Long-term exposure to traffic noise and mortality: a systematic review and meta-analysis of epidemiological evidence between 2000-2020

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Abstract

We aimed to update the evidence-base of long-term noise exposures from road, rail, and aircraft traffic on both non-accidental and cardiovascular mortality.

A systematic review and meta-analysis were conducted following PRISMA guidelines. The literature was searched using PubMed, Scopus, Web of Science, and EMBASE for the period between 01/01/2000 and 05/10/2020. 13 studies were selected for final review. The risk of bias and overall quality of evidence was evaluated using a pre-defined list of criteria. Risk estimates from each study were converted into per 10dB higher of L_{den} for each traffic source. Inverse-Variance heterogeneity (I-Vhet) meta-analysis was used to pool these individual risk estimates, along with assessment of heterogeneity and publication bias. Sensitivity analyses include using random-effect model and leave-one-out meta-analysis. Subgroup analyses by study design and noise exposure assessment were conducted to explore potential sources of heterogeneity.

For road traffic, the pooled relative risk (RR) per 10 dB higher L_{den} for mortality from non-accidental causes was 1.01 (95% CI: 0.98, 1.05) (5 studies, I^2=78%), CVD was 1.01 (95% CI: 0.98, 1.05) (5 studies, I^2=41%), ischemic heart disease (IHD) was 1.03 (95% CI: 0.99, 1.08) (7 studies, I^2=46%), and stroke was 1.05 (95% CI: 0.97, 1.14) (5 studies, I^2=62%). The overall quality of evidence for most meta-analyses was rated as *very low* to *low*, except for CVD or IHD mortality, for which the quality of evidence was rated as *moderate*. A possible threshold of 53dB was visually suggested for CVD-related mortality from road traffic noise in the trend analysis. For aircraft noise, pooled estimates were based on fewer studies and varied by mortality outcomes.

Evidence of long-term exposure to traffic noise on mortality remains weak except the association between road traffic noise and IHD mortality. High-quality longitudinal studies are required to better characterise mortality effects of traffic noise.

Key words: noise exposure, transportation, death, fatality, cardiovascular disease

Capsule

In this updated meta-analysis, we found that exposure to higher road traffic noise levels was associated with a modest increase in risk of mortality from ischemic heart disease.

1. Introduction

In the past decade, evidence has emerged to suggest that traffic noise pollution is an important public health problem affecting children, adults, and the elderly. Noise pollution, as a non-specific psychological and physiological stressor, has been linked to a range of non-auditory health outcomes including cardiovascular diseases (CVD), metabolic disorders, cognitive dysfunction, poor sleep and mental health in a chronic exposure timeframe (Basner *et al.*, 2014).

In 2018, the World Health Organization (WHO) for the European region published updated Environmental Noise Guidelines, recommending new thresholds above which adverse health effects may be observed for different sources of environmental noise (*Environmental Noise Guidelines for the European Region (2018)*, no date). These new guidelines were underpinned by evidence from eight systematic reviews on both critical health outcomes (e.g. CVD) and new important outcomes (e.g. birth outcomes). One of these reviews was conducted by Van Kempen and colleagues (van Kempen *et al.*, 2018), in which associations of traffic noise with both cardiovascular and metabolic outcomes were meta-analysed from studies published between 2000-2015. A key finding is that long-term exposure to road traffic noise was associated with incident ischemic heart disease (IHD) (relative risk (RR) of 1.08 (95% CI: 1.01 - 1.15) per 10dB higher of noise levels). However, as the authors concluded, quality of evidence for most other CVD outcomes, including mortality, was low to moderate. For example, the pooled RR of road traffic noise on IHD mortality was 1.05 (95% CI: 0.97 - 1.13), which were only based on two cohort and one case-control studies published by year 2014.

Since 2015, 16 new studies (Tobias *et al.*, 2015; Tobías *et al.*, 2015; Evrard *et al.*, 2015; Halonen *et al.*, 2015; Barceló *et al.*, 2016; Roswall *et al.*, 2016; Tonne *et al.*, 2016; Recio *et*

al., 2016, 2017; Roswall, Bidstrup, *et al.*, 2017; Héritier *et al.*, 2018, 2019; Nieuwenhuijsen *et al.*, 2018; Andersson *et al.*, 2020; Thacher *et al.*, 2020; Klompmaker *et al.*, 2020) of traffic noise and mortality outcomes with various study designs, study origins, and sample sizes were published. In particular, new evidence of associations with cardiovascular mortality has emerged from several large studies with sample sizes ranging from hundreds of thousands (Klompmaker *et al.*, 2020) to millions (Evrard *et al.*, 2015; Halonen *et al.*, 2015; Héritier *et al.*, 2018, 2019). In addition, to the best of our knowledge, evidence of traffic noise effects on non-accidental mortality has not yet been synthesised. We were motivated by these new available studies to update the previous WHO review (van Kempen *et al.*, 2018) by conducting a systematic review and meta-analysis. We set out to review all available epidemiological evidence from January 2000 up to early October 2020 on mortality outcomes from traffic noise of road, rail, and aircraft sources, thereby contributing to policy formulation to protect public health from traffic noise.

2. Methods

We followed the PRISMA guidelines ('Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement', 2009) in conducting and reporting this review. The PRISMA checklist is available on **Supplementary-1**. The research question was formulated *a priori* as: "What is the exposure-response relationship between long-term (i.e. at least annual) residential noise exposure from each traffic source (road, rail, aircraft) and non-accidental or cardiovascular mortality in the general population?".

2.1 Identification and selections of studies

Studies that analysed road, rail, and aircraft traffic noise as exposures and mortality (either cause-specific or all non-accidental) as outcomes were searched. The search was conducted in PubMed, EMBASE, Scopus and Web of Science for such studies published in English

language between 1st January 2000 and 5th October 2020 (date of the final search). The keywords used in the search included “traffic noise”, “transportation noise”, “environmental noise”, “community noise”, “urban noise”, “mortality”, “fatality” and “death”. Detailed search strings for each electronic database are available in **Supplementary-2.** Additional search was conducted in non-peer reviewed literature by scanning International Society for Environmental Epidemiology (ISEE) 2020 conference abstract book during the peer-review stage of this review. Study selection criteria are given in **Table 1**, which generally follows the PECO (Population, Exposure, Comparator and Outcome) approach(Morgan *et al.*, 2018).

2.2.Data extraction

Using a pre-defined abstraction form in Microsoft Excel, the following data from each retained study were extracted: lead author, publication year, study region, study design, number, mean age and sex of the study population, follow-up periods, traffic noise assessment methods, mean or median and range of traffic noise estimate (by sources, where available), adjusted covariates, outcomes ascertainment, and risk estimate. If in a given study, multiple relative risks were presented from different adjusted models, we *a priori* decided to extract risk estimate from the model that was adjusted for age, sex, at least one individual-level or area-level socioeconomic status (SES) (i.e. education level, household income, area deprivation index etc.), air pollution (in preferred order, nitrogen dioxide (NO_2), nitrogen oxides (NO_x), particulate matter with a diameter <2.5μm ($PM_{2.5}$), <10μm (PM_{10}), etc.), and where applicable, at least one lifestyle factor (i.e. smoking status, physical activity, alcohol consumption etc or their surrogates such as comorbidity).

In the case of multiple publications reporting on the same mortality outcomes based on the same cohort, we only chose the most recent publications to extract risk estimates for meta-analysis due to a longer period of follow-up. For example, two earlier studies(Sørensen *et al.*,

2012; Sorensen *et al.*, 2014) from the Danish Diet, Cancer and Health cohort were not included in this review as a more recent study (Thacher *et al.*, 2020) with a longer follow-up period on the same mortality outcomes has been published, using the same set of covariate adjustments. There were four studies from the Swiss National Cohort, all of which analysed associations between traffic noise exposures from road, rail and aircraft and cardiovascular mortality (Heritier *et al.*, 2017; Héritier *et al.*, 2018, 2019; Vienneau *et al.*, 2019). Two of them specifically investigated the roles of noise intermittency ratio (Heritier *et al.*, 2017) or facades/floors of residence (Vienneau *et al.*, 2019) on the main associations already reported by the other two studies (Héritier *et al.*, 2018, 2019). Hence, we only kept these latter two studies for meta-analysis. Using the same Swiss National Cohort, there was an earlier study (Huss *et al.*, 2010) in 2010 that specifically investigated aircraft noise and cardiovascular mortality outcomes. We did not include this study for meta-analysis on IHD mortality as these results have been updated in a recent analysis (Héritier *et al.*, 2019) but we kept this study (Huss *et al.*, 2010) for the meta-analysis of aircraft noise and all CVD or stroke mortality. Two studies (Héritier *et al.*, 2019; Klompmaker *et al.*, 2020) reported risk estimates of each traffic source in a single publication and we extracted these estimates separately for each source as if they came from separate publications.

One author (Y.C) extracted the data and a second author (R.R) double-checked data accuracy. Five questions were raised by the second author, mainly to check the adjusted models that the data were extracted from. These questions were then resolved through mutual discussion and concurrent examination of relevant parts of the original papers.

2.3.Risk of bias evaluation in individual studies

There is no universally adopted tool to evaluate risk of bias at study-level for systematic reviews on observational studies of environmental exposures, with different tools including

different bias domains (Steenland *et al.*, 2020). To increase transparency of the assessment process, we followed a comprehensive review protocol developed jointly by the WHO and International Labour Organisation (ILO)(Teixeira *et al.*, 2019), in which the risk of bias assessment was largely adapted from the Navigation Guide. For each individual study, we assessed nine risk of bias domains: (1) source population representation; (2) exposure assessment; (3) outcome assessment; (4) confounding; (5) blinding; (6) incomplete outcome data; (7) selective outcome reporting; (8) conflict of interest and (9) other sources of bias. For each of these domains, risk of bias was assigned to one of the five categories: *low, probably low, probably high, high, not applicable*. We used the detailed instructions from the WHO/ILO protocol to assign rating to each domain for each study (**Supplementary-3)**. The overall risk of bias at study level was decided by the worst rating in any bias domain.

2.4.Data synthesis and analysis

To answer the research question, we only included studies that investigated long-term exposure on mortality outcomes in the general populations for meta-analysis. Studies of time-series or case-crossover design, studies in specific sub-populations, and non-peer review conference abstracts are described in **Supplementary-4**.

Retained studies had used different noise metrics (e.g. L_{den}, L_{DN}, L_{day}, L_{night}, L_{Aeq24h}, L_{Aeq16h}) (definitions on **Supplementary-5**) to estimate their respective mortality effects, though most studies used L_{den} (weighted 24-hour noise). Before pooling individual studies for meta-analysis, conversions of different noise metrics to L_{den} were made following the conversion terms derived by Brink and colleagues (Brink *et al.*, 2018) for the western European context. Such conversions, specifically, L_{Aeq24h}+3.6dB, L_{Aeq16h}+2.3dB, $L_{day(7\text{-}21h)}$ +2.3dB, were made in four studies (Halonen *et al.*, 2015; Barceló *et al.*, 2016; Nieuwenhuijsen *et al.*, 2018;

Andersson *et al.*, 2020) of road traffic noise that were retained for meta-analysis (**Supplementary-6**).

For three studies (Beelen *et al.*, 2009; Huss *et al.*, 2010; Hansell *et al.*, 2013) that had only reported risk estimates by categorical noise exposures, a transformation into an exposure-response relationship was performed. The midpoint of each exposure interval was assigned as the median exposure corresponding to the risk estimate. Since the lowest/highest exposure interval was defined as being lower/greater than a specific value, the median exposure for these intervals were imputed assuming a linear function and the width of the exposure interval (Woodcock *et al.*, 2011). Categorical estimates from these studies were then converted into a linear exposure-response relationship per 10dB higher in L_{den} (where necessary, L_{DN}+0.3dB, L_{Aeq16h}+2dB) (Vienneau *et al.*, 2015).

Relative risk (RR) per 10 dB higher L_{den} were either directly extracted or converted from each study before meta-analysis, for which we used the inverse-variance heterogeneity (I-Vhet) model suggested by Doi and colleagues (Doi *et al.*, 2015). It is an estimator under the fixed-effect model assumption with a quasi-likelihood-based variance structure. In contrast to the random-effect (RE) model, which is typically used for meta-analysis of heterogenous studies, I-Vhet model favours larger studies, retains a relatively correct coverage probability and a lower observed variance, thereby avoiding the overconfident estimates from the RE model. Between-study heterogeneity was confirmed if Cochran's Q at the $p<0.1$ or $I^2>30\%$ (Dzhambov and Dimitrova, 2018). Risk of publication bias was tested using Doi plot. Doi plot asymmetry was assessed using the Luis Furuya-Kanamori (LFK) index (<1: no asymmetry; 1-2: minor asymmetry; >2: major asymmetry)(Barendregt and Doi, 2016). To facilitate comparisons of the pooled estimates with previous reviews, we nonetheless repeated all the meta-analyses using random-effect model. All meta-analyses were conducted using the MetaXL software V5.3 (EpiGear International Pty Ltd, Queensland, Australia).

In addition, as the majority of studies focused on road traffic noise, we estimated the trend for every 10 dB higher in road traffic L_{den} and mortality from non-accidental, all CVD, IHD, and stroke respectively using variance-weighted least squares (VWLS) method (Orsini, Bellocco and Greenland, 2006). We also investigated potential departure from linearity for these associations and estimated the trend by using linear spline transformation with three knots except for CVD for which only two knots were found to be sufficient. These analyses were conducted in STATA v16.

For the main meta-analyses of traffic noise from road and aircraft sources on each mortality outcome, we used the leave-one-out method to exclude each study one-at-a-time to check the robustness of the main results. We then conducted sub-group analyses by study characteristics to explore potential sources of heterogeneity due to methodological concerns: study design (cohort/case-control vs. ecological study) and noise exposure assignment (address-level vs. postcode/block/census track level).

2.5.Quality of evidence assessment

As with risk of bias assessment, there is no agreed method to assess quality of evidence at study level for systematic reviews on environmental health research(Teixeira *et al.*, 2019). In our review, the quality of evidence of each association between traffic noise and non-accidental or CVD mortality was assessed following a modified version of the GRADE considerations, which has been previously used in WHO reviews(van Kempen *et al.*, 2018; Teixeira *et al.*, 2019). Quality of evidence was defined as "to what extent we were confident that an estimate of an association between traffic noise and mortality is accurate", and was categorised using four levels of certainty (*High, Moderate, Low, Very Low*)(van Kempen *et al.*, 2018). As with previous reviews on traffic noise and health outcomes(Dzhambov and Dimitrova, 2018; van Kempen *et al.*, 2018), the quality of evidence was initially rated as

'high' for cohort and case-control studies and *'very low'* for ecological studies. The quality of evidence was downgraded by one category if any of the following aspects applied: (1) high risk of bias; (2) inconsistent findings across studies (i.e. high heterogeneity, I^2>50%), (3) imprecision of the pooled relative risk (i.e. wide 95%CI with a lower limit <0.75 and an upper limit>1.25), (4) presence of publication bias as assessed by Doi plots and LFK index, or (5) evidence was only based on one study. The quality of evidence was upgraded (if it was not downgraded before) by one category if the magnitude of the pooled effect was large (i.e. RR>=1.5)(van Kempen *et al.*, 2018).

3. Results

3.1. Search results

The extensive search resulted in a total of 1,690 publications from the four electronic databases after removing duplicate records (**Figure 1**). After screening the titles and abstracts, we further excluded 1,667 records, leaving 23 studies satisfying inclusion criteria for full-text screening (Beelen *et al.*, 2009; Huss *et al.*, 2010; Gan *et al.*, 2012; Hansell *et al.*, 2013; Tobias *et al.*, 2014, 2015; Tobías *et al.*, 2015; Evrard *et al.*, 2015; Halonen *et al.*, 2015; Barceló *et al.*, 2016; Recio *et al.*, 2016, 2017; Roswall *et al.*, 2016; Tonne *et al.*, 2016; Roswall, Bidstrup, *et al.*, 2017; Heritier *et al.*, 2017; Nieuwenhuijsen *et al.*, 2018; Héritier *et al.*, 2018, 2019; Vienneau *et al.*, 2019; Andersson *et al.*, 2020; Klompmaker *et al.*, 2020; Thacher *et al.*, 2020). Through manual searching of the reference lists of these 23 studies, two studies (Sørensen *et al.*, 2012; Sorensen *et al.*, 2014) were additionally identified.

Of the 25 records that were retained for full-text screening, we excluded four studies (Sørensen *et al.*, 2012; Sorensen *et al.*, 2014; Heritier *et al.*, 2017; Vienneau *et al.*, 2019) due to multiple publications on the same mortality outcomes using the same dataset. Only 13 studies (Beelen *et al.*, 2009; Huss *et al.*, 2010; Gan *et al.*, 2012; Hansell *et al.*, 2013; Evrard

et al., 2015; Halonen *et al.*, 2015; Barceló *et al.*, 2016; Nieuwenhuijsen *et al.*, 2018; Héritier *et al.*, 2018, 2019; Andersson *et al.*, 2020; Klompmaker *et al.*, 2020; Thacher *et al.*, 2020) were eligible for quantitative data synthesis; all were of cohort, case-control or ecological study design and conducted in general populations.

The remaining 10 studies and (Tobias *et al.*, 2014, 2015; Tobías *et al.*, 2015; Recio *et al.*, 2016, 2017; Roswall *et al.*, 2016; Tonne *et al.*, 2016; Roswall *et al.*, 2017; Ancona, 2020; Andersen, 2020) (five of time-series design, three of specific patients only (myocardial infarction or cancer), and two conference abstracts) were excluded from meta-analysis.

3.2.Description of included studies

Among the 13 included studies (**Table 2**), 12 studies were from western/northern European countries (Denmark, France, Switzerland, Sweden, Spain, the Netherlands and the UK) and one from Canada (Gan *et al.*, 2012).

Nine studies (Beelen *et al.*, 2009; Huss *et al.*, 2010; Gan *et al.*, 2012; Héritier *et al.*, 2018, 2019; Nieuwenhuijsen *et al.*, 2018; Andersson *et al.*, 2020; Klompmaker *et al.*, 2020; Thacher *et al.*, 2020) were cohort studies analysing data at individual-level, other study designs included ecological study (Hansell *et al.*, 2013; Evrard *et al.*, 2015; Halonen *et al.*, 2015), case-control study (Barceló *et al.*, 2016). The majority of studies focused on road traffic noise, with a few studies on aircraft noise (Huss *et al.*, 2010; Hansell *et al.*, 2013; Evrard *et al.*, 2015; Héritier *et al.*, 2019), whilst studies on railway noise were scant (Héritier *et al.*, 2019; Klompmaker *et al.*, 2020). Mortality from all CVD or cause-specific CVD were the most commonly investigated outcomes, while a very small number of studies focused on other mortality outcomes such as respiratory (Klompmaker *et al.*, 2020; Thacher *et al.*, 2020), diabetes (Barceló *et al.*, 2016), cancer (Klompmaker *et al.*, 2020; Thacher *et al.*, 2020) and neurodegenerative disease (Klompmaker *et al.*, 2020).

Risk of bias assessment for these 13 studies is individually presented in **Supplementary-3**. For most studies, the overall risk of bias was rated as '*probably high*' or '*high*', except only four studies(Huss *et al.*, 2010; Héritier *et al.*, 2018, 2019; Andersson *et al.*, 2020) in which the overall risk of bias was rated as '*probably low*'. Most studies with high risk of bias did not adjust for individual-level SES in the statistical analysis or assigned noise exposure at postcode- or area-level rather than individual address-level.

For each reported association with non-accidental or CVD-related mortality, the risk estimates per 10dB higher of the original noise metric used are listed in **Table 2** (other mortality outcomes on **Supplementary-7**). Seven studies used L_{den} as the noise metric while others used various noise metrics; for the specific meta-analysis purpose we converted these metrics into L_{den} for other studies (Huss *et al.*, 2010; Hansell *et al.*, 2013; Halonen *et al.*, 2015; Barceló *et al.*, 2016; Nieuwenhuijsen *et al.*, 2018; Andersson *et al.*, 2020). All studies either modelled traffic noise from a valid method or obtained traffic noise exposure from a European Union noise map. Not all studies reported the range of absolute noise level, but of the available information, the absolute noise level ranged at least from 29 to 90 dB for L_{den}, based on the original reports from two studies (Beelen *et al.*, 2009; Gan *et al.*, 2012).

3.3.Meta-analysis on non-accidental mortality

All pooled relative risks per 10dB higher L_{den} on non-accidental mortality were summarised in **Table 3** for each traffic source and respective forest plots and Doi plots were shown in **Supplementary-8**.

Pooling estimates of road traffic noise only, the RR was 1.01 (95%CI: 0.98 to 1.05), with an I^2 of 78%. The only study of rail traffic noise (Klompmaker *et al.*, 2020) reported a null association (RR: 0.99, 95%CI: 0.97-1.00). Subgroup analyses by study design did not yield

material differences on the pooled relative risks. Overall, the quality of evidence was rated as very low to low.

3.4.Meta-analysis on CVD mortality

Nine estimates (five of road traffic, three of aircraft traffic, one of rail traffic) from eight studies (Beelen *et al.*, 2009; Huss *et al.*, 2010; Hansell *et al.*, 2013; Evrard *et al.*, 2015; Halonen *et al.*, 2015; Andersson *et al.*, 2020; Klompmaker *et al.*, 2020; Thacher *et al.*, 2020) were included for meta-analysis on all CVD mortality (**Table 4**). The pooled RRs for road traffic and aircraft noise were 1.01 (95%CI: 0.98-1.05) and 1.17 (95%CI: 1.10-1.25) with an I^2 of 41% and 0% respectively. Overall, the quality of evidence was rated as very low to low, except for road traffic noise studies of cohort or case-control design, for which the quality of evidence was rated as moderate.

Twelve estimates (seven of road traffic, three of aircraft traffic, two of rail traffic) from nine studies (Beelen *et al.*, 2009; Hansell *et al.*, 2013; Evrard *et al.*, 2015; Halonen *et al.*, 2015; Barceló *et al.*, 2016; Héritier *et al.*, 2019; Andersson *et al.*, 2020; Klompmaker *et al.*, 2020; Thacher *et al.*, 2020) were included for meta-analysis on IHD mortality (**Table 4**). For road traffic noise, the observed pooled RR was 1.03 (95%CI: 0.99-1.08) with an I^2 of 46% (**Figure 2**). For aircraft noise, the observed pooled RR was 1.03 (95%CI: 0.82-1.29) with an I^2 of 82%. For rail traffic noise, the observed pooled RR from the two studies (Héritier *et al.*, 2019; Klompmaker *et al.*, 2020) was 1.01 (95%CI: 1.01-1.03) with an I^2 of 84%. Overall, the quality of evidence was rated as very low to low, except for road traffic noise studies of cohort or case-control design, for which the quality of evidence was rated as moderate.

Nine estimates (five of road traffic, three of aircraft traffic and one of rail traffic) from eight studies (Beelen *et al.*, 2009; Huss *et al.*, 2010; Hansell *et al.*, 2013; Evrard *et al.*, 2015; Halonen *et al.*, 2015; Andersson *et al.*, 2020; Klompmaker *et al.*, 2020; Thacher *et al.*, 2020)

were included for meta-analysis on stroke mortality (**Table 4**). The pooled RR was 1.05 (95%CI: 0.97-1.14) for road traffic noise and 1.06 (95%CI: 0.93-1.20) for aircraft noise, although for the latter no evidence of between-study heterogeneity (I^2=0%) was found. Overall, the quality of evidence was rated as very low to low.

For each of the aforementioned meta-analyses, forest plot and Doi plot was available in **Supplementary-9**.

3.5.Trend estimation between road traffic noise and mortality

The shape of a linear trend was less clear for non-accidental mortality (**Figure 3A**). For mortality from all CVD, IHD, and stroke (**Figure 3 B-D**), evidence of non-linearity was observed for IHD (p-value <0.001) and stroke (p-value=0.023). Visual inspection revealed that, for all CVD and IHD mortality outcomes, risk started to increase from approximately 53dB, although such risk was possibly only significantly higher at levels exceeding 55dB.

3.6. Sensitivity meta-analyses (random-effect model, leave-one-out method, subgroups)

When each meta-analysis was performed using a random-effect model, all pooled RRs remain unchanged or were similar to those of using I-Vhet model, although most of the 95% confidence intervals were narrower as expected (**Supplementary-10**). In the leave-one-out analyses, all pooled RRs and associated 95% confidence intervals remained rather stable (**Supplementary-11**), except for aircraft noise and IHD mortality, when the study of the Swiss National Cohort (Héritier *et al.*, 2019) was excluded, the pooled RR (95%CI) changed from 1.03 (95% CI: 0.82-1.29) to 1.23 (95% CI: 1.11-1.37), but the latter was only based on two ecological studies (Hansell *et al.*, 2013; Evrard *et al.*, 2015). For subgroup analyses (**Supplementary-12**), when pooling studies that assigned noise exposure at address-level, the 95%CIs of the pooled RR were generally narrower, indicating more certainty of the estimate.

3.7.Narrative review of other mortality outcomes

Studies on other mortality outcomes remain few. Two studies reported significant positive associations between traffic noise and mortality from hypertensive diseases (Barceló *et al.*, 2016; Héritier *et al.*, 2018) and one reported no association with atrial fibrillation (Andersson *et al.*, 2020). Whilst some time-series studies reported significant associations between road traffic noise and respiratory mortality (Tobias *et al.*, 2014; Recio *et al.*, 2016), this was not observed in the other two large individual-level cohort studies (Klompmaker *et al.*, 2020; Thacher *et al.*, 2020). Studies on other mortality outcomes including diabetes, cancer, and neurodegenerative disease generally reported no associations (Barceló *et al.*, 2016; Klompmaker *et al.*, 2020). While there was a small non-significant elevated risk on non-accidental mortality for exposure to road traffic noise among myocardial infarction patients (Tonne *et al.*, 2016); such elevated risk was not observed among cancer patients (Roswall *et al.*, 2016; Roswall *et al.*, 2017).

4. Discussion

4.1. Summary of findings

First, current evidence based on a limited number of studies does not suggest an association between different types of traffic noise and non-accidental mortality. Second, supporting the WHO review on incident IHD, we found that every 10dB higher in road traffic L_{den} was associated with a 3% increase in risk of IHD mortality with moderate evidence of between-study heterogeneity. Associations with all other CVD outcomes by each traffic source were weak and not consistent across studies except the one between aircraft noise and all CVD mortality. Third, a potential threshold of 53dB was suggested for road traffic noise on CVD-related mortality.

4.2.Comparison with previous reviews

For road traffic noise, the WHO review reported a RR per 10dB higher noise level for IHD and stroke mortality was 1.05 (95%CI: 0.97-1.13) and 0.87 (95%CI: 0.71-1.06), respectively (van Kempen *et al.*, 2018), each based on three studies. Our current review has further updated these estimates by including studies published after year 2015. We herein reported a positive pooled estimate (RR:1.03, 95%CI: 0.99-1.08) for IHD mortality and (RR: 1.05, 95%CI: 0.97-1.14) for stroke mortality per 10dB higher road traffic L_{den} level. The point estimate for IHD mortality remained materially similar, but the confidence interval of our estimated effect size was narrower. It should be noted that our pooled estimate of road traffic noise on IHD mortality was likely influenced by a recent large study by Héritier and colleagues (Héritier *et al.*, 2019), which reported a RR of 1.03 (95%CI: 1.01-1.06) per 10dB higher in road L_{den} in a population of 4.4 millions. In the leave-one-out analysis, excluding this study yielded a pooled RR of 1.02 (95%CI: 0.97-1.08). The pooled estimate for stroke mortality has been updated to a greater extent in our review, by further including positive estimates from three large recent cohort studies (Andersson *et al.*, 2020; Klompmaker *et al.*, 2020; Thacher *et al.*, 2020).

For aircraft noise, the WHO review reported a RR per 10dB higher noise level for IHD and stroke mortality was 1.04 (95%CI: 0.97-1.12) and 1.07 (95%CI: 0.98-1.17) respectively, based on two ecological studies. Our updated estimates remained similar to these as only two aircraft noise studies, one ecological study and one cohort study (Evrard *et al.*, 2015; Héritier *et al.*, 2019), on IHD or stroke mortality were published in the last five years. More aircraft noise studies at individual-level are therefore much needed to strengthen this evidence base on mortality effects.

The much higher pooled estimate (RR: 1.17, 95%CI: 1.10-1.25) of aircraft noise on all CVD mortality should be interpreted with a greater caution. First, this pooled estimate, based on two ecological studies (Hansell *et al.*, 2013; Evrard *et al.*, 2015) and one census-linkage

cohort study (Huss *et al.*, 2010), was largely influenced by results from one ecological study (Evrard *et al.*, 2015) that is subject to ecological fallacy; therefore, it is not certain whether these associations would be observed at individual level. An individual-level longitudinal study, where important predictors of mortality such as tobacco smoking and diet are usually collected, is better placed to elucidate this association. Second, it is challenging to interpret this association as all CVD includes a wide range of cardiovascular diseases which likely have different associations with aircraft noise. Unlike IHD and stroke, more chronic CVD outcomes such as heart failure, which usually is the end stage of CVD, may be particularly vulnerable to mortality effects from traffic exposure including noise (Carey *et al.*, 2016). In fact, heart failure mortality was found to have the strongest association, among all other common CVD outcomes, with combined traffic noise sources in a nationwide study in Switzerland (Héritier *et al.*, 2018).

To our knowledge, this is the first meta-analysis that attempted to estimate linear trends for road traffic noise and mortality effect, based on all currently available studies. Previously, Babisch used a categorical meta-analysis to evaluate potential non-linear relationships and reported a threshold at around 57dB L_{den} for road traffic noise on incident IHD (Babisch, 2014). This approach, however, may have to be built on assumptions made on different noise categories and metrics used across different studies. Vienneau and colleagues estimated a linear trend for each individual study (Vienneau *et al.*, 2015). They reported a possible threshold at around 50dB L_{den} for all traffic noise sources combined on incident IHD. In contrast, we combined all available studies to estimate the linear trends, in which a possible threshold of 53dB was visually suggested for CVD-related mortality, the same threshold suggested in the recently updated WHO guidelines on the health effects of road traffic noise (*Environmental Noise Guidelines for the European Region (2018)*, no date). Our results echo with these previous reports that the associations between road traffic noise and IHD outcomes

391 are likely non-linear. We, however, cannot fully evaluate the shapes of exposure-response
392 relationships for all CVD and stroke mortality particularly at higher noise levels (i.e.>60dB),
393 as data was limited by the range of noise exposures from available studies.

394 4.3.Biological mechanisms

395 There are already a number of comprehensive reviews (Münzel *et al.*, 2014, 2018) on the
396 possible biological mechanisms underlying the associations between traffic noise and
397 cardiovascular outcomes; we, therefore, refer readers to these reviews. In short, a main
398 hypothesis is that chronic exposure to noise, as a general stressor, leads to activation of the
399 autonomic nervous system and endocrine system, and a cascade of stress effects (Münzel,
400 Sørensen, *et al.*, 2017). Physiological adaptions to these stress effects in a chronic timeframe
401 will generate unfavourable alterations in many CVD biomarkers, oxidative stress, and
402 vascular function which, if left untreated, will manifest as CVD and contribute to premature
403 mortality (Münzel *et al.*, 2018). Other pathways suggest that traffic noise might indirectly
404 affect health through emotional response (i.e. noise annoyance) and/or sleep quality, although
405 some studies suggested that impacts of traffic noise on the cardiovascular system are likely to
406 be independent of these factors (Münzel, Sørensen, *et al.*, 2017). In addition, an important
407 study recently reported that there may exist a neurobiological pathway linking noise and
408 CVD (Osborne *et al.*, 2020). It was found that the amygdala may participate in processing
409 stress responses to noise and increase CVD risk via heightened arterial inflammation.

410 Health effects of traffic noise could vary by its sources, characteristics, and intensity (Münzel
411 *et al.*, 2018). Studies in both healthy adults and mice suggested that controlled higher
412 exposure (i.e. >60dB) to aircraft noise in a short period was associated with elevated blood
413 pressure and vascular dysfunction through oxidative stress and inflammation (Schmidt *et al.*,
414 2013; Münzel, Daiber, *et al.*, 2017). Whether these biological pathways could also be seen

with road traffic noise remain to be investigated. In a recent study, aircraft noise was found to be more annoying than rail or road traffic noise (Brink *et al.*, 2019), suggesting intensity of acute variations of noise over time may potentially mediate the health effects.

4.4.Limitations and future research

We conducted the search in *a priori* selected medical literature databases and in English language only. It is still possible we missed some studies, in particular those published in non-English language. For one study (Nieuwenhuijsen *et al.*, 2018), we treated all-cause as non-accidental mortality in the meta-analysis while for studies which only reported on myocardial infarction mortality, we still included them in the analysis of overall IHD mortality. While we cannot separate these different outcomes, the pooled estimates, however, are likely to remain similar (Khosravipour and Khanlari, 2020).

Due to the limited number of studies we could only test departure from linearity for studies that reported road traffic noise. Additionally, the results for linear trend estimation could have been influenced by the small number of studies that were included in these analyses.

Due to the small number of available studies, the potential sources of heterogeneity observed in most of our meta-analyses were not formally investigated. The descriptive subgroup analyses however indicated likely sources may include study designs, noise exposure assessment, bias from covariate adjustment and sample size, amongst others.

Although covering some typical sources of potential bias, the pre-defined criteria to evaluate risk of bias at study-level in this review was somewhat arbitrary. This subject matter is still debated and no such a standard tool exists, as acknowledged in a recent commentary which called for a comprehensive approach to identify and quantify possible bias, specifically their directions and magnitude, and the overall importance on the effect estimate, instead of using a pre-defined checklist approach (Steenland *et al.*, 2020).

More high-quality studies on traffic noise and mortality outcomes are needed on several aspects. For example, studies combining different sources of traffic noise, as well as other environmental noise (e.g. wind turbine noise) are crucial to assess the relative importance of each source on health risks and also to decide which model (energetic noise addition model vs. epidemiological risk multiplication model) performs better on predicting these health risks (Seidler *et al.*, 2019). In terms of covariate adjustment in the statistical analysis, we suggest future studies should use directed acyclic graphs (Greenland, Pearl and Robins, 1999) or similar tools to select covariates for adjustment to avoid a potential over-adjustment issue. Ideally, the sequence of models should be presented as follows: unadjusted, further adjusted for age, sex, individual-level and/or area-level SES (i.e. no adjustment for potential mediators), further adjusted for lifestyle factors, and finally further adjusted for air pollution if data were available. Some recent studies observed positive associations between road traffic noise exposure and non-participation in leisure sports (Roswall *et al.*, 2017), consumption of alcohol and tobacco smoking (Roswall *et al.*, 2018), and BMI (Cai *et al.*, 2020), suggesting that these lifestyle factors could be on the pathway between traffic noise exposure and CVD outcomes. As mentioned earlier, noise characteristics and eventfulness of a noise situation should be further elucidated in relation to health effects. Studies on railway noise on health outcomes are still rare. Outcomes other than CVD should be paid more attention, for example, morbidity and mortality relating to mental/neurobiological health. As with previous reports (Vienneau *et al.*, 2015), the majority of current evidence seems to suggest that traffic-related air pollution is likely not confounding the role of traffic noise on CVD outcomes. However, we suggest future noise and health studies should still consider accounting for traffic air pollution as well as greenspace if possible, which may provide useful information to understand whether there exist synergistic or antagonistic health effects

of these common urban exposures. Lastly, traffic noise and health studies are urgently needed from regions outside Europe to better understand these associations in a global context.

5. Conclusion

Evidence of long-term exposure to traffic noise on mortality remain weak except the association between road traffic noise and IHD mortality. High-quality longitudinal studies are required to better characterise mortality effects of traffic noise.

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Conflict of Interest

We declared no conflict of interest.

Authors' contribution

Yutong Cai – Conceptualization, data curation, formal analysis, methodology, validation, visualization, writing – original draft; writing – review & editing;

Rema Ramakrishnan – data curation, formal analysis, methodology, validation, visualization, writing – review & editing;

Kazem Rahimi - Writing - review & editing

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Figure legends

Figure 1 Flowchart of study selection for the review.

Figure 2 Forest plot of the association between per 10dB higher road traffic L_{den} and ischemic heart disease mortality; RR- relative risk, Q and I^2 – heterogeneity statistics.

Figure 3 Trend estimation of road traffic noise effects on mortality outcomes based on currently available studies: A) non-accidental mortality, B) all-CVD mortality, C) IHD mortality and D) stroke mortality.

Table 1 Eligibility criteria to screen studies for the review

Components	**Inclusion criteria**	**Exclusion criteria**
Population	Adults, general population	Children, animals, occupational populations, and pregnant women
Exposure	Residential traffic noise from road, rail and aircraft, measured or modelled	Self-reported, occupational noise, wind turbine and construction noise, neighbour noise, noise annoyance
Comparator	Risk estimates adjusted for at least age and sex; two or more exposure groups or provision of a linear trend	Unadjusted effect estimates only; no comparison groups
Outcome	Objectively defined using ICD-10 (A00-R99) or equivalent codes of earlier ICD version for non-accidental cause mortality	Self-reported or non-objectively measurement.

Table 2 The fully adjusted associations (risk estimate (95%CI) between exposure to traffic noise and all-cause and CVD mortality outcomes from each reviewed study.

Study	Region/Country	Study Design	Analytical Sample size	Participants: sex and mean age at baseline	Outcome definitions	Noise metric (mean and min-max, dB)±	Number of mortality cases	Non-accidental or all-cause mortality	All CVD mortality	IHD Mortality	Stroke Mortality
(Andersson *et al.*, 2020)	Gothenburg, Sweden	Cohort Study (Follow-up: 36 years)	6,304	M (100%); 58.2 years	ICD10: A00-R99; I00-I99; I20-I25; I61-64	Modelled Road-L_{Aeq24h} (55; range unavailable)	3,182 (natural mort.) 1,569 (CVD mort.)	1.01 (0.94-1.07)	1.03 (0.94-1.14)	1.09 (0.99-1.19)	1.06 (0.94-1.20)
(Thacher *et al.*, 2020)	Copenhagen and Aarhus, Denmark	Cohort Study (Follow-up: 19 years)	52,758	M(47%), F(53%); 57.5years	ICD10: A00-R99 I00-I99; I20-I25; I60-I64; J00-J99; C00-C97	Modelled Road-L_{den} (Median 55.8; 5%-95%: 44-69)	11,596 (all mort.) 2,623 (CVD mort.)	1.08 (1.04-1.12)	1.10 (1.02-1.17)	1.04 (0.92-1.16)	1.12 (0.97-1.29)
(Klompmaker *et al.*, 2020)	the Netherlands	Cohort study (Follow-up: 5 years)	339,633	M (46%), F(54%); 63 years	ICD10: A00-R99 I00-I99 J00-J99 I20-I25 I60-I69	Modelled Road and Rail - L_{den} (Median for road: 53; rail: 29, range unavailable)	26,886 (natural mort.) 8,020 (CVD mort.)	0.99 (0.96-1.01) (road); 0.99 (0.97-1.00) (rail)	1.00 (0.96-1.04) (road); 0.98 (0.94-1.01) (rail)	0.95 (0.87-1.01) (road); 0.93 (0.86-0.99) (rail)	1.07 (0.99-1.15) (road); 0.96 (0.91-1.03) (rail)
(Héritier *et al.*, 2019)	Switzerland	Cohort study (Follow-up: 8 years)	4.4 millions	M (48%), F(52%); 48 years	ICD10: I21-I22	Modelled Road, rail and Aircraft - L_{den} (Median: 54.1, range unavailable)	19,261 (MI mort.)	-	-	1.034 (1.014-1.055) (road); 1.020 (1.008-1.034) (rail); 1.026 (1.006-1.047) (aircraft)	-

(Nieuwenhuijsen *et al.*, 2018)	Barcelona, Spain	Cohort study (Follow-up: 4 years)	792,649	M (53%) F(47%); 51 years	All-cause mortality extracted from relevant database	Measured Road-L_{Aeq16h} (64; range unavailable)	28,391 (all mort.)	0.98 (0.94-1.02)	-	-	-
(Héritier *et al.*, 2018)	Switzerland	Cohort study (Follow-up: 8 years)	4.4 millions	M (48%), F(52%); 48 years	ICD10: I00-I99; I20-I25; I60-I64; I21-I22; I50 I10-I15	Modelled combined (Road, rail and aircraft) -L_{den} (55; 35-89)	142,995 (CVD mort.)	-	1.024 (1.016-1.031)	1.023 (1.011-1.035)	1.003 (0.985-1.023)
(Barceló *et al.*, 2016)	Barcelona, Spain	Case-control study	12,878 (6,439 cases: 6,439 controls)	Unclear	ICD-10: I21-I22	Measured Road-L_{day} (65; range unavailable)	6,439 (MI mort.)	-	-	1.22 (1.10-1.51) men only;	-
(Halonen *et al.*, 2015)	London, England	Ecological study	8.61 millions	unclear	ICD10: A00-R99 I00-I99 I20-I25 I61,I63,I64	Modelled Road-L_{Aeq16h} (Median: 56.6, range unavailable)	442,560 (all mort.); 151,585 (CVD mort.)	1.02 (0.98-1.06)	1.00 (0.96-1.06)	1.00 (0.94-1.06)	1.04(0.96-1.12)
(Evrard *et al.*, 2015)	Paris, Lyon, Toulouse, France	Ecological study	1.9 millions	unclear	ICD10: I00-I52; I20-I25 I21-I22 I60-I64	Modelled Aircraft-L_{den} (50; 42-64)	*unclear*	-	1.18 (1.10-1.26)	1.23 (1.10-1.38	1.06 (0.93-1.21)
(Hansell *et al.*, 2013)	London, England	Ecological study	3.6 millions	unclear	ICD10: I00-I99 I20-I25 I61,I63,I64	Modelled Aircraft - L_{day} and L_{night} (mean and range unavailable)	48,347 (CVD mort.)	-	1.16 (1.04-1.29) for L_{day}>63 vs <=51dB; 1.14 (1.03-1.26) for L_{night} >55 vs.<=50dB 1.20 (0.88-1.61)*	1.15 (1.02-1.30) L_{day} >63 vs. <=51dB; 1.11 (0.99-1.24) for L_{night} >55 vs.<=50dB 1.27 (0.91-1.76)*	1.21 (0.98-1.49) L_{day} >63 vs. <=51dB; 1.23 (1.02-1.49) L_{night} >55 vs.<=50dB 1.37 (0.77-2.46)*

(Gan *et al.*, 2012)	Vancouver, Canada	Cohort study (Follow-up years: 4 years)	445,868	M (46%), F(54%); 59 years	ICD9: 410-414, 429.2 ICD10: I20-I25	Modelled Community - L_{den} (63; 33-90)	3095 (CHD mort.)	-	-	1.12 (1.05-1.21)	-
(Huss *et al.*, 2010)	Switzerland	Cohort study (Follow-up: 5 years)	4.6 millions	M (50%), F(50%); 52 years	ICD10: I21, I22 I00-I99 I60-64	Modelled Aircraft - L_{dn} (mean and range unavailable)	15,532 (MI mort.)	-	>=60 vs <45 dB, 0.99 (0.89-1.09); 1.12 (0.94-1.32)*	>=60 vs <45dB, 1.30 (0.96-1.76); 1.42 (0.78-2.59)*	>=60 vs <45dB 0.83 (0.61-1.13); 0.84 (0.52-1.37)*
(Beelen *et al.*, 2009)	the Netherlands	Cohort Study (Follow-up: 9 years)	117,528	M (48%), F(52%);63 years	ICD9: 400-440 410-414 430-438 428 427	Modelled Road – max L_{den} (52; 29-75)	6,137 (CVD mort.)	-	>65 vs <= 50dB, 1.17 (0.94-1.45) ; 0.88 (0.57-1.36)*	>65 vs <= 50dB, 1.01 (0.74-1.36); 0.88 (0.48-1.60)*	>65 vs <= 50dB 0.95 (0.55-1.66); 0.23 (0.09-0.64)*

Effect size from each exposure-response relationship was presented as per 10dB higher traffic noise level unless specified otherwise in the table. Original noise metric (L_{den}, L_{Aeq24h}, L_{Aeq16h}, L_{DN} etc) was kept for each study. Risk estimates were obtained from fully adjusted models where available including adjustment for air pollution. *For studies of Hansell, Huss and Beelen, original categorical effect estimates were converted to a linear exposure-response relationship per 10dB higher in L_{den}. ±: mean and range of noise indicators were presented for each study unless specified otherwise in the table. L_{day} – daytime noise, L_{night}- nighttime noise. CVD: cardiovascular disease; IHD: ischemic heart disease; CHD: coronary heart disease; MI: Myocardial Infarction.

Table 3 Summary of results from Inverse-Variance heterogeneity meta-analysis on associations (pooled RR [risk estimate] (95%CI)) between per 10dB higher in L_{den} levels and non-accidental mortality.

Noise source	N	Main Pooled RR (95%CI)	I^2	N	Study design	Pooled RR (95%CI)	I^2	Number of participants (cases)	Quality of evidence[Δ]
Road traffic	5	1.01 (0.98-1.05)	78%	4	Cohort/ Case-control	1.01 (0.96-1.05)	83%	1,191,344 (70,055)	Low
				1	Ecological	1.02 (0.98-1.05)	-	8,610,000 (442,560)	Very Low
Rail traffic	1	0.99 (0.97-1.00)	-	1	Cohort/ Case-control	0.99 (0.97-1.00)	-	339,633 (26,886)	Low

N=number of individual estimates; I^2=variation in estimated effect attributable to heterogeneity; [Δ]: *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; *Very Low* – any estimate of effects is very uncertain.

Table 4 Summary of results from Inverse-Variance heterogeneity meta-analysis on associations (pooled RR[risk estimate] (95%CI)) between per 10dB higher in L_{den} levels and CVD mortality

All CVD mortality									
Noise source	N	Main Pooled RR (95%CI)	I2	N	Study design	Pooled RR (95%CI)	I2	Number of participant (cases)	Quality of evidence$^{\Delta}$
Road traffic	5	1.01 (0.98-1.05)	41%	4	Cohort/Case-control	1.02 (0.97-1.08)	50%	516,223 (18,349)	Moderate
				1	Ecological	1.00 (0.97-1.05)	-	8,610,000 (151,585)	Very Low
Aircraft traffic	3	1.17 (1.10-1.25)	0%	1	Cohort/Case-control	1.12 (0.94-1.32)	-	4,600,000 (177,836)	Low
				2	Ecological	1.18 (1.11-1.26)	0%	5,500,000 (48,347*)	Very Low
Rail traffic	1	0.98 (0.94-1.01)	-	1	Cohort/Case-control	0.98 (0.94-1.01)	-	339,633 (8,020)	Low
IHD mortality									
Noise source	N	Main Pooled RR (95%CI)	I2	N	Study design	Pooled RR (95%CI)	I2	Number of participant (cases)	Quality of evidence$^{\Delta}$
Road traffic	7	1.03 (0.99-1.08)	46%	6	Cohort/Case-control	1.03 (0.98-1.09)	48%	4,929,101 (33,784)	Moderate
				1	Ecological	1.00 (0.95-1.05)	-	8,610,000 (69,163)	Very Low

Aircraft traffic	3	1.03 (0.82-1.29)	82%	1	Cohort/Case-control	1.03 (1.01-1.05)	-	4,400,000 (19,261)	Low
				2	Ecological	1.23 (1.11-1.37)	0%	5,500,000 (22,613*)	Very Low
Rail traffic	2	1.02 (0.91-1.14)	84%	2	Cohort/Case-control	1.02 (0.91-1.14)	84%	4,739,633 (21,247)	Low
Stroke mortality									
Noise source	N	Main Pooled RR (95%CI)	I2	N	Study design	Pooled RR (95%CI)	I2	Number of participant (cases)	Quality of evidence[Δ]
Road traffic	5	1.05 (0.97-1.14)	62%	4	Cohort/Case-control	1.06 (0.94-1.20)	70%	516,223 (4,492)	Low
				1	Ecological	1.03 (0.97-1.10)	-	8,610,000 (29,036)	Very Low
Aircraft traffic	3	1.06 (0.93-1.20)	0%	1	Cohort/Case-control	0.84 (0.52-1.37)	-	4,600,000 (25,231)	Very Low
				2	Ecological	1.07 (0.94-1.22)	0%	5,500,000 (9,803*)	Very Low

N=number of individual estimates; I^2=variation in estimated effect attributable to heterogeneity; *Numbers of CVD-mortality cases was not reported in the original study by Evrard et al, hence was not included in the overall cases; [Δ]: *Moderate* − Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; *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; *Very Low* – any estimate of effects is very uncertain.

Supplementary files

Long-term exposure to traffic noise and mortality: a systematic review and meta-analysis of epidemiological evidence between 2000-2020

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Table of Contents

Supplementary-1 PRISMA checklist for this systematic review

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2,3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5,6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5,6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n/a
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7,8

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7,8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	10,11

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	11
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12,13
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	36-39
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	14
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	36-39 and supplementary files
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	40-43
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	17,18

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19,20,22,23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19,20,23
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	25

Supplementary-2 Literature search terms for each database

Pubmed

All FIELDS=((road) OR (traffic) OR (automobile) OR (vehicle) OR (transport) OR (transportation) OR (rail) OR (aircraft) OR (airport) OR (environmental) OR (community) OR (urban)) AND (noise) AND ((mortality) OR (fatality) OR (death))

Scopus

(TITLE-ABS-KEY(((road) OR (traffic) OR (automobile) OR (vehicle) OR (transport) OR (transportation) OR (rail) OR (aircraft) OR (airport) OR (environmental) OR (community) OR (urban)) AND (noise) AND ((mortality) OR (fatality) OR (death))) AND PUBYEAR > 1999 AND (LIMIT-TO (LANGUAGE,"English")))

Web of Science

TOPIC: (((road) OR (traffic) OR (automobile) OR (vehicle) OR (transport) OR (transportation) OR (rail) OR (aircraft) OR (airport) OR (environmental) OR (community) OR (urban)) AND (noise) AND ((mortality) OR (fatality) OR (death)))

Refined by: LANGUAGES: (ENGLISH)

Timespan: 2000-2020.

EMBASE

'noise exposure' OR 'traffic noise' OR 'transport noise' OR 'community noise' OR 'road noise' OR 'rail noise' OR 'rail traffic noise' OR 'aircraft noise' OR 'railway noise' AND 'mortality' OR 'fatality' OR 'death'.

Supplementary- 3 Risk of Bias Assessment

Detailed instructions and rationales on rating for each domain could be found in **Appendix H** in the review protocol by Teixeira, L. R. *et al.* (2019) '**WHO/ILO work-related burden of disease and injury: Protocol for systematic reviews of exposure to occupational noise and of the effect of exposure to occupational noise on cardiovascular disease.**', *Environment international*. Netherlands, 125, pp. 567–578. doi: 10.1016/j.envint.2018.09.040.

Rating: Low (L), Probably Low (PL), Probably High (PH), High (H) and not applicable (NA).

1. Andersson et al 2020

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	PL	PL	L	L	NA	L	L	L	PL	**Probably Low**
Rationale	insufficient information about participant selection to permit a judgment of low risk of bias, but there is indirect evidence which suggests that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups.	Robust exposure assessment methods with complete residential records, and methods have been tested for validity and reliability. Evidence of exposure misclassification risk, but was not expected to have substantial bias.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study appropriately assessed and accounted for Age, Sex and SES, and other potentially important confounders; all these potential confounders were measured consistently across study participants.	n/a	No missing outcome data.	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The final reporting model may have a potential over-adjustment issue.	

2. Thacher et al 2020

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	PH	PL	L	L	NA	L	L	L	PL	**Probably High**
Rationale	There is insufficient information about participant selection to permit a judgment of high risk of bias, but there is indirect evidence which suggests that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were inconsistent across groups (participants were older, more females, had higher SES, and a lower mortality rate)	Robust exposure assessment methods with complete residential records, and methods have been tested for validity and reliability. Evidence of exposure misclassification risk, but was not expected to have substantial bias.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study appropriately assessed and accounted for Age, Sex and SES, and other potentially important confounders; all these potential confounders were measured consistently across study participants.	n/a	No missing outcome data.	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The final reporting model may have a potential over-adjustment issue.	

3. Klompmaker et al 2020

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	H	PL	L	L	N/A	PL	L	L	PH	**High**
Rationale	There were indications from descriptions of the source population, recruitment ,enrolment procedures, participation and follow-up rates, or data on the distribution of relevant study sample and population characteristics that risk of selection effects were substantial (e.g. elderly were over-sampled, and only individuals living in non-institutionalized households were recruited).	Robust exposure assessment methods with residential records, and methods have been tested for validity and reliability. Evidence of exposure misclassification risk, but was not expected to have substantial bias.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study appropriately assessed and accounted for Age, Sex and SES, and other potentially important confounders; all these potential confounders were measured consistently across study participants.	n/a	While there are no missing outcome data but Participants were only followed for 4 years	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	Only a main model with potential over-adjustment issue was presented.	

4. Heritier et al 2019

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	L	PL	L	PL	N/A	L	L	L	L	**Probably Low**
Rationale	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed to support the assertion that risk of selection effects was minimal (This is a study based on national census of the whole Switzerland).	Robust exposure assessment methods with considerations of both façade and residence floor, and methods have been tested for validity and reliability. Evidence of exposure misclassification risk, but was not expected to have substantial bias.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study appropriately assessed and accounted for Age, Sex and SES, but did not consider other potentially important confounders; However, this is not expected to introduce substantial bias.	n/a	No missing outcome data.	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

5. Nieuwenhuijsen et al 2018

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	L	H	L	L	NA	PL	L	L	L	**High**
Rationale	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed to support the assertion that risk of selection effects was minimal (this study is based on a registration system, covering 80% of all Barcelona populations>= 18 years old).	There is low confidence in the accuracy of the exposure assessment methods, which was based on census-tract but not individual address.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records	The study appropriately assessed and accounted for Age, Sex and SES, and other potentially important confounders; all these potential confounders were measured consistently across study participants.	n/a	While there is no missing outcome data, specific cause of death was unknown. The follow-up period was also short (4 years).	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

6. Heritier et al 2018

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	L	PL	L	PL	N/A	L	L	L	L	**Probably Low**
Rationale	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed to support the assertion that risk of selection effects was minimal (This is a study based on national census of the whole Switzerland).	Robust exposure assessment methods with considerations of both façade and residence floor, and methods have been tested for validity and reliability. Evidence of exposure misclassification risk, but was not expected to have substantial bias.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study appropriately assessed and accounted for Age, Sex and SES, but did not consider other potentially important confounders; However, this is not expected to introduce substantial bias.	n/a	No missing outcome data.	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

7. Barcelo et al 2016

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	PH	PL	L	PH	NA	PL	L	L	L	**Probably High**
Rationale	insufficient information about participant selection to permit a judgment of high risk of bias, but there is indirect evidence which suggests that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were inconsistent across groups. (This is a case-control study).	Robust exposure assessment methods based on EU noise map, and methods have been tested for validity and reliability. Evidence of exposure misclassification risk, but was not expected to have substantial bias.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study only accounted for Age, Sex but did not considered individual-level SES and other potential confounding variables.	n/a	While there are no missing outcome data but death counts were only available for 3 years	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

8. Halonen et al 2015

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	PL	PH	L	PH	NA	L	L	L	L	**Probably High**
Rationale	insufficient information about participant selection to permit a judgment of low risk of bias, but there is indirect evidence which suggests that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups (This small-area study covered all the populations in London)	insufficient information about the exposure assessment methods to permit a judgment of high risk of bias, but there is indirect evidence that suggests that methods were not robust (exposure estimates assigned on small-area/postcode level).	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study only accounted for Age, Sex, area-level SES but did not considered individual-level SES and other potential confounding variables.	n/a	There were no missing outcome data.	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

9. Evard et al 2015

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	PL	PH	L	PH	NA	PL	L	L	L	**Probably High**
Rationale	insufficient information about participant selection to permit a judgment of low risk of bias, but there is indirect evidence which suggests that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups (This study of aircraft noise selected all communes in the vicinity of airport – reasonably representative of these specific populations).	insufficient information about the exposure assessment methods to permit a judgment of high risk of bias, but there is indirect evidence that suggests that methods were not robust (exposure estimates assigned on commune level).	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study only accounted for Age, Sex, area-level SES but did not considered individual-level SES and other potential confounding variables.	n/a	While there are no missing outcome data but mortality outcomes were only followed for 3 years	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

10. Hansell et al 2013

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	L	PH	L	PH	NA	PL	L	L	L	**Probably High**
Rationale	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed to support the assertion that risk of selection effects was minimal ((This study of aircraft noise selected all boroughs in the vicinity of London LHR airport – reasonably representative of these specific populations).	insufficient information about the exposure assessment methods to permit a judgment of high risk of bias, but there is indirect evidence that suggests that methods were not robust (exposure estimates assigned on census output level).	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study only accounted for Age, Sex, ethnicity but did not considered individual-level SES and other potential confounding variables	n/a	While there are no missing outcome data but mortality outcomes were only followed for 4 years	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

11. Gan et al 2011

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	L	PH	L	PH	NA	PL	L	L	PL	**Probably High**
Rationale	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed to support the assertion that risk of selection effects was minimal ((This study was based on a mandatory health insurance program that had covered all metropolitan Vancouver residents).	insufficient information about the exposure assessment methods to permit a judgment of high risk of bias, but there is indirect evidence that suggests that methods were not robust (exposure estimates assigned on postal code level; details on how different sources of traffic noise were modelled not sufficient).	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study only accounted for Age, Sex, area-level SES but did not considered individual-level SES (although used comorbid as a surrogate) and other potential confounding variables	n/a	While there are no missing outcome data but mortality outcomes were only followed for 4 years.	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The final reporting model may have a potential over-adjustment issue.	

12. Huss et al 2010

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	L	PL	L	PL	NA	PL	L	L	L	**Probably Low**
Rationale	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed to support the assertion that risk of selection effects was minimal (This is a study based on national census of the whole Switzerland).	Robust exposure assessment methods, and methods have been tested for validity and reliability. Evidence of exposure misclassification risk, but was not expected to have substantial bias.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study appropriately assessed and accounted for Age, Sex and SES, but did not consider other potentially important confounders; However, this is not expected to introduce substantial bias.	n/a	Most deaths (95%) could be linked to a census record.	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

13. Beelen et al 2009

Domain	Source population representation	Exposure assessment	Outcome assessment	confounding	blinding	Incomplete outcome data	Selective outcome reporting	Conflict of interest	Other sources of bias	Overall risk of bias
Rating	L	PH	L	L	NA	L	L	L	L	**Probably High**
Rationale	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed to support the assertion that risk of selection effects was minimal (This is a study based on nationwide cohort throughout the Netherlands).	insufficient information about the exposure assessment methods to permit a judgment of high risk of bias, but there is indirect evidence that suggests that methods were not robust – e.g. using traffic data in 2000 to model traffic noise back in 1986, and missing information on other data which may have misclassified exposures.	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures such as solid medical records.	The study appropriately assessed and accounted for Age, Sex , area-level SES and other potentially important confounders; all these potential confounders were measured consistently across study participants.	n/a	Almost no missing outcome data (over 99.7% had a cause of death in the certificate)	All of the study's pre-specified outcomes in the published manuscript that are of interest in this review have been reported in the pre-specified way.	The study did not receive support from a company, study author, or other entity having a financial interest in the outcome of the study.	The study appears to be free of other sources of bias.	

Supplementary-4 Descriptions of studies not eligible for meta-analysis in this review

Study	Region/Country	Study Design	Analytical Sample size	Participants: sex and mean age at baseline	Outcome definitions	Noise metric (mean and min-max, dB)±	Number of mortality cases	Natural or all-cause mortality	All CVD mortality	IHD Mortality	Stroke Mortality
(Roswall *et al.*, 2017)	Copenhagen and Aarhus, Denmark	Cohort Study (Follow-up: 4 years)	1,234 (colorectal cancer cases)	M(56%), F(44%); 67 years	ICD10: A00-R99 C18-C20	Modelled Road-L_{den} (Median 58; 5%-95%: 50-71)	594 (all mort.)	1.00 (0.88-1.13)	-	-	-
(Tonne *et al.*, 2016)	London, England	Cohort study (Follow-up: 7 years)	18,138 (MI cases)	M (68%), F(32%); 68 years	ICD10: A00-R99	Modelled Road-L_{Aeq16h} (58; range unavailable)	5,129 (all mort.)	1.04 (0.98 - 1.12)	-	-	-
(Recio *et al.*, 2017)	Madrid, Spain	Time-series study	3.15 millions	Unclear	ICD-10: I00-I99 I20-I25 I21 I60-I69 J00-J99 E10-E14	Measured Road - L_{eqd} (63; 59-67)	18 (daily CVD mort.)	-	Lag0 per 1dB:1.033 (1.017-1.049), >=65 years; 1.050 (1.004-1.098) <65 years	Lag0 per 1dB: 1.029 (1.010-1.048) >=65 years; 1.108 (1.042-1.177) <65 years	Lag0 per 1dB: 1.024 (1.001-1.048) >=65 years; 1.001 (0.897-1.118) <65 years
(Roswall *et al.*, 2016)	Copenhagen and Aarhus, Denmark	Cohort Study (Follow-up: 7 years)	1,759(breast cancer cases)	F (100%); 65 years	ICD10: A00-R99	Modelled Road-L_{den} (Median 58; 5%-95%: 50-71)	402 (all mort.)	0.94(0.81-1.08)	-	-	-
(Tobias *et al.*, 2015)	Madrid, Spain	Case-crossover study	3.15 millions	unclear	ICD9: 390-459	Measured Road-L_{eqd} (64; 61-66)	18 (daily CVD mort.)	-	1.062 (1.021-1.106) per 1 dB at Lag1	-	-

During the peer-review stage of this review, two new studies (based in Rome and Denmark) of road traffic noise and all-cause and CVD mortality were presented at the ISEE2020 conference. While all the results were preliminary and subject to peer-review, both studies reported that long-term higher road traffic noise exposure was significantly linked to either all-cause mortality or specific CVD mortality(Ancona, 2020; Andersen, 2020). These studies, when published after peer-review, will be included for future updates on this review.

Supplementary-5 Definitions of different noise indicators

Noise Indicator	Definition	Time period
L_{den}	Average sound level over all 24 h periods of a year, with a penalty of 5 dB added for the evening hours and penalty of 10 dB added for the night hours	24-h
L_{day} or L_{eqd}	The A-weighted equivalent sound pressure level over the day period	12-h or 16-h
L_{night} or L_{eqn}	The A-weighted equivalent sound pressure level over the night period	8-h
L_{dn}	The weighted average noise level over 24-h periods, with a penalty of 10dB typically applied for night hours (e.g.22:00-07:00)	24-h
L_{Aeq24h}	The A-weighted equivalent sound pressure level over the 24-hperiod	24-h
L_{Aeq16h}	The A-weighted equivalent sound pressure level over 16-h (0700-2300) period	16-h

Note: there are no universal definitions of the time period for 'day', 'evening' and 'night' across different noise indicators, for details, please refer to the following reference.

Brink M, Schäffer B, Pieren R, Wunderli JM. Conversion between noise exposure indicators Leq24h, LDay, LEvening, LNight, Ldn and Lden: Principles and practical guidance. Int J Hyg Environ Health [Internet]. 2018;221(1):54–63. Available from: http://www.sciencedirect.com/science/article/pii/S1438463917304819

Supplementary-6 Conversions from different noise metrics to L_{den} in each study

	Original noise metrics	Natural or all-cause mortality	All CVD mortality	IHD mortality	Stroke mortality	Conversion to L_{den}		Natural or all-cause mortality	All CVD mortality	IHD mortality	Stroke mortality
Andersson, 2020	Road-LAeq24h	1.01 (0.94-1.07)	1.03 (0.94-1.14)	1.09 (0.99-1.19)	1.06 (0.94-1.20)	+3.6dB	L_{den}	1.01 (0.96-1.05)	1.02 (0.96-1.10)	1.07 (0.99-1.14)	1.04 (0.96-1.14)
Nieuwenhuijsen, 2018	Road-LAeq16h	0.98 (0.94-1.02)				+2.3db	L_{den}	0.98 (0.95-1.02)			
Barcelo, 2016	Road - Lday (7-21h)			1.22 (1.10-1.51)		+2.3dB	L_{den}			1.17 (1.08-1.40)	
Halonen, 2015	Road-LAeq16h	1.02 (0.98-1.06)	1.00 (0.96-1.06)	1.00 (0.94-1.06)	1.04 (0.96-1.12)	+2.3dB	L_{den}	1.02 (0.98-1.05)	1.00 (0.97-1.05)	1.00 (0.95-1.05)	1.03 (0.97-1.10)

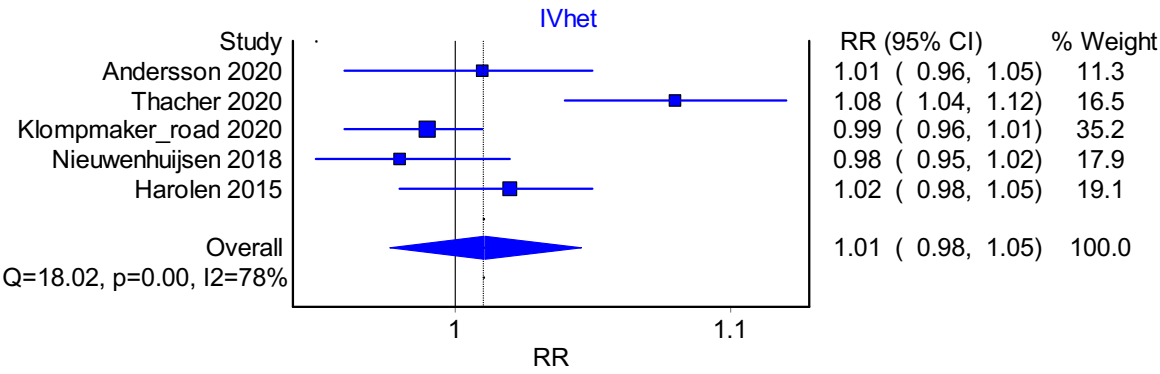
Supplementary-7 traffic noise and mortality outcomes other than CVD-related in the reviewed studies.

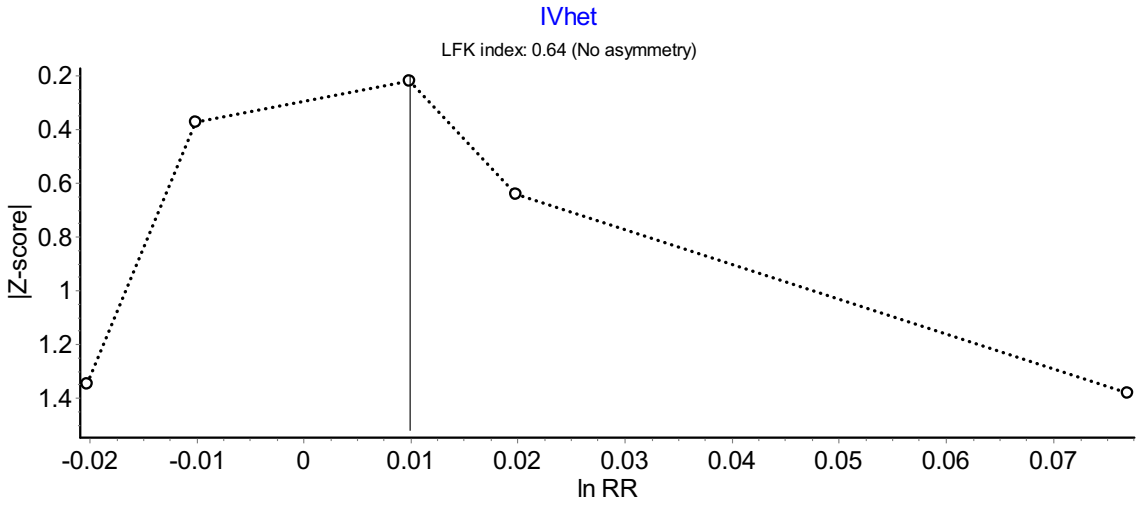
Author, Year	Respiratory Mortality	Cancer mortality	Diabetes mortality	Neurodegenerative disease mortality
Thacher, 2020	1.02 (0.95-1.11)	0.99 (0.94-1.04)		
Klompmaker, 2019	0.93 (0.86-1.00) (road); 1.03 (0.98-1.11)(rail)	0.96 (0.89-1.04) [Lung cancer only] (road); 0.99 (0.93-1.05)(rail)		0.95 (0.88-1.03) (road); 0.98 (0.91-1.03)(rail)
Roswall, 2017		0.98 (0.85-1.13) for colorectal cancer		
Recio, 2016	Lag1: 1.022 (1.002-1.043) >=65 years; 1.004 (0.934-1.079) <65 years, per 1dB		Lag 1: 1.110 (1.040-1.192) >=65 years; 1.082 (0.850-1.379) <65 years, per 1dB	
Barcelo, 2016			1.26 (1.11-1.60) - men only	
Tobias, 2015			1.094 (1.030-1.162)	

Tobias, 2014	1.062 (1.006-1.119) per 1 dB	
Huss, 2010 (Aircraft noise)		1.01 (0.74-1.37) >=60 vs<45 dB, lung cancer only

Supplementary -8: Forest plot and Doi plot for the meta-analysis of traffic noise and non-accidental mortality

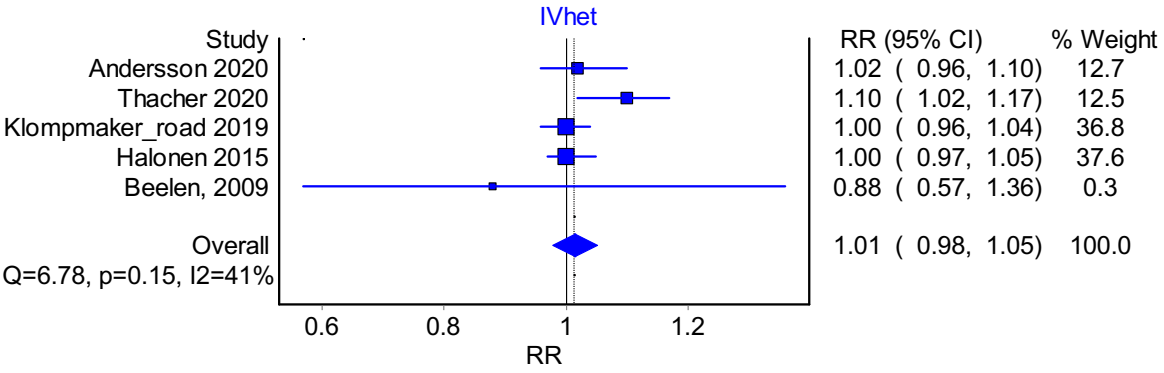
Road traffic source

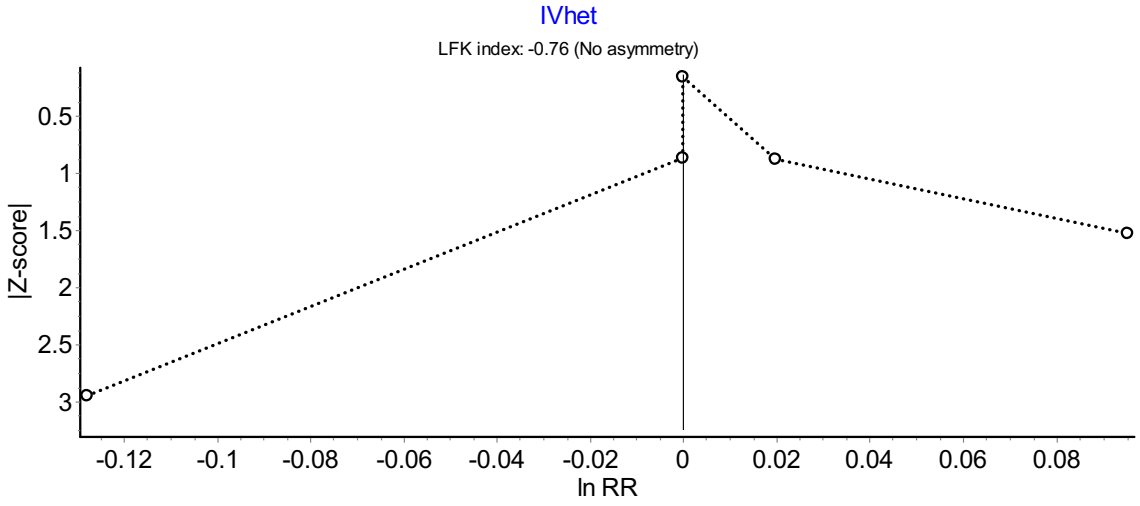




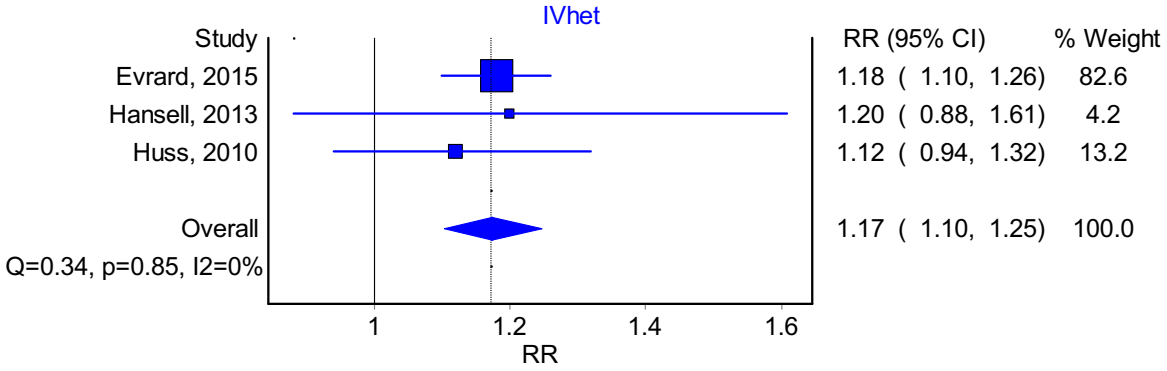
Supplementary-9: Forest plot and Doi plot for the meta-analysis of traffic noise and CVD-related mortality

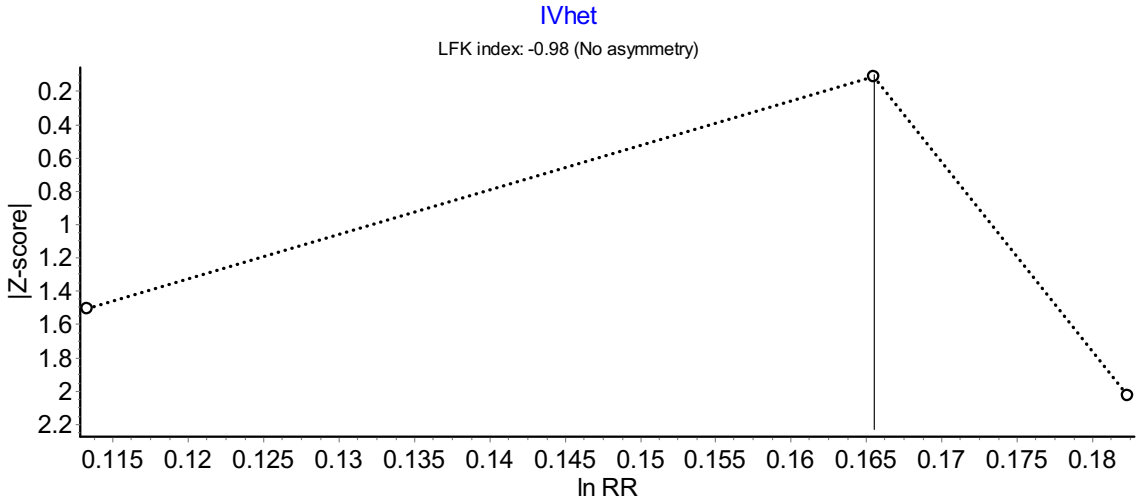
(1a) All CVD mortality – road traffic source



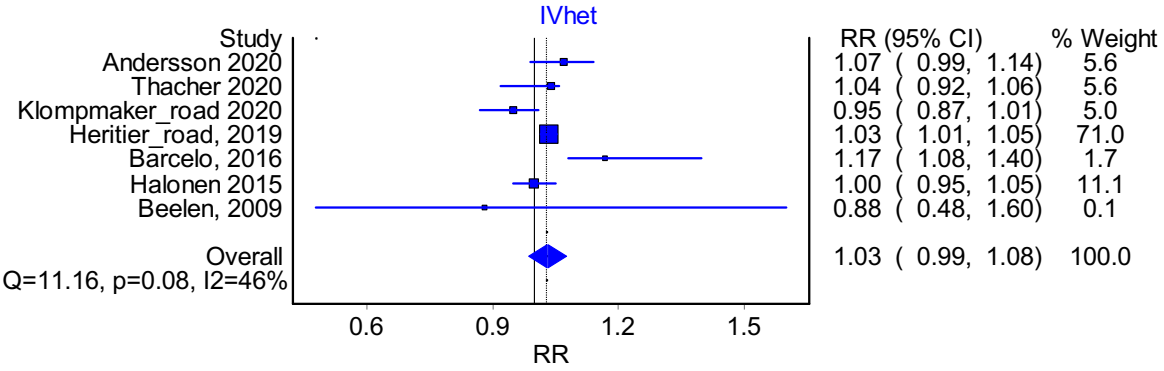


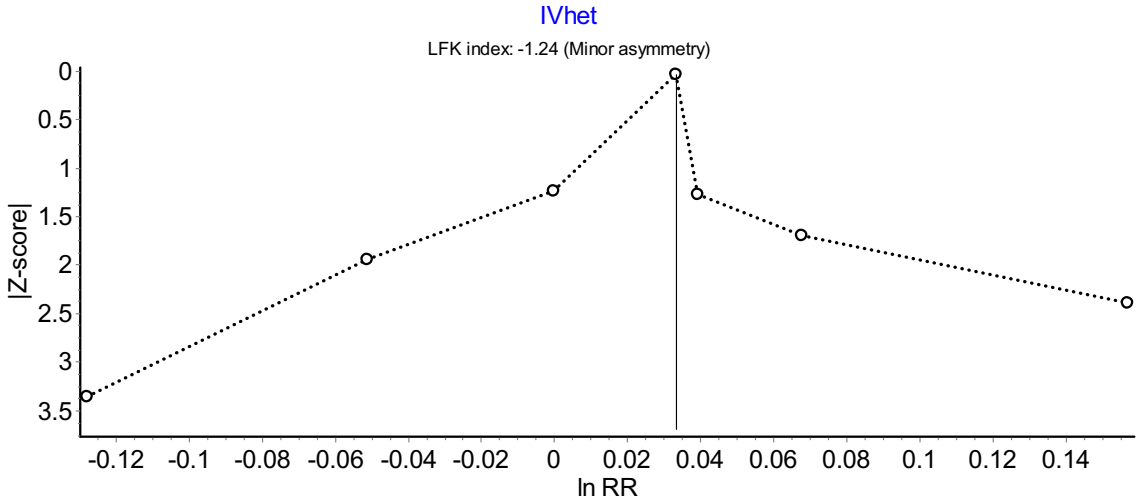
(1b) All CVD mortality – aircraft traffic source



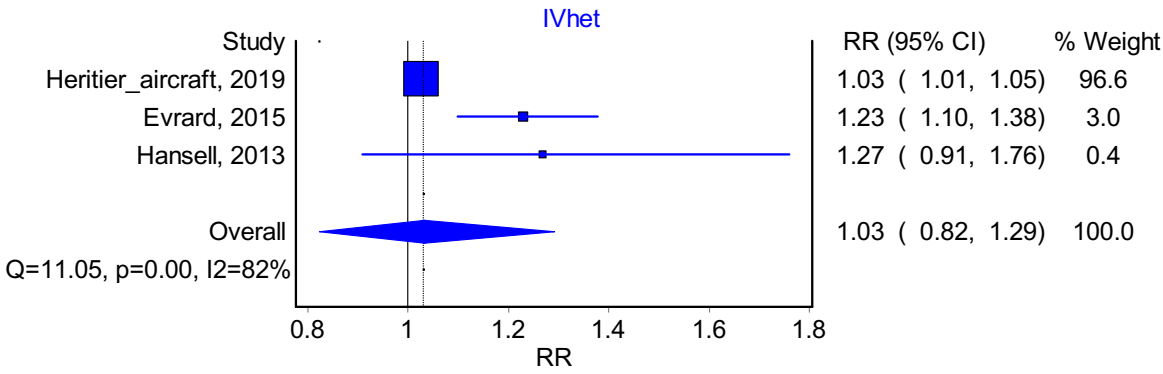


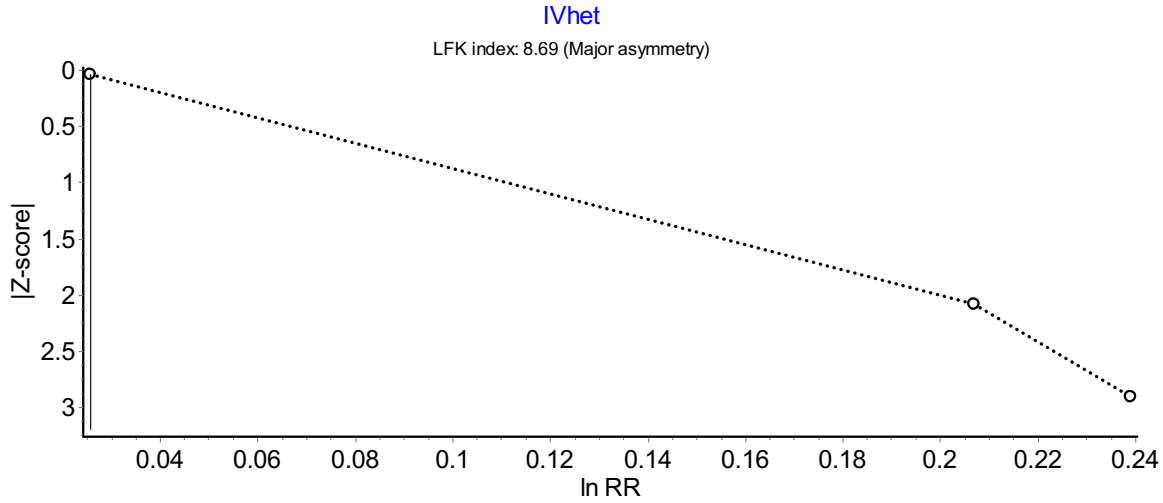
(2a) IHD mortality – road traffic sources



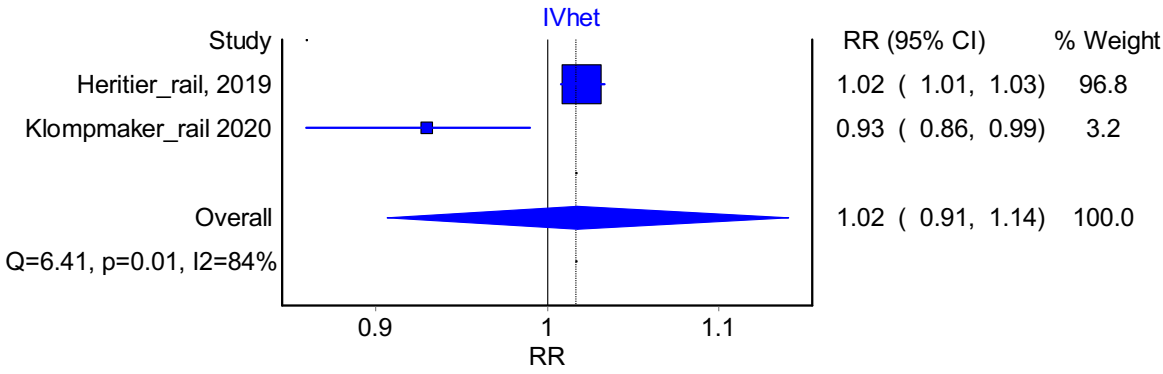


(2b) IHD mortality – aircraft traffic sources

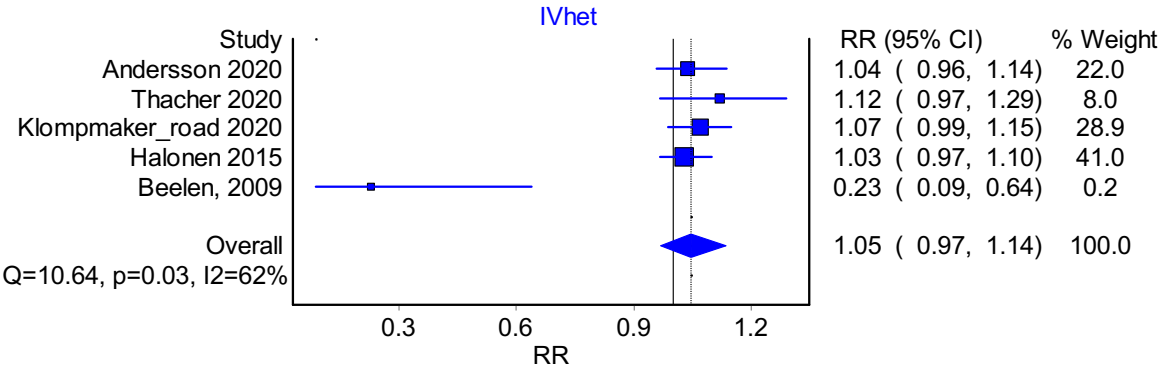


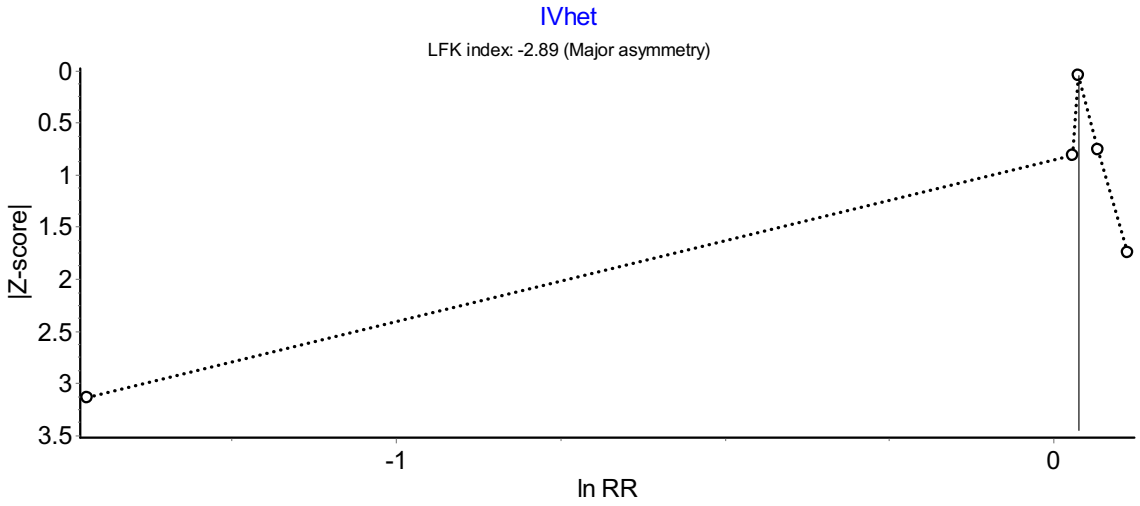


(2c) IHD mortality – rail traffic sources

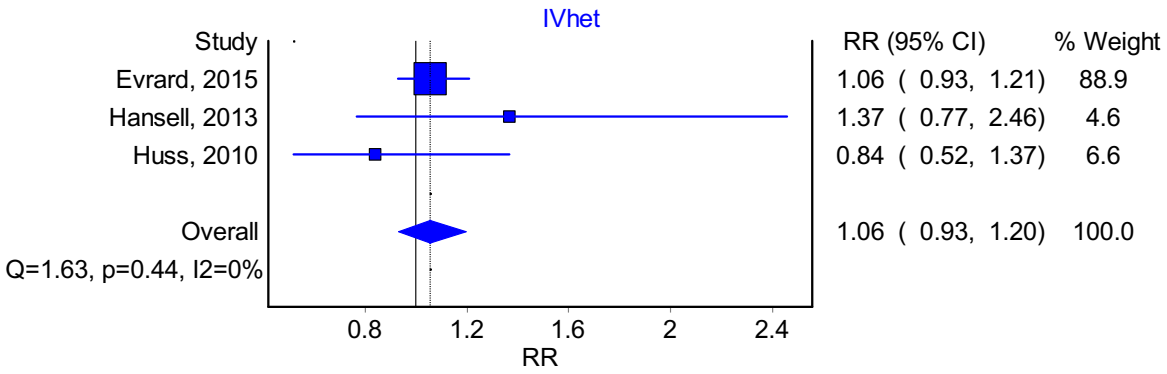


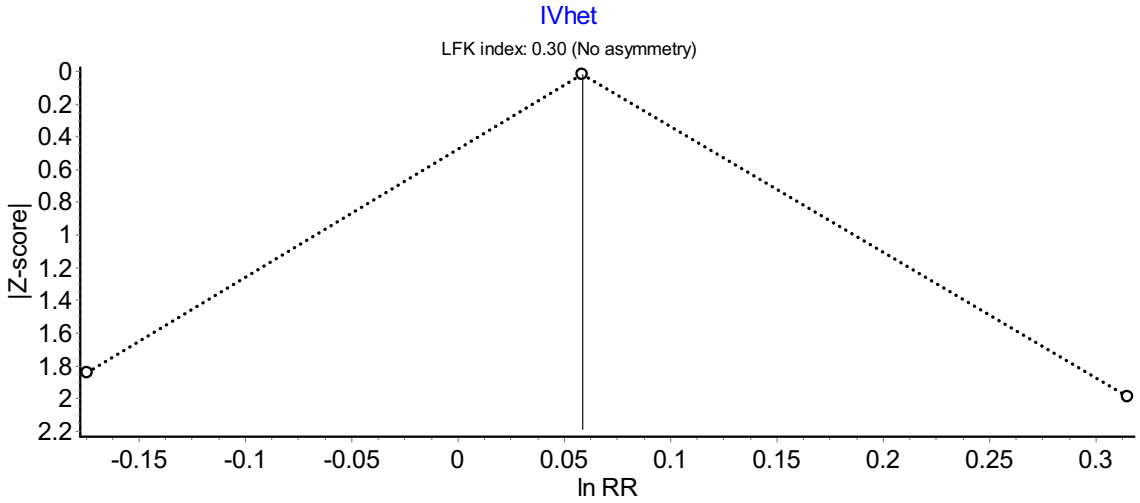
(3a) Stroke mortality – road traffic source





(3b) Stroke mortality – aircraft traffic source





Supplementary-10: Comparisons of pooled RR(95%CI) from meta-analysis using IVhet model and random effects model

Noise source	N	All-cause	I^2	N	All-CVD	I^2	N	IHD	I^2	N	Stroke	I^2
Road	5	1.01 (0.98-1.05)	78%	5	1.01 (0.98-1.05)	41%	7	1.03(0.99-1.08)	46%	5	1.05 (0.97-1.13)	62%
		1.01 (0.98-1.05)	78%		1.02 (0.98-1.06)	41%		1.03(0.99-1.06)	46%		1.05 (0.97-1.13)	62%
Aircraft	-	-	-	3	1.17 (1.10-1.25)	0%	3	1.03 (0.82-1.29)	82%	3	1.06 (0.93-.1.20)	0%
					1.17 (1.10-1.25)	0%		1.14 (0.97-1.13)	82%		1.06 (0.93-1.20)	0%
Rail	1	0.99 (0.97-1.00)	-	1	0.98 (0.94-1.01)	-	2	1.02(0.91-1.14)	84%	1	0.96 (0.91-1.03)	-
								0.98 (0.90-1.07)	84%			

N=number of individual estimates; I2=heterogeneity statistics; Pooled RR (95%CI) in black colour indicated results from IVhet model, while red colour indicated results from random-effect model.

Supplementary-11: Leave-one-out analyses on the main meta-analyses

Road traffic source

Road traffic Sources			
ALL causes mortality			
	Pooled RR (95%CI)	Between-study heterogeneity	LFK index Doi plot asymmetry
All studies	1.01 (0.98-1.05)	P=0.00; I^2=78%	0.64 (No asymmetry)
Excluded study			
Andersson et al	1.01 (0.97-1.05)	P=0.00; I^2=83%	1.98 (Minor)
Thacher et al	1.00 (0.98-1.01)	P=0.36; I^2=6%	1.71 (Minor)
Klompmaker_road et al	1.02 (0.98-1.06)	P=0.00; I^2=79%	0.06 (No asymmetry)
Nieuwenhuijsen et al	1.02 (0.98-1.06)	P=0.00; I^2=79%	1.44 (Minor)
Halonen et al	1.01 (0.96-1.05)	P=0.00; I^2=83%	1.85 (Minor)
ALL CVD mortality			
	Pooled RR (95%CI)	Between-study heterogeneity	LFK index Doi plot asymmetry
All studies	1.01 (0.98-1.05)	P=0.15; I^2=41%	-0.76 (No asymmetry)
Excluded study			
Andersson et al	1.01 (0.97-1.06)	P=0.08; I^2=56%	-1.58 (Minor)
Thacher et al	1.00 (0.98-1.03)	P=0.89; I^2=0%	-3.19 (Major)
Klompmaker_road et al	1.02 (0.97-1.08)	P=0.11; I^2=50%	-1.10 (Minor)
Halonen et al	1.02 (0.97-1.08)	P=0.11; I^2=50%	-2.02 (Major)
Beelen et al	1.01 (0.98-1.05)	P=0.09; I^2=53%	2.86 (Major)
IHD mortality			
	Pooled RR (95%CI)	Between-study heterogeneity	LFK index Doi plot asymmetry
All studies	1.03 (0.99-1.08)	P=0.08; I^2=46%	-1.24 (Minor)
Excluded study			
Andersson et al	1.03 (0.98-1.08)	P=0.08; I^2=50%	-2.22 (Major)
Thacher et al	1.03 (0.98-1.09)	P=0.05; I^2=55%	-1.98 (Minor)
Klompmaker_road et al	**1.03 (1.00-1.07)**	P=0.27; I^2=22%	-0.11 (No asymmetry)

Heritier_road et al	1.02 (0.97-1.08)	P=0.06; I^2=53%	0.04 (No asymmetry)
Barcelo et al	1.03 (0.99-1.06)	P=0.19; I^2=32%	-4.02 (Major)
Halonen et al	1.03 (0.98-1.09)	P=0.09; I^2=48%	-0.74 (No asymmetry)
Beelen et al	1.03 (0.98-1.08)	P=0.05; I^2=54%	1.31 (Minor)

Stroke mortality			
	Pooled RR (95%CI)	Between-study heterogeneity	LFK index Doi plot asymmetry
All studies	1.05 (0.97-1.14)	P=0.03; I^2=62%	-2.89 (Major)
Excluded study			
Andersson et al	1.05 (0.93-1.18)	P=0.00; I^2=72%	-3.78 (Major)
Thacher et al	1.04 (0.95-1.14)	P=0.02; I^2=69%	-4.19 (Major)
Klompmaker_road et al	1.04 (0.92-1.18)	P=0.02; I^2=71%	-3.43 (Major)
Halonen et al	1.06 (0.94-1.20)	P=0.02; I^2=70%	-3.98 (Major)
Beelen et al	1.05 (1.01-1.09)	P=0.70; I^2=0%	2.86 (Major)

Aircraft traffic source

Aircraft traffic Sources			
ALL CVD mortality			
	Pooled RR (95%CI)	Between-study heterogeneity	LFK index Doi plot asymmetry
All studies	1.17 (1.10-1.25)	P=0.85; I^2=0%	-0.98 (No asyemmetry)
Excluded study			
Evard et al	1.14 (0.98-1.32)	P=0.70; I^2=0%	n/a
Hansell et al	1.17 (1.10-1.25)	P=0.58; I^2=0%	n/a
Huss et al	1.18 (1.11-1.26)	P=0.92; I^2=0%	n/a
IHD mortality			
	Pooled RR (95%CI)	Between-study heterogeneity	LFK index Doi plot asymmetry
All studies	1.03 (0.82-1.29)	P=0.00; I^2=82%	8.69 (Major)
Excluded study			
Heriter et al	1.23 (1.11-1.37)	P=0.86; I^2=0%	n/a
Evrard et al	1.03 (0.86-1.23)	P=0.21; I^2=38%	n/a
Hansell et al	1.03 (0.82-1.30)	P=0.00; I^2=90%	n/a
Stroke mortality			
	Pooled RR (95%CI)	Between-study heterogeneity	LFK index Doi plot asymmetry
All studies	1.06 (0.93-1.20)	P=0.44; I^2=0%	0.30 (No asymmetry)
Excluded study			
Evrard et al	1.03 (0.64-1.65)	P=0.20; I^2=38%	n/a
Hansell et al	1.04 (0.92-1.18)	P=0.36; I^2=0%	n/a
Huss et al	1.07 (0.94-1.22)	P=0.40; I^2=0%	n/a

Supplementary-12: Subgroup analyses on the main meta-analyses

Road sources			
All CVD mortality			
	N	Pooled RR (95%CI)	Between-study heterogeneity
Address-level noise	4	1.02 (0.97-1.08)	P=0.11; I^2=50%
Postcode/census/block level noise	1	1.00 (0.97-1.05)	n/a
IHD mortality			
	N	Pooled RR (95%CI)	Between-study heterogeneity
Address-level noise	5	1.03 (0.99-1.07)	P=0.19; I^2=34%
Postcode/census/block level noise	2	1.02 (0.85-1.22)	P=0.03; I^2=80%
Stroke mortality			
	N	Pooled RR (95%CI)	Between-study heterogeneity
Address-level noise	4	1.06 (0.94-1.20)	P=0.02; I^2=70%
Postcode/census/block level noise	1	1.03 (0.97-1.10)	n/a