies were available, we started with a grading of "high" (4); a) In all the studies, the participants were randomly selected. For six studies, the response rate was higher than 60%; in all the cohort studies, the loss to follow-up was less than 20%. Methods to assess exposure: In three of the included studies, exposure

was assessed by noise models incorporated in GIS. The noise models used were able to estimate the noise levels at individual level. In three other studies, noise exposure assessment was based on noise measurements in the direct living area of the participant; b) Results across studies differed only in the magnitude of effect estimates (see Figure 5.3). The results of the heterogeneity analyses demonstrated no clear evidence for heterogeneity; c) The study assessed population, exposure and outcome of interest; d) We considered the results as precise: The number of participants and cases were much larger than 200, and the 95%CI did not contain values below 0.75 or above 1.25; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias. However, when combining these studies with the ecological study that investigated the association between road traffic noise and the incidence of IHD, the number of estimates became large enough to test for publication bias. The funnel plot (Figure 5.6) was somewhat a-symmetric, but the Egger test provided only weak evidence for small-study effects; f) Most studies found that the risk of IHD increased when road traffic noise level increased (RR per 10 dB > 1). There was evidence of a significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a significant effect size of 1.08 per 10 dB. The noise range of the studies under evaluation was 40-80 dB. This means that if road traffic noise level increases from 40 to 80 dB, the RR = 1.36; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table IV.7

Question	Does exposure to aircraft noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in the UK and the Netherlands			
Outcome	Mortality due to IHD			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.04 (95%CI: 0.97 – 1.12)		
	Number of participants (# studies)	3,897,645 (2)		
	Number of cases	26,066		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	2 ecological studies	1 (very low) [#]
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

[#] Since only ecological studies were available, we started with a grading of "very low" (0);

a) Both ecological studies worked with a purposeful sample; so randomization and response rate is not an issue. Studies were not able to adjust for important confounders at

individual level. Studies were unable to apply individual exposure estimates; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 5.1). This was not confirmed by the results of the heterogeneity analyses, demonstrating “low” heterogeneity ($I^2_{\text{residual}} = 39.7\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be precise: Both the number of participants and cases were much larger than 200; the 95%CI did not contain values below 0.75 or above 1.25; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) One of the two studies found that the risk of IHD increased when air traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.04 per 10 dB. The noise range of the studies under evaluation was 40-65 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table IV.8

Question	Does exposure to aircraft noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting: people living in Switzerland			
Outcome	Mortality due to IHD			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.04 (95%CI: 0.98 – 1.11) per 10 dB		
	Number of participants (# studies)	4,580,311 (1)		
	Number of cases	15,532		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cohort study	4 (high) [#]
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Na ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			2 (low) ^{h)}

[#] Since a cohort study was available, we started with a grading of “high” (4); a) Aircraft noise levels were available at 100x100 m grids and the study suffered from a lack of

information about important life style factors; b) Only one study was evaluated, so inconsistency was not an issue (see Figure 5.1); c) The study assessed population, exposure and outcome of interest. d) We considered the results to be precise: Both the number of participants and cases were much larger than 200. The 95%CI did not contain values below 0.75 or above 1.25; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) There was evidence of a non-significant exposure-response gradient: We found a non-significant effect size of 1.04 per 10 dB across a noise range of 40 to 60 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of evidence as “moderate”. Since only one study was available, we downgraded the overall level of evidence to “low” (2).

Table IV.9

Question	Does exposure to road traffic noise increase the risk of IHD			
People	Adult population (men and women)			
Setting	Residential setting; people living several cities in Europe			
Outcome	Mortality due to IHD			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	1.05 (95%CI: 0.97 – 1.13) per 10 dB		
	Number of participants (# studies)	532,268 (3)		
	Number of cases	6,884		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cohort studies, 2 case-control studies	4 (high) [#]
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			3 (moderate)	

[#] Since cohort and case-control studies were available, we started with a grading of “high” (4); a) For the largest of the three studies, there was a possible risk of bias since there were worries with regard to exposure assessment, and one was not able to adjust for smoking; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 5.5). This was not confirmed by the heterogeneity analyses, demonstrating “low” heterogeneity ($I^2_{residual} = 34.9\%$); c) The study assessed population, exposure and outcome of interest; d) We considered the results to be precise: Both the number of participants and cases were much larger than 200. The 95%CI did not contain

values below 0.75 or above 1.25; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) Most studies found that the risk of IHD increased when road traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.05 per 10 dB. The noise range of the studies under evaluation was 42-70 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Appendix V. Summary of findings tables dealing with studies on the impact of noise on stroke

Table V.1

Question	Does exposure to aircraft noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in Europe and the Netherlands			
Outcome	The prevalence of stroke			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.02 (95%CI: 0.80 – 1.28)		
	Number of participants (# studies)	14,098 (2)		
	Number of cases	151		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) Response rates were in both studies below 60%. In the studies, stroke was ascertained by means of a questionnaire only; one of the two studies was not able to adjust for smoking; b)

Results between studies differed in the magnitude and direction of effect estimates (see Figure 6.1). This was not confirmed by the result of the heterogeneity analysis, demonstrating "low" heterogeneity ($I^2_{residual} = 0.0\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The number of cases was smaller than 200, and the 95%CI was judged as not sufficiently narrow; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) One the two studies found that the risk of stroke increased when air traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the results of the

evaluated studies, we found a non-significant effect size of 1.02 per 10 dB. The noise range of the studies under evaluation was 30-75 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table V.2

Question	Does exposure to road traffic noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in Europe and the Netherlands			
Outcome	The prevalence of stroke			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	1.00 (95%CI: 0.91 – 1.10) per 10 dB		
	Number of participants (# studies)	14,098 (2)		
	Number of cases	151		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) Response rates were in both studies below 60%. In the studies, stroke was ascertained by means of a questionnaire only; one of the two studies was not able to adjust for smoking; b)

Results between studies differed in the magnitude and direction of effect estimates (see Figure 6.2). This was not confirmed by the result of the heterogeneity analysis, demonstrating "low" heterogeneity ($I^2_{residual} = 0.0\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be imprecise since the number of cases was smaller than 200. The 95%CI was judged as sufficiently narrow; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) One the two studies found that the risk of stroke increased when road traffic noise level increased (RR per 10 dB > 1). There was no evidence of an exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.00 per 10 dB. The noise range of the studies under evaluation was 30-75 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table V.3

Question	Does exposure to rail traffic noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities around airports in the Netherlands			
Outcome	The prevalence of stroke			
Summary of findings	RR per 10 dB increase in road traffic noise level (L _{DEN})	1.07 (95%CI: 0.92 – 1.25) per 10 dB		
	Number of participants (# studies)	9,365 (1)		
	Number of cases	89		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cross-sectional study [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small, but non-significant ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low) ^{h)}

Since one cross-sectional study was available, we started with a grading of "low" (2); a) Response rate was below 60%, and stroke was ascertained by means of a questionnaire only; b) NA; c) The study assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: Although the 95%CI was considered as sufficiently narrow, we considered the number of cases to be small; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) The evaluated study found that the risk of stroke increased when rail traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: We found a non-significant effect size of 1.07 per 10 dB. The noise range of the study under evaluation was 30-65 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be "very low" (0). Grading the overall judgement of the quality of evidence down with one level was not considered to be useful. Despite the fact that only one study was available,

Table V.4

Question	Does exposure to aircraft noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in the UK and USA			
Outcome	The incidence (hospital admissions) of stroke			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.05 (95%CI: 0.96 – 1.15)		
	Number of participants (# studies)	9,619,082 (2)		
	Number of cases	97,949		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 ecological studies	1 (very low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non- significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

Since only ecological studies were available, we started with a grading of “very low” (1); a) Both ecological studies worked with a purposeful sample; so randomization and response rate is not an issue. Studies were not able to adjust for important confounders at individual level. Studies were unable to apply individual exposure estimates; b) Results between studies differed in the magnitude and direction of effect estimates (see Figure 6.1). This was confirmed by the result of the heterogeneity analysis, indicating “strong” heterogeneity ($I^2_{residual} = 82.7\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be precise: Both the number of participants and cases were much larger than 200. The 95%CI did not contain values below 0.75 or above 1.25; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) One the two studies found that the risk of stroke increased when air traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.05 per 10 dB. The noise range of the studies under evaluation was 40 to approximately 65 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table V.5

Question	Does exposure to road traffic noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in several cities in Denmark			
Outcome	The incidence of stroke			
Summary of findings	RR per 10 dB increase in road traffic noise level (L _{DEN})	1.14 (95%CI: 1.03 – 1.25) per 10 dB		
	Number of participants (# studies)	51,485 (1)		
	Number of cases	1,881		
			Rating	Adjustment to rating
Quality assessment		Starting rating	1 cohort study	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of an exposure-response gradient ^{f)}	Upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			3 (moderate) ^{h)}

Since one cohort study was available, we started with a grading of "high" (4); a) No limitations in study design found; b) Only one study was evaluated, so inconsistency was not an issue; c) The study assessed population, exposure and outcome of interest; d) We considered the results of the study to be precise: Both the number of participants and cases were much larger than 200. The 95%CI did not contain values below 0.75 or above 1.25; e) The number of available effect estimates was too small to test for publication bias; f) The evaluated study found that the risk of stroke increased when road traffic noise level increased (RR per 10 dB > 1). There was evidence of a significant exposure-response gradient: We found a significant effect size of 1.14 per 10 dB. The noise range of the study under evaluation was approximately 50 to 70 dB. This means that if the road traffic noise level increases from 50 to 70 dB, the RR = 1.30; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be "high" (4). Since only one study was available, we downgraded the overall level of evidence to "moderate" (3).

Table V.6

Question	Does exposure to aircraft noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in the UK and the Netherlands			
Outcome	Mortality due to stroke			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.07 (95%CI: 0.98 – 1.17)		
	Number of participants (# studies)	3,897,645 (2)		
	Number of cases	12,086		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	2 ecological studies	1 (very low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

Since we only ecological studies were available, we started with a grading of "very low" (1); a) Both ecological studies worked with a purposeful sample; so randomization and response rate is not an issue. Studies were not able to adjust for important confounders at individual level. Studies were unable to apply individual exposure estimates; b) Results between studies differed in the magnitude of effect estimates (see Figure 6.1). The result of the heterogeneity analysis demonstrated "low" heterogeneity ($I^2_{residual} = 28.5\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be precise: Both the number of participants and cases were much larger than 200. The 95%CI did not contain values below 0.75 or above 1.25; e) Due to the low number of available effect estimates, it was not possible to test for publication bias or small study bias; f) Both studies found that the risk of stroke increased when air traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: After aggregating the results of the evaluated studies, we found a non-significant effect size of 1.07 per 10 dB. The noise range of the studies under evaluation was approximately 40 to 65 dB. This means that if the aircraft noise level increases from 40 to 65 dB, the RR = 1.18; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table V.7

Question	Does exposure to air traffic noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in several cities near airports in Switzerland			
Outcome	Mortality due to stroke			
Summary of findings	RR per 10 dB increase in air traffic noise level (L_{DEN})	0.99 (95%CI: 0.94 – 1.04) per 10 dB		
	Number of participants (# studies)	4,580,311 (1)		
	Number of cases	25,231		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cohort study	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	None ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			3 (moderate) ^{h)}	

Table V.8

Question	Does exposure to road traffic noise increase the risk of stroke			
People	Adult population (men and women)			
Setting	Residential setting: people living in several cities in Denmark, the Netherlands and Canada			
Outcome	Mortality due to stroke			
Summary of findings	RR per 10 dB increase in road traffic noise level (L_{DEN})	0.87 (95%CI: 0.71 – 1.06) per 10 dB		
	Number of participants (# studies)	581,517 (3)		
	Number of cases	2,634		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	3 cohort studies	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Limited ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			3 (moderate)	

Since cohort studies were available, we started with a grading of "high" (4): a) No limitations in study design found; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 6.2). This was confirmed by the results of the heterogeneity analysis, demonstrating "strong" heterogeneity ($I^2_{residual} = 78.0\%$); c) The study assessed population, exposure and outcome of interest; d) We considered the results to be precise enough: Both the number of participants and cases were much larger than 200. However, the 95%CI did contain values below 0.75; e) The number of available effect estimates were too small to test for publication bias; f) Only one of the evaluated studies found that the risk of stroke increased when road traffic noise level increased (RR per 10 dB > 1). There was no evidence of an exposure-response gradient: After aggregating the results of the studies, a non-significant effect size of 0.87 per 10 dB across a noise range of -50 to 70 dB was found; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Appendix VI. Summary of findings tables dealing with studies on the impact of noise on diabetes

Table VI.1

Question	Does exposure to aircraft noise increase the risk of diabetes			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in the Netherlands			
Outcome	The prevalence of diabetes			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	1.01 (95%CI: 0.78 – 1.31)		
	Number of participants (# studies)	9,365 (1)		
	Number of cases	89		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cross-sectional study [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low) ^{h)}

Since only one cross-sectional study was available, we started with a grading of "low" (2); a) The response rates was below 60%. Diabetes was ascertained by means of a questionnaire only; the study was not able to adjust for smoking; b) Since only one study is available, this criterion is not applicable; c) The study assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The number of cases was small, and the 95%CI was not sufficiently narrow; e) Since the results of only one study were available it was not possible to test for publication bias or small study bias; f) The evaluated study found that the risk of diabetes increased when air traffic noise level increased (RR per 10 dB > 1). There was evidence of a non-significant exposure-response gradient: we found a non-significant effect size of 1.01 per 10 dB. The noise range of the studies under evaluation was 30-65 dB. this means that if the air traffic noise level increases from 30 to 65 dB, the RR = 1.04; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We

graded overall quality of the evidence to be “very low” (0). Despite the fact that only one study was available, it was not useful to downgrade the overall quality of evidence.

Table VI.2

Question	Does exposure to road traffic noise increase the risk of diabetes			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in the Netherlands and Stockholm			
Outcome	The prevalence of diabetes			
Summary of findings	RR per 10 dB increase in road noise level (L_{DEN})	NR		
	Number of participants (# studies)	11,460 (2)		
	Number of cases	242		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional study [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

Since only cross-sectional studies were available, we started with a grading of “low” (2);

a) In one of the studies, the response rate was below 60%. In the studies, diabetes was ascertained by means of a questionnaire only; b) Results of the studies differed in the magnitude of effect estimates; c) The studies assessed population, exposure and outcome of interest; d) We considered the results of the studies to be imprecise: Although the number of cases was > 200, the 95% CIs of the separate studies were not sufficiently narrow; e) Since the results of only two studies were available it was not possible to test for publication bias or small study bias; f) Both studies found that the risk of diabetes increased when road traffic noise level increased (RR per 10 dB > 1). A meta-analysis was not carried out; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VI.3

Question	Does exposure to rail traffic noise increase the risk of diabetes			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities located around airports in the Netherlands			
Outcome	The prevalence of diabetes			
Summary of findings	RR per 10 dB increase in rail noise level (L _{DEN})	0.21 (95%CI: 0.05 – 0.82)		
	Number of participants (# studies)	9,365 (1)		
	Number of cases	89		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cross-sectional study [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
	Factors increasing confidence	Publication bias	NA ^{e)}	No downgrading
		Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low) ^{h)}	

Since only one cross-sectional study was available, we started with a grading of “low” (2); a) The response rate was below 60%. Diabetes was ascertained by means of a questionnaire only; b) Since only one study is available, this criterion is not applicable; c) The study assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The number of cases was small, and the 95%CI was not sufficiently narrow; e) Since the results of only one study were available, it was not possible to test for publication bias or small study bias; f) In the evaluated study a health promoting effect of noise was found; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be “very low”(0). Despite the fact that only one study was available, it was not useful to downgrade the overall quality of evidence.

Table VI.4

Question	Does exposure to noise from wind turbines increase the risk of diabetes			
People	Adult population (men and women)			
Setting	Residential setting: people in the neighbourhood of wind turbines in the Netherlands and Sweden			
Outcome	The prevalence of diabetes			
Summary of findings	RR per 10 dB increase in wind turbine noise level (SPL)	-		
	Number of participants (# evaluated studies)	1,830 (3)		
	Number of cases	NR		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	3 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Very serious ^{a)}	Downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	Serious bias cannot be ruled out ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

[#] Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) Methods used to select the population: response rates were in two of the three studies below 60%. The participants were randomly selected, taking into account the distance between their house and a wind turbine (park); diabetes was in all cases measured by means of a questionnaire; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 7.1); c) The evaluated studies assessed population, exposure, and outcome of interest; d) We considered the results to be imprecise: We assessed that the number of cases is probably lower than 200. The 95% CIs of the separate studies contained values below 0.5 and above 2.0; e) Due to the low number of available effect estimates it was not possible to test for publication bias or small study bias; f) Only one of the evaluated studies found that We decided not to carry out a meta-analysis; g) The studies were unable to adjust for important confounders

Table VI.5

Question	Does exposure to aircraft noise increase the risk of diabetes			
People	Adult population (men and women)			
Setting	Residential setting: people living in Stockholm (Sweden)			
Outcome	The incidence of diabetes			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	0.99 (95%CI: 0.47 – 2.09)		
	Number of participants (# studies)	5,156 (1)		
	Number of cases	1,346		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cohort [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			2 (low) ^{h)}	

Since we have a cohort study, we start at 4 (high evidence); a) The loss-to-follow-up was estimated as > 20%; b) Since only one study is available, this criterion is not applicable; c) The study assessed population, exposure and outcome of interest; d) Although the number of cases was large, the 95%CI was judged as not sufficiently narrow; e) Since the results of only one study were available it was not possible to test for publication bias or small study bias; f) The evaluated study found that the risk of diabetes decreased when air traffic noise level increased (RR per 10 dB < 1). No evidence of an exposure-response gradient was found: the evaluated study found a non-significant effect size of 0.99 per 10 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be "moderate" (3). Since only one study was available, we downgraded the overall level of evidence to "low" (2).

Table VI.6

Question	Does exposure to road traffic noise increase the risk of diabetes			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities in Denmark			
Outcome	The incidence of diabetes			
Summary of findings	RR per 10 dB increase in road traffic noise level (L _{DEN})	1.08 (95%CI: 1.02 – 1.14)		
	Number of participants (# studies)	57,053 (1)		
	Number of cases	2,752		
			Rating	Adjustment to rating
Quality assessment		Starting rating	1 cohort [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Limited ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a significant exposure-response gradient ^{f)}	Upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			3 (moderate) ^{h)}

Since one cohort study is available, we started with a grading of "high" (4); a) The quality of the study was judged as high; b) Since only one study is available, this criterion is not applicable; c) The study assessed population, exposure and outcome of interest; d) We considered the results of the study to be precise: The number of cases was large, and the 95%CI was sufficiently narrow; e) Since the results of only one study were available it was not possible to test for publication bias or small study bias; f) The evaluated study found that the risk of diabetes increased when road traffic noise level increased (RR per 10 dB < 1). There was evidence of a significant exposure-response gradient: In the evaluated study a statistically significant RR of 1.08 per 10 dB across the noise range of 50-70 dB was found. This means that if the road traffic noise level increases from 50 to 70 dB, the RR = 1.17; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be "high" (4). Since only one study was available, we downgraded the overall level of evidence to "moderate" (3).

Table VI.7

Question	Does exposure to rail traffic noise increase the risk of diabetes			
People	Adult population (men and women)			
Setting	Residential setting: people living in cities in Denmark			
Outcome	The incidence of diabetes			
Summary of findings	RR per 10 dB increase in aircraft noise level (L_{DEN})	0.97 (95% CI: 0.89 – 1.05)		
	Number of participants (# studies)	57,053 (1)		
	Number of cases	2,752		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cohort [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Limited ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			3 (moderate) ^{h)}	

[#] Since, a cohort study is available, we started with a grading of "high" (4); a) The quality of the study was judged as high; b) Since only one study is available, this criterion is not applicable; c) The study assessed population, exposure and outcome of interest; d) We considered the results of the studies as precise: the number of cases was large, and the 95%CI was judged as sufficiently narrow; e) Since the results of only one study were available it was not possible to test for publication bias or small study bias; f) The evaluated study found that the risk of diabetes decreased when rail traffic noise level increased (RR per 10 dB < 1). No evidence of an exposure-response gradient was found: the evaluated study found a non-significant effect size of 0.97 per 10 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be "high" (4). Since only one study was available, we downgraded the overall level of evidence to "moderate" (3).

Appendix VII. Summary of findings tables dealing with studies on the impact of noise on obesity

Table VII.1

Question	Does exposure to aircraft noise increase the risk of obesity			
People	Adult population (men and women)			
Setting	Residential setting: people living in Stockholm in areas located around the airport			
Outcome	Change in BMI (kg/m ³)			
Summary of findings	Change in BMI per 10 dB increase in aircraft noise level (L _{DEN})	0.14 (95%CI: -0.18 – 0.45) kg/m ²		
	Number of participants (# studies)	5,156 (1)		
	Number of cases	NR		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	1 cohort study [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			2 (low) [#]	

Since a cohort study was available, we started with a grading of "high" (4); a) The quality of the study was judged as high; b) Since only one study is available, this criterion is not applicable; c) The study assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in BMI; e) Since the results of only one study were available, it was not possible to test for publication bias or small study bias; f) In the evaluated study, a harmful effect of noise was found. There was evidence of a non-significant exposure-response gradient: we found a non-significant effect size of 0.14 kg/m² per 10 dB. The noise range of the study under evaluation was 48-65 dB. This means that in case the air traffic noise level increases from 48 to 65 dB, the BMI increased with 0.24 kg/m² (this is less than 3-5% change in BMI, which is considered clinically significant); g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be "moderate" (3). Because only one study was available, we downgraded the overall quality of evidence to "low" (2).

Table VII.2

Question	Does exposure to road traffic noise increase the risk of obesity			
People	Adult population (men and women)			
Setting	Residential setting: people living in Stockholm in areas located around the airport (Sweden), people living in Oslo (Norway), People living in Aarhus or Copenhagen (Denmark)			
Outcome	Change in BMI (kg/m ³)			
Summary of findings	Change in BMI per 10 dB increase in road traffic noise level (L _{DEN})	0.03 (95%CI: -0.10 – 0.15) kg/m ²		
	Number of participants (# studies)	71,431 (3)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	3 cross-sectional studies#	2 (low)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as high; b) Results across studies differed in the magnitude and direction of effect estimate (see Figure 8.1). This was confirmed by the results of the heterogeneity analysis, demonstrating "strong" heterogeneity ($I^2_{\text{residual}} = 84.4\%$); c) The study assessed population, exposure and outcome of interest. d) We considered the results to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in BMI; e) Since the number of available estimates was small, it was not possible to test for publication bias or small study bias; f) In one of the evaluated studies, a harmful effect of noise was found. There was evidence of a non-significant exposure-response gradient: After aggregating the results of the studies, we found a non-significant effect size of 0.03 kg/m² per 10 dB. The noise range of the studies under evaluation was ~40-65 dB. This means that if the road traffic noise level increases from 40 to 65 dB, the BMI increased with 0.08 kg/m² (this is probably less than 3-5% change in BMI, which is considered clinically significant); g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VII.3

Question	Does exposure to rail traffic noise increase the risk of obesity			
People	Adult population (men and women)			
Setting	Residential setting: people living in Stockholm in areas located around the airport (Sweden), and people living in Aarhus or Copenhagen (Denmark)			
Outcome	Change in BMI (kg/m ³)			
Summary of findings	Change in BMI per 10 dB increase in rail traffic noise level (L _{DEN})	-		
	Number of participants (# studies)	57,531 (2)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional studies#	2 (low)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Limited ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
Possible confounding		No conclusions can be drawn ^{g)}	No upgrading	
Overall judgement of quality of evidence			1 (very low)	

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as high; b) Results varied between the studies; c) Results across studies differed in the magnitude of effect estimates. The direction of the effects was consistent; c) The study assessed population, exposure and outcome of interest; d) We considered the results to be precise: For both studies, the standard deviations of the reported effect were smaller than the reported effect size; e) Since the number of available estimates was small, it was not possible to test for publication bias or small study bias; f) Both studies found a harmful effect of rail traffic noise. We decided not to carry out a meta-analysis; g) Residual confounding primarily due to the way exposure was assessed, cannot be ruled out. For the other factors, we were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VII.4

Question	Does exposure to aircraft noise increase the risk of obesity			
People	Adult population (men and women)			
Setting	Residential setting: people living in Stockholm in areas located around the airport			
Outcome	Change in waist circumference (cm)			
Summary of findings	Change in waist circumference per 10 dB increase in aircraft noise level (L _{DEN})	3.46 (95%CI: 2.13 – 4.77) cm		
	Number of participants (# studies)	5,156 (1)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	1 cohort study [#]	4 (high)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	NA ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Limited ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Large ^{f)}	Upgrading
		Exposure-response gradient	Evidence of a significant exposure-response gradient ^{f)}	Upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			3 (moderate) ^{h)}

Since a cohort study was available, we started with a grading of "high" (4); a) The quality of the study was judged as high; b) Since only one study is available, this criterion is not applicable; c) The study assessed population, exposure and outcome of interest; d) We considered the results of the study to be precise: The standard deviation of the reported effect size was smaller than the mean difference in waist circumference; e) Since the results of only one study were available, it was not possible to test for publication bias or small study bias; f) The study found a harmful effect of aircraft noise. There was evidence of a significant exposure-response gradient: we found a significant effect size of 3.46 cm per 10 dB. The noise range of the study under evaluation was 48-65 dB. This means that if the air traffic noise level increases from 48 to 65 dB, the waist circumference increased more than 5.88 cm; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate; h) We graded the overall quality of the evidence to be "high" (4). Because only one study was available, we downgraded the overall quality of evidence to "moderate" (3).

Table VII.5

Question	Does exposure to road traffic noise increase the risk of obesity			
People	Adult population (men and women)			
Setting	Residential setting: people living in Stockholm in areas located around the airport (Sweden), people living in Oslo (Norway), People living in Aarhus or Copenhagen (Denmark)			
Outcome	Change in waist circumference (cm)			
Summary of findings	Change in waist circumference per 10 dB increase in road traffic noise level (L_{DEN})	0.17 (95%CI: -0.06 – 0.40) cm		
	Number of participants (# studies)	71,431 (3)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	3 cross-sectional studies#	2 (low)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	Small ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			1 (very low)	

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as high b) Results across studies differed in the magnitude and direction of effect estimate (see Figure 8.1). This was confirmed by the results of the heterogeneity analysis, demonstrating "strong" heterogeneity ($I^2_{residual} = 84.4\%$); c) The study assessed population, exposure and outcome of interest; d) We considered the results to be precise enough: The standard deviation of the reported effect size was smaller than the mean difference in waist circumference; e) Since the number of available estimates was small, it was not possible to test for publication bias or small study bias; f) Two studies found a harmful effect of road traffic noise. There was evidence of a non-significant exposure-response gradient: After aggregating the results of the three evaluated studies, we found a non-significant effect size of 0.17 per 10 dB. The noise range of the study under evaluation was ~40-65 dB. This means that if the road traffic noise level increases from 40 to 65 dB, the waist circumference increased with 0.43 cm (this is probably less than 3-5% change in waist circumference, which is considered clinically significant); g) Residual confounding primarily due to the way exposure was assessed cannot be ruled out. For the rest we were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VII.6

Question	Does exposure to rail traffic noise increases the risk of obesity			
People	Adult population (men and women)			
Setting	Residential setting: people living in Stockholm in areas located around the airport (Sweden), and people living in Aarhus or Copenhagen (Denmark)			
Outcome	Change in waist circumference (cm)			
Summary of findings	Change in waist circumference per 10 dB increase in rail traffic noise level (L _{DEN})	-		
	Number of participants (# studies)	57,531 (2)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional studies#	2 (low)
	Factors decreasing confidence	Risk of bias	Limited ^{a)}	No downgrading
		Inconsistency	Limited ^{b)}	No downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Limited ^{d)}	No downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			2 (low)

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as high; b) Results across studies only differed in magnitude of effect estimates; c) The study assessed population, exposure and outcome of interest; d) We considered the results to be precise: For both studies, the standard deviations of the reported effect were smaller than the reported effect size; e) Since the number of available estimates was small, it was not possible to test for publication bias or small study bias; f) Both studies found a harmful effect of rail traffic noise. We decided not to carry out a meta-analysis; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Appendix VIII. Summary of findings tables dealing with studies on the impact of noise on children's blood pressure

Table VIII.1

Question	Does exposure to aircraft noise affect blood pressure			
People	Children (boys and girls)			
Setting	Residential setting: Children (aged 6-11 yrs.) living in cities around Schiphol Amsterdam airport (the Netherlands), London Heathrow (United Kingdom) and Kingsford-Smith airport (Australia)			
Outcome	Change in systolic blood pressure (mmHg)			
Summary of findings	Change in systolic blood pressure level per 10 dB increase in aircraft noise level (L_{DEN})	-		
	Number of participants (# studies)	2,013 (2)		
	Number of cases	NR		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	2 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	A lot is unclear ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

[#] Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) The quality of the studies was judged as low, since response rates in both studies were higher than 60%, and because of the difficulty to judge the quality of the blood pressure measurements; b) One study found a positive effect; the other found a negative effect (see Figure 9.1); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the results of only two studies were available it was not possible to test for publication bias or small study bias; f) One of the studies found a harmful effect of noise. It was not possible to combine the results of both studies. A meta-analysis was not carried out; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VIII.2

Question	Does exposure to aircraft noise affect blood pressure			
People	Children (boys and girls)			
Setting	Residential setting: Children (aged 6-11 yrs.) living in cities around Schiphol Amsterdam airport (the Netherlands), London Heathrow (United Kingdom) and Kingsford-Smith airport (Australia)			
Outcome	Change in diastolic blood pressure (mmHg)			
Summary of findings	Change in diastolic blood pressure level per 10 dB increase in aircraft noise level (L_{DEN})	-		
	Number of participants (# studies)	2,013 (2)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	A lot is unclear ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) The quality of the studies was judged as low, since response rates in both studies were higher than 60% and because of the difficulty to judge the quality of the blood pressure measurements; b) One study found a positive effect; the other found a negative effect (see Figure 9.2); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the results of only two studies were available it was not possible to test for publication bias or small study bias; f) One of the evaluated studies found a harmful effect of noise. It was not possible to combine the results of both studies. A meta-analysis was not carried out; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VIII.3

Question	Does exposure to aircraft noise affect blood pressure			
People	Children (boys and girls)			
Setting	Educational setting: Children (aged 6-11 yrs.) visiting primary schools in cities around Schiphol Amsterdam airport (the Netherlands), London Heathrow (United Kingdom) and Kingsford-Smith airport (Australia)			
Outcome	Change in systolic blood pressure (mmHg)			
Summary of findings	Change in systolic blood pressure level per 10 dB increase in aircraft noise level (L _{DEN})	-		
	Number of participants (# studies)	2,013 (2)		
	Number of cases	NR		
			Rating	
			Adjustment to rating	
Quality assessment		Starting rating	2 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	A lot is unclear ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
	Overall judgement of quality of evidence			0 (very low)

Since only cross-sectional studies were available, we started the grading with "low" (2);

a) The quality of the studies was judged as low, since response rates in both studies were higher than 60% and because of the difficulty to judge the quality of the blood pressure measurements; b) One study found a positive effect; the other found a negative effect

(see Figure 9.1); c) The studies assessed population, exposure and outcome of interest; d) The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the results of only two studies were available it was not possible to test for publication bias or small study bias; f) It was not possible to combine the results of both studies. A meta-analysis was not carried out; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VIII.4

Question	Does exposure to aircraft noise affect blood pressure			
People	Children (boys and girls)			
Setting	Educational setting: Children (aged 6-11 yrs.) visiting primary schools in cities around Schiphol Amsterdam airport (the Netherlands), London Heathrow (United Kingdom) and Kingsford-Smith airport (Australia)			
Outcome	Change in diastolic blood pressure (mmHg)			
Summary of findings	Change in diastolic blood pressure level per 10 dB increase in aircraft noise level (L _{DEN})	-		
	Number of participants (# studies)	2,013 (2)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	2 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	A lot is unclear ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	NA ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

Since only cross-sectional studies were available, we started with a grading of "low" (2);

a) The quality of the studies was judged as low, since response rates in both studies were higher than 60% and because of the difficulty to judge the quality of the blood pressure measurements; b) One study found a positive effect; the other found a negative effect

(see Figure 9.2); c) The studies assessed population, exposure and outcome of interest; d) The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the results of only two studies were available it was not possible to test for publication bias or small study bias; f) It was not possible to combine the results of both studies. A meta-analysis was not carried out; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VIII.5

Question	Does exposure to road traffic noise affect blood pressure			
People	Children (boys and girls)			
Setting	Residential setting: Children (aged 6-11 yrs.) living in cities in the Netherlands, the United Kingdom, Germany, Croatia, Serbia and the United States of America			
Outcome	Change in systolic blood pressure (mmHg)			
Summary of findings	Change in systolic blood pressure level per 10 dB increase in road traffic noise level (L_{DEN})	0.08 (95%CI: -0.48 – 0.64) mmHg		
	Number of participants (# studies)	4,197 (6)		
	Number of cases	NR		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	6 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as low, since response rates in both studies were higher than 60% and because of the difficulty to judge the quality of the blood pressure measurements. Also studies were not always able to adjust for confounding or were able to attribute individual exposure estimates; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 9.1). This was not confirmed by the results of the heterogeneity analysis, demonstrating only "low" heterogeneity ($I^2_{residual} = 8.9\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the number of available effect estimates was less than 10, it was not possible to test for publication bias or small study bias; f) Three of the evaluated studies found a harmful effect of noise. There was evidence of a non-significant exposure-response gradient: after combining the results of the evaluated studies, we found a non-significant effect size of 0.08 mmHg per 10 dB. The noise range was ~35-80 dB. This means that if the road traffic noise level increases from 35 to 80 dB, the blood pressure increased with 0.36 mmHg; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VIII.6

Question	Does exposure to road traffic noise affect blood pressure			
People	Children (boys and girls)			
Setting	Residential setting: Children (aged 6-11 yrs.) living in cities in the Netherlands, the United Kingdom, Germany, Croatia, Serbia and the United States of America			
Outcome	Change in diastolic blood pressure (mmHg)			
Summary of findings	Change in diastolic blood pressure level per 10 dB increase in road traffic noise level (L_{DEN})	0.47 (95%CI: -0.30 – 1.24) mmHg		
	Number of participants (# studies)	4,197 (6)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	6 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a non-significant exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as low, since response rates in both studies were higher than 60%, and because of the difficulty to judge the quality of the blood pressure measurements. Also studies were not always able to adjust for confounding or were able to attribute individual exposure estimates; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 9.2). This was confirmed by the results of the heterogeneity analysis, demonstrating "strong" heterogeneity ($I^2_{residual} = 76.0\%$); c) The studies assessed population, exposure and outcome of interest; d) The results were considered to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the number of available effect estimates was less than 10, it was not possible to test for publication bias or small study bias; f) Three of the evaluated studies found a harmful effect of noise. There was evidence of a non-significant exposure-response gradient: After combining the results of the evaluated studies we found a non-significant effect size of 0.47 mmHg per 10 dB. The noise range was ~35-80 dB. This means that if the road traffic noise level increases from 35 to 80 dB, the blood pressure increased with 2.1 mmHg; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VIII.7

Question	Does exposure to road traffic noise affects blood pressure			
People	Children (boys and girls)			
Setting	Educational setting: Children (aged 6-11 yrs.) living in cities in the Netherlands, the United Kingdom, Croatia, Serbia and the United States of America			
Outcome	Change in systolic blood pressure (mmHg)			
Summary of findings	Change in systolic blood pressure level per 10 dB increase in road traffic noise level (L _{DEN})	-0.60 (95%CI: -1.51 – 0.30) mmHg		
	Number of participants (# studies)	4,520 (5)		
	Number of cases	NR		
		Rating	Adjustment to rating	
Quality assessment		Starting rating	5 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	No evidence of an exposure-response gradient ^{f)}	No upgrading
		Possible confounding	No conclusions can be drawn ^{g)}	No upgrading
Overall judgement of quality of evidence			0 (very low)	

Since we only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as low, since response rates in both studies were higher than 60% and because of the difficulty to judge the quality of the blood pressure measurements. Also studies were not always able to adjust for confounding or were able to attribute individual exposure estimates; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 9.1). This was confirmed by the results of the heterogeneity analysis, demonstrating "moderate" heterogeneity ($I^2_{\text{residual}} = 61.6\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the number of available effect estimates was less than 10, it was not possible to test for publication bias or small study bias; f) Three studies found a harmful effect. There was no evidence of an exposure-response gradient: after combining the results of the evaluated studies, we found a non-significant effect size of -0.60 mmHg per 10 dB; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Table VIII.8

Question	Does exposure to road traffic noise affect blood pressure			
People	Children (boys and girls)			
Setting	Educational setting: Children (aged 6-11 yrs.) living in cities in the Netherlands, the United Kingdom, Croatia, Serbia and the United States of America			
Outcome	Change in diastolic blood pressure (mmHg)			
Summary of findings	Change in diastolic blood pressure level per 10 dB increase in road traffic noise level (L_{DEN})	0.46 (95%CI: -0.60 – 1.53) mmHg		
	Number of participants (# studies)	4,520 (5)		
	Number of cases	NR		
			Rating	Adjustment to rating
Quality assessment		Starting rating	5 cross-sectional studies [#]	2 (low)
	Factors decreasing confidence	Risk of bias	Serious ^{a)}	Downgrading
		Inconsistency	Serious ^{b)}	Downgrading
		Indirectness	None ^{c)}	No downgrading
		Imprecision	Serious ^{d)}	Downgrading
		Publication bias	NA ^{e)}	No downgrading
	Factors increasing confidence	Strength of association	NA ^{f)}	No upgrading
		Exposure-response gradient	Evidence of a statistically non-significant exposure-response gradient ^{f)}	No upgrading
Possible confounding		No conclusions can be drawn ^{g)}	No upgrading	
Overall judgement of quality of evidence			0 (very low)	

Since only cross-sectional studies were available, we started with a grading of "low" (2); a) The quality of the studies was judged as low, since response rates in both studies were higher than 60% and because of the difficulty to judge the quality of the blood pressure measurements. Also studies were not always able to adjust for confounding or were able to attribute individual exposure estimates; b) Results across studies differed in the magnitude and direction of effect estimates (see Figure 9.1). This was not confirmed by the results of the heterogeneity analysis, demonstrating "low" heterogeneity ($I^2_{residual} = 16.0\%$); c) The studies assessed population, exposure and outcome of interest; d) We considered the results to be imprecise: The standard deviation of the reported effect size was larger than the mean difference in blood pressure; e) Since the number of available effect estimates was less than 10, it was not possible to test for publication bias or small study bias; f) There was evidence of a statistically non-significant exposure-response gradient: after combining the results of the evaluated studies, we found a non-significant effect size of 0.46 mmHg per 10 dB. The noise range was ~35-80 dB. This means that if the road traffic noise level increases from 35 to 80 dB, the blood pressure increased with 2.1 mmHg; g) We were not able to draw any conclusions whether possible residual confounders or biases would reduce our effect estimate.

Appendix IX References excluded because of lack of information

This appendix presents the references that we excluded because we were not able to overtake more information of the publication than is given below. As a consequence, we were not able to judge whether the publication meet our inclusion criteria.

Excluded references

1. *Cardiovascular disease and aircraft noise-the cologne-bonn airport study.*
2. *Effects of train noise and vibration on human heart rate during sleep: An experimental study.*
3. *Sounds of silence.*
4. *Gesundheitliche Folgen von Fluglärm: Aktueller Stand der Evidenz. [Health effects of aircraft noise: current evidence].*
5. *Fluglärm lässt den blutdruck steigen Aircraft noise-induced hypertension.*
6. *Pathogenesemechanismen bei lärminduzierten krankheitsbildern - Schlussfolgerungen aus dem Spandauer Gesundheits-Survey Pathogenesis mechanism by noise induced clinical pictures - Lessons from the Spandau Health-Survey.*
7. *Customer health: A new role for occupational physicians.*
8. *Gezondheidsklachten bij omwonenden van een internationale luchthaven: Een transversaal onderzoek Enquiry about health problems in a population living near an international airport.*
9. *Gesundheitsbezogene Aspekte der extra-auralen Lärmwirkungsforschung. Health-related aspects of research on noise effects other than on the ear.*
10. *Qualitätsziele zur Vermeidung von Beeinträchtigungen und Belastungen durch Fluglärm. Quality goals in preventing detrimental effects and stress caused by aircraft noise.*
11. *Lärm trifft nicht nur die Ohren. Aber lassen sich Schaden für die Gesundheit auch objektivieren? Noise effects not only the ears. But can damage to health be objectively evaluated?*
12. *Reproductive outcomes associated with noise exposure - A systematic review of the literature.*
13. *Residential proximity to major roads and term low birth weight: The roles of air pollution, heat, noise, and road-adjacent trees.*
14. *Associations between road traffic noise and body composition.*
15. *Association of long-term exposure to traffic-related air pollution with blood pressure and hypertension in an adult population-based cohort in Spain (the REGICOR Study).*
16. *The associations between urban traffic emissions on myocardial infarction risk.*
17. *Reported heart disease and stroke in relation to aircraft and road traffic noise in six european countries - the hyena study.*
18. *Increased traffic exposure and negative birth outcomes: A prospective cohort in Australia.*
19. *Noise hurts boys and girls.*

20. *Association between the rates of low birth-weight and/or preterm infants and aircraft noise exposure.*
21. *Physiological hemodynamical reactions to road-traffic noise in an experimental setting.*
22. *Polygraphy and noise sensitivity do not predict effects of night-time aircraft noise on vascular function and stress hormone release.*
23. *Road traffic noise exposure and risk of hypertension in Taiwan.*
24. *Road traffic noise and hypertension - Results from the kora study.*
25. *Role du bruit dans le developpement de l'hypertension arterielle en milieu aeroportuaire Relationship between noise and blood pressure in an airport environment.*
26. *Blood pressure and particulate air pollution in schoolchildren of Lahore, Pakistan.*
27. *Does traffic noise influence respiratory mortality?*
28. *The influence of daytime road-traffic noise on blood pressure of school children.*
29. *Risk of hypertension related to road traffic noise among reproductive-age women.*
30. *Criteria of noise pathologies in aviation specialists and their prognostic implications.*
31. *Gesundheitliche auswirkungen von fluglärm Health consequences of aircraft noise.*
32. *Study on the health status of the residents near military airbases in Pyeongtaek City.*
33. *Larmbedingte Belastigung und Erkrankungsrisiko. Ergebnisse des paneuropaischen LASER-Survey Noise induced annoyance and morbidity. Results from the pan European LARES-Survey.*
34. *Plane pollution.*
35. *Medically relevant effects of noise from military low-altitude flights. Results of an interdisciplinary pilot study.*
36. *Influence of physical factors on the ro-ro vessel over selected parameters of the circulatory system.*
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