

# **Association between Exposure to Noise and Risk of Hypertension: A Meta-Analysis of Observational Epidemiological Studies**

**Running title:** Noise and hypertension

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## Abstract

**Background and Objective:** An increasing amount of original studies suggested that exposure to noise could be associated with the risk of hypertension, but the results remain inconsistent and inconclusive. We aimed to synthesize available epidemiological evidence about the relationship between various types of noise and hypertension, and to explore the potential dose-response relationship between them in an up-to-date meta-analysis.

**Methods:** We conducted a literature search of PubMed and Embase from these databases' inception through December 2016 to identify observational epidemiological studies examining the association between noise and risk of hypertension. A Random-effects model was used to combine the results of included studies. Dose-response meta-analysis was conducted to examine the potential dose-response relationship.

**Results:** Thirty-two studies (five cohort studies, one case-control study, and twenty-six cross-section Studies) involving 264,678 participants were eligible for inclusion. Pooled result showed that living or working in environment with noise exposure was significantly associated with increase risk of hypertension (OR 1.62; 95% CI: 1.40 to 1.88). We found no evidence of a curve linear association between noise and risk of hypertension. Dose-response analysis suggested that, for an increment of per 10 dB(A) of noise, the combined odds ratio of hypertension was 1.06 (95% CI: 1.04 to 1.08).

**Conclusions:** Integrated epidemiological evidence supports the hypothesis that exposure to noise may be a risk factor of hypertension, and there is a positive dose-response association between them.

**Keywords:** noise, hypertension, dose-response, meta-analysis

## **Introduction**

Hypertension is the most common condition seen in primary care that can lead to renal failure, cardiovascular disease, and death<sup>1-2</sup>. According to the World Health Organization, about 24.8% of the global population are affected by hypertension<sup>3</sup>. Reducing modifiable risk factors may contribute to the prevention and control of hypertension, which is of considerable public health importance.

Noise pollution has been increasingly investigated as an environmental risk factor for hypertension recently. Some studies suggested that exposure to noise were associated with many health problems, including annoyance<sup>4</sup>, hearing loss<sup>5</sup>, sleep disturbance<sup>6</sup>, type 2 diabetes<sup>7</sup>, and ischemic heart disease<sup>8</sup>. For example, a multi-airport study published in 2013 found that exposure to aircraft noise increased the relative rate of hospitalization for cardiovascular diseases<sup>9</sup>.

Recently, the association between noise exposure and the risk of hypertension has drawn researchers' attention and it was the topic for dozens of epidemiological studies. Although there were several meta-analyses that evaluated the relationship between noise and the risk of hypertension, their results were not comprehensive without considering all types of noises, and many new studies have been recently published.

Taken into consideration of the inconsistent conclusions of existing epidemiological studies and the flaw of previous meta-analyses, we conducted an updated meta-analysis of observational epidemiological studies to evaluate the association between noise and the risk of hypertension.

## **Materials and Methods**

Ethical approval is not required for this systematic review.

### **Literature search strategy**

We conducted this meta-analysis in accordance with the preferred reporting items for systematic

reviews and meta-analysis (PRISMA) <sup>10</sup> and the checklist of items in the meta-analysis of observational studies in epidemiology (MOOSE) <sup>11</sup>. We performed a literature search on PubMed and Embase in December 2016. The following keywords were used to identify relevant citations: “noise” in combination with “hypertension” or “blood pressure”. The language was restricted to English. Only human studies were considered. Additionally, reference lists of the retrieved original articles and relevant review articles were also scrutinized to identify further pertinent studies.

### **Study selection**

We included studies according to the following criteria: (1) the study design was cohort, case-control, or cross-sectional; (2) any type of noise was an exposure variable and the outcome was the incidence of hypertension; and (3) the study reported the odds ratio (OR) or relative risk (RR) with the corresponding 95% confidence intervals of hypertension related to noise exposure. Studies providing data on the relationship between noise exposure and the change of blood pressure but not reporting the association of noise with the risk of hypertension were excluded. If there is more than one report from the same study, we only included the one with the most detailed information for both noise exposure and the incidence of hypertension.

### **Data extraction and quality assessment**

Two authors (WF and SC) independently extracted the following information from the included studies: first author, publication year, country (state), study design, sex, age, number of participants, noise type, exposure levels, adjusted OR/RR with 95% CI, and adjusted factors. Disagreements were resolved by discussion with a third author (ZL).

We used the Newcastle-Ottawa Scale to evaluate the quality of cohort studies and case-control studies<sup>12</sup>. The scale score is calculated based on the three factors: selection of participants,

comparability of groups, and exposure/outcome ascertainment. This scale awards a maximum of 9 points to a study. Studies scoring 0-3 points, 4-6 points, and 7-9 points were categorized as low, moderate, and high quality of studies, respectively. The assessment tool involving 11 items recommended by the Agency for Healthcare Research and Quality was applied for cross sectional studies<sup>13</sup>. An item is given '1' point if it was considered in a study, and '0' point if the item was not considered or we were unable to determine whether it was considered in a study. Each study was rated independently by two authors (WF and SC). Discrepancies were resolved by discussion with a third investigator (ZL).

### **Statistical analyses**

We considered OR as the common measure of the association between noise and risk of hypertension. The reported RR was considered approximately as OR. When OR was reported separately by different levels of noise exposure, the highest level of noise exposure was defined as the exposure group. We calculated an overall pooled OR using a random effects model for the main analysis<sup>14</sup>. In addition, if the articles included at least three quantitative categories of noise or the results were already reported as OR per 10 dB(A) of noise, they were used in a dose-response meta-analysis, in which the dose-response result was measured by OR of hypertension per 10 dB(A) of noise.

We calculated the natural logarithm of the OR and its variance per 10 dB(A). If a study reported an OR per unit of noise, the natural logarithm of the OR per unit of noise could be directly used.

However, most studies gave a series of grouped dose-specific OR, with one noise exposure group as the referent group. These were transformed into a risk estimate per unit of noise. In addition, a dose value for each noise exposure group was assigned as suggested by<sup>15</sup>: The median or mean level of noise within each category was used as the corresponding dose value. When the median or mean per

unit of noise was not available, the midpoint of the upper and lower boundaries was considered the dose of each category. If the highest category was open-ended, the midpoint of the category was set at 1.5 times that of the lower category. When the number of participants were not available, the odds ratios comparing the highest vs. lowest categories of noise were used to obtain a summary estimate. Restricted cubic splines with three knots at percentiles 10%, 50%, and 90% of the distribution were used to evaluate a potential curve linear relationship between noise and risk of hypertension. We calculated the  $P$  value for curve linearity or nonlinearity by testing the null hypothesis in which the coefficient of the second spline is equal to 0<sup>16</sup>.

We used  $Q$  statistic with a significance level at  $P < 0.10$  and  $I^2$  statistic to test the heterogeneity. The  $I^2$  statistic measures the percentage of total variation across studies due to heterogeneity rather than chance. It was calculated according to the formula by Higgins<sup>17</sup>. The substantial heterogeneity is  $I^2$  value of  $\geq 50\%$ .

We conducted subgroup analyses to determine the possible influence of some factors such as study design, noise type, state, controlling for age, body mass index, sex, and smoking. The Begg's rank correlation and the Egger's linear regression tests were used to assess potential publication bias<sup>18-19</sup>.

Duval and Tweedie's nonparametric trim-and-fill method was used to adjust potential publication bias<sup>20</sup>. We used STATA statistical software (version 12.0; College Station, TX, USA) to analyze data.

All statistical tests were two-sided with a significance level of 0.05.

## **Results**

### **Literature search**

Figure 1 shows the process of study identification and inclusion. Initially, we retrieved 1346 citations

from the PubMed and 1248 citations from the Embase. After excluding 151 duplicates, we identified 2446 citations. After assessing the eligibility of the 2446 records based on titles and abstracts, we excluded 2193 records. After retrieving and assessing full-text of the remaining 253 articles, we excluded 221 articles, because 191 studied only the relationship between noise and blood pressure and thirty studies did not provide useful data to calculate them. Finally, 32 studies<sup>21-52</sup> were included (five cohort studies, one case-control study, and twenty-six cross-sectional studies).

### **Characteristics of the included studies**

Table 1 shows the main characteristics of the 32 studies included in the systematic review. The included studies were published between 1984 and 2016, and included a total of 264,678 participants. Among these, nineteen studies were from the Europe, twelve studies were from Asia, and one study was from the South America. In total, seventeen studies were occupational noise and fifteen were community noise (including seven road noise, six air noise and two were unknown). Two studies were published before 2000 and the other thirty after 2000. In addition, there were five cohort studies, and the quality assessment scores ranged from 6 to 9, with an average score of 7 points. The quality assessment score for one case-control study was 7 points. There were a total of 26 cross-sectional studies, and the scores from our assessment of study quality ranged from 5 to 10, with a mean score of 7.2 points.

### **Results of meta-analysis**

#### **Association between noise and risk of hypertension**

Figure 2 shows the results from the random-effects model combining the ORs for hypertension in relation to noise. Twenty-eight studies investigated the relationship between noise and risk of hypertension. Of the 28 studies, twenty-one suggested a positive relationship between noise and the



risk of hypertension, while the others did not. The pooled OR of hypertension for noise was 1.62 (95%CI: 1.40 to 1.88), with substantial heterogeneity across studies ( $P = 0.000$ ,  $I^2 = 84.3\%$ ).

### **Dose-response analysis**

Sixteen studies reported the dose-response analysis of noise and risk of hypertension. As shown in Fig. 3, a curve linear association between per 10 dB(A) of noise and risk of hypertension was not observed ( $P = 0.420$ ). The pooled OR of hypertension for an increment of per 10 dB(A) in noise was 1.06 (95% CI: 1.04 to 1.08; Figure 4). We saw a substantial heterogeneity among studies ( $P = 0.000$ ,  $I^2 = 79.4\%$ ).

### **Results of subgroup analyses and sensitivity analyses**

Table 2 shows the results of subgroup analyses. Subgroup analyses by study design, noise type, state or country, **nighttime or daytime noise**, and controlling for **the concomitant effects of air pollution**, age, BMI, sex, smoking were conducted for the increase of hypertension risk, relating to noise exposure, respectively. In general, these subgroup analyses showed no statistically significant difference in results. Every single pooled result of subgroup showed the positive and statistically significant relationship between exposure to noise and the risk of hypertension.

Of note, subgroup analyses by noise type showed that the heterogeneity was mainly from occupational noise:  $I^2=88.7\%$  for occupational noise and 12.4%, 69.0%, and 0 % for road, air, or unknown noise, respectively.

To identify the potential influence of single study on the pooled results, any single study was excluded in turn and pooled the results of the remaining included studies. The pooled OR did not materially change, with a range from 1.57 (95% CI: 1.36-1.82) to 1.69 (95%CI: 1.43-2.01).

### **Publication bias**

Visual inspection of the funnel plot indicated substantial asymmetry (Figure 5). The Egger test

indicated evidence of publication bias, but the Begg test did not (Egger,  $p=0.000$ , Begg,  $p=0.12$ ). We used the trim-and-fill method to evaluate the impact of any potential publication bias, the results showed that two potentially missing studies would be needed to obtain funnel plot symmetry for hypertension (Figure 6). By using the trim-and-fill method, the corrected OR was 1.57 (95% CI: 1.35 to 1.82; random-effects model,  $p=0.000$ ). Therefore, the pooled OR was not substantially changed by the correction for potential publication bias.

## **Discussion**

Noise exposure is a widely existing environment factor around the world and a number of previous studies suggested that noise may affect human being's health. In the study by Munzel (2017), some generalized pathways are possible to explain the potential mechanisms: (1) noise cause perturbation of vegetative nerve or Sympathetic adrenal activation; (2) noise can lead to release of pro-inflammatory mediators and active leukocyte populations; and (3) endothelial dysfunction caused by oxidative stress. Therefore, both reaction chains can initiate physiological stress responses, involving the hypothalamus, the autonomous nervous system with activation of the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic-adrenal-medulla axis, that may lead to the incidence of hypertension. Meanwhile, noise can increase the psychological stress, which is considered to be an important factor in the formation and development of hypertension. The mechanism of psychological stress leading to hypertension is mainly as follows: psychological stress can lead to excessive activation and unbalanced adjustment of the sympathetic nervous system. Thus, the sympathetic adrenal medulla system, the hypothalamus pituitary adrenal axis system and the renin-angiotensin system are regulated directly or indirectly, which increases the secretion of hormones such as angiotensin, catecholamine

hormones, and aldosterone abnormally regulates. The endothelial system and the immune system, resulting in increased secretion of endothelin-1 and inflammatory factors, raised the amount of vasoconstrictor substance and decreased vasodilator substance, leading to vascular dysfunction. The combined effect is the elevated blood pressure.<sup>54-59</sup>

This meta-analysis focusing on the association between exposure to noise and the risk of hypertension included 32 observational epidemiological studies involving 264,678 participants<sup>21-52</sup>. Evidence from these studies suggested that people living or working in noise environment have an increased risk of hypertension by 62% compared with control participants.

Since substantial heterogeneity was found among the included studies, we conducted subgroup analyses by various factors, including study design, noise type, state or country, nighttime or daytime noise, and controlling for the concomitant effects of air pollution, age, BMI, and sex. Our results showed that the association between noise and hypertension risk was similar across subgroups. However, subgroup analyses suggested that type of noise may be the main cause of heterogeneity. For noise from community (road noise, air noise, or unknown type of community noise), no obvious heterogeneity was found. For occupational noise, the heterogeneity was substantial, indicating that different occupation has very different type of noise. Of note, occupational factories have different standard, and different methods were used to control noise, so there is discrepancy in the type of occupational noise. In community, a majority of individuals may spend less daytime at home, and in the evening the noise may be smaller than that during the day.

Of the included studies, 16 articles reported the ORs of hypertension for an increment of per 10 dB(A) of noise or respective ORs for different levels of noise exposure dB(A). Based on these data, we conducted a dose-response analysis and found that the combined OR of hypertension was 1.06

(95% CI: 1.04 to 1.08) for an increment of 10 dB(A) of noise. The present quantitative review supported the positive, statistically significant dose-response relationship between the exposure level of noise and the risk of hypertension. Given the insufficiency of available data, we failed to identify whether the duration of noise exposure changed the risk of hypertension.

There are several strengths in our study. Firstly, sensitivity analysis and consistent results from various subgroup analyses indicated that our findings were reliable and robust, although heterogeneity existed among the included studies. Secondly, not only did we identified the increased hypertension risk of people regularly living or working in noise environment compared with control people, but also the dose-response relationship between exposure level of noise and the risk of hypertension.

Some limitations should be of concern in the present meta-analysis. First, majority of the included studies had a cross-sectional study design, the methodological weakness of which may weak the validity of our results. Secondly, potential confounding factors were adjusted differently in the included studies, as what and how many covariates should be adjusted in data analyses were usually unclear.

In summary, our meta-analysis of observational epidemiological studies with the most up-to-date evidence suggests that noise exposure is significantly associated with an increased risk of hypertension. A positive, statistically significant dose-response relationship is found between the exposure level of noise and the hypertension risk. **Since most of the included studies were of a cross-sectional design with considerable risk of bias, well designed prospective cohort studies with sufficiently long follow up period are needed to confirm our findings.**

**Author Contributions:** Zuxun Lu, Shiyi Cao and Zhihong Wang had full access to all the data in the

study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Shiyi Cao and Wenning Fu independently extracted the related data information.

Check the related data information again: Chao Wang, Qiaoyan Liu and Li Zou.

Data analysis and writing articles: Shiyi Cao , Wenning Fu and Fujian Song.

Analysis, or interpretation of data: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

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**Table 1 Main characteristics of the included studies involving noise exposure and the risk of hypertension.**

Author	Country(state)	Study design	Sex, age	Number of participants	Noise type	Exposure levels[dB(A)]	Adjustment
Belli S	Italy (Europe)	Cross	M. 35-56	940	Occupational	78-105	NR
Herbold M	Germany (Europe)	Cross	M. 30-69	2295	Occupational	NR	NR
Belojevic G	Pancevo (Europe)	Cross	M&F. NR	3622	Community (Road)	53-70	Age, smoking and BMI
Rosenlund M	Sweden (Europe)	Cross	M&F. 19-80	2959	Community (Air)	<72 versus ≥72	Age, sex, smoking and education
Souza TCFD	Brazil (South America)	Cross	M&F. NR	1729	Occupational	≤75 75-85 ≥85	Age, sex and BMI
Inoue M	Japanese (Asia)	Cross	M. 20-59	415	Occupational	75 versus 92	Age, BMI, smoking, alcohol drinking, exercise, diet and family history of hypertension
Bluhm GL	Sweden (Europe)	Cross	M&F. 19-80	667	Community (Road)	≤45 45-50 50-55 >55	Age, type of residence, occupational status ,smoking status and number of cigarettes
Eriksson C	Sweden (Europe)	Cohort	M. 35-56	2754	Community (Air)	50-65 versus >65	Age and BMI
Belojevic GA	Serbia (Europe)	Cross	M&F. 18-96	2503	Community (Road)	>45 versus ≤45	Age, BMI, physical activity, education, family history of hypertension and alcohol consumption

Rhee MY	Korea (Asia)	Cross	M&F. >18	875	Community (Air)	80-89 105-115 114-116	Age, sex, BMI, smoking, alcohol drinking, diabetes and regular exercise
Barregard L	Sweden (Europe)	Cross	M&F. 18-75	1953	Community (Road)	45-50 51-55 56-70	Age, sex, BMI and heredity for hypertension
Bodin T	Sweden (Europe)	Cross	M&F. 18-80	24238	Community (Road)	<45 45-49 50-54 55-59 60-64 >64	NR
Chang TY	Taiwan (Asia)	Cross	M&F. NR	59	Occupational	50-120	Age, sex, BMI, smoking, regular exercise and family history of hypertension
Eriksson C	Sweden (Europe)	Cohort	M&F. 35-56	4721	Community (Air)	<50 50-54 55-59 ≥60	Age, sex, socioeconomic status, smoking and BMI
Nawaz SK	Pakistan (Asia)	Cross	M. 30-50	389	Occupational	≤80 81-94 ≥95□	Age, weight, BMI, smoking and family history of hypertension
Bendokiene I	Lithuania (Europe)	Cross	M. 20-45	3121	Community (Road)	≤50 51-69 ≥61	Age, social status, marital status, education, alcohol drinking, ethnic, BMI, chronic disease and exposure duration
Chang TY	Taiwan (Asia)	Cross	M&F. NR	820	Community (Road)	<77 versus ≥83	Sex, BMI, smoking, alcohol drinking, tea consumption, coffee consumption, regular exercise and family history of hypertension

La TG	Italian (Europe)	Csae - control	M&F. NR	241	Community (NR)	NR	NR
Attarchi M	Iran (Asia)	Cross	M. 19-55	331	Occupational	72-100	Age, work of duration, BMI, smoking, dietary salt, regular exercise and family history of hypertension
Babisch W	Germany (Europe)	Cross	M&F. 25-74	4166	Occupational (Road)	per 10dB(A)	Age, anti hypertension medication, employment duration, BMI, educational level, cigarette use, alcohol drinking and regular exercise
Chang TY	Taiwan (Asia)	Cross	M&F. 23-58	188	Occupational	≥80 versus <80	Sex, BMI, triglyceride level, BMI, educational level, smoking, working activity, alcohol drinking, regular exercise and family history of hypertension
Weinmann T	Germany (Europe)	Cross	M&F. 8-65	1742	Community (NR)	40-115	NR
Chang TY	Taiwan (Asia)	Cohort	M. NR	578	Occupational	<80 80-85 ≥85	Age, anti hypertension medication, employment duration, BMI, educational level, cigarette use, alcohol drinking and regular exercise

Attarchi M	Iran (Asia)	Cross	M. 20-58	471	Occupational	61-102	Age, work of duration, BMI, smoking, dietary salt, regular exercise, shift working, nature of job and family history of hypertension
Stokholm ZA	Denmark (Europe)	Cohort	M&F. NR	145190	Occupational	<75 75-79 80-84 85-89 90-94 95-99 >100	Age, socioeconomic status, calendar year and employment status
Babisch W	Germany (Europe)	Cross	M&F. 25-74	4166	Occupational (Road)	per 10dB(A)	Age, BMI, other chronic disease
Babisch W	Germany (Europe)	Cross	M&F. 35-74	1770	Occupational (Road)	per 10dB(A)	NR
Banerjee D	India (Asia)	Cross	M&F. 18-80	909	Occupational	<60 60-65 65-70 ≥70	Age, gender, BMI, physical activity, alcohol consumption and professional activity
Chang TY	Taiwan (Asia)	Cross	M. NR	820	Occupational	<47 versus ≥63	Sex, age, BMI, smoking status, alcohol drinking, salt intake, physical activity, family history of hypertension and the total traffic flow rate
Rapisarda V	Italy (Europe)	Cross	M. NR	105	Occupational	NR	NR
Evrard AS	France (Europe)	Cross	M&F. >18	1244	Community (Air)	per 10dB(A)	Age, sex, triglyceride level, the use of hearing-protective

Liu CS	Taiwan (Asia)	Cohort	M&F. NR	1002	Occupational	<75 75-79 ≥80	devices, BMI, smoking, alcohol drinking, regular exercise and family history of hypertension Age, sex, triglyceride level, the use of hearing-protective devices, BMI, smoking, alcohol drinking, regular exercise and family history of hypertension
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Abbreviation: NR= not reported; BMI=body mass index

**Table 2 Results of subgroup analyses about noise and hypertension risk.**

<b>Subgroup</b>	<b>Number of studies</b>	<b>OR/RR</b>	<b>95% confidence intervals</b>	<b>P for heterogeneity</b>	<b>I-square(%)</b>
<b>Study design</b>					
Cohort	26	1.088	1.058-1.119	0.000	85.10
Case-control	5	1.203	1.097-1.319	0.086	51.00
Cross	1	2.090	0.993-4.397	—	0.00
<b>Noise type</b>					
Occupational	17	1.080	1.049-1.113	0.000	88.70
Road	7	1.443	1.221-1.682	0.335	12.40
Air	6	1.121	1.048-1.198	0.006	69.60
Unknown	2	1.588	1.150-2.193	0.422	0.00
<b>State</b>					
Europe	19	1.978	1.049-1.107	0.000	59.90
Asia	12	1.58	1.100-2.270	0.000	86.50
South America	1	1.959	1.671-2.297	—	—
<b>Nighttime or daytime noise</b>					
nighttime noise	2	1.344	1.043-1.733	0.145	53.00
daytime noise	9	1.225	1.121-1.339	0.000	89.90
nighttime and daytime noise	21	1.082	1.052-1.113	0.000	76.90
<b>Controlling for the concomitant effects of air pollution</b>					
Yes	3	1.141	1.049-1.241	0.000	87.10
No	29	1.092	1.062-1.123	0.000	82.60
<b>Controlling for age</b>					

Yes	22	1.165	1.113-1.218	0.000	79.20
No	10	1.064	1.030-1.100	0.000	87.50
<b>Controlling for body mass index</b>					
Yes	21	1.174	1.118-1.232	0.000	78.90
No	11	1.067	1.034-1.102	0.000	87.20
<b>Controlling for sex</b>					
Yes	10	1.338	1.198-1.495	0.324	12.90
No	22	1.085	1.056-1.115	0.000	86.800
<b>Controlling for smoking</b>					
Yes	15	1.049	1.275-1.558	0.000	80.00
No	17	1.078	1.048-1.108	0.000	81.70

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## **Figure legends**

Figure 1 Flow diagram of identification of relevant observational studies of noise in relation to the risk of hypertension.

Figure 2 Association between exposure to noise and the risk of hypertension in a meta-analysis of observational studies.

Figure 3 Dose-response relationships for the association between noise and risk of hypertension. CI = confidence Interval

Figure 4 Forest plot of the summary odds ratio of hypertension for an increase of per10 dB(A) of noise. CI = confidence interval

Figure 5 Funnel plot with 95% confidence limits

Figure 6 Filled funnel plot of OR from studies that investigated the association between noise and the risk of hypertension