The relationship between transportation noise exposure and ischemic heart disease: a meta-analysis

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ABSTRACT

Background: There is a growing body of evidence that exposure to transportation related noise can adversely affect health and wellbeing. More recently, research on cardiovascular disease has specifically explored the hypothesis that exposure to transportation noise increases the risk for ischemic heart disease (IHD). Our objective was to review and conduct a meta-analysis to obtain an overall exposure-response association. **Methods and Results:** We conducted a systematic review and retained published studies on incident cases of IHD using sources of transportation noise as exposure. Study-specific results were transformed into risk estimates per 10dB increase in exposure. Subsequently we conducted a random effects meta-analysis to pool the estimates. We identified 10 studies on road and aircraft noise exposure conducted since the mid-1990s, providing a total of 12 risk estimates. Pooled relative risk for IHD was 1.06 (1.03-1.09) per 10dB increase in noise exposure with the linear exposure-response starting at 50dB. Based on a small number of studies, subgroup analyses were suggestive of higher risk for IHD for males compared to females (p=0.14), and for persons over 65 years of age compared to under (p=0.22). Air pollution adjustment, explored only in a subset of four studies, did not substantially attenuate the association between noise exposure and IHD. **Conclusions:** The evidence for an effect of transportation noise with IHD necessitates further research into the threshold and the shape of the exposure-response association, potential sources of heterogeneity and effect modification. Research in different cultural contexts is also important to derive regional and local estimates for the contribution of transportation noise to the global burden of disease.

Keywords: Transport Noise; Exposure; Ischemic heart disease; Myocardial infarction; meta-analysis

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Highlights:

- We review and conduct a meta-analysis on transportation noise exposure and IHD.
- Novel approach to pool studies with a diversity of metrics and exposure categories.
- We verify the assumption of a linear ER association by targeted statistical analyses.
- The overall RR is 1.06 (1.03-1.09) per 10dB increase in noise, starting at 50dB.
- More studies are needed to refine the shape and threshold for the ER relationship.

1. INTRODUCTION

Noise exposure from transportation, especially in urban areas, is one of the most widespread sources of environmental stress in the daily lives. There is much evidence supporting the relationship between exposure to environmental noise and wellbeing. Basner, et al. [1] and Munzel, et al. [2] provide a concise review of the effects of noise, including environmental noise, on health. In addition to causing sleep disturbance and psychological effects such as annoyance, noise is postulated to induce biological stress on the cardiovascular system, leading to changes in blood pressure and to cause hypertension. [3-8] Most studies have investigated these and other non-auditory health effects of noise from road and aircraft traffic (e.g. cognitive impairment in children [9] and diabetes in adults [10]), although noise from railways is also a concern. For example, Croy, et al. [11] demonstrated experimentally that night-time freight train noise and vibration can accelerate heart rate during sleep, which may in turn be linked to cardiovascular disease (CVD). Although less studied, recent research on the potential relationship between transportation noise and ischemic heart disease (IHD) has yielded inconsistent results.[12-16]

Babisch previously performed meta-analyses on studies of road traffic noise exposure and IHD. The first included five studies on incident myocardial infarction (MI) and reported a relative risk of 1.17 (95% CI 0.87-1.57) per 10dB increase in daytime (Lday) noise.[8] Recently updated, the study by Babisch [17] included 17 studies (incidence or prevalence) suggesting a relative risk of 1.08 (95% CI 1.04-1.13) per 10dB increase (Ldn) in road noise. Other transportation sources, however, were not considered. In this paper, we also perform a meta-analysis on available studies on the association between exposure to any transportation noise and IHD. We expanded the previous meta-analysis[17] to aircraft noise by giving both a main effect estimate and estimates by source. Further, we systematically evaluate the threshold and the shape of the exposure-response association, as well as potential sources of

heterogeneity and effect modification. Recent noise exposure studies also include evaluation of co-exposure to air pollution, an important consideration given that both exposures derive from the same sources and are further both associated with CVD.[18-20]

2. METHODS

2.1. Study Selection and Data Extraction

We conducted a systematic review to identify papers using road, rail or aircraft noise as exposure and myocardial infarction (MI) or coronary heart disease (referred to here as ischemic heart disease [IHD]) as outcomes (ICD10 codes I20-I25). We included both non-fatal and fatal incident cases. Studies on prevalence (i.e. cross-sectional) were excluded. The search was conducted in PubMed and EMBASE, for the 20 year period prior to January 2014 and reference lists of relevant articles including the WHO burden of diseases report[21] were screened. No geographic constraints were defined, however the search was conducted in and limited to publications in the English language. The search strings are provided in Appendix A. Further inclusion criteria were: eligible studies had to quantify the association between modelled or measured exposure to the transportation noise source, and myocardial infarction (MI) or ischemic heart disease (IHD) had to be in the title and/or abstract. Studies which quantified this relationship in dB, either categorically or by a linear trend (i.e. increase in risk is constant per exposure interval), including a measure of precision (e.g. 95% confidence intervals), were retained. We conducted a double data extraction of retained studies. Data extraction included recording the risk estimates by noise exposure categories (including reference level value), noise metric (e.g. Lday, Lden – see Appendix B for description), noise source, study population by sex, study design, and whether the risk estimate was adjusted for air pollution. Where available, risk estimates for specific subsets of the study population were also extracted (e.g. age and sex stratified, and for continuous years at the same residential

address [referred to as years in residence]).

2.2. Linear Exposure-Response (Trend) Estimation

Risk estimates from individual studies based on categorical noise exposures were transformed into a linear exposure-response (per 10dB increase in Lden). For each study, a log-normal model in SAS was fitted to the data to estimate the mean level of exposure in each of the exposure intervals. Model fit was based on the proportion of person years or number of cases within different exposure intervals for cohort and case-control studies, respectively. If necessary, the study specific interval means were converted to Lden using approximations from the literature: L16h+2dB; Ldn+0.3dB; and LAeq,24 + 1.5dB.[22]

Trend per 10dB noise increment, zeroed for the study specific reference level, was estimated using generalised least squares (STATA glst). If the covariance matrix could not be specified, the variance-weighted least squares (STATA vwls) method was used.[23] This approach was tested in a sensitivity analysis with studies providing risk estimates both categorically and as a linear exposure-response. We further explored individual studies for departure of the exposure-response from linearity by including a quadratic term for exposure level, and also performed a meta-analysis of the respective estimates. As a final check, we performed a meta-regression of the original effect estimates on the study's mean exposure level since a non-linear exposure-response relationship might only be seen when comparing across studies. A positive (negative) association between study-specific estimates and mean exposure levels would be suggestive of an exposure-response relationship with positive (negative) curvature.

2.3. Meta-analysis

Random effects meta-analysis (using STATA metan [24]) was conducted based on the

risk estimates per 10dB increase in Lden noise for the individual studies. The percent total variance due to between-study heterogeneity was assessed with the I^2 statistic. Between strata heterogeneity was assessed on the basis of the p value of a Chi^2 test. To specify the starting point for the pooled linear exposure-response association, we pooled the study specific reference values using the derived meta-analysis weights of each study.

We used the following effect estimates in the main analysis: non-fatal IHD, for studies reporting separate estimates for non-fatal vs. fatal cases; both sexes combined, for studies reporting males, females and both. Subsequent stratified analyses were also conducted to explore potential sources of heterogeneity due to methodological considerations, including: outcome definition (non-fatal vs. fatal and MI specific vs. unspecified IHD); study date (<=2005 vs. >2005) because studies after 2005 explored potential confounding due to air pollution; type of transportation noise source (road, rail, aircraft); study design (case control, cohort, small area study [i.e. individual health data aggregated on the level of census areas with exposure assigned on this group level]); method of linear trend estimation (estimated from categorical vs. linear model in the original study); adjustment for air pollution (no, yes); and noise reference level. Reference levels were defined on the basis of the computed mid-point of the reference exposure category. For studies providing linear exposure-response estimates, we used the reference value reported in the text. If not specified we assigned the category "no threshold." We also explored potential effect modification using stratified analyses, due to: age (<65 years, >=65 years); sex; and years in residence (not specified, >10 years).

The influence of individual risk estimates was assessed by performing repeated meta-analyses with one study left out each time (further referred to as leave-one-out meta-analysis). The effect of leaving out sets of studies on the basis of methodological features was also explored (i.e. small area studies, North American studies, those potentially over-adjusted,

studies not adjusted for air pollution, and those not adjusted for smoking). Analyses were conducted in STATA 12.

3. RESULTS

3.1. Selected Studies

We have identified 10 studies, conducted mainly in Europe, focussing on road and aircraft noise and incident cases of IHD.[12-15, 25-30] No studies specifically investigating effects of railway traffic on IHD were found. A summary of retained studies is provided in Table 1 and an overview of risk estimates per exposure category is shown in Figure 1.

Six of the studies[12, 13, 25, 28-30] related to road traffic noise while three large population studies focussed on aircraft noise: 65 civil airports and airfields in Switzerland,[15] Heathrow airport in London UK[26] and 89 airports in the USA.[27] The Vancouver study[14] looked at the effects of community noise, defined as noise from both road and aircraft traffic. Half of the studies investigated associations in a subset of persons living long term at a single address. Earlier studies, those conducted prior to the end of 2005, did not specifically explore potential confounding due to air pollution. All of the more recent studies, however, included models adjusted for air pollution, and some provided age and sex stratified risk estimates.

Two papers reported the results of the NaRoMi (BerlinIII); we selected the original paper by Babisch, et al. [28] instead of Willich, et al. [16] because the latter excluded participants living at smaller streets with low traffic intensities likely producing selection bias. Babisch, et al. [28] included these individuals, who are likely exposed <60dB, in the corresponding reference category. To avoid double counting, we also excluded the paper by Selander, et al. [31] which used the same population as in Selander, et al. [12] The paper by de Kluizenaar, et al. [32] was not included because separate effect estimates for IHD were not available (effect estimates were reported for cerebrovascular disease which included stroke). We further

excluded cross-sectional studies such as Floud, et al. [33] and Banerjee, et al. [34]

The GLST command was used to estimate linear trend for all studies except Babisch, et al. [28] where the covariance matrix would not compute without exact number of cases and controls by exposure category. For this study, we therefore used VLWS.

<<Table 1 hereabouts>>

<<Figure 1 hereabouts>>

3.2. Main Effect Estimates

All studies combined, regardless of outcome definition and noise source, resulted in an overall risk estimate of 1.06 (95% CI: 1.03-1.09) per 10dB increase in noise exposure (Figure 2 and Table 2). We calculated a pooled reference level of 50dB as the starting point for the linear exposure-response association.

Stratified by disease state, non-fatal IHD was 1.07 (1.05-1.09) compared to 1.05 (1.01-1.09) for risk of death. The difference in these risk estimates was not statistically significant (between strata p value = 0.49).

<<Figure 2 hereabouts>>

<<Figure 3 hereabouts>>

3.3. Potential Sources of Heterogeneity

The effect of individual studies on the main effect estimate was assessed via leave-one-out meta-analysis (Figure 3). No substantial impact of a specific study was found. The highest estimate (1.07 [1.05-1.08]) was found when Beelen, et al. [13] was omitted, and lowest estimate (1.05 [1.03-1.08]) when Gan, et al. [14] was omitted. We further explored the impact of

leaving out sets of studies with specific methodological features (Figure 4). Neither omitting the two small area studies,[26, 27] nor those studies which did not adjust for air pollution [28-30] had a noticeable impact on the main estimate. However, dropping the three studies with potential over adjustments (e.g. adjusted for high blood pressure or both traffic and air pollution),[13, 27, 28] slightly increased the relative risk and reduced the 95% confidence intervals; while dropping studies conducted in North America[14, 27] or those which did not adjust for smoking slightly reduced the relative risk.[14, 15, 26, 27] In terms of other methodological issues, there was no evidence of heterogeneity due to outcome definition, study date, nor study design (Table 2). Studies that specifically reported MI risk did not differ from those that reported unspecified IHD (1.06 [1.02-1.09] vs. 1.05 [1.01-1.10]; p=0.92). As shown in Table 3, only four studies reported estimates for models which were adjusted and not adjusted for air pollution. Although adjustment very slightly attenuated the risk, there was no difference between these strata (p=0.77).

<<Figure 4 hereabouts>>

<<Table 2 hereabouts>>

<<Table 3 hereabouts>>

The method used for trend estimation in individual studies introduced some heterogeneity (p= 0.05). The relative risk was ~6% higher based on studies where linear trend was reported as opposed to derived using our method. We tested and found good agreement for our linearisation approach in a sensitivity analysis of two studies publishing risk estimates both categorically and as linear exposure-response (1.10 [0.97-1.25] vs. reported 1.12 [0.90-1.35] per 10dB;[12] 1.12 [1.01-1.24] vs. reported 1.13 [1.06-1.21][14]). More recent studies also tended to report linear trend.[14, 25, 27] We further found that a meta-estimate of the quadratic

exposure term, introduced in models for individual studies, was not statistically significant except for in Babisch, et al. [29] where we found indications for a stronger than linear effect of noise. Excluding Babisch, et al. [29] the meta-estimate of the quadratic terms was close to 0 and not statistically significant which generally supports our decision to treat the exposure-response for all studies as linear. The meta-regression of study-specific effect estimates on mean exposure levels provided a slightly negative but not statistically significant slope further supporting the concept of a linear exposure-response relationship.

Fewer studies were available for aircraft noise compared to road noise (Table 2). The results seem to suggest some heterogeneity between the groups (p=0.1), however, this is mainly attributed to the study by Gan, et al. [14] in which the noise sources were already combined as a measure of community noise.

We did not find strong indications that the reference level used in the individual studies had an impact on the slope of the linear exposure-response association, although the between strata p value was relatively low due to one study which did not define a threshold (p=0.08).[14]

3.4. Effect Modification

Table 3 shows results for potential effect modification due to age, sex and years in residence. Three studies looked at IHD risk by age, showing indications of higher risk in the older age group (1.09 [1.03-1.16] in 65 years and older vs. 1.04 [0.98-1.10] for under 65; p=0.22). Relative risk for males (1.09 [1.04-1.13]) tended to be greater than for females (1.02 [0.95-1.10]) (p=0.14). Persons residing longer term at the same address also tended to have higher relative risks ([1.08 [1.03-1.14] resident for 10+ years vs. 1.04 [1.00-1.08] years in residence not specified; p=0.15). These results, however, are only suggestive given that the 95% CIs between strata overlap.

4. DISCUSSION

4.1. Comparison with the literature

We found indications for a linear exposure-response association between IHD and transportation noise starting as low as 50dB and increasing by 1.06 (95% CI: 1.03-1.09) per 10dB Lden. Babisch [17] recently reported a relative risk of 1.08 (95% CI 1.04-1.13) per 10dB increase in Ldn, though with a slightly higher starting point (~52.3dB Lden) for the linear exposure-response association. There are, however, several differences between our two meta-analyses. Babisch focussed on road noise exposure only whereas we have considered all type of transportation noise sources. A further key difference between ours and the recent meta-analysis by Babisch [17] is that we focussed only on studies addressing incident cases of IHD whereas Babisch also included prevalence studies. By excluding studies on prevalence we avoid potential bias which would be introduced if fatality is related to the exposure. In other words, we may see fewer prevalent cases in areas with greater exposure simply because the fatal IHD cases are removed from the prevalence pool. Further differences between the two meta-analyses include methodological details in the derivation of study specific linear exposure-response relationships. Of note, we used air pollution adjusted effect estimates, whenever available in a study, whereas Babisch relied on unadjusted estimates. Despite all these differences our pooled estimates are relatively similar, with both our studies suggesting that noise induced risk of IHD starts to increase at lower level than previously presumed.[8]

4.2. Assumption of linear trend

Whether the exposure-response association between transportation noise and IHD is linear is not yet known. In principle a categorical meta-analysis would enable the evaluation of a non-linear relationship. This is the approach taken in the original meta-analysis by

Babisch [8] where the relationship between IHD and road traffic noise was represented by a polynomial function (OR=1.63 – 0.000613 · $(L_{day,16h})^2$ + 0.00000736 · $(L_{day,16h})^3$) with a rather high threshold (55dB Lday ≈ 57dB Lden).[21] Our decision is to assume a linear relationship for the exposure-response is supported by the more recent studies included in our meta-analysis. Sørensen, et al. [25] for example, visually confirmed a linear relationship between MI and road traffic noise across an exposure range of 42-84dB Lden for a cohort in Denmark (although depicted on a log scale, the relationship is linear). Furthermore, Sørensen, et al. [35] report a similar finding for the association between road noise and stroke incidence.

Nevertheless, as illustrated in Figure 1, assuming a linear exposure-response relationship may be an over simplification in some studies, potentially masking a non-linear association in one or both of the noise sources.[1] For the two aircraft studies, we see indications that the linear association with a higher threshold (between 55-60dB, Lden) is likely appropriate. The relevant threshold level and shape of the exposure-response association is less obvious for road traffic noise.

While the categorical approach used by Babisch [8] can account for non-linear associations and help determine possible threshold effects, the disadvantage is that definition of exposure categories in individual studies must be the same. The diversity of exposure categories and noise metrics in our studies would have implied too many assumptions about choice of appropriate categories. The linear approach is also less sensitive to differences in exposure modelling across studies if the slopes are consistent and offset of the modelled value is the only concern.

Our decision to first estimate linear trend for each study was better justified, and further supported by our analyses testing this assumption. We also confirmed our general approach to trend estimation in two studies, showing good agreement.[12, 14]

4.3. Effect Modification

We found some suggestion that vulnerability differs across the population. The number of studies in each stratum, however, was small and the differences were not statistically significant (95% CIs for between strata comparisons were overlapping (Tables 2 and 3). As a general trend, studies found men to be at greater risk for noise-related IHD. The source of noise (road vs. aircraft) or the outcome (MI and unspecified IHD) did not seem to play a role in this respect. Nevertheless, in experimental short-term studies with physiological parameters as endpoints, evidence regarding gender differences in susceptibility to transportation noise remains inconclusive.[36] In an experimental setting, exposure to railway noise during sleep was associated with somewhat stronger heart rate acceleration among men compared to women.[11] Indications for more a pronounced effect of noise exposure on objective sleep quality was also found in men compared to women in Basel, Switzerland.[37]

We also saw a tendency for higher risk in persons living long term at the same address, in line with the hypothesis that chronic transportation noise exposure is needed to induce IHD.[28] An alternative explanation is that long term residency implies poorer insulated houses. Housing stock was not considered in our included studies which were all based on available noise maps or modelling. Some support for this hypothesis, however, comes from Huss, et al. [15] who found higher noise exposure and risk of death by MI for people residing in older compared to newer constructions or recently renovated buildings. We also found a tendency for higher relative risk in the older age group compared to those <65 years. Older persons may be more vulnerable to noise; but it is also possible that risk may be higher because they are likely to stay longer at the same address or live in older buildings with less noise insulation.

4.4. Methodological issues

Several methodological issues are potential limitations to our study. First is our combination of noise sources into a pooled risk estimate, which cannot be justified based on the few aircraft and lack of railway studies on IHD risk. In previous studies annoyance response curves for aircraft were above that for road noise exposures. [38] It is less clear, however, whether this also affects the linear relationship (i.e. slope) or whether this is only an offset issue. Further, self-reported annoyance is rather different from objectively measured outcomes and these findings may not be transferable to disease risk. Recent research indicates that while the effect of noise exposure on health related quality of life is mediated by annoyance and sleep disturbance,[39] the effect of noise exposure on objective sleep outcomes (e.g. measured sleep efficiency) is also observed in people who are not annoyed by noise.[37] Some of the more recent studies have investigated combined community noise[14] or confounding by other transportation noise sources.[25] Many factors influence the decibels of noise (Leq), including acoustical characteristics of the source as well as non-acoustical characteristics (e.g. environmental setting and timing of event). Our stratified results, however, do not indicate heterogeneity between the studies on road versus aircraft noise (Table 2).

Newer and older studies alike adjusted for typical confounders; common covariates across studies were age, sex (if included) and socio-economic status. Some also adjusted for factors such as employment status, occupational noise exposure, BMI, family history, pre-existing comorbidities, and smoking status. Only Babisch, et al. [29], however, included information for window opening behaviour − a practice which would directly influence the noise exposure. Studies before year 2000 derived exposure on the basis of gridded road noise maps, and may be subject to greater exposure misclassification than recent studies which are typically based on more sophisticated receptor noise models to assign exposure at the home address. All studies conducted after 2005 also adjusted for air pollution exposure. Our results

show only slight, if any at all, attenuation of risk due to air pollution adjustment. This supports the recent findings from a systematic review suggesting minimal confounding by air pollution on the relationship between cardiovascular disease and noise.[20] There is, however, also recent evidence suggesting that the correlations between these two exposures changes spatially.[19]

We explored the effect of additional methodological differences through leave-one-out meta-analysis (Figure 3) and subgroup meta-analysis (Table 2, Table 3 and Figure 4). In general, not adjusting for air pollution had little impact on the results (Figure 4). Although potential over adjustment may be a problem. For example adjustment for high blood pressure, as was done in Babisch, et al. [28], is not appropriate if this is on the causal pathway. Beelen, et al. [13] and Correia, et al. [27] are also potentially over-adjusted as both air pollution and traffic intensity or road density are included as confounders and thus some of the noise effects may have been attributed to these variables. The influence plot of individual studies (Figure 3) shows that the risk estimate slightly increased from 1.06 to 1.07 when Beelen, et al. [13] was removed. The individual effect of Babisch, et al. [28] and Correia, et al. [27] however, was less pronounced. Although slightly attenuated, the effect of noise persisted after removing studies not adjusting for smoking, which were also the large population studies (1.052 [1.016-1.016]).

Based on the original meta-analysis by Babisch [8] the annual burden of environmental noise in Western Europe is an estimated loss of 1 million healthy life-years (DALYS; disability adjusted life-years).[21] Although this used a higher risk estimate than ours, we expect this is an underestimation of the risk due to the higher threshold (57dB Lden vs. our 50dB Lden). The polynomial exposure-response function used for the WHO burden of disease assessment crosses our exposure-response function at a noise level of 71dB Lden with a relative risk of approximately 1.13. This implies that people exposed between 50 and

71dB have a higher risk for ischemic heart disease according to our meta-analysis than previously assumed in the WHO assessment. In Switzerland, 73% of the population live in areas within this exposure range for road traffic;[40] although the relative risk is small, this translates into a substantial number of additional DALYs. The specific cut-off used to define the threshold may be context specific. Exposure assessment should therefore include a careful assessment of the noise exposure, including recognition of the uncertainties in the data, especially those based on regulatory noise maps.

5. CONCLUSIONS

Using a linear exposure-response relationship between transportation noise and IHD, our meta-analysis supports a relative 6% increase in IHD per 10dB Lden increase in exposure. Based on the reference levels of included studies, we suggest that the association starts as low as 50dB. More studies are needed to further support research into the shape of this relationship, threshold of effect and susceptibilities of at-risk populations. More studies on aircraft and rail, and studies from different cultural contexts are also needed to derive regional and local estimates for the contribution of transportation noise to the global burden of disease.

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Figure 1. Association between noise exposure (Lden) and IHD reported in original studies

Dot size is proportional to 95% CI for studies reporting categorical relative risks; noise level based on midpoint of respective exposure category. Dashed lines represent studies reporting linear trend.

Figure 2. Forest plot of effect estimates per 10dBA increase in transportation noise (Lden) and association with IHD

Figure 3. Influence plot of association between transportation noise exposure (Lden) and IHD

Leave-one-out meta-analysis (random effects) where study name indicates the left-out study

Figure 4. Sensitivity of the effect estimate when leaving out sets of studies based on methodological differences

Table 1. Summary of retained studies

Location	Citation	Source[a]	Noise data	Original metric	Reference (Lden)	Study design	Method for linear ER estimation [b]	Sample size[c]	Outcome [d]	Sex	Age at baseline	Available stratified risk estimates[e]			
												Air pollution adjustment	Age	Sex	Years in residence
Berlin I	Babisch 1994	Road	Map	Lday	62	case control	derived	243	MI	Male	41-70	-	-	-	15
Berlin II	Babisch 1994	Road	Map	Lday	62	case control	derived	4035	MI	Male	31-70	-	-	-	15
Caerphilly & Speedwell, UK	Babisch 1999	Road	Map and measures	Lday	57	cohort	derived	~23700	IHD	Male	45-63	-	-	-	15
Berlin III	Babisch 2005	Road	Model	Lday	62	case control	derived	4115	MI	Male + Female	20-69	-	-	Yes	10

NL	Beelen 2009	Road	Model	Max dB	50	cohort	derived	~1.2 mil	IHD (f)	Both	58-67	Yes	NA	NA	-
Stockholm	Selander 2009	Road	Model	LAeq, 24h	51.5	case control	derived	3518; 2320	MI (b)	Both	45-70	NA	NA	NA	-
Switzerland	Huss 2010	Aircraft	Model	Ldn	45.3	cohort	derived	~22.5 mil	MI (f)	Both	>30	Yes	Yes	Yes	15
Denmark	Sørensen 2012	Road	Model	Lden	42	cohort	original	~496000	MI (b)	Both	50-64	Yes	Yes	Yes	5
Vancouver	Gan 2012	Community	Model	Lden	none	cohort	original	~1.8 mil	IHD (f)	Both	45-85	Yes	Yes	Yes	-
London, UK	Hansell 2013	Aircraft	Model	Lday	52	small area	derived	~20 mil	MI (b)	Both	all ages	Yes	-	-	-
USA	Correia 2013	Aircraft	Model	Ldn	45.3	small area	original	~6 mil	IHD	Both	>65+	Yes	-	-	-

a. Community noise refers to noise from both road and aircraft traffic

b. ER = exposure-response; derived = linear trend estimated, original = original studies reported linear ER

c. N persons for case control studies; Person-years for cohort studies and Hansell (2013)

d. MI = myocardial infarction; IHD = ischemic heart disease; Risk estimates are for non-fatal cases unless indicated in brackets, where f = fatal

cases only, b = individual estimates available for fatal and non-fatal cases

e. Dash (-) indicates not analysed; NA indicates analysed by authors, but not available for inclusion in meta-analysis

Table 2. Association between transportation noise exposure and IHD, including stratified analyses to explore potential heterogeneity due to methodological differences

Subgroup	Number of estimates	Risk Estimate per 10dB (95% CI)	Heterogeneity[a]	
			Between strata (p value)	Between studies within strata (I^2)
None	12	1.06 (1.03-1.09)		28.3%
Outcome definition			0.92	
MI specific	7	1.06 (1.02-1.09)		0.0%
Unspecified IHD	5	1.05 (1.01-1.10)		62.1%
Disease state[b]			0.49	
Non-fatal IHD	9	1.07 (1.05-1.09)		0.0%
Fatal IHD	6	1.05 (1.01-1.09)		54.1%
Study date			0.98	
<= 2005	4	1.06 (0.99-1.13)		0.0%
> 2005	8	1.06 (1.03-1.09)		48.3%
Noise reference level			0.08	
No threshold	1	1.13 (1.06-1.21)		-
<55dBA (Lden)	6	1.05 (1.02-1.08)		38.0%
>=55dBA (Lden)	5	1.04 (0.98-1.11)		0.0%
Type of Noise[c]			0.10	
Road	8	1.04 (1.00-1.10)		26.4%
Aircraft	3	1.06 (1.04-1.08)		0.0%
Community	1	1.13 (1.06-1.21)		-
Study design			0.93	
Case control	5	1.06 (1.00-1.13)		0.0%
Cohort	5	1.05 (1.00-1.12)		67.7%

Small area	2	1.07 (1.04-1.09)		0.0%
Linear ER Estimation			0.05	
Original (linear)	3	1.10 (1.05-1.15)		15.0%
Derived	9	1.04(1.02-1.07)		19.4%

a. p value of the Chi2 test used to assess between-strata heterogeneity; I^2 statistic used to assess between-study heterogeneity

b. Study N exceeds 12 because cause-specific estimates used where available

c. Community noise refers to noise from both road and aircraft traffic

Table 3. Association between transportation noise exposure and IHD restricted to studies with estimates in both strata

Subgroup	Number of estimates	Risk Estimate (per 10dBA)	Heterogeneity[a]	
			Between strata (p value)	Between studies within strata (I^2)
Age			0.22	
<65 years	3	1.04 (0.98-1.10)		0.0%
≥65 years	3	1.09 (1.03-1.16)		39.2%
Sex			0.14	
Males	4	1.09 (1.04-1.13)		0.0%
Females	4	1.02 (0.95-1.10)		33.2%
Years in residence			0.15	
Not specified (full data)	6	1.04 (1.00-1.08)		0.0%
>10 years (subset)	6	1.08 (1.03-1.14)		0.0%
Air pollution adjustment			0.77	
no	4	1.06 (1.00-1.12)		68.2%
yes	4	1.05 (1.00-1.11)		57.0%

a. p value of the Chi2 test used to assess between-strata heterogeneity; I2 statistic used to assess between-study heterogeneity

APPENDIX A.

PubMed Search String

(“noise exposure” [Title/Abstract] OR “traffic noise” [Title/Abstract] OR “community noise” [Title/Abstract] OR “traffic noise exposure” [Title/Abstract] OR “road traffic noise” [Text Word] OR “road noise” [Text Word] OR “rail traffic noise” [Text Word] OR “rail noise” [Text Word] OR “rail traffic noise” [Text Word] OR “railway noise” [Text Word] OR “air traffic noise”[Text Word] OR “aircraft noise” [Text Word]) AND

(“etiology”[MeSH Subheading] OR “etiology”[Title/Abstract] OR “etiological”[Title/Abstract] OR “epidemiologic studies”[MeSH Terms] OR “risk factors”[MeSH Terms] OR “case control study”[Title/Abstract] OR “case-control” [Title/Abstract] OR “cohort study”[Title/Abstract] NOT “occupational” [Title/Abstract] NOT “industrial” [Title/Abstract]) AND

(“incidence” [Title/Abstract] OR “mortality” [Title/Abstract] OR “risk” [Title/Abstract] NOT “prevalence” [Title/Abstract]) AND

(“myocardial infarction” [Title/Abstract] OR “MI” [Title/Abstract] OR “ischemic heart disease” [Title/Abstract] OR “IHD” [Title/Abstract] OR “cardiovascular” [Title/Abstract] OR “coronary heart disease” [Title/Abstract])

EMBASE Search String

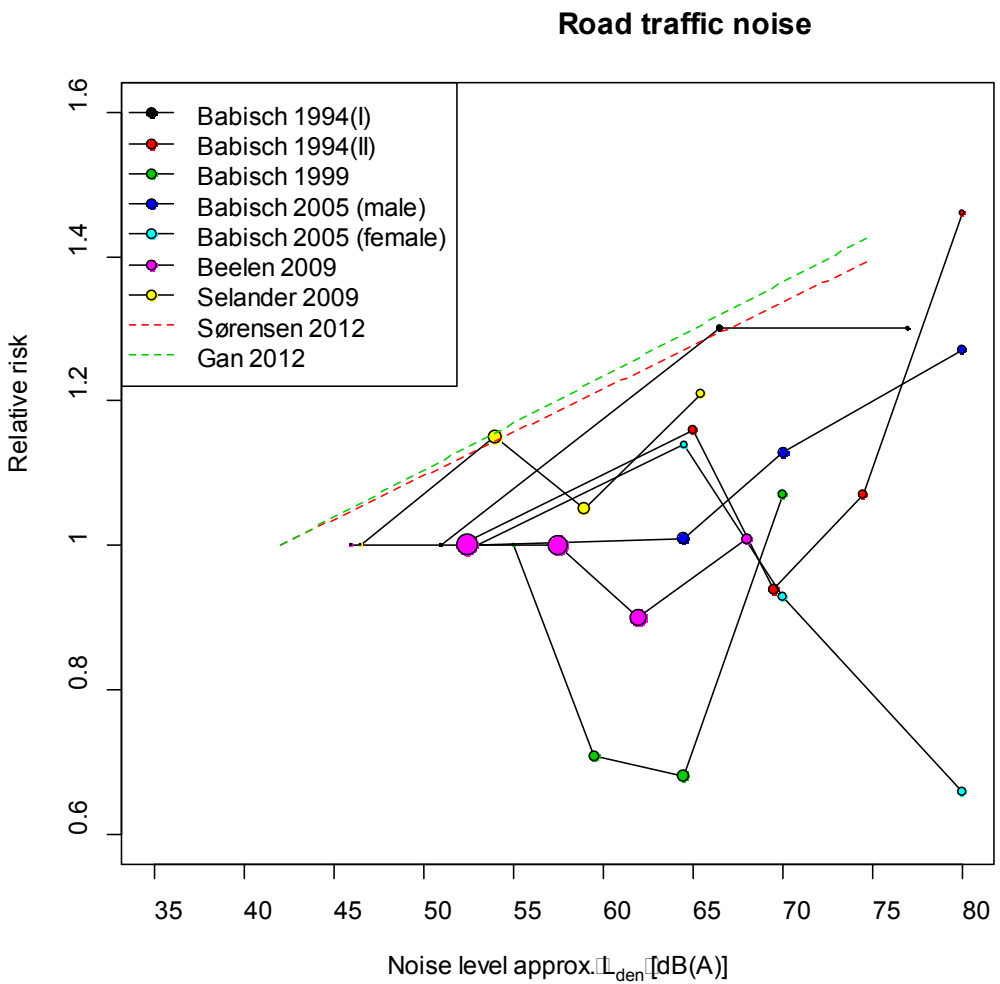
('noise exposure':ti,ab OR 'traffic noise':ti,ab OR 'community noise':ti,ab OR 'traffic noise exposure':ti,ab OR 'road traffic noise' OR 'road noise' OR 'rail traffic noise' OR 'rail noise' OR 'rail traffic noise' OR 'railway noise' OR 'air traffic noise' OR 'aircraft noise') AND ('etiology'/exp OR 'etiology':ti,ab OR 'etiological':ti,ab OR 'epidemiology'/exp OR 'risk factor'/exp OR 'case control study':ti,ab OR 'case-control':ti,ab OR 'cohort study':ti,ab NOT 'occupational':ti,ab NOT 'industrial':ti,ab) AND ('incidence':ti,ab OR 'mortality':ti,ab OR 'risk':ti,ab NOT 'prevalence':ti,ab) AND ('myocardial infarction':ti,ab OR 'MI':ti,ab OR 'ischemic heart disease':ti,ab OR 'IHD':ti,ab OR 'cardiovascular':ti,ab OR 'coronary heart disease':ti,ab)

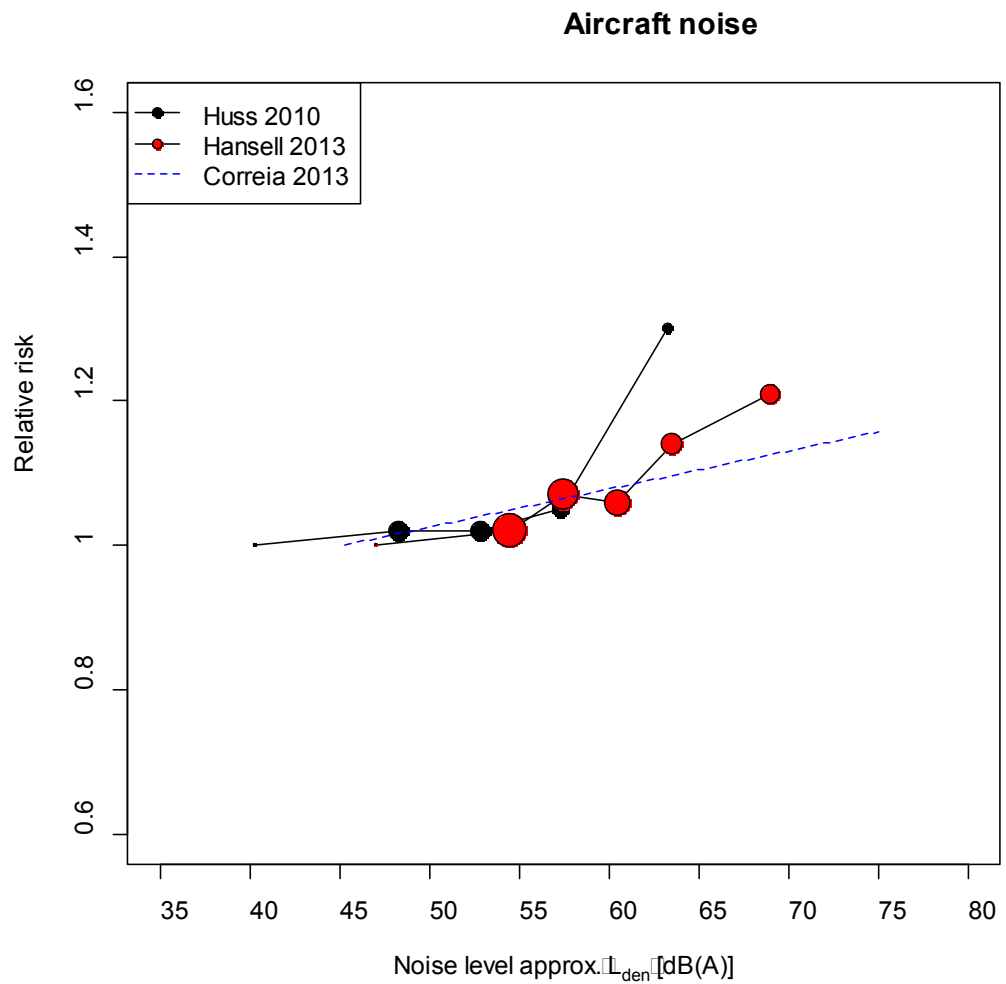
APPENDIX B.

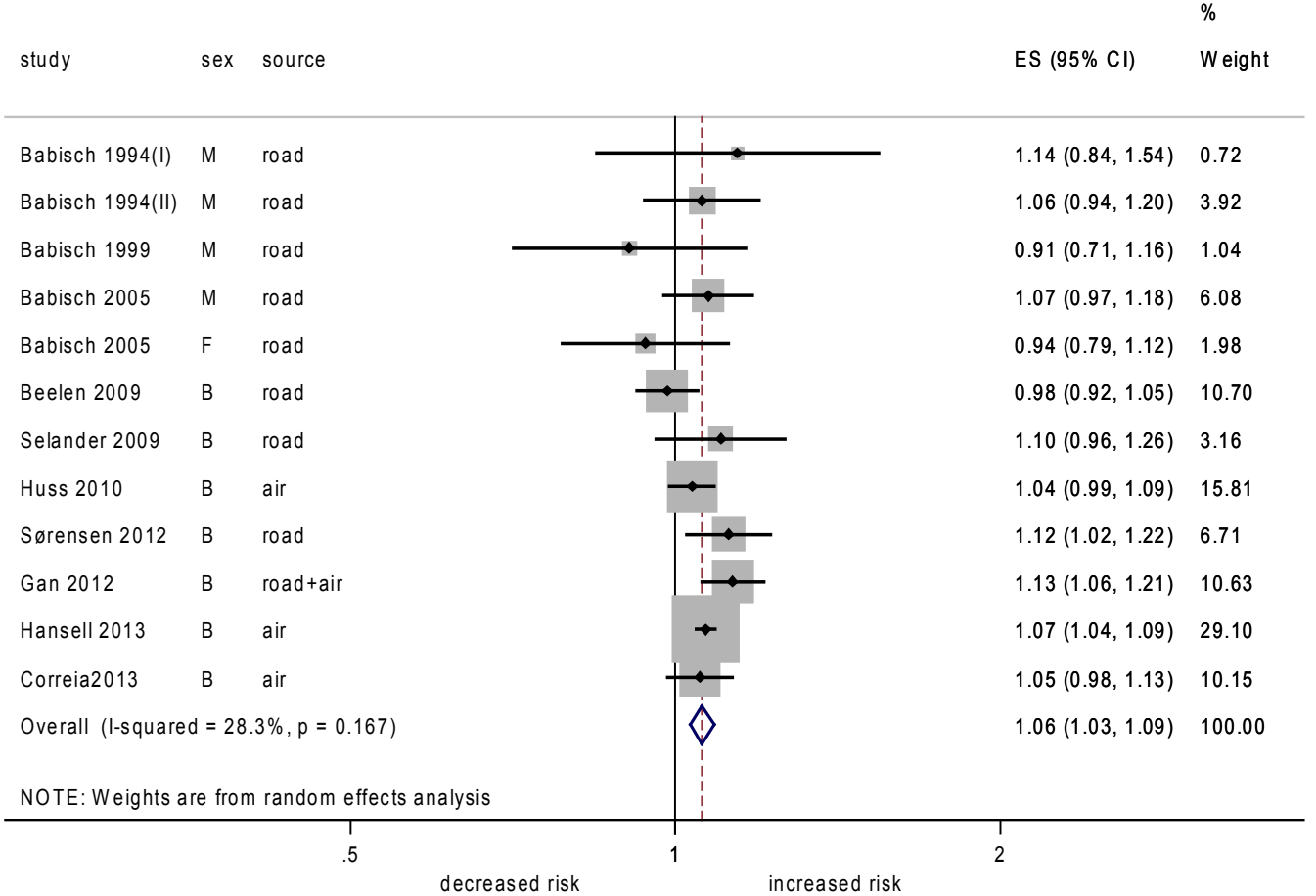
Noise Indicators

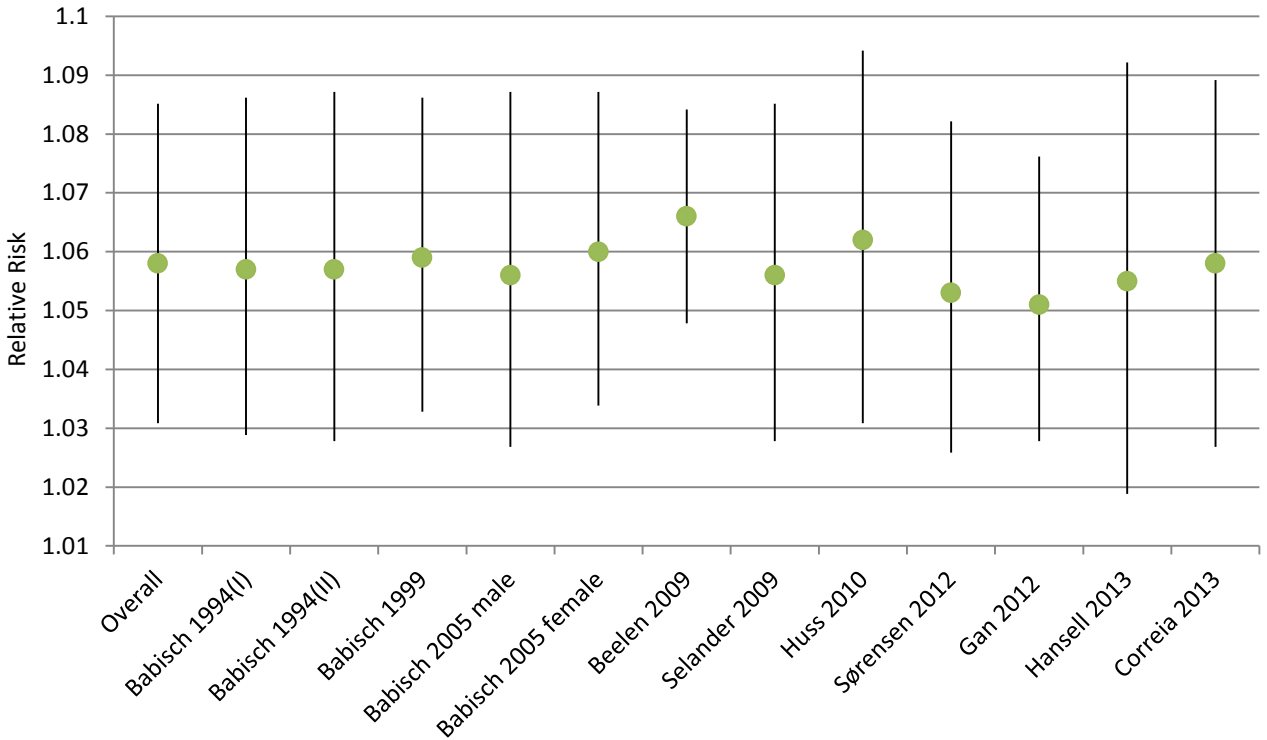
Indicator	**Description**	**Period**
Lday	Average sound level over all the day periods of a year	12 hours or 16 hours
Ldn ($L_{day\text{-}night}$)	Average sound level over all 24 hour periods of a year, with a penalty of 10 dB added for the 8 night hours	24 hours
Lden ($L_{day\text{-}evening\text{-}night}$)	Average sound level over all 24 hour periods of a year, with a penalty of 5 dB added for the 4 evening hours penalty of 10 dB added for the 8 night hours	24 hours

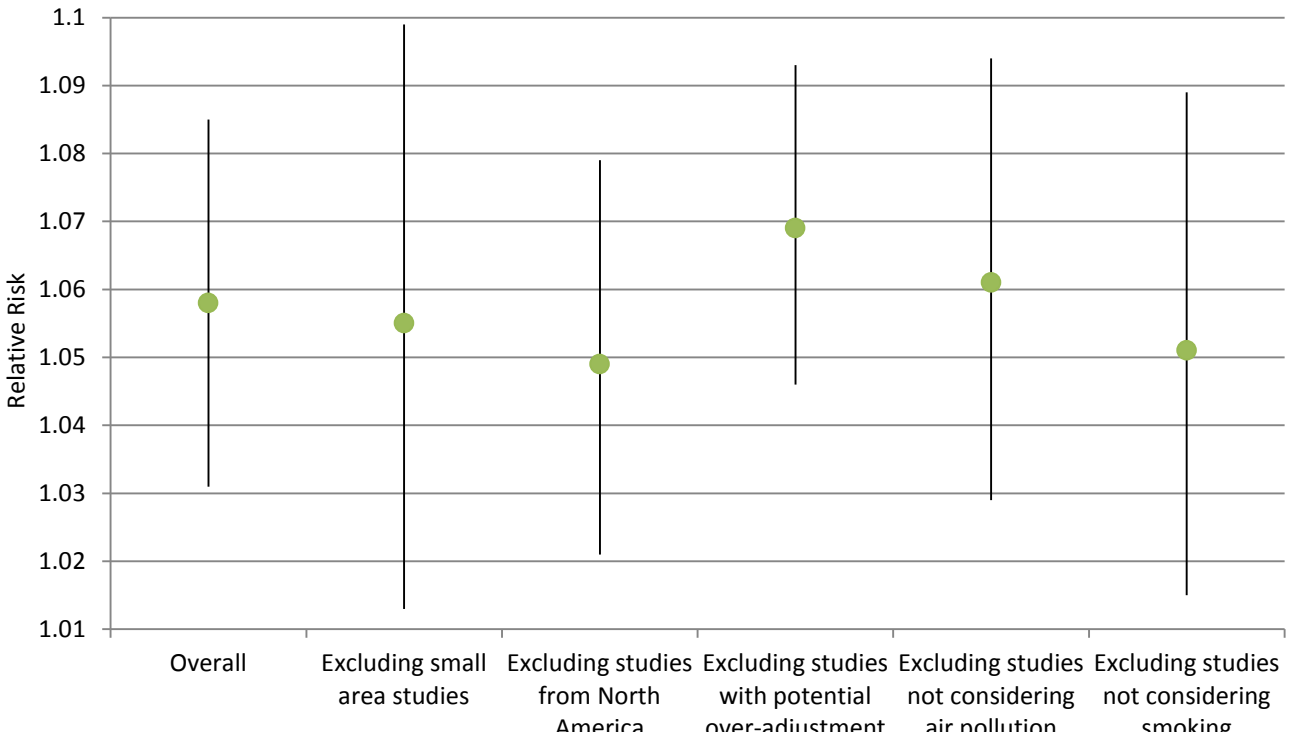
adapted from EEA 2010 Good Practice Guide[22]


Road traffic noise
Babisch 1994(I)
Babisch 1994(II)
Babisch 1999
Babisch 2005 (male)
Babisch 2005 (female)
Beelen 2009
Selander 2009
Sørensen 2012
Gan 2012
Relative risk
0.6
0.8
1
1.2
1.4
1.6
35
40
45
50
55
60
65
70
75
80
Noise level approx. L_{den} [dB(A)]


Aircraft noise
Huss 2010
Hansell 2013
Correia 2013
Relative risk
0.6
0.8
1
1.2
1.4
1.6
35
40
45
50
55
60
65
70
75
80
Noise level approx. L_{den} [dB(A)]


study
sex
source
ES (95% CI)
% Weight
Babisch 1994(I) M road 1.14 (0.84, 1.54) 0.72
Babisch 1994(II) M road 1.06 (0.94, 1.20) 3.92
Babisch 1999 M road 0.91 (0.71, 1.16) 1.04
Babisch 2005 M road 1.07 (0.97, 1.18) 6.08
Babisch 2005 F road 0.94 (0.79, 1.12) 1.98
Beelen 2009 B road 0.98 (0.92, 1.05) 10.70
Selander 2009 B road 1.10 (0.96, 1.26) 3.16
Huss 2010 B air 1.04 (0.99, 1.09) 15.81
Sørensen 2012 B road 1.12 (1.02, 1.22) 6.71
Gan 2012 B road+air 1.13 (1.06, 1.21) 10.63
Hansell 2013 B air 1.07 (1.04, 1.09) 29.10
Correia2013 B air 1.05 (0.98, 1.13) 10.15
Overall (I-squared = 28.3%, p = 0.167) 1.06 (1.03, 1.09) 100.00
NOTE: Weights are from random effects analysis
.5
1
2
decreased risk
increased risk


1.1
1.09
1.08
1.07
1.06
1.05
1.04
1.03
1.02
1.01
Relative Risk
Overall
Babisch 1994(I)
Babisch 1994(II)
Babisch 1999
Babisch 2005 male
Babisch 2005 female
Beelen 2009
Selander 2009
Huss 2010
Sørensen 2012
Gan 2012
Hansell 2013
Correia 2013


1.1
1.09
1.08
1.07
1.06
1.05
1.04
1.03
1.02
1.01
Relative Risk
Overall
Excluding small area studies
Excluding studies from North America
Excluding studies with potential over-adjustment
Excluding studies not considering air pollution
Excluding studies not considering smoking