



## Does air pollution confound associations between environmental noise and cardiometabolic outcomes? - A systematic review

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### ABSTRACT

**Background** - Exposure to road traffic noise can lead to adverse health effects. It is important to understand how associations may be affected by air pollution exposure.

**Objectives** - To update the current state of evidence on environmental noise on cardiometabolic outcomes, evaluating both confounding and interactions with air pollution.

**Methods** - Papers were identified from previous reviews from 2013 and 2015, reviews for the WHO 2018 noise guidelines and a literature search 2016-2020, using Medline and PubMed databases. Additional papers were identified from colleagues. Study selection was according to PECOS inclusion criteria. Studies were evaluated against a checklist for risk of bias.

**Results** - 81 publications were identified. Most, but not all, papers suggested independent associations of air pollution and noise but only nine provided quantitative estimates of interaction. Several of these found highest associations in highest air pollution – highest noise strata.

**Conclusions** - Current methods to assess quality of evidence of associations are not optimal when evaluating confounding. More studies are needed that examine interactions between noise and air pollution, which may occur whether or not there is confounding.

### Introduction

There is evidence that exposure to environmental noise pollution is associated with cardiovascular diseases, hypertension and metabolic health outcomes, and there is also evidence that exposure to environmental air pollution is associated with these outcomes [1-3]. Early research often focused on only one exposure, noise or air. However, since road transport is a major source of both air- and noise-pollution, there could be interaction or confounding to account for. For public health policy planning, it is important to understand the noise effects on health outcomes in the context of air pollution.

### METHODS

This review assessed studies that evaluated the combined effects of noise and air pollution. Our main research questions were:

- Does air pollution confound studies of noise and health?
- Are there sufficient studies to provide exposure-response relationships for interactions between noise and air pollution exposure?

### **Paper identification and selection**

#### **Paper Identification**

The identification process consisted of identifying and reviewing papers in the following sequence:

Two review papers [4, 5] were identified which evaluated the combined effect of environmental noise and air pollution and cardiovascular outcomes. All papers in these reviews were scanned for eligibility and then put forward for data extraction or excluded.

Searching for 'Noise' AND 'Air pollution' did not identify a number of key papers. Therefore, we searched for relevant noise exposure and relevant health outcomes and manually determined those that also included air pollution.

An initial literature search of Medline and PubMed databases was conducted for the years 2016 - 7th September 2020 to identify published studies looking at both environmental noise and air pollution. An updated search was subsequently carried out to December 31st, 2020.

The search terms for noise exposure related to road traffic, railway, aircraft and wind turbine. Search terms for health outcomes focused on cardiovascular disease, hypertension, diabetes and obesity.

We identified all papers considering noise and cardiometabolic outcomes included in systematic reviews conducted for the WHO noise guidelines for Europe [6] and included in systematic reviews published 2016 - present identified in Chen et al, Internoise proceedings 2021. We manually determined those including air pollution.

We searched for conference proceedings from: Internoise 2017, 2018 and 2019; Eurnoise 2018; IC BEN 2017, ICA 2019 and ICSV 2017, 2018 and 2019.

#### **Title scanning, abstracts, full paper reading**

Title scanning and abstract reading was by single reviewer. Studies were selected according to the PECOS inclusion criteria. Duplicates, papers for intervention, in-vitro, toxicological, animal, or controlled exposure studies, health outcomes of unclear clinical health relevance (e.g. epigenetics, metabolomics, methylation) and exposures out of scope (e.g. occupational, industrial, construction or laboratory-based noise) were excluded. Full paper reading was by single reviewer and determined papers that also included air pollution.

#### **PECO statement**

- Populations of interest: General population
- Exposures: Noise - road (RTN), rail (RWN), aircraft (ACN), transport, wind turbine, environmental
- Comparators: Comparison group with lower exposure, comparison expressed per specified dB increase of noise
- Outcomes: CVD (incl. IHD, stroke), Metabolic (incl. DM), Hypertension and Obesity

#### **Data extraction and preparation**

A standardised data extraction form was used to collect the following variables from each study: first author (publication year); journal; type of study; outcome measure; noise exposure; air pollution exposure; location; sample; sample size; exposure response coefficient without adjustment for air pollution; exposure coefficient including adjustment for air pollution and interaction analysis. Data extraction was by single reviewer.

### Quality assessment

**Individual study risk of bias evaluation** - Studies were evaluated against the WHO template [7] for assessment of quality and risk of bias for individual studies. Studies were assessed based on specific factors including exposure assessment, confounding, participant selection and non-blinded outcome.

**Quality of evidence assessment** - We considered using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [8]. However, it has been designed to evaluate effect estimates and several of the criteria are difficult or not possible to apply when evaluating confounding or interactions. As it was not possible to conduct a formal quality of evidence assessment, we have therefore commented on number of studies available, consistency of findings in terms of both direction of effects and changes in effect estimate from significant to non-significant.

## RESULTS

### Numbers of records identified

The initial search from 2016 to September 2020, identified 486 records through Medline and 87 through PubMed (Figure 1). After duplicates were removed, 436 papers progressed to record scanning. After title and abstract screening, 219 records were excluded. Papers could not be readily excluded at this stage as confounders were not often described in the abstract. 217 records progressed to full-text assessment for eligibility where a further 163 records were excluded, leaving 54 studies. A further 20, 5 and 1 eligible studies were identified from existing reviews, the WHO systematic review and own archives, respectively. The second literature search to December 2021 contributed one further study, giving a total of 81 papers.

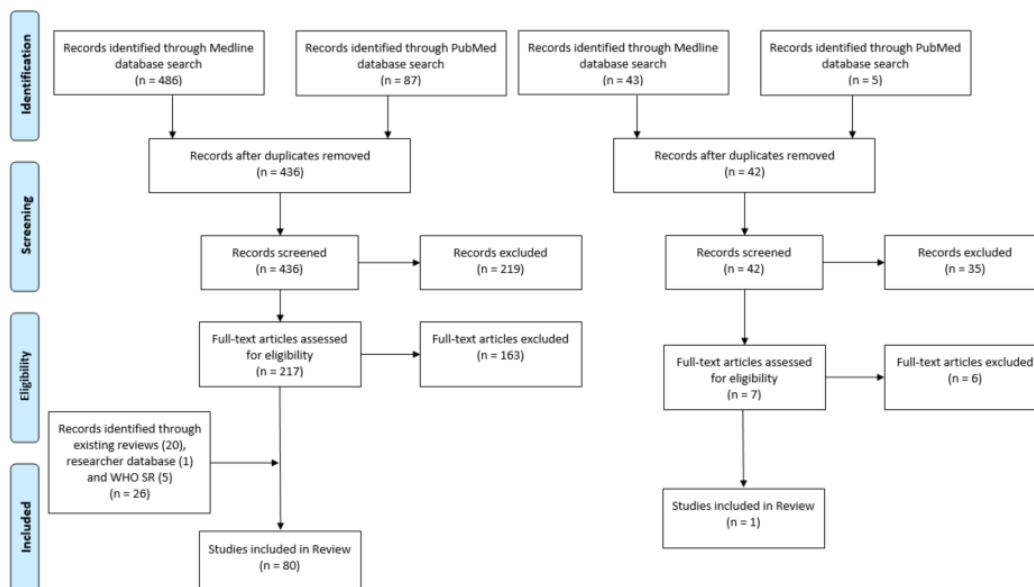


Figure 1: Medline and PubMed search flow diagram

## Main findings

Studies were grouped by outcomes and further grouped into noise type-outcome pairs to examine evidence for confounding or interactions of noise and air pollutants.

### Cardiovascular disease

14 studies investigated the combined effect of noise and air pollution (AP) on cardiovascular disease (CVD).

**Confounding** - Two of nine studies evaluating the combined effect of RTN and AP on CVD outcomes suggested potential confounding by AP [9, 10]. Both evaluated the effect on CVD mortality and looked at multiple cardiovascular outcomes. Potential confounding by air pollution was not consistent across outcomes. Beelen et al., 2009 [9] reported an attenuation of the strength of the association after adjustment for AP and traffic intensity. However, the simultaneous adjustment for traffic intensity and black smoke makes the evaluation of confounding by black smoke difficult. Thacher et al., 2020 [10] found that adjustment for NO<sub>2</sub> or PM<sub>2.5</sub> attenuated estimates slightly. The association remained significant after adjustment.

Neither of the two studies evaluating the combined effect of RWN and AP on CVD outcomes suggested that noise associations were confounded by AP.

One of five studies evaluating the combined effect of ACN and AP on CVD outcomes, suggested potential confounding by AP. Correia et al., 2013 [11] found that in the 90<sup>th</sup> centile of noise exposure, the association between ACN and CVD hospitalisations became statistically significant after adjustment for AP. However, the authors conclude that the association is not confounded by AP.

**Interactions** - Two of 14 studies investigated interaction. Yang et al., 2018 [12] evaluated associations between co-exposure groups and the prevalence of cardiovascular disease. Results showed that the co-exposure groups with high noise ( $\geq 80$  dBA) and high PM<sub>10</sub> ( $\geq 58$   $\mu\text{g}/\text{m}^3$ ), as well as co-exposure to high noise ( $\geq 80$  dBA) and high NO<sub>2</sub> ( $\geq 20$  ppb), had the highest adjusted odds ratios compared with the reference groups, OR: 2.20 (0.73, 6.62) and OR: 1.84 (0.79, 4.31), respectively. However, no categorised co-exposure groups were found to be statistically significant.

Thacher et al., 2020 [10] evaluated associations between combined residential exposure to RTN and PM<sub>2.5</sub> and CVD mortality risk (10-year mean exposure). In interaction analysis, results suggested that high exposure to both noise and PM<sub>2.5</sub> resulted in the highest risk for CVD mortality, HR: 1.70 (1.28, 2.27).

**Comments** - Overall, there is little evidence to suggest that noise estimates of CVD outcomes are confounded by AP. Only two studies investigated interactions, and both found highest effects in high noise and high AP exposure groups, but this was only statistically significant in one study.

### Ischemic heart disease (coronary heart disease)

17 studies investigated the combined effect of different types of noise and AP on IHD/CHD.

**Confounding** - Five of 12 studies evaluating the combined effect of RTN and AP presented evidence of potential confounding [9, 10, 13-15]. However, none of these found a statistically significant association between noise and IHD outcomes and none became significant after adjustment for AP.

Neither of two studies evaluating the combined effect of RWN and AP on IHD outcomes suggested that there was any confounding by AP.

Two of six studies evaluating the combined effect of ACN and AP found that effect estimates were changed by adjustment for AP [13, 16]. Evrard et al., 2015 [16] found a significant association between ACN and CHD mortality and that this effect estimate was reduced when adjusted for PM<sub>10</sub> but did not change relevantly after adjustment for NO<sub>2</sub>. Floud et al., 2013 [13] found non-significant associations between ACN and 'heart disease and stroke' and that effect estimates rose slightly after adjustment for NO<sub>2</sub>, but the association did not become significant after adjustment and the change in estimate (CIE) was <10%.

One of two studies evaluating the combined effect of transportation noise and AP found some evidence of confounding, however, the result was not consistent across air pollutants. Gan et al., 2012 [17] found a significant association between environmental noise and CHD mortality and that the noise estimate remained essentially unchanged when adjusted for NO<sub>2</sub> or NO<sub>2</sub> and PM<sub>2.5</sub>. However, when additionally adjusted for black carbon, the estimate was attenuated slightly.

**Interactions** - Gan et al., 2012 [17] evaluated the relative risk of death from CHD by decile of noise level and quartile of black carbon concentration. The study found that there was not any positive interaction between noise and black carbon on risk of CHD mortality when they were assessed on either additive or multiplicative scales.

**Comments** - Five of 12 RTN, neither of two RWN, two of six ACN and one of two combined noise studies found that noise estimates were changed after adjustment for AP. However, the CIEs were generally small, the pollutants adjusted for varied and results were not fully consistent. Interactions were only assessed in one study with no evidence for interactions.

### **Myocardial infarction/ acute myocardial infarction/ heart attack**

18 studies investigated the combined effect of noise and air pollution on myocardial infarction (MI) or heart attack.

**Confounding** – Four of 12 studies evaluating the combined effect of RTN and AP on MI outcomes suggested potential confounding [15, 18-20]. Two found significant associations between noise and MI outcomes before or after adjustment for AP [18, 20]. Bai et al., 2020 [18] found a significant association, but found that adjusting for ultrafine particles (UFPs) and NO<sub>2</sub> slightly attenuated noise estimates for incident AMI. However, the association remained significant and the percentage CIE was small. Roswall et al., 2017 [20] found a significant association for all exposure windows, but found that adjustment for NO<sub>2</sub> attenuated the estimates of MI incidence. Results were no longer significant for 10-year exposure.

None of the studies evaluating the combined effect of RWN, transportation noise or WTN and AP suggested potential confounding.

One of five studies evaluating ACN suggested potential confounding by AP, but the results were not consistent across air pollutants [16]. A significant association was found but the noise estimates for mortality from MI were attenuated by adjustment for PM<sub>2.5</sub> but increased after adjustment for NO<sub>2</sub>. The CIE for both pollutants was small.

**Interactions** - Four of 18 studies evaluated interaction effects. Three evaluated interactions in MI incidence [15, 20, 21]. Bodin et al., 2016 [15] estimated rate ratios for MI in relation to combined exposure to L<sub>den</sub> and NO<sub>x</sub> combined, for both current and medium-term exposure. Results showed associations between RTN and MI were strongest in the high noise, high AP category for both current and medium-term exposure, however, associations did not reach statistical significance. Roswall et al., 2017 [20] evaluated the combined effects of 10-year mean exposure to RTN and NO<sub>2</sub> in relation to risk of MI. Results showed the highest HRs for

both outcomes were among those with a combination of either high or medium noise exposure and high NO<sub>2</sub> exposure. Selander et al., 2009 [21] evaluated the risk of MI in subcategories defined by residential exposure to AP (NO<sub>2</sub> µg/m<sup>3</sup>) and noise (dBL<sub>Aleq,24h</sub>) from RTN. The reference category included individuals with low exposure to both AP and RTN. No strong interaction effect in relation to MI risk was seen between the two variables.

Heritier et al., 2019 [22] evaluated the combined impact of RTN and AP on MI mortality. The study tested interactions in categorical models to evaluate potential thresholds for interaction. Results did not reveal any relevant interactions for PM<sub>2.5</sub> or NO<sub>2</sub> with RTN. For instance, interaction terms were close to unity for people exposed to high levels of noise and air pollutants.

**Comments** - Four of 12 RTN, neither of two RWN, one of five ACN, none of one combined and neither of two WTN studies found that noise estimates were changed after adjustment for AP. However, the CIE was generally small, the pollutants adjusted for varied, and results were not fully consistent. There was no consistent evidence supporting interactions between air pollution and noise for MI incidence or mortality – two studies suggested highest risks in high noise and high AP categories, while two studies didn't find interaction effects.

### Stroke

18 studies investigated the combined effect of noise and air pollution on stroke or cerebrovascular disease.

**Confounding** - Eight of 12 studies identified evaluating the combined effect of RTN and AP on stroke outcomes found that noise estimates changed after adjustment for AP [9, 10, 13, 14, 23-26]. Three found estimates reduced [13, 14, 23], four increased and one had mixed results [10]. Six found significant associations pre-adjustment for AP [13, 14, 23-26].

Andersson et al., 2020 [14] found that adjusting for NO<sub>x</sub> reduced noise estimates for the association of RTN and stroke incidence and the association was no longer statistically significant. However, the CIE was still small. Both Sorensen et al., 2011 and 2014 [25, 26] found significant association between RTN and stroke incidence pre-adjustment for AP. Noise estimates increased after adjustment for AP, but the percentage CIE was low. Floud et al., 2013 [13] found that noise associations for 'heart disease and stroke' prevalence were attenuated after adjustment for NO<sub>2</sub>. In the subsample analysis, the CIE was >100%. Halonen et al., 2015 [24] found that daytime noise estimates increased after adjustment for AP but, again, the percentage CIE is low. Vivanco-hidalgo et al., 2019 [23] found that noise estimates for the association between RTN and stroke hospitalisations were attenuated, and became non-significant, after adjustment for PM<sub>2.5</sub>. However, the simultaneous adjustment for greenspace (NDVI) made assessing the confounding effect from AP difficult.

Thacher et al., 2020 [10] found mixed results for confounding. Noise estimates for the association between RTN and stroke mortality were attenuated by adjustment for PM<sub>2.5</sub> but increased after adjustment for NO<sub>2</sub>. Estimates were generally non-significant both before and after adjustment for AP with low percentage changes in estimates. However, the estimate for 1-year exposure became significant after adjustment for NO<sub>2</sub>. Beelen et al., 2009 [9] found that noise estimates increased after adjustment but the simultaneous adjustment for black smoke and traffic intensity means it is difficult to assess the confounding impact of black smoke.

There was no evidence for RWN estimates for stroke outcomes being confounding by AP, however, this is based on only one study.

Two of the five studies identified evaluating the combined effect of ACN and AP on stroke outcomes found that estimates changed after adjustment for AP. Floud et al., 2013 [13] found that noise estimates increased slightly after adjustment for NO<sub>2</sub>. The association remained non-significant, but the percentage CIEs were high. Evrard et al., 2015 [16] found that noise estimates were unchanged after adjustment for PM<sub>10</sub>, but adjustment for NO<sub>2</sub> led to a slight reduction. The percentage CIE was small.

One of two studies evaluating the combined effect of WTN and AP found evidence of potential confounding by AP [27]. Noise estimates for stroke mortality or hospitalisations were attenuated after adjustment for NO<sub>x</sub> but the CIE was low.

**Interactions** - One study evaluated interaction effects. Results from Sorensen et al., 2014 [26] showed exposure–response relationships between RTN and ischemic stroke within all three tertiles of exposure to NO<sub>2</sub>. The strongest association was found for the combination of the highest exposure to both noise and NO<sub>2</sub>.

**Comments** - Eight of 12 RTN, none of one RWN, two of five ACN, none of one combined and one of two WTN studies found that noise estimates were changed after adjustment for AP. However, the direction of change was not consistent and, with the exception of Floud et al., 2013 [13], the percentage CIE was low. Only one of the 18 studies on stroke or cerebrovascular disease examined interaction effects, finding highest associations in the highest noise + NO<sub>2</sub> tertile.

### **Heart failure/ congestive heart failure**

Seven studies investigated the combined effect of noise and air pollution on heart failure or congestive heart failure.

**Confounding** - Two of five studies identified that evaluated the combined effect of RTN and AP on heart failure outcomes, found some evidence that noise estimates were confounded by AP. Sorensen et al., 2017 [28] found that adjustment for NO<sub>2</sub> consistently attenuated the risk estimates for the association between RTN and heart failure incidence. Associations became non-significant after adjustment for NO<sub>2</sub> in the 1- and 5-year exposure windows. Beelen et al., 2009 [9] found that adjustment for black smoke and traffic intensity attenuated risk estimates for the association between RTN and heart failure mortality with the association becoming non-significant. However, the simultaneous adjustment for traffic intensity makes judgment on confounding by black smoke difficult.

No studies that evaluated RWN, ACN, or combined transportation noise presented any evidence of potential confounding by AP. However, comments on potential confounding was not possible for some of these studies.

**Interactions** - One study evaluated interaction effects. Sorensen et al., 2017 [28] evaluated combined effects of 10-year mean RTN (L<sub>den</sub>) and AP (NO<sub>2</sub>) in relation to risk of heart failure. Results showed that the strongest association was found for the combination of high exposure to both noise and NO<sub>2</sub>. Also, combinations of medium-medium and medium-high exposures yielded significantly increased estimates.

**Comments** - Both studies identified as having potential confounding found significant exposure-response associations before adjustment for AP [16, 50], which became non-significant after adjustment. However, the CIE for both these studies was low, <10%.

Only one of seven studies on heart failure examined interaction effects, finding highest associations in the highest noise + NO<sub>2</sub> grouping.

### **Atrial fibrillation**

Four studies investigated the combined effect of noise and AP on atrial fibrillation.

**Confounding** - Two of four studies evaluating the combined effect of noise and AP on atrial fibrillation outcomes found some evidence of potential confounding by AP. Andersson et al., 2020 [14] and Monrad et al., 2016 [29] both found that noise estimates for the association between RTN and atrial fibrillation incidence were reduced by adjustment for NO<sub>x</sub>. Estimates in Monrad et al., 2016 [29] were attenuated more so by adjustment for NO<sub>2</sub>. Only Monrad et al., 2016 [29] found a significant exposure-response association before adjustment for AP. Noise estimates were reduced from IRR: 1.06 (1.00, 1.12) to IRR: 1.01 (0.94, 1.09) meaning that the association became non-significant after adjustment for AP. The CIE was <10% for both NO<sub>x</sub> and NO<sub>2</sub>.

**Interactions** - No studies evaluated the potential interaction effects.

**Comments** - Few studies evaluated the combined effect of environmental noise and AP on atrial fibrillation outcomes. Only one study found a significant exposure-response association before adjustment for AP, but this became null after adjustment.

### Hypertension

24 studies were identified that investigated the combined effect of noise and AP on hypertension and blood pressure outcomes in adults. 21 of these were in the general adult population, and three were in pregnant women.

**Confounding** - Two of three studies that found significant associations between RTN and blood pressure, found that estimates were slightly attenuated by adjustment for AP. However, when looking across all BP studies, the results on potential confounding by AP are inconsistent with some increasing and some decreasing after adjustment.

Six studies evaluating RTN and hypertension outcomes suggested potential confounding from AP [31-36]. Four found significant associations before adjustment for AP [32, 34-36]. Babisch et al., 2014 [34] found inconsistent results across the two samples in the study. De Kluizenaar et al., 2007 [35] also found mixed results between study samples, generally, effect estimates increased after adjustment for PM<sub>10</sub>. Sears et al., 2018 [36] and Pedersen et al., 2017 [32] both found significant associations between RTN and HDP. However, in one study, adjustment for ECAT increased noise estimates [36], while in the other, adjustment for NO<sub>2</sub> reduced noise estimates and associations became non-significant [32]. In both, the percentage CIE was <10%.

One of five studies evaluating RWN found that noise estimates changed after adjustment for AP [37]. Dratva et al., 2012 [37] found that the estimated change in SBP increased from 0.79 (0.17, 1.41) to 0.84 (0.22, 1.46) for night time noise exposure.

None of the studies evaluating ACN or combined transportation noise suggested potential confounding from AP.

**Interactions** - No studies looked at interactions.

**Comments** - Surprisingly, out of 24 studies on hypertension in adults, no studies examined interactions between noise and AP. Evidence of confounding was low and inconsistent.

### Blood pressure in children

Three studies investigated the combined effect of noise and AP on blood pressure in children.

**Confounding** - The confounding effect of AP in these three studies evaluating noise and children's blood pressure are mixed. Pedersen et al., 2019 [38] saw some attenuation of



estimates after adjusting for NO<sub>2</sub>. Clark et al., 2012 [39], also saw a slight attenuation of estimates but suggests that moderate levels of AP do not appear to confound associations of noise on health, but further studies of higher AP levels are needed. In Enoksson Wallis et al., 2019 [40], ORs remained virtually unchanged after adjustment for NO<sub>x</sub>.

**Interactions** - No studies looked at interactions.

**Comments** - More studies are needed that evaluate the combined effect of environmental noise and AP in relation to blood pressure in children.

### **Metabolic outcomes (diabetes mellitus and gestational diabetes)**

14 studies investigated the combined effect of noise and AP on metabolic outcomes.

**Confounding** - Six of 11 studies evaluating the combined effect of RTN and AP on metabolic outcomes found statistically significant associations with noise before adjustment for AP [19, 41-45]. One found no confounding by AP [44], one found estimates were attenuated [19], two found estimate increased [43, 45] and two were not clear [41, 42]. In all cases, the percentage CIE was low. In one study, however, the association between RTN and diabetes incidence became significant after adjustment for AP. Eze et al., 2017 [46] found that the relative risk increased from 1.20 (0.92, 1.56) to 1.35 (1.02, 1.78) after adjustment for NO<sub>2</sub>.

Of the three studies that evaluated the combined impact of railway noise and AP on metabolic outcomes, only one study presented estimates both before and after adjustment for AP [46] and there was no indication of confounding.

One of two studies evaluating the combined impact of aircraft noise and AP on metabolic outcomes presented estimates both before and after adjustment for AP [46]. The association between ACN and diabetes was non-significant, but the estimate increased after adjustment for NO<sub>2</sub>. The percentage CIE was low.

Of the three studies that evaluated the combined effect of transportation noise and AP on metabolic outcomes, only Clark et al., 2017 [79] found any evidence of potential confounding. Results were not consistent across air pollutants.

**Interactions** - No studies looked at interactions.

**Comments** - Overall, evidence that the association between environmental noise and diabetes is confounded by AP is low. More studies are needed, and these should present estimates pre- and post- adjustment for AP and also look at interactions of air- and noise-pollution.

### **Obesity**

Ten studies were identified that investigated the combined effect of noise and AP on markers of obesity. Outcomes evaluated included BMI; waist circumference; obesity; overweight; central obesity; lean body mass index (LBMI); body fat mass index (BFMI); weight gain and percentage body fat.

**Confounding** - Overall, little evidence was found to suggest that transportation noise estimates in obesity outcomes are confounded by AP. Only Cai et al., 2020 [47] suggested any potential confounding and results were not consistent across outcomes, cohorts or air pollutants.

**Interactions** - No studies looked at interactions.

**Comments** - There was no consistent evidence for confounding by AP in ten studies identified. No studies had examined interactions.

## Quality of evidence

Overall, risk of bias was generally low across the studies. 60% of studies with hypertension or obesity outcomes were judged to have a low overall risk of bias, while 79%, and 80% had low overall risk of bias for CVD and metabolic outcomes, respectively.

## DISCUSSION

This review aimed to assess whether environmental air pollution confounds the effects of environmental noise pollution on health outcomes, and to assess any interaction effect. In general, the results of the 81 studies reviewed here show that there was little consistent evidence for confounding. Very few papers have considered interactions.

Studies were initially identified as showing potential for confounding from air pollution, if the noise estimates were changed after adjustment for air pollution. Many studies that showed a change in estimate after adjustment for air pollution, found no significant associations between environmental noise and health outcomes, before or after adjustment. By definition, a confounder is a variable whose presence modifies the association between the exposure and the outcome. Therefore, to evaluate the effect of confounding, an association should exist at least before, or after adjustment for air pollution. Evaluation of the change in estimate in studies with non-significant associations, may not be particularly relevant.

In studies finding a significant association between the noise exposure and the health outcomes where estimates were affected by adjustment for air pollution, the percentage CIEs was low. In many cases results were inconsistent across air pollutants. In a few studies with significant associations, it was difficult to evaluate the effect of confounding by air pollution, as there was simultaneous adjustment for another potential confounder, e.g. traffic intensity or green space.

We identified two previous reviews which specifically evaluated the combined effect of environmental noise and air pollution and cardiovascular outcomes. There has been a significant increase in the literature of studies that control for air pollution since these previous reviews were undertaken. However, our findings are similar. Stansfeld et al., 2015 [1] found that, in general, the studies reviewed suggest independent associations of environmental noise, from road traffic, aircraft and rail, and air pollution with cardiovascular outcomes. Similarly, Tétreault, et al., 2013 [2] suggests that confounding of cardiovascular effects by noise or air pollutants is low.

A strength of this study is its systematic approach, it followed the same criteria as WHO reviews. However, there are some limitations. Firstly, study screening and data extraction was carried out by single reviewer, which increases the risk of studies being missed. Secondly, for some outcomes there were few studies, which could decrease the strength of the results. Publication bias is always a possibility with reviews. For example, in this study we only included English language studies. We did try to minimise potential publication bias by searching grey literature in a range of conference proceedings. Another limitation could be the heterogeneity across studies and that studies use many different exposure measure and different air pollutants as confounders. Some studies had adjusted for air pollution, but then did not include both the pre- and post-adjusted effect estimates, meaning that comments on confounding could not be further assessed. It is possible that these studies found that adjustment for air pollution had no significant effect and so the result was omitted. If future studies consistently reported both estimates it could strengthen our findings.

## CONCLUSION

We identified 81 papers for cardiometabolic outcomes. Most, but not all, studies found little evidence of confounding by air pollution. Very few papers (nine of 81) considered potential interaction effects but there were no consistent findings. Further evidence is needed on interactions to better evaluate co-exposures to noise and air pollution from transport sources.

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Please note, due to page limits, this reference list does not contain all papers identified in the review.

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