Journal of the American Heart Association

SYSTEMATIC REVIEW AND META-ANALYSIS

Effects of Ambient Air Pollution on Blood Pressure Among Children and Adolescents: A Systematic Review and Meta-Analysis

Miao Huang, MD*; Jingyuan Chen, MD*; Yiping Yang, BM; Hong Yuan, MD, PhD; Zhijun Huang, MD; Yao Lu, MD, PhD

BACKGROUND: Previous studies have investigated the association of ambient air pollution with blood pressure (BP) in children and adolescents, however, the results are not consistent. We conducted a systematic review and meta-analysis to assess the relationship between short-term and long-term ambient air pollutant exposure with BP values among children and adolescents.

METHODS AND RESULTS: We searched PubMed, Web of Science, and Embase before September 6, 2020. Two reviewers independently searched and selected studies, extracted data, and assessed study quality. The studies were divided into groups by composition of air pollutants (NO_2, particulate matter (PM) with diameter ≤10 μm or ≤2.5 μm) and length of exposure. The beta regression coefficients (β) and their 95% CIs were calculated to evaluate the strength of the effect with each 10 $\mu g/m^3$ increase in air pollutants. Out of 36 650 articles, 14 articles were included in this meta-analysis. The meta-analysis showed short-term exposure to PM with diameter ≤10 μm (β=0.267; 95% CI, 0.033−0.501) was significantly associated with elevated systolic BP values. In addition, long-term exposure to PM with diameter ≤2.5 μm (β=1.809; 95% CI, 0.962−2.655), PM with diameter ≤10 μm (β=0.526; 95% CI, 0.095−0.958), and NO_2 (β=0.754; 95% CI, 0.541−0.968) were associated with systolic BP values and long-term exposure to PM with diameter ≤2.5 μm (β=0.931; 95% CI, 0.157−1.705), and PM with diameter ≤10 μm (β=0.378; 95% CI, 0.022−0.735) was associated with diastolic BP.

CONCLUSIONS: Our study indicates that both short-term and long-term exposure to some ambient air pollutants may increase BP values among children and adolescents.

Key Words: blood pressure ■ children ■ gaseous pollutants ■ meta-analysis ■ particulate matter

High blood pressure (BP) or hypertension has become 1 of the 10 largest contributors to global disease burden,[1] which contributed to 211.8 million disability adjusted life-years per year. In particular, the increasing prevalence of childhood hypertension has gained worldwide concern.[2] Childhood and adolescence are periods of rapid growth and in this period organ systems are particularly susceptible to injury, leading to lifelong consequences. In recent years, a growing body evidence indicates that elevated BP in childhood and adolescence is a risk factor for hypertension and cardiovascular disease in adults.[3,4] Therefore, it is important to identify the possible causes.

Previous studies have found that the lungs of children may be exposed to higher concentrations of ambient particles than adults,[5] suggesting that children would be at greater risk from the adverse effects of air pollution. Recent epidemiological studies have

Correspondence to: Yao Lu, MD, PhD, Center of Clinical Pharmacology, The Third Xiangya Hospital, Central South University, 138 Tongzipo Road, Changsha, 410013 Hunan, China. E-mail: luyao0719@163.com and Zhijun Huang, MD, Center of Clinical Pharmacology, The Third Xiangya Hospital, Central South University, 138 Tongzipo Road, Changsha, 410013 Hunan, China. E-mail: huangzj@csu.edu.cn

Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.017734

*Dr Miao Huang and Dr Chen contributed equally to this work.

For Sources of Funding and Disclosures, see page 9.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- This is the first meta-analysis to assess the quality and magnitude of the associations between air pollution and blood pressure values among children and adolescents.
- In the present meta-analysis of 14 articles, short-term exposure to particulate matter with diameter ≤10 μm and long-term exposure to NO_x, particulate matter with diameter ≤10 μm and particulate matter with diameter ≤2.5 μm were significantly associated with elevated blood pressure values.

What Are the Clinical Implications?

- Our findings raise concerns for the health of children and adolescents in areas with high air pollution, by providing evidence toward a positive association between both short-term and long-term exposure to some ambient air pollutants and blood pressure among children and adolescents.

Nonstandard Abbreviations and Acronyms

DBP	diastolic blood pressure
PM	particulate matter
PM_1	particulate matter with diameter ≤1 μm
PM_{10}	particulate matter with diameter ≤10 μm
$PM_{2.5}$	particulate matter with diameter ≤2.5 μm
SBP	systolic blood pressure

evaluated the effect of short-term and long-term exposure to air pollutants on BP values among children and adolescents. However, the results are not consistent. Some studies revealed that exposure to air pollutants increase BP values,[6–9] while others found that there was no association between air pollution and BP value.[10–12] To better understand the effects of air pollution on blood pressure among children and adolescents, this inconsistency needs to be resolved. Systematic reviews and meta-analysis are useful methods for quantitatively synthesizing and interpreting existing evidence. However, no meta-analysis specifically addressing the effect of air pollution on BP values among children and adolescents has been published to date.

To provide more information about the association of air pollutant exposure with BP values in childhood and adolescence for researchers and medical personnel, we pooled the evidence from epidemiological studies to assess the effect of short-term and long-term air pollutant exposure on BP values among children and adolescents in this systematic review and meta-analysis.

METHODS

The authors declare that all supporting data are available within the article.

Data Sources and Search Strategies

This meta-analysis was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines (Table S1).[13] We searched 3 electronic databases (PubMed, Web of Science, and Embase) for articles published before September 6, 2020. The search strategies were composed of keywords related to ambient air pollutants (air pollution, particulate matter [PM], particles, air pollutants, SO_X, SO_2, NO_x, NO_2, O_3, and CO), BP (hypertension, high BP, hypertensive, BP, systolic BP [SBP], diastolic BP [DBP]) and children/adolescents (child, children, childhood, adolescent, teenager, and kids) (Table S2). We also searched the references of the included articles.

Study Selection

Studies were included if they: (1) were original studies exploring the effect of ambient air pollution exposure (long-term: ≥30 days or/and short-term exposure: <30 days) on BP among adolescents or/and children; (2) provided quantitative estimates and their 95% CI (or sufficient data to calculate these estimates). The studies were not included if they: (1) were reviews, case reports, repeated studies, or animal studies; (2) only involved hypertension without including specific BP values.

All references retrieved from the databases were imported into a reference manager (EndNote X9, Thomson ResearchSoft, US). Duplicate references were deleted directly through the software. We then screened the titles and abstracts of the remaining articles. Studies were excluded if they did not explore the effect of ambient air pollution exposure on BP among children or adolescents. Finally, we evaluated the full text of the remaining references using the same criteria (Figure 1). Two researchers (Miao Huang and Jingyuan Chen) independently searched and screened all the studies.

Data Extraction

The following information was extracted from all of the included articles: last name of the first author, publication year, country of the study, study design, study period, short-term or long-term effect,

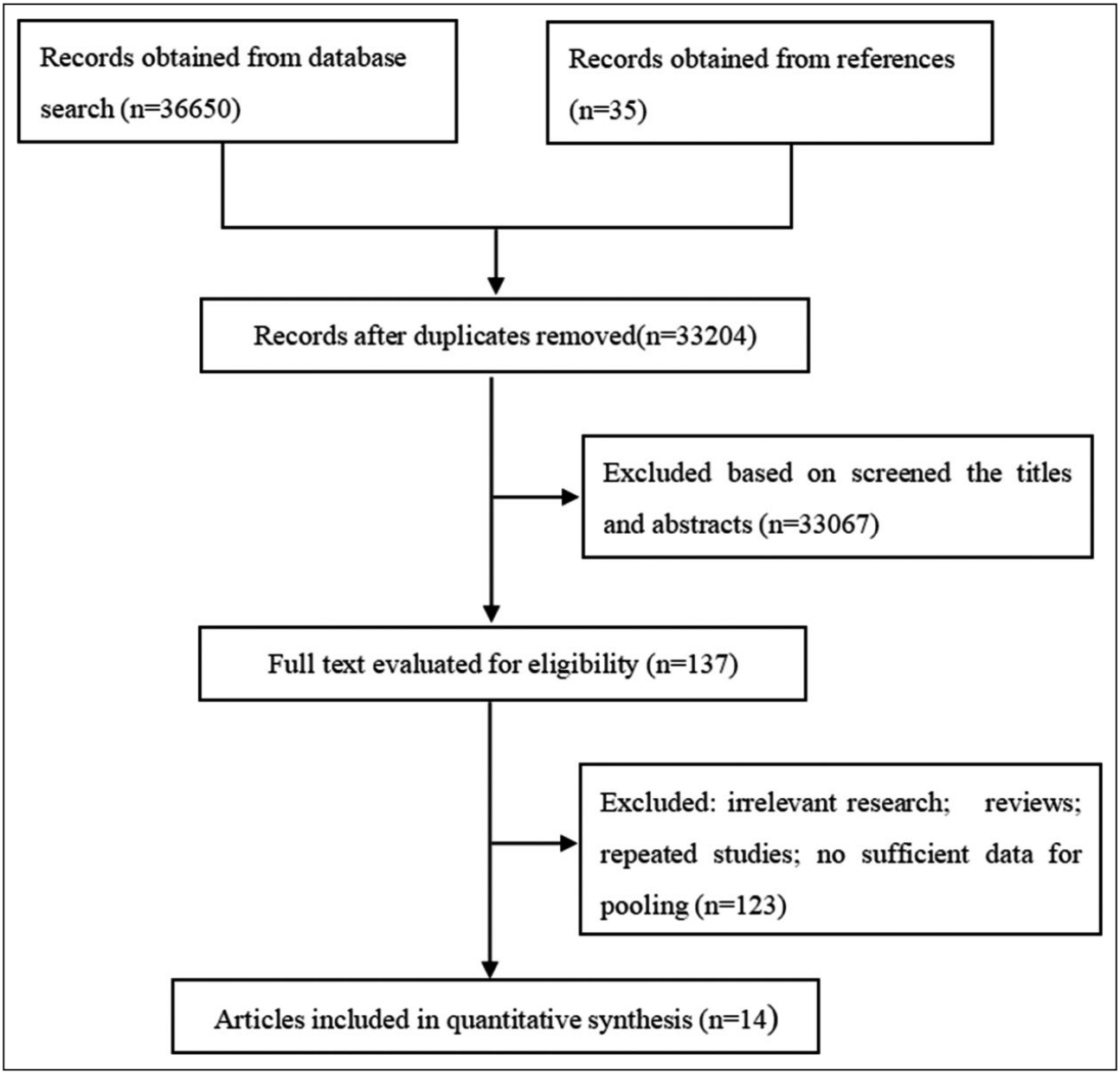

Figure 1. Flowchart of study selection.

study population, sample size, age, sex proportion, assessment method of air pollution exposure, BP measurement method, effect sizes and 95% CI, and confounding factors. We tried to contact the author if quantitative information was not provided in the articles. The data for each article were extracted independently by 2 researchers (Miao Huang and Jingyuan Chen).

Quality Evaluation

Two investigators, Miao Huang and Jingyuan Chen, independently assessed the quality of each study. Any disagreement was resolved through discussion. The quality of included studies was assessed using the Newcastle-Ottawa Scale[14] for cohort and panel studies and the Joanna Briggs Institute[15] meta-analysis of statistics assessment and review instrument for cross-sectional studies. The score range for the Newcastle-Ottawa Scale is 0 to 9 and the score range of Joanna Briggs Institute meta-analysis of statistics assessment and review instrument is 0 to 20. Higher scores corresponded to higher quality.

Data Synthesis and Statistical Analysis

In this review, we used beta regression coefficients (β) as the effect size of exposure to air pollutants on BP among children and adolescents. All of the effect sizes were converted to a common exposure unit increase

(10 μg/m^3) so that we were able to quantitatively pool effect sizes from different studies. In studies evaluating the effect of air pollution short-term exposure, different studies have assessed different lag patterns, with some reporting 1-day lags and some reporting cumulative lags. We followed the methodology presented by Atkinson et al to choose lag patterns.[16] Briefly, if only 1 lag pattern was provided, this estimated effect was recorded. If several lag patterns were provided, we chose the lag that was statistically significant or stated as a priority. In studies included in short-term exposure analysis, only Yang et al (2019) reported lag patterns, and the statistically significant lag (lag 0–6) was chosen. Some studies reported several estimated effect sizes from different models that adjusted for different covariates/confounding factors. In the present meta-analysis, we only extracted the estimated effect sizes from the main analysis or full-adjusted model performed by investigators.

We used the meta-analysis model to calculate the pooled effect size. The weight of the forest plots was based on the sample size of each study and on the estimated effect trend and 95% CI of each study. Heterogeneity between studies was assessed using Cochran Q statistic and I^2 statistic. P_Q value was obtained by comparing the Q statistic with a χ^2 distribution with k–1 degrees of freedom, where k was the number of included studies. If the P_Q value was <0.05, the random-effect model was selected; otherwise, the fixed-effect model was selected. A value of the coefficient of inconsistency (I^2) >50% indicated that the heterogeneity was statistically significant. We used funnel plot and Egger regression to detect the potential publication bias. Egger regression was applied to test the funnel plot symmetry, in which the standard error of the estimated effect was the independent variable and the estimated effect was the dependent variable.[17]

We performed subgroup analyses of the type of study (cross-sectional versus cohort) for the long-term exposure effect. Because of the limited number of studies that assessed the short-term exposure effect, we could not perform subgroup analysis. To explore potential modification effects of age, male proportion, and study location, we conducted single variable and multiple variable meta-regression analysis for long-term exposure groups, which was a method for detecting more sources of heterogeneity. Both age and male proportion were included as continuous variables in the meta-regression model. Study location was included as a classification variable, specifically, China is coded as 1 and other countries are coded as 2. Finally, we performed sensitivity analyses to test the stability of the pooled effect size by sequentially removing each study and recalculating the meta-analysis. We only conducted sensitivity analyses for the meta-analyses that included >3 studies.

All statistical analyses were performed using STATA version 16 (StataCorp, College Station, TX). P<0.05 (2-side) was considered to be statistically significant unless otherwise stated.

RESULTS

Search Results and Characteristic of the Included Studies

As shown in Figure 1, 36 650 articles were identified through preliminary search through the electronic databases. After removing duplicate articles, 33 204 articles were screened. After screening the titles and abstracts, 33 067 articles were excluded as not meeting the inclusion criteria. Among the remaining 137 articles, 14 articles were included after examing the full text. These 14 articles finally were included in this meta-analysis.

The characteristics of the included studies[6–11,18–25] are shown in Table and Table S3. The study designs included cross-section and cohort. Of all the 14 studies, 8 were conducted in China, 2 were conducted in the Netherlands, 1 was conducted in Belgium, 1 was conducted in Germany, 1 was conducted in the United Kingdom, and 1 was conducted in Europe (United Kingdom, France, Spain, Lithuania, Norway, and Greece). Four focused on the effects of short-term exposure on BP values, 9 studies focused on the effects of long-term exposure, and 1 focused on both short-term and long-term exposure. The total sample size was 351 766. The mean ages of the study populations ranged from 5.4 to 12.7 years. Most studies measured air pollutant concentration based on data from monitoring stations or models including a land-use regression model, a machine learning method with a Random Forests model, or a combined emission-dispersion and regression model.

Short-Term Effects of Air Pollutants on SBP and DBP Values

Three studies investigated the effect of short-term PM with diameter ≤10 μm (PM_{10}) exposure on SBP values among children and adolescents. A 10 μg/m^3 PM_{10} increase was significant associated with 0.276 mm Hg (95% CI, 0.033−0.501) increase in SBP (Figure 2, Figure S1). Three studies evaluated the short-term effects of PM with diameter ≤2.5 μm ($PM_{2.5}$) exposure on DBP values and 4 studies evaluated the short-term effects of PM_{10} exposure on DBP values (Figure 3 and Figures S2, S3). We did not find a statistically significant relationship of DBP values with $PM_{2.5}$ (β=−0.107; 95% CI, −1.036 to 0.823) or PM_{10} (β=0.215; 95% CI, −0.070 to 0.500). The heterogeneity analyses revealed that the above meta-analyses had significant heterogeneity: 95.99% for PM_{10} with SBP, 70.60% for $PM_{2.5}$ with DBP,

Table. Characteristics of the Studies Included in the Meta-Analysis

Author (Publication, y)	Period	Location	Sample Size	Mean Age (y)	Male (%)	Design	Pollutants	Duration	Outcome	Quality Score
Zhang et al (2020)[18]	2017	China	7225	9.1	54.0	Cross-sectional	$PM_{2.5}$ PM_{10}	Long-term	SBP DBP	18 (JBI)
Wu et al (2020)[19]	2012–2013	China	9354	10.9	51.0	Cross-sectional	$PM_{2.5}$	Long-term	SBP DBP	18 (JBI)
Warembourg et al (2019)[20]	2014–2015	Europe (UK, France, Spain, Lithuania, Norway, and Greece)	1277	8.0	54.6	Cohort	NO_2 $PM_{2.5}$ PM_{10}	Long-term	SBP DBP	8 (NOS)
Ntarladima et al (2019)[21]	2010	Netherlands	733	5.4	51.3	Cross-sectional	NO_2 $PM_{2.5}$ PM_{10}	Long-term	SBP DBP	18 (JBI)
Yang et al (2019)[9]	2016	China	194 104	10.2	53.0	Cross-sectional	$PM_{2.5}$ PM_{10}	Short-term	SBP DBP	18 (JBI)
Zhang et al (2019)[8]	2013	China	43 745	11.3	50.4	Cross-sectional	$PM_{2.5}$ PM_{10}	Long-term	SBP DBP	19 (JBI)
Li et al (2018)[22]	2010	China	71 763	12.5	50.0	Cross-sectional	PM_{10}	Long-term	SBP DBP	17 (JBI)
Zeng et al (2017)[7]	2012–2013	China	9354	10.9	51.0	Cross-sectional	PM_{10}	Short-term	SBP DBP	18 (JBI)
Pieters et al (2015)[11]	2011	Belgium	130	9.0	50.0	Panel	$PM_{2.5}$ PM_{10}	Short-term	DBP	6 (NOS)
Bilenko et al (2015)[6]	2009–2010	Netherlands	1400	12.7	49.1	Cohort	NO_2 $PM_{2.5}$ PM_{10}	Both	SBP DBP	7 (NOS)
Dong et al (2014)[23]	2012	China	9354	10.9	51.0	Cross-sectional	NO_2 PM_{10}	Long-term	SBP DBP	19 (JBI)
Liu et al (2014)[10]	1997–2009	Germany	2368	10.2	51.1	Cohort	NO_2 $PM_{2.5}$ PM_{10}	Long-term	SBP DBP	7 (NOS)
Baumgartner et al (2012)[24]	2008–2009	China	240	10.3	52.0	Cross-sectional	$PM_{2.5}$	Short-term	SBP DBP	16 (JBI)
Clark et al (2012)[25]	2002	UK	719	10.0	45.6	Cross-sectional	NO_2	Long-term	SBP DBP	18 (JBI)

DBP indicates diastolic blood pressure; JBI, the Joanna Briggs Institute meta-analysis of statistics assessment and review instrument; NOS, Newcastle Ottawa Scale; $PM_{2.5}$, particulate matter with diameter ≤2.5 μm; PM_{10}, particulate matter with diameter ≤10 μm; and SBP, systolic blood pressure.

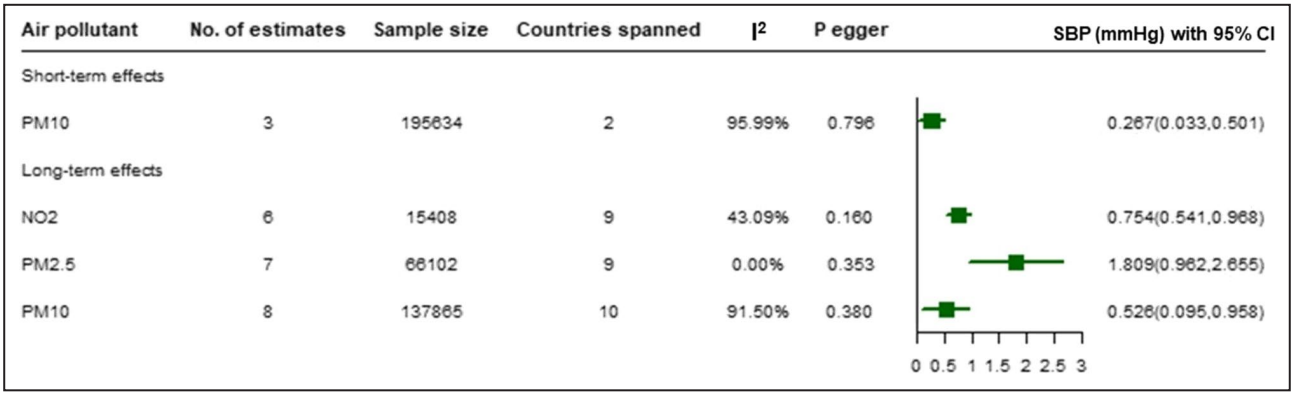

Figure 2. Forest plots for the pooled association between air pollutants (per 10 μg/m³ increment) and systolic blood pressure (mm Hg).
The green boxes represent the pooled mean effect estimates. The horizontal bars represent 95% CIs of pooled mean effect estimates. The I^2 statistic was used to evaluate study heterogeneity and Egger regression was used to detect publication bias. PM_{10} indicates particulate matter with diameter ≤10 μm; $PM_{2.5}$, particulate matter with diameter ≤2.5 μm; and SBP, systolic blood pressure.

and 97.19% for PM_{10} with DBP (Figures S1 through S3). The funnel plot and the results of Egger test showed significant publication bias for the association of $PM_{2.5}$ with DBP (P=0.009) and of PM_{10} with DBP (P=0.009), but not for PM_{10} with SBP (P=0.796) (Figures S4 through S6).

Sensitivity analysis showed that the association of PM_{10} with DBP was not robust (Table S4). Because of the limited number of studies that investigated the effect of PM_{10} on SBP and $PM_{2.5}$ on DBP, we could not perform a sensitivity analysis.

Long-Term Effects of Air Pollutants on SBP and DBP Values

The effect of long-term exposure to NO_2, $PM_{2.5}$, and PM_{10} on BP values was investigated in 6, 7, and 8 studies, respectively. For SBP, significant association was found for $PM_{2.5}$ (β=1.809; 95% CI, 0.962–2.655), PM_{10} (β=0.526; 95% CI, 0.095–0.958), and NO_2 (β=0.754; 95% CI, 0.541–0.968) (Figures S7 through S9). For DBP, significant association was found for $PM_{2.5}$ (β=0.931; 95% CI, 0.157–1.705) and PM_{10} (β=0.378; 95% CI, 0.022–0.735), but not for NO_2 (Figures S10 through S12). The heterogeneity analyses revealed that most of the above meta-analyses did not have significant heterogeneity except for PM_{10} with SBP (91.50%) and NO_2 (54.82%) and PM_{10} (90.65%) with DBP (Figures S7 through S12). The funnel plot and the Egger test found no publication bias for the association of $PM_{2.5}$, PM_{10}, and NO_2 with SBP and the association of $PM_{2.5}$, PM_{10}, and NO_2 with DBP (Figures S13 through S18).

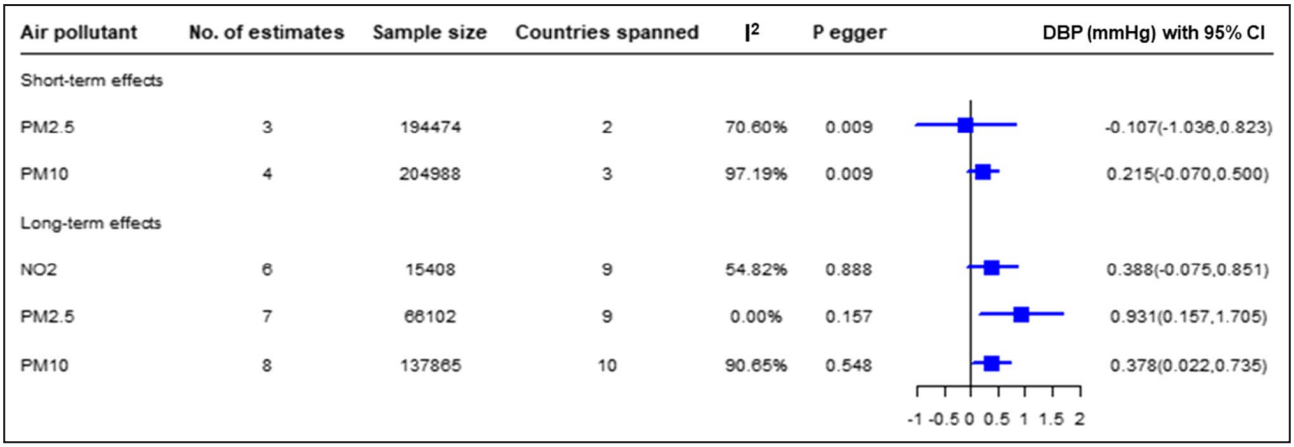

Figure 3. Forest plots for the pooled association between air pollutants (per 10 μg/m³ increment) and diastolic blood pressure (mm Hg).
The blue boxes represent the pooled mean effect estimates. The horizontal bars represent 95% CIs of pooled mean effect estimates. The I^2 statistic was used to evaluate study heterogeneity and Egger regression was used to detect publication bias. DBP indicates diastolic blood pressure; PM_{10}, particulate matter with diameter ≤10 μm; and $PM_{2.5}$, particulate matter with diameter ≤2.5 μm.

The sensitivity analyses showed that the pooled estimates were generally robust except for the association between NO_2 and SBP (Tables S5 through S10).

Subgroup analyses by type of study showed that the associations were generally significant or more apparent in cross-sectional studies (Tables S11 and S12).

The results of single variable meta-regression showed that a 1-year increase in age of the subjects was significantly associated with the effect sizes of long-term exposure to PM_{10} (β=−0.361, P<0.001) on SBP and PM_{10} (β=−0.322, P<0.001) on DBP, a 1% increase in the proportion of males in the population was significantly associated with the effect sizes of long-term exposure to PM_{10} (β=0.512, P<0.001) on SBP and NO_2 (β=0.461, P<0.001) on DBP, and the study location was significantly associated with the effect sizes of long-term exposure to NO_2 on SBP (β=−0.657, P=0.016) and DBP (β=−0.794, P=0.001) (Table S13). Multiple variable meta-regression showed that a 1-year increase in age was still significantly associated with the effect sizes of long-term exposure to PM_{10} (β=−0.693, P=0.001) on SBP and PM_{10} (β=−0.536, P=0.003) on DBP and that the study location was still significantly associated with the effect sizes of long-term exposure to NO_2 on SBP (β=−0.562, P=0.007) and DBP (β=−0.860, P=0.001) (Table S14). The results showed that the heterogeneity of the meta-analysis may be attributable to the age and sex distribution of the study population and the study location of the studies.

DISCUSSION

Principal Finding

A total of 14 studies encompassing 351 766 participants from 10 countries were enrolled in this systematic review and meta-analysis. To the best of our knowledge, we have conducted the most detailed assessment of all of the data from studies that have been published to date on the relationship between exposure to 3 ambient air pollutants (NO_2, $PM_{2.5}$, and PM_{10}) and BP values in children and adolescents. The overall meta-analysis showed that short-term exposure to PM_{10} was significantly associated with elevated SBP values. Long-term exposure to NO_2, $PM_{2.5}$, and PM_{10} were associated with SBP values and long-term exposure to $PM_{2.5}$, PM_{10} was associated with DBP. Subgroup analyses showed that the association between long-term exposure to NO_2 and PM_{10} and BP values of children and adolescents was significantly positive in cross-sectional studies.

Short-Term Exposure Effects on BP

Numerous previous studies have demonstrated some degree of positive relationship between short-term (<30 days) ambient outdoor air pollution exposure and higher BP in adults.[9,11] A recent meta-analysis by Yang and colleagues using pooled data from 100 studies, reported that short-term exposure to some ambient air pollutants showed a significant association with hypertension and BP levels in the general population.[26]

Childhood high BP is a significant predictor of hypertension and cardiovascular risk later in life.[27] However, few studies have previously explored the association between short-term air pollution exposure and BP among children and adolescents. Sughis et al investigated the effect of particulate air pollution (PM with diameter ≤1 μm [PM_1], $PM_{2.5}$, and PM_{10}) on BP among 179 children in Pakistan, including 100 children in high-air pollution areas and 79 children in low-air pollution areas. Results showed that BP values were significantly higher in children living in the high-pollution areas (115.9/70.9 mm Hg) compared with in the low-pollution areas (108.3/66.4 mm Hg).[28] Zeng et al reported on the relationship between short-term exposure to 4 ambient air pollutants (PM_{10}, NO_2, SO_2, and O_3) and childhood BP in a highly polluted area of China. Their findings indicated that there was no significant association between SO_2 or NO_2 and elevated BP in children, however, they observed an association between elevated BP and an increased interquartile range for PM_{10} and O_3.[7] Yang et al conducted a study on 194 104 children in Suzhou, China and concluded that short-term exposure to ambient PM ($PM_{2.5}$ and PM_{10}) was significantly associated with elevation of SBP and DBP. However, Pieters et al enrolled 130 schoolchildren in Belgium and concluded that short-term exposure to air pollution ($PM_{2.5}$ and PM_{10}) was not significantly associated with blood pressure.[11] Baumgartner et al investigated 240 schoolchildren in Yunnan, China, and found that increased personal exposure to $PM_{2.5}$ were not associated with higher BP among children in households cooking with biomass fuel.[24] A cohort study among 1432 children in the Netherlands reported that short-term air pollution exposure (NO_2, O_3, and PM_{10}) was not associated with BP.[29] Considering these inconsistent results, we conducted this current meta-analysis, which showed only short-term exposure to PM_{10} was significantly associated with SBP values. In conclusion, there was evidence that short-term exposure to air pollution was associated with increased BP among children and adolescents.

Long-Term Exposure Effects on BP

Numerous epidemiological studies have consistently suggested that long-term exposure to ambient air pollutants increases cardiovascular morbidity and mortality rates. Moreover, increasing scientific proofs also

concluded that long-term air pollution exposure was associated with hypertension and elevated BP values in adults.[26] However, few studies explored the association of childhood long-term exposure to air pollutants with BP values. Most published articles consistently demonstrated that long-term exposure to $PM_{2.5}$ and PM_{10} was significantly associated with elevated BP, which was consistent with our results.[6,8,22,23,30] Few parts of studies reached an inconsistent conclusion. For example, Ntarladima et al assessed the association between long-term exposure to $PM_{2.5}$ and PM_{10} and SBP/DBP among the 733 5-year-old children in the Netherlands, and found that no associations were observed.[21]

Numerous epidemiological studies supported that long-term exposure to NO_2 (a marker of traffic exhaust emissions) was significantly associated with elevated BP among children and adolescents.[6,8,22,23,30] However, there are some inconsistent conclusions. Clark et al enrolled 719 children in the UK and observed no association between long-term exposure to NO_2 and BP. The Prevention and Incidence of Asthma and Mite Allergy birth cohort study from the Netherlands also found there was no significant association with long-term exposure to NO_2 with BP in adolescents.[25] Ntarladima et al assessed 733 5-year-old children in the Netherlands and concluded that there was no association between long-term exposure to NO_X and BP.[21] Long-term exposure to ultrafine particles (<0.1 mm), associated with traffic emission, was associated with higher SBP in adults.[31] Among children, short-term exposure to ultrafine particles was associated with increased SBP.[11] Volatile organic compounds, another component of traffic-derived air pollution exposure, were associated with oxidative stress and increased BP in adults,[32] and contributed to the risk of preeclampsia.[33] These results indicated that volatile organic compounds may be associated with the variation in BP among children and adolescents. Furthermore, a relationship between long-term exposure to other air pollutants (SO_2 and O_3) and childhood BP has been reported. Dong et al enrolled 384 Chinese children and found long-term exposure to SO_2 and O_3 were significantly associated with increased BP.[23]

In our meta-analysis, the results of the heterogeneity analysis showed significant heterogeneity for the association between long-term exposure to PM_{10} and SBP/DBP. The heterogeneity among the enrolled studies may result from differences in the study settings, research design, exposure evaluation, constituents of air pollutants, and confounder adjustment. The meta-regression results indicated that the effects of air pollution exposure on BP varied with age, sex, and location. Subgroup analyses by type of study showed that the effects of long-term exposure to air pollutants were generally significant in cross-sectional studies.

In addition, our meta-analysis focuses on the association between postnatal long-term air pollution exposures and BP among children and adolescents. However, maternal or in-utero exposures to air pollutants could also affect the children's BP. Previous evidence supported that utero tobacco exposure is associated with elevated child BP.[34,35] A recent study indicated that prenatal exposure to NO_2 was associated with higher SBP in 11-year-old children.[36] A prospective study including 1131 infants born in the United States showed that higher mean $PM_{2.5}$ and black carbon exposures during the third trimester (90 days before birth) were associated with higher newborn SBP.[37]

In summary, many epidemiologic studies support an association of long-term exposure to $PM_{2.5}$, PM_{10}, and NO_2 with increased BP among children and adolescents, consistent with our meta-analysis results.

Mechanism of Blood Pressure and Air Pollution Association

The exact mechanisms by which exposure to ambient air pollutants contribute to the elevated BP values remain unclear. PM may increase BP by influencing the cardiovascular system.[38] The body exposure to environmental stressors could trigger autonomic reflexes via pulmonary receptors, or impair them in baroreceptors and chemoreceptors to promote arterial constriction. The outcome of these responses may lead to further arterial vasoconstriction.[39] PM could induce endothelial dysfunction and further impair hemodynamics.[40,41] PM exposure can also trigger systemic inflammation and oxidative stress, which can affect vascular function and hemodynamics and ultimately cause arterial remodeling.[42–44] Other air pollutants, such as NO_2 and O_3, may affect the cardiovascular system via autonomic imbalance favoring sympathetic modulation.[45,46] Another possible mechanism linking elevated BP and O_3 exposure is increased serotonin-induced vasoconstriction and decreased acetylcholine-induced vasodilation.[47] Experimental studies demonstrated acute exposure to SO_2 and SO_x may cause a decrease in blood pressure of the rat in both dose-dependent and time-dependent manners.[48] Moreover, animal experiments showed that co-exposure to SO_2, NO_2, and $PM_{2.5}$ may induce inflammatory response and endothelial dysfunction in the heart.[49] In addition, certain constituents of air pollutants (eg, metals, nano-sized particles) may be able to pass through the systemic circulation and directly affect the cardiovascular system.[50–52]

Strengths and Limitations

A significant strength of our meta-analysis was that, to our knowledge, we are the first to evaluate the association

between short-term and long-term exposure ambient air pollution and BP among children and adolescents using meta-analysis. And our study provided strong evidence supporting the positive association between short-term or long-term exposure to some ambient air pollutants and BP among children and adolescents. However, there are some limitations to our review. First, the number of included articles of our study is limited, which possibly limits how generalizable the results of the meta-analysis are. Furthermore, we could not conduct a meta-analysis to assess the effect of some air pollutants, such as O_3, NO_x, SO_2, and CO, because of too few studies. Second, the large variation in sample size (130–194 104) of included studies could prevent us from drawing a robust conclusion between ambient air pollutants and BP among children and adolescents. Several included studies that comprised small sample sizes could be difficult to evaluate the association with sufficient statistical power. Third, most enrolled studies used a single-pollutant model to estimate the association between each pollutant and BP despite the fact that there are possible interactions between different pollutants. Fourth, although all enrolled original studies calculated adjusted estimates, the covariates adjusted in these studies were not the same. In particular, traffic noise, as a significant risk factor for increased BP, which often coexists with many urban air pollutants,[53] was not adjusted in some included studies. Furthermore, considering the highly variable correlations between traffic noise and air pollution,[54] the effects of air pollution on BP may be confounded if not adjusting traffic noise.

CONCLUSIONS

This is the first meta-analysis to assess the quality and magnitude of the associations between air pollution and blood pressure values among children and adolescents. Our study indicates that both short-term and long-term exposure to some ambient air pollutants may increase BP values among children and adolescents. Lower exposure to air pollutants during childhood and adolescence might decrease the risk of hypertension and cardiovascular disease in adulthood. Furthermore, the existing evidence we reviewed cannot test for the association between some air pollutants (NO_X, SO_2, O_3, and CO) exposure and BP values because of limited studies. Therefore, further high-quality studies should focus on the multiple air pollutants and BP of children and adolescents.

ARTICLE INFORMATION

Received October 14, 2020; accepted January 4, 2021.

Affiliations

From the Center of Clinical Pharmacology, The Third Xiangya Hospital, Central South University, Changsha, China (M.H., J.C., Y.Y., H.Y., Z.H., Y.L.); National-Local Joint Engineering Laboratory of Drug Clinical Evaluation Technology, Changsha, China (H.Y., Z.H., Y.L.); and Department of Life Science and Medicine, King's College London, London, United Kingdom (Y.L.).

Sources of Funding

The study was supported by the National Natural Science Foundation of China (81800393, 81673520), Hunan Youth Talent Project (2019RS2014), the Natural Science Foundation of Hunan Province (2018JJ3783), and the Fundamental Research Funds for Central Universities of Central South University (No. 2019zzts1058). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the article.

Disclosures

None.

Supplementary Material

Tables S1–S14
Figures S1–S18

REFERENCES

1. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388:1659–1724. DOI: 10.1016/S0140-6736(16)31679-8.
2. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365:217–223. DOI: 10.1016/S0140-6736(05)17741-1.
3. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation*. 2008;117:3171–3180. DOI: 10.1161/CIRCULATIONAHA.107.730366.
4. Liang Y, Mi J. Pubertal hypertension is a strong predictor for the risk of adult hypertension. *Biomed Environ Sci*. 2011;24:459–466. DOI: 10.3967/0895-3988.2011.05.002.
5. Bennett WD, Zeman KL, Jarabek AM. Nasal contribution to breathing and fine particle deposition in children versus adults. *J Toxicol Environ Health A*. 2008;71:227–237. DOI: 10.1080/15287390701598200.
6. Bilenko N, Rossem LV, Brunekreef B, Beelen R, Eeftens M, Hoek G, Houthuijs D, de Jongste JC, Kempen EV, Koppelman GH, et al. Traffic-related air pollution and noise and children's blood pressure: results from the PIAMA birth cohort study. *Eur J Prev Cardiol*. 2015;22:4–12. DOI: 10.1177/2047487313505821.
7. Zeng X-W, Qian ZM, Vaughn MG, Nelson EJ, Dharmage SC, Bowatte G, Perret J, Chen D-H, Ma H, Lin S, et al. Positive association between short-term ambient air pollution exposure and children blood pressure in China—result from the Seven Northeast Cities (SNEC) study. *Environ Pollut*. 2017;224:698–705. DOI: 10.1016/j.envpol.2017.02.054.
8. Zhang Z, Dong B, Li S, Chen G, Yang Z, Dong Y, Wang Z, Ma J, Guo Y. Exposure to ambient particulate matter air pollution, blood pressure and hypertension in children and adolescents: a national cross-sectional study in China. *Environ Int*. 2019;128:103–108. DOI: 10.1016/j.envint.2019.04.036.
9. Yang HB, Teng CG, Hu J, Zhu XY, Wang Y, Wu JZ, Xiao Q, Yang W, Shen H, Liu F. Short-term effects of ambient particulate matter on blood pressure among children and adolescents: a cross-sectional study in a city of Yangtze River delta, China. *Chemosphere*. 2019;237:124510. DOI: 10.1016/j.chemosphere.2019.124510.
10. Liu C, Fuertes E, Tiesler CM, Birk M, Babisch W, Bauer CP, Koletzko S, von Berg A, Hoffmann B, Heinrich J. The associations between traffic-related air pollution and noise with blood pressure in children: results from the GINIplus and LISAplus studies. *Int J Hyg Environ Health*. 2014;217:499–505. DOI: 10.1016/j.ijheh.2013.09.008.
11. Pieters N, Koppen G, Van Poppel M, De Prins S, Cox B, Dons E, Nelen V, Panis LI, Plusquin M, Schoeters G, et al. Blood pressure and same-day exposure to air pollution at school: associations with nano-sized to coarse PM in children. *Environ Health Perspect*. 2015;123:737–742. DOI: 10.1289/ehp.1408121.
12. Bloemsma LD, Gehring U, Klompmaker JO, Hoek G, Janssen NAH, Lebret E, Brunekreef B, Wijga AH. Green space, air pollution, traffic noise and cardiometabolic health in adolescents: the PIAMA birth cohort. *Environ Int*. 2019;131:104991. DOI: 10.1016/j.envint.2019.104991.

13. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine*. 2009;6:e1000097. DOI: 10.1371/journal.pmed.1000097.
14. Stang A. Critical evaluation of the newcastle-ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603–605.DOI: 10.1007/s10654-010-9491-z.
15. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int J Evid Based Healthc*. 2015;13:147–153. DOI: 10.1097/XEB.0000000000000054.
16. Atkinson RW, Cohen A, Mehta S, Anderson HR. Systematic review and meta-analysis of epidemiological time-series studies on outdoor air pollution and health in Asia. *Air Qual Atmos Health*. 2012;5:383–391. DOI: 10.1007/s11869-010-0123-2.
17. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629–634.
18. Zhang J, Cai LI, Gui Z, Wang S, Zeng X, Lai L, Lv Y, Tan K, Wang H, Huang C, et al. Air pollution-associated blood pressure may be modified by diet among children in Guangzhou, China. *J Hypertens*. 2020;38:2215–2222. DOI: 10.1097/HJH.0000000000002521.
19. Wu QZ, Li S, Yang BY, Bloom M, Shi Z, Knibbs L, Dharmage S, Leskinen A, Jalaludin B, Jalava P, et al. Ambient airborne particulates of diameter ≤1 μm, a leading contributor to the association between ambient airborne particulates of diameter ≤2.5 μm and children's blood pressure. *Hypertension*. 2020;75:347–355. DOI: 10.1161/HYPERTENSIONAHA.119.13504.
20. Warembourg C, Maitre L, Tamayo-Uria I, Fossati S, Roumeliotaki T, Aasvang GM, Andrusaityte S, Casas M, Cequier E, Chatzi L, et al. Early-life environmental exposures and blood pressure in children. *J Am Coll Cardiol*. 2019;74:1317–1328. DOI: 10.1016/j.jacc.2019.06.069.
21. Ntarladima AM, Vaartjes I, Grobbee DE, Dijst M, Schmitz O, Uiterwaal C, Dalmeijer G, van der Ent C, Hoek G, Karssenberg D. Relations between air pollution and vascular development in 5-year old children: a cross-sectional study in the Netherlands. *Environ Health*. 2019;18:50. DOI: 10.1186/s12940-019-0487-1.
22. Li Q, Guo Y, Song J-Y, Song Y, Ma J, Wang H-J. Impact of long-term exposure to local PM10 on children's blood pressure: a Chinese national cross-sectional study. *Air Qual Atmos Health*. 2018;11:705–713. DOI: 10.1007/s11869-018-0577-1.
23. Dong GH, Qian ZM, Trevathan E, Zeng XW, Vaughn MG, Wang J, Zhao Y, Liu YQ, Ren WH, Qin XD. Air pollution associated hypertension and increased blood pressure may be reduced by breastfeeding in chinese children: the Seven Northeastern Cities Chinese Children's Study. *Int J Cardiol*. 2014;176:956–961. DOI: 10.1016/j.ijcard.2014.08.099.
24. Baumgartner J, Zhang Y, Schauer JJ, Ezzati M, Patz JA, Bautista LE. Household air pollution and children's blood pressure. *Epidemiology*. 2012;23:641–642.
25. Clark C, Crombie R, Head J, van Kamp I, van Kempen E, Stansfeld SA. Does traffic-related air pollution explain associations of aircraft and road traffic noise exposure on children's health and cognition? A secondary analysis of the United Kingdom sample from the RANCH project. *Am J Epidemiol*. 2012;176:327–337. DOI: 10.1093/aje/kws012.
26. Yang BY, Qian Z, Howard SW, Vaughn MG, Fan SJ, Liu KK, Dong GH. Global association between ambient air pollution and blood pressure: a systematic review and meta-analysis. *Environ Pollut*. 2018;235:576–588. DOI: 10.1016/j.envpol.2018.01.001.
27. Lauer RM, Burns TL, Clarke WR, Mahoney LT. Childhood predictors of future blood pressure. *Hypertension*. 1991;18:I74–I81. DOI: 10.1161/01.HYP.18.3_Suppl.I74.
28. Sughis M, Nawrot TS, Ihsan-ul-Haque S, Amjad A, Nemery B. Blood pressure and particulate air pollution in schoolchildren of lahore, Pakistan. *BMC Public Health*. 2012;12:378. DOI: 10.1186/1471-2458-12-378.
29. Bilenko N, Brunekreef B, Beelen R, Eeftens M, de Hoogh K, Hoek G, Koppelman GH, Wang M, van Rossem L, Gehring U. Associations between particulate matter composition and childhood blood pressure—the PIAMA study. *Environ Int*. 2015;84:1–6. DOI: 10.1016/j.envint.2015.07.010.
30. Wang X, Zou Z, Dong B, Dong Y, Ma Y, Gao D, Yang Z, Wu S, Ma J. Association of school residential PM(2.5) with childhood high blood pressure: results from an observational study in 6 cities in China. *Int J Environ Res Public Health*. 2019;16:2515. DOI: 10.3390/ijerph16142515.
31. Corlin L, Woodin M, Hart JE, Simon MC, Gute DM, Stowell J, Tucker KL, Durant JL, Brugge D. Longitudinal associations of long-term exposure to ultrafine particles with blood pressure and systemic inflammation in Puerto Rican adults. *Environ Health*. 2018;17:33. DOI: 10.1186/s12940-018-0379-9.
32. Chuang HC, Ho KF, Lin LY, Chang TY, Hong GB, Ma CM, Liu IJ, Chuang KJ. Long-term indoor air conditioner filtration and cardiovascular health: a randomized crossover intervention study. *Environ Int*. 2017;106:91–96. DOI: 10.1016/j.envint.2017.06.008.
33. Nobles CJ, Williams A, Ouidir M, Sherman S, Mendola P. Differential effect of ambient air pollution exposure on risk of gestational hypertension and preeclampsia. *Hypertension*. 2019;74:384–390. DOI: 10.1161/HYPERTENSIONAHA.119.12731.
34. Oken E, Huh SY, Taveras EM, Rich-Edwards JW, Gillman MW. Associations of maternal prenatal smoking with child adiposity and blood pressure. *Obes Res*. 2005;13:2021–2028. DOI: 10.1038/oby.2005.248.
35. Hogberg L, Cnattingius S, Lundholm C, D'Onofrio BM, Langstrom N, Iliadou AN. Effects of maternal smoking during pregnancy on offspring blood pressure in late adolescence. *J Hypertens*. 2012;30:693–699. DOI: 10.1097/HJH.0b013e32835168f4.
36. Breton CV, Yao J, Millstein J, Gao LU, Siegmund KD, Mack W, Whitfield-Maxwell L, Lurmann F, Hodis H, Avol ED, et al. Prenatal air pollution exposures, DNA methyl transferase genotypes, and associations with newborn LINE1 and Alu methylation and childhood blood pressure and carotid intima-media thickness in the Children's Health Study. *Environ Health Perspect*. 2016;124:1905–1912. DOI: 10.1289/EHP181.
37. van Rossem L, Rifas-Shiman SL, Melly SJ, Kloog I, Luttmann-Gibson H, Zanobetti A, Coull BA, Schwartz JD, Mittleman MA, Oken E, et al. Prenatal air pollution exposure and newborn blood pressure. *Environ Health Perspect*. 2015;123:353–359. DOI: 10.1289/ehp.1307419.
38. Brook RD, Rajagopalan S, Pope CA III, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, et al. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation*. 2010;121:2331–2378. DOI: 10.1161/CIR.0b013e3181dbece1.
39. Perez CM, Hazari MS, Farraj AK. Role of autonomic reflex arcs in cardiovascular responses to air pollution exposure. *Cardiovasc Toxicol*. 2015;15:69–78.DOI: 10.1007/s12012-014-9272-0.
40. Kelly FJ, Fussell JC. Role of oxidative stress in cardiovascular disease outcomes following exposure to ambient air pollution. *Free Radic Biol Med*. 2017;110:345–367. DOI: 10.1016/j.freeradbiomed.2017.06.019.
41. Rao X, Zhong J, Brook RD, Rajagopalan S. Effect of particulate matter air pollution on cardiovascular oxidative stress pathways. *Antioxid Redox Signal*. 2018;28:797–818. DOI: 10.1089/ars.2017.7394.
42. Boos CJ, Lip GY. Is hypertension an inflammatory process? *Curr Pharm Des*. 2006;12:1623–1635. DOI: 10.2174/138161206776843313.
43. Brook RD, Urch B, Dvonch JT, Bard RL, Speck M, Keeler G, Morishita M, Marsik FJ, Kamal AS, Kaciroti N, et al. Insights into the mechanisms and mediators of the effects of air pollution exposure on blood pressure and vascular function in healthy humans. *Hypertension*. 2009;54:659–667. DOI: 10.1161/HYPERTENSIONAHA.109.130237.
44. Miller MR. The role of oxidative stress in the cardiovascular actions of particulate air pollution. *Biochem Soc Trans*. 2014;42:1006–1011. DOI: 10.1042/BST20140090.
45. Weichenthal S, Kulka R, Dubeau A, Martin C, Wang D, Dales R. Traffic-related air pollution and acute changes in heart rate variability and respiratory function in urban cyclists. *Environ Health Perspect*. 2011;119:1373–1378. DOI: 10.1289/ehp.1003321.
46. Gold DR, Litonjua A, Schwartz J, Lovett E, Larson A, Nearing B, Allen G, Verrier M, Cherry R, Verrier R. Ambient pollution and heart rate variability. *Circulation*. 2000;101:1267–1273. DOI: 10.1161/01.CIR.101.11.1267.
47. Paffett ML, Zychowski KE, Sheppard L, Robertson S, Weaver JM, Lucas SN, Campen MJ. Ozone inhalation impairs coronary artery dilation via intracellular oxidative stress: evidence for serum-borne factors as drivers of systemic toxicity. *Toxicol Sci*. 2015;146:244–253. DOI: 10.1093/toxsci/kfv093.
48. Meng Z, Geng H, Bai J, Yan G. Blood pressure of rats lowered by sulfur dioxide and its derivatives. *Inhal Toxicol*. 2003;15:951–959.DOI: 10.1080/08958370390215785.
49. Zhang Y, Ji X, Ku T, Sang N. Inflammatory response and endothelial dysfunction in the hearts of mice co-exposed to SO(2), NO(2), and PM(2.5). *Environ Toxicol*. 2016;31:1996–2005. DOI: 10.1002/tox.22200.
50. Furuyama A, Kanno S, Kobayashi T, Hirano S. Extrapulmonary translocation of intratracheally instilled fine and ultrafine particles via direct and

alveolar macrophage-associated routes. *Arch Toxicol*. 2009;83:429–437. DOI: 10.1007/s00204-008-0371-1.
51. Geiser M, Kreyling WG. Deposition and biokinetics of inhaled nanoparticles. *Part Fibre Toxicol*. 2010;7:2. DOI: 10.1186/1743-8977-7-2.
52. Cascio WE, Gilmour MI, Peden DB. Ambient air pollution and increases in blood pressure: role for biological constituents of particulate matter. *Hypertension*. 2015;66:469–471. DOI: 10.1161/HYPERTENSIONAHA.115.05563.
53. Fuks KB, Weinmayr G, Basagaña X, Gruzieva O, Hampel R, Oftedal B, Sørensen M, Wolf K, Aamodt G, Aasvang GM, et al. Long-term exposure to ambient air pollution and traffic noise and incident hypertension in seven cohorts of the european study of cohorts for air pollution effects (ESCAPE). *Eur Heart J*. 2017;38:983–990. DOI: 10.1093/eurheartj/ehw413.
54. Fecht D, Hansell AL, Morley D, Dajnak D, Vienneau D, Beevers S, Toledano MB, Kelly FJ, Anderson HR, Gulliver J. Spatial and temporal associations of road traffic noise and air pollution in London: implications for epidemiological studies. *Environ Int*. 2016;88:235–242. DOI: 10.1016/j.envint.2015.12.001.

SUPPLEMENTAL MATERIAL

Table S1. PRISMA 2009 Checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n/a
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10-11
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-11
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10-11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	18

Table S2. Literature search strategy.

Database	Search strategies	Results
PubMed	(("air pollution"[Mesh Terms] OR "air pollution"[All Fields]) OR ("particulate matter"[Mesh Terms] OR "particulate matter"[All Fields]) OR "particles"[All Fields] OR ("air pollutants"[Mesh Terms] OR "air pollutants"[All Fields]) OR "fine particulate" [All Fields] OR ("sulfur dioxide"[Mesh Terms] OR "sulfur dioxide"[All Fields]) OR ("sulfur oxide" [Mesh Terms] OR " sulfur oxide"[All Fields]) OR ("nitrogen dioxide"[Mesh Terms] OR "nitrogen dioxide"[All Fields]) OR("nitrogen oxide"[Mesh Terms] OR "nitrogen oxide"[All Fields]) OR ("ozone"[Mesh Terms] OR "ozone"[All Fields]) OR ("carbon monoxide"[Mesh Terms] OR "carbon monoxide"[All Fields]) OR ("black carbon" [Mesh Terms] OR "black carbon"[All Fields]) OR "$PM_{2.5}$"[All Fields] OR "PM_{10}"[All Fields] OR "SO_2"[All Fields] OR "SO_X"[All Fields] OR "NO_2"[All Fields] OR "NO_X"[All Fields] OR "O_3"[All Fields] OR "CO"[All Fields] OR "BC"[All Fields]) AND (("hypertension"[Mesh Terms] OR "hypertension"[All Fields]) OR "high blood pressure"[All Fields] OR hypertensive[All Fields] OR ("blood pressure"[Mesh Terms] OR "blood pressure"[All Fields]) OR "systolic blood pressure"[All Fields] OR "diastolic blood pressure"[All Fields]) OR ("hypotension" [Mesh Terms] OR "hypotension"[All Fields]) OR "hypotensive"[All Fields] OR ("arterial pressure" [Mesh Terms] OR "arterial pressure"[All Fields]) OR ("arterial tension" [Mesh Terms] OR "arterial tension"[All Fields]) OR ("elevated blood pressure" [Mesh Terms] OR "elevated blood pressure"[All Fields])) AND (("child"[Mesh Terms] OR "child"[All Fields]) OR ("children"[Mesh Terms] OR "children"[All Fields]) OR "childhood"[All Fields] OR ("adolescent"[Mesh Terms] OR "adolescent"[All Fields]) OR ("teenager" [Mesh Terms] OR "teenager"[All Fields]) OR "kids"[All Fields])	19689 records
Embase	('air pollution'/exp OR 'air pollution' OR 'particulate matter'/exp OR 'particulate matter' OR 'particles' OR 'air pollutants'/exp OR 'air pollutants' OR 'fine particulate' OR 'sulfur dioxide'/exp OR 'sulfur dioxide' OR 'sulfur oxide'/exp OR 'sulfur oxide' OR 'nitrogen dioxide'/exp OR 'nitrogen dioxide' OR 'nitrogen oxide'/exp OR 'nitrogen oxide' OR 'ozone'/exp OR ozone OR 'carbon monoxide'/exp OR 'carbon monoxide' OR 'black carbon'/exp OR 'black carbon' OR '$PM_{2.5}$' OR 'PM_{10}' OR 'SO_2' OR 'SO_X' OR 'NO_2' OR 'NO_X' OR 'O_3' OR 'CO' OR 'BC') AND ('hypertension'/exp OR hypertension OR 'high blood pressure'/exp OR 'high blood pressure' OR hypertensive OR 'blood pressure'/exp OR 'blood pressure' OR 'systolic blood pressure'/exp OR 'systolic blood pressure' OR 'diastolic blood pressure'/exp OR 'diastolic blood pressure' OR 'hypotension'/exp OR 'hypotension' OR	14878 records

	'hypotensive' OR 'arterial pressure'/exp OR 'arterial pressure' OR 'arterial tension' OR 'arterial tension' OR 'elevated blood pressure' OR 'elevated blood pressure') AND ('child'/exp OR 'child' OR 'children'/exp OR 'children' OR 'childhood' OR 'adolescents'/exp OR 'adolescents' OR 'teenager'/exp OR 'teenager' OR 'kids')	
Web of Science	TS=(“air pollution” OR "particulate matter" OR "particles" OR "air pollutants" OR "fine particulate" OR "sulfur dioxide" OR "sulfur oxide" OR "nitrogen dioxide" OR "nitrogen oxide" OR "ozone" OR "carbon monoxide" OR "black carbon" OR "$PM_{2.5}$" OR "PM_{10}" OR "SO_2" OR "SO_X" OR "NO_2" OR "NO_X" OR "O_3" OR "CO" OR "BC") AND TS=("hypertension" OR "high blood pressure" OR "hypertensive" OR "blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR "hypotension" OR "hypotensive" OR "arterial pressure" OR "arterial tension" OR "elevated blood pressure") AND TS=(“child” OR “children” OR “childhood” OR “adolescents” OR “teenager” OR “kids”)	2083 records

Table S3. Contextual details of included studies: exposure and blood pressure measurements and confounding factors.

Author (Publication year)	Subjects	Pollutants	NO_2	$PM_{2.5}$	PM_{10}	Exposure assessment method	Confounding factors
Zhang et al.(2020)[18]	Children from five schools in five districts of Guangzhou	$PM_{2.5}$ PM_{10}	-	39.00	61.10	Monitoring stations and inverse distance weighting interpolation method	age, sex, weight status, humidity, breast, outdoor physical activity time, parental education, parental smoking status and family history of hypertension
Wu et al.(2020)[19]	Children from the Chinese Seven Northeast Cities (SNEC) Study	$PM_{2.5}$	-	54.16	-	Monitoring station	age, sex, parental education, income, passive tobacco smoke exposure,

							home coal use, exercise time, and BMI.
Warembourg et al.(2019)[20]	Child from the HELIX (Human Early-Life Exposome) project	NO_2 $PM_{2.5}$ PM_{10}	22.10	13.50	25.60	Land use regression or dispersion models	age, sex, height, maternal age, maternal education level, maternal pre-pregnancy body mass index, parity, parental country of birth and cohort
Ntarladima et al.(2019)[21]	Children from the Wheezing Illnesses Study Leidsche Rijn (WHISTLER)	NO_2 $PM_{2.5}$ PM_{10}	29.40	16.70	25.00	Land use regression model	sex, age, parental socio-economic status characteristics, exposed to smoke during pregnancy, child exposed to smoke later in life
Yang et al.(2019)[9]	Children from the 2016 Health Promotion Program for Children and Adolescents (HPPCA)	$PM_{2.5}$ PM_{10}	-	45.70	76.20	Monitoring station	gender, age, body mass index, outdoor temperature, O3

Zhang et al.(2019)[8]	Children and adolescents from seven provinces/municipalities (Chongqing, Hunan, Guangdong, Liaoning, Ningxia, Shanghai and Tianjin) in China	$PM_{2.5}$ PM_{10}	-	60.10	99.40	Machine learning method with Radom Forests model	age, sex, height, body mass index, exercise, dietary, parental education, parental smoking, parental hypertension, region (south vs north), rurality (urban vs rural),annual average temperature and GDP per capita
Li et al(2018)[22]	Primary or middle school students from the 2010 Chinese National Survey on Students' Constitution and Health(CNSSCH)	PM_{10}	-	-	97.00	Monitoring station	effect of school, age, gender, height, weight of each child, GDP per capital, relative humidity in 2010 of each city, the spline term of temperature, NO2, SO2, children's physical activity level

Zeng et al(2017)[7]	Children from the Chinese Seven Northeast Cities (SNEC) Study	PM_{10}	-	-	108.80	Monitoring station	temperature, age, sex, BMI, breast feeding, birth weight, exercise time, personal area, passive smoking exposure, parental education, family income, family history of hypertension, and district.
Piters et al.(2015)[11]	Primary schools students from Health Effects of Air Pollution in Antwerp Schools(HEAPS) study	$PM_{2.5}$ PM_{10}		35.00	24.00	Air pollution monitoring devices	sex, age, height and weight of the child, parental education, neighborhood SES, fish consumption, heart rate, school, day of the week, season, wind, speed, relative humidity, temperature

Bilenko et al.(2015)[6]	Children from the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study	NO_2 $PM_{2.5}$ PM_{10}	13.3（short-term） 7.8(long-term)	1.1(long-term)	11.1(short-term) 1(long-term)	Land use regression model	sex, age, height, and BMI, cuff size, gestational age at birth, birthweight, weight gain during the first year of life, breast feeding, maternal smoking during pregnancy, parental smoking in child's home, physical activity, puberty development scale, maternal education, maternal hypertension during pregnancy, pneumonia and/or otitis media during the first 2 years of life, ambient temperature, and

							room temperature
Dong et al.(2014)[23]	Children from the Seven Northeastern Cities Chinese Children's Study (SNECCS)	NO_2 PM_{10}	36.44	-	88.90	Monitoring station	age, sex, BMI, parental education, low birth weight, premature birth, breast, income, passive smoking exposure, home coal use, exercise time, area residence per person, family history of hypertension, and district

Liu et al.(2014)[10]	Children from the German Infant Nutritional Intervention plus environmental and genetic influences on allergy development study (GINIplus)	NO_2 $PM_{2.5}$ PM_{10}	23.31	14.88	22.12	Land use regression model	cohort study, area, gender, age of child, BMI, physical activity, maternal smoking during pregnancy, parental education level, parental history of hypertension,7-day level of air pollutants, 7-day temperature
Baumgartner et al.(2012)[24]	Children from villages in Yunnan, China	$PM_{2.5}$	-	53.00	-	Portable, battery-operated pump	sex, age, height, body mass index, passive smoking, socioeconomic status, salt intake, monosodium glutamate use, physical activity

Clark et al.(2012)[25]	Children from the Road Traffic and Aircraft Noise Exposure and Children's Cognition and Health (RANCH) project	NO_2	42.73	-	-	Combined emission-dispersion and regression model	age, gender, employment status, crowding, home ownership, mother's educational level, long-standing illness, main language spoken at home, parental support for schoolwork, body mass index, cuff-size, room temperature, birth weight, parental high blood pressure, and prematurity.

Abbreviations: O_3, ozone; GDP, Gross Domestic Product; SES, socio-economic status; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; BMI, body mass index. The levels of pollutants are present with mean/interquartile range: Piters et al.(2015) and Bilenko et al.(2015) are present with interquartile range and the rest are present with mean.

Table S4. Results of the sensitivity analysis for short-term exposure to PM_{10} and change in DBP.

Excluded article	Estimated effect	95% CI	P	I^2	P of publication bias
Yang et al.(2019)[9]	0.051	-0.506, 0.608	0.858	84.23%	0.001
Zeng et al(2017)[7]	0.041	-0.407, 0.49	0.857	76.15%	0.007
Pieters et al.(2015)[11]	0.327	0.16, 0.493	<0.001	93.35%	0.120
Bilenko et al.(2015)[6]	0.358	0.229, 0.487	<0.001	87.59%	0.039

Table S5. Results of the sensitivity analysis for long-term exposure to $PM_{2.5}$ and change in SBP.

Excluded article	Estimated effect	95%CI	P	I^2	P of publication bias
Zhang et al.(2020)[18]	1.978	1.114,2.841	<0.001	0.00%	0.850
Wu et al.(2020)[19]	1.268	0.097,2.439	0.03	0.00%	0.702
Warembourg et al.(2019)[20]	1.826	0.951,2.701	<0.001	10.49%	0.355
Ntarladima et al.(2019)[21]	1.778	0.924,2.631	<0.001	5.90%	0.177
Zhang et al.(2019)[8]	2.003	0.946,3.059	<0.001	4.72%	0.269
Bilenko et al.(2015)[6]	1.84	0.988,2.692	<0.001	4.04%	0.4787
Liu et al.(2014)[10]	1.786	0.925,2.647	<0.001	9.57%	0.2525

Table S6. Results of the sensitivity analysis for long-term exposure to $PM_{2.5}$ and change in DBP.

Excluded article	Estimated effect	95%CI	P	I^2	P of publication bias
Zhang et al.(2020)[18]	0.952	0.156,1.748	0.0191	1.89%	0.1128
Wu et al.(2020)[19]	1.041	0.069,2.012	0.0357	0.20%	0.1714
Warembourg et al.(2019)[20]	0.835	0.037,1.633	0.0404	0.00%	0.2433
Ntarladima et al.(2019)[21]	0.867	0.087,1.646	0.0293	0.00%	0.4043
Zhang et al.(2019)[8]	1.048	0.017,2.080	0.0464	0.62%	0.1588
Bilenko et al.(2015)[6]	0.86	0.079,1.641	0.0310	0.00%	0.3735
Liu et al.(2014)[10]	1.002	0.209,1.795	0.0133	0.00%	0.0668

Table S7. Results of the sensitivity analysis for long-term exposure to PM_{10} and change in SBP.

Excluded article	Estimated effect	95%CI	P	I^2	P of publication bias

Zhang et al.(2020)[18]	0.529	0.074,0.983	0.0226	93.11%	0.3685
Warembourg et al.(2019)[20]	0.548	0.066,1.030	0.0257	93.68%	0.3556
Ntarladima et al.(2019)[21]	0.516	0.085,0.948	0.0189	92.57%	0.5363
Zhang et al.(2019)[8]	0.409	-0.007,0.826	0.0540	90.68%	0.5709
Li et al(2018)[22]	0.692	0.573,0.811	0.0000	0.00%	0.6841
Bilenko et al.(2015)[6]	0.529	0.094,0.964	0.0173	92.72%	0.2996
Dong et al.(2014)[23]	0.079	0.062,0.096	0.0000	20.54%	0.0429
Liu et al.(2014)[10]	0.538	0.064,1.012	0.0262	93.52%	0.3705

Table S8. Results of the sensitivity analysis for long-term exposure to PM_{10} and change in DBP.

Excluded article	Estimated effect	95%CI	P	I^2	P of publication bias
Zhang et al.(2020)[18]	0.387	0.009,0.766	0.045	92.50%	0.4827
Warembourg et al.(2019)[20]	0.359	-0.027,0.744	0.068	92.60%	0.6129
Ntarladima et al.(2019)[21]	0.37	0.013,0.727	0.042	91.88%	0.8301
Zhang et al.(2019)[8]	0.332	-0.068,0.731	0.104	92.67%	0.6291
Li et al(2018)[22]	0.626	0.524,0.727	0.000	0.00%	0.8247
Bilenko et al.(2015)[6]	0.366	0.008,0.725	0.045	91.91%	0.7731
Dong et al.(2014)[23]	0.081	0.067,0.095	0.000	0.00%	0.1672
Liu et al.(2014)[10]	0.435	0.068,0.802	0.020	91.91%	0.2444

Table S9. Results of the sensitivity analysis for long-term exposure to NO_2 and change in SBP.

Excluded article	Estimated effect	95%CI	P	I^2	P of publication bias
Warembourg et al.(2019)[20]	0.436	-0.156, 1.028	0.1488	53.14%	0.897
Ntarladima et al.(2019)[21]	0.487	-0.001,0.976	0.0506	51.81%	0.262
Bilenko et al.(2015)[6]	0.824	0.603,1.045	<0.001	0.00%	0.682
Dong et al.(2014)[23]	0.228	-0.251,0.707	0.3508	0.00%	0.311
Liu et al.(2014)[10]	0.791	0.571,1.012	<0.001	42.48%	0.866
Clark et al.(2012)[25]	0.481	-0.057,1.019	0.0796	53.82%	0.160

Table S10. Results of the sensitivity analysis for long-term exposure to NO_2 and change in DBP.

Excluded article	Estimated effect	95%CI	P	I2	P of publication bias
Warembourg et al.(2019)[20]	0.408	-0.133,94.90%	0.139	59.72%	0.7251

Ntarladima et al.(2019)[21]	0.371	-0.095,83.80%	0.119	60.65%	0.0154
Bilenko et al.(2015)[6]	0.439	-0.095,97.30%	0.108	57.09%	0.7392
Dong et al.(2014)[23]	0.090	-0.320,50.10%	0.667	0.00%	0.2082
Liu et al.(2014)[10]	0.800	0.613,98.70%	0.000	39.85%	0.189
Clark et al.(2012)[25]	0.384	-0.137,90.40%	0.148	61.59%	0.7535

Table S11 Subgroup analysis for the association between long-term exposure and SBP

Air pollutant	design	No. of estimates	Sample size	I^2	P_{egger}	P	Estimated effect (95%CI)
NO_2							
	cross-sectional	3	10363	0.00%	0.874	<0.001	0.880 (0.644,1.115)
	cohort	3	5045	8.56%	0.141	0.5023	0.173 (-0.333,0.680)
$PM_{2.5}$							
	cross-sectional	4	61057	41.29%	0.322	<0.001	1.837 (0.940,2.734)
	cohort	3	5045	0.00%	0.692	0.2284	1.575 (0.988,4.134)
PM_{10}							
	cross-sectional	5	132820	96.55%	0.2179	0.0439	0.575(0.016,1.135)
	cohort	3	5045	0	0.9543	0.3376	0.466(-0.487,1.419)

Table S12 Subgroup analysis for the association between long-term exposure and DBP

Air pollutant	design	No. of estimates	Sample size	I^2	P_{egger}	P	Estimated effect (95%CI)
NO_2							
	cross-sectional	3	10363	0.00%	0.795	<0.001	0.876 (0.660,1.093)
	cohort	3	5045	0.00%	0.973	0.7873	0.066(-0.412,0.543)
$PM_{2.5}$							
	cross-sectional	4	61057	0.00%	0.304	0.0509	0.825 (-0.003,1.653)
	cohort	3	5045	26.01%	0.392	0.1343	1.657 (-0.512,3.825)
PM_{10}							
	cross-sectional	5	132820	94.88	0.398	0.0442	0.408(0.011,0.806)
	cohort	3	5045	23.94	0.5719	0.6735	0.198(-0.722,1.117)

Table S13. The results of univariate meta-regression in the long-term exposure group.

	Age		Male proportion		Study location	
	β(95%CI)	P	β(95%CI)	P	β(95%CI)	P
SBP						
NO_2	-0.176(-0.514,0.162)	0.308	0.066(-0.148, 0.281)	0.545	-0.657(-1.192,-0.122)	0.016

$PM_{2.5}$	0.043(-0.716,0.802)	0.912	-0.302(-1.034,0.431)	0.420	0.045(-2.506,2.595)	0.973
PM_{10}	-0.361(-0.433,-0.288)	<0.001	0.512(0.403,0.621)	<0.001	0.423(-0.520,1.366)	0.379
DBP						
NO_2	0.085(-0.151,0.321)	0.479	0.018(-0.133,0.170)	0.814	-0.794(-1.251,-0.338)	0.001
$PM_{2.5}$	-0.343(-1.039,0.352)	0.333	0.123(-0.509,0.754)	0.704	1.282(-0.938,3.502)	0.258
PM_{10}	-0.322(-0.384,-0.260)	<0.001	0.461(0.368,0.555)	<0.001	0.165(-0.745,1.076)	0.722

Table S14. The results of multivariate meta-regression in the long-term exposure group.

	Age		Male proportion		Study location	
	β(95%CI)	P	β(95%CI)	P	β(95%CI)	P
SBP						
NO_2	-0.266(-0.625,0.093)	0.308	-0.051(-0.293,0.192)	0.683	-0.800(-1.377,-0.223)	0.007
$PM_{2.5}$	-0.481(-1.908,0.946)	0.912	-0.695(-1.874,0.484)	0.248	0.197(-3.289,3.683)	0.912
PM_{10}	-0.693(-1.093,-0.293)	<0.001	-0.493(-1.109,0.122)	0.116	-0.562(-1.611,0.487)	0.293
DBP						
NO_2	-0.088(-0.406,0.231)	0.479	-0.044(-0.240,0.152)	0.663	-0.860(-1.372,-0.348)	0.001
$PM_{2.5}$	-0.493(-1.855,0.869)	0.333	-0.343(-1.442,0.755)	0.540	0.856(-1.920,3.633)	0.546
PM_{10}	-0.536(-0.887,-0.185)	<0.001	-0.309(-0.849,0.231)	0.262	-0.785(-1.796,0.226)	0.128

Figure S1. Forest plot for the association between short-term exposure to PM_{10} (per 10 μg/m^3 increment) and SBP (mmHg). The blue boxes represent estimated effects of included studies. The blue horizontal bars represent 95% CIs of the estimated effects. The green box represents the pooled mean estimated effect. CI indicates confidence interval.

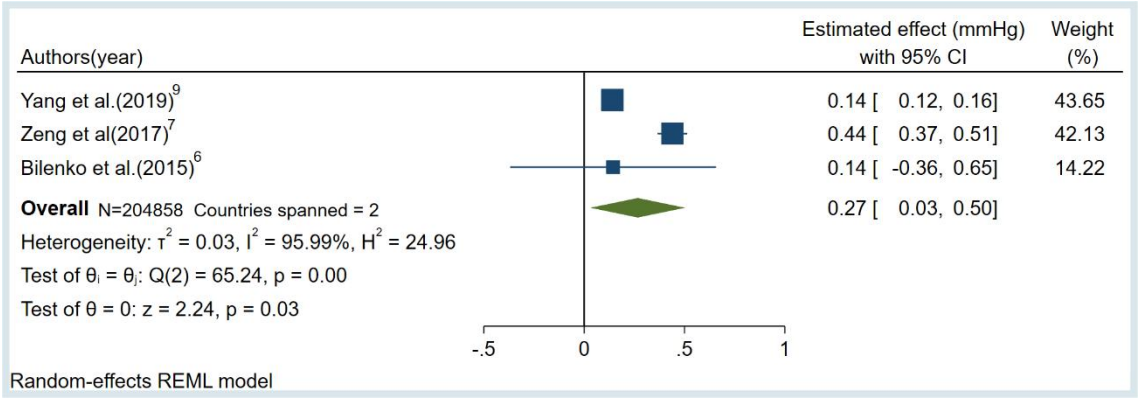

Figure S2. Forest plot for the association between short-term exposure to $PM_{2.5}$ (per 10 μg/m^3 increment) and DBP (mmHg).

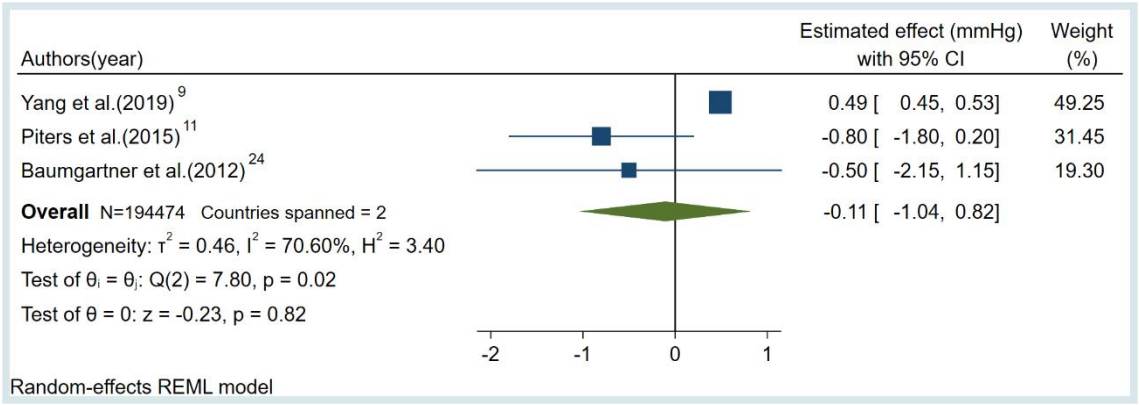

Figure S3. Forest plot for the association between short-term exposure to PM_{10} (per 10 μg/m^3 increment) and DBP(mmHg).

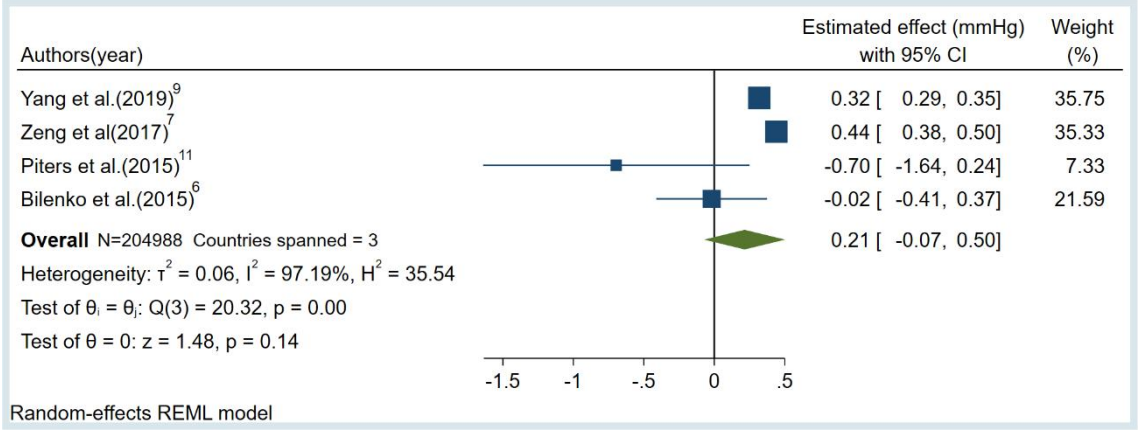

Figure S4. Funnel plot analysis in the meta-analysis of the association between short-term exposure to PM_{10} and SBP. The x-coordinate is the estimated effect and the y-coordinate is the standard error of estimated effect. The two diagonal lines are the edges of the funnel plot. The black dots represent studies that were included in the meta-analysis. The study with small simple size is at the bottom of funnel plot, while the study with large sample is at the top of funnel plot.

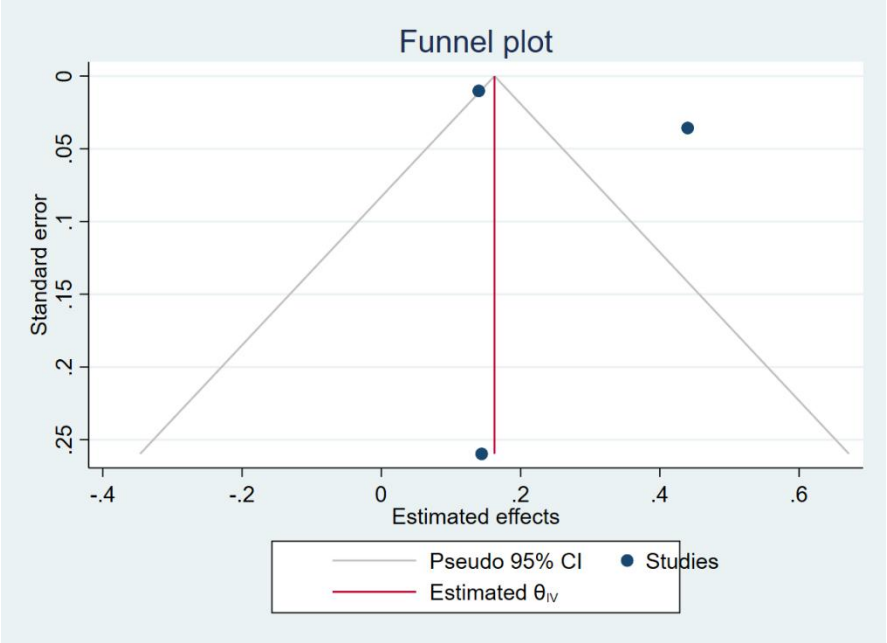

Figure S5. Funnel plot analysis in the meta-analysis of the association between short-term exposure to $PM_{2.5}$ and DBP.

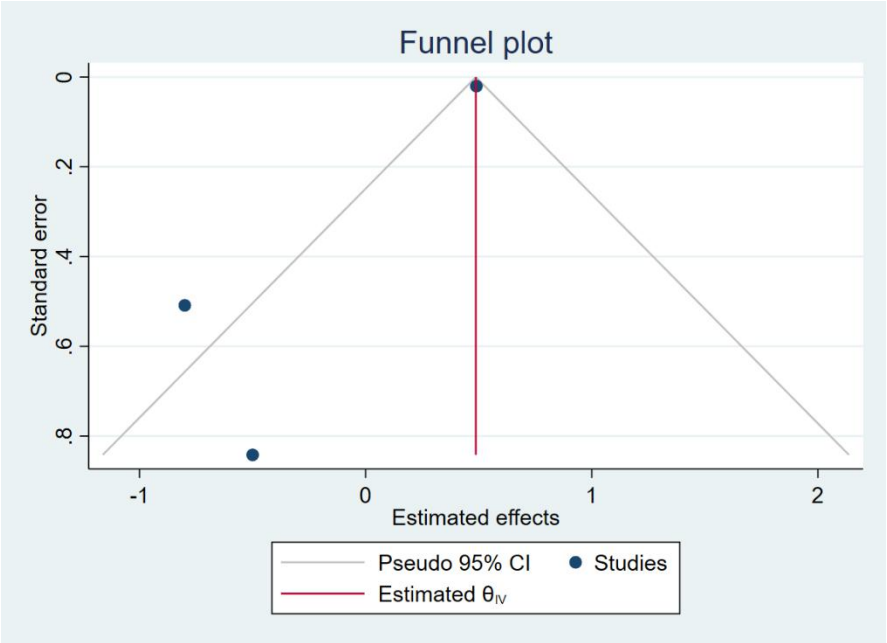

Figure S6. Funnel plot analysis in the meta-analysis of the association between short-term exposure to PM_{10} and DBP.

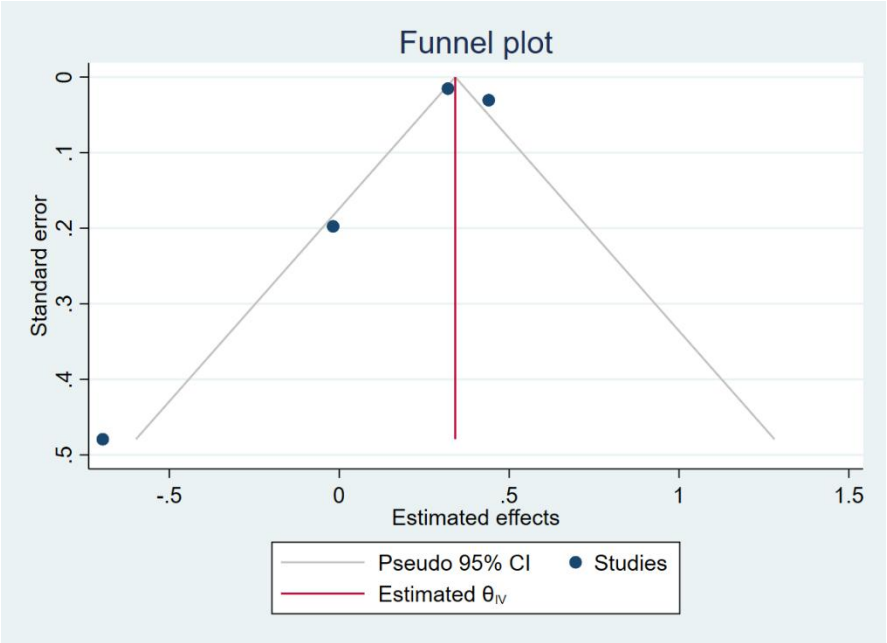

Figure S7. Forest plot for the association between long-term exposure to $PM_{2.5}$ (per 10 μg/m^3 increment) and SBP (mmHg).

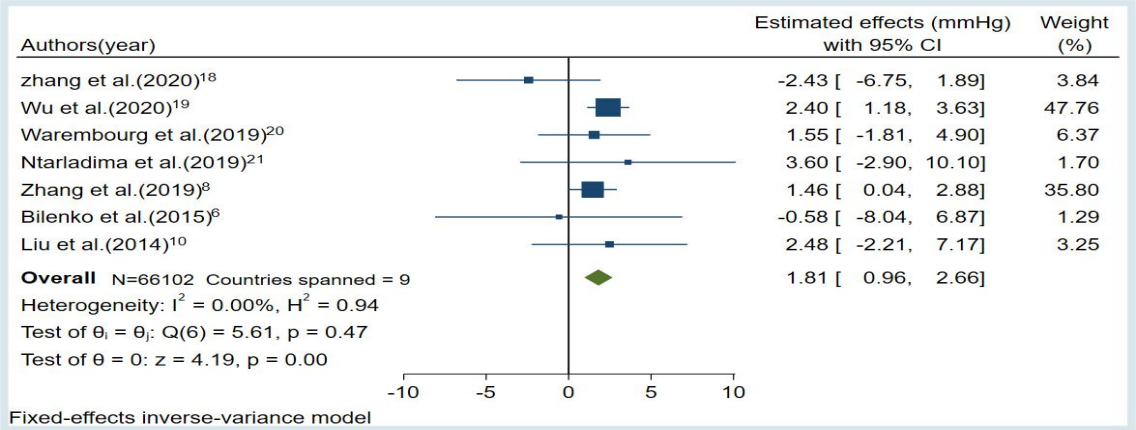

Figure S8. Forest plot for the association between long-term exposure to PM_{10} (per 10 μg/m^3 increment) and SBP (mmHg).

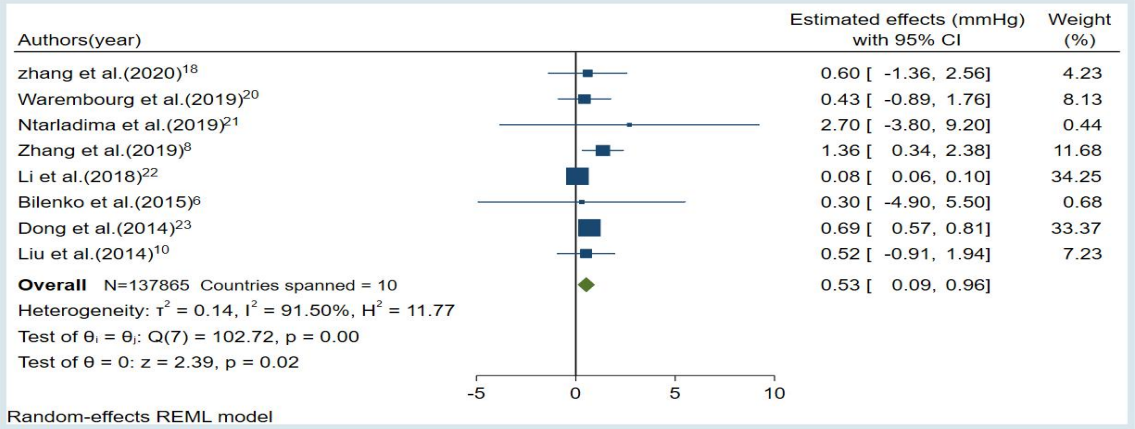

Figure S9. Forest plot for the association between long-term exposure to NO_2 (per 10 μg/m^3 increment) and SBP (mmHg).

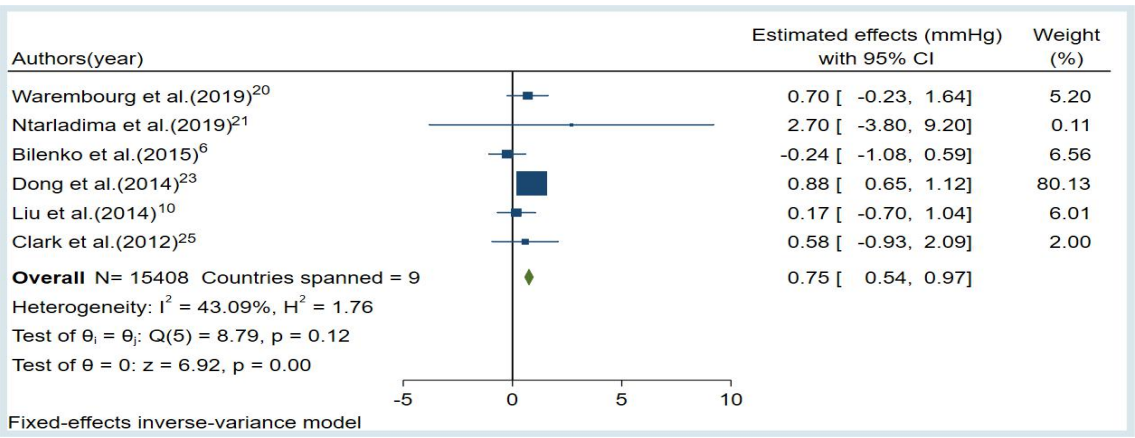

Figure S10. Forest plot for the association between long-term exposure to $PM_{2.5}$ (per 10 μg/m^3 increment) and DBP (mmHg).

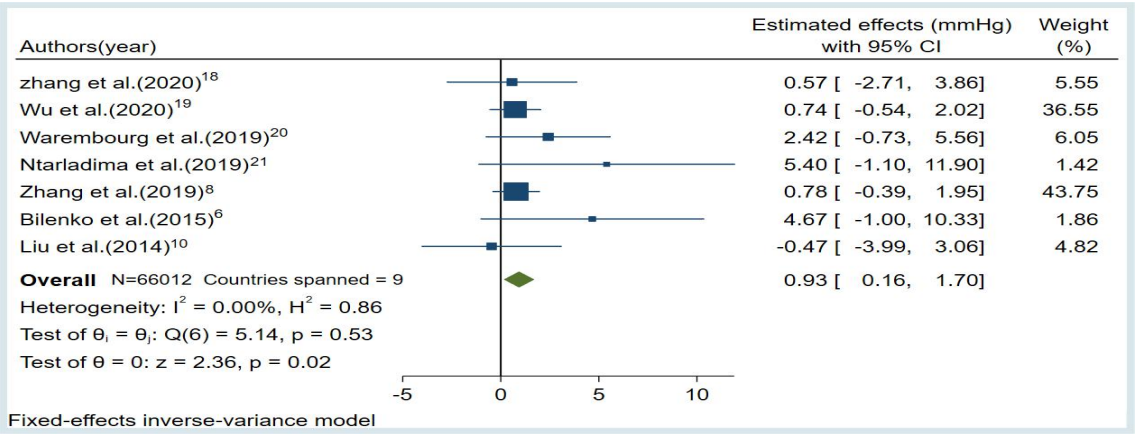

Figure S11. Forest plot for the association between long-term exposure to PM_{10} (per 10 $\mu g/m^3$ increment) and DBP (mmHg).

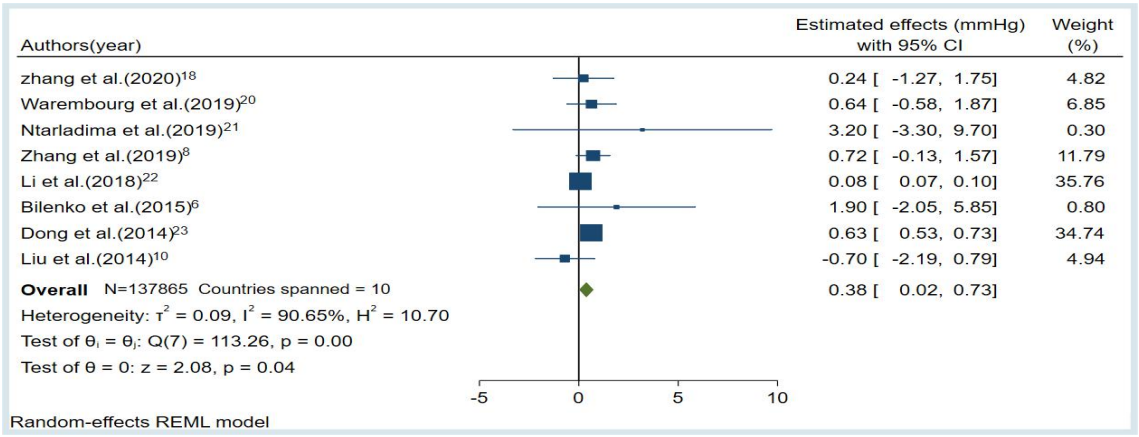

Figure S12. Forest plot for the association between long-term exposure to NO_2 (per 10 $\mu g/m^3$ increment) and DBP (mmHg).

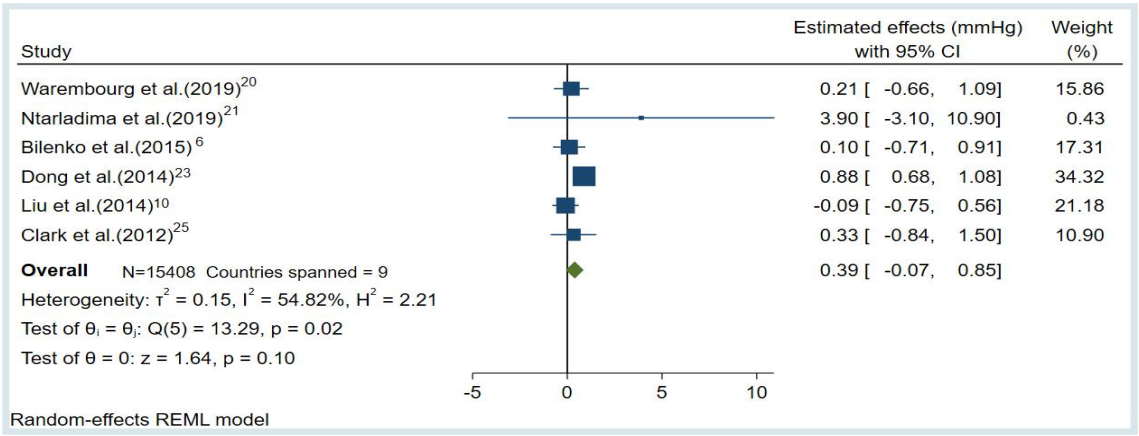

Figure S13. Funnel plot analysis in the meta-analysis of the association between long-term exposure to $PM_{2.5}$ and SBP.

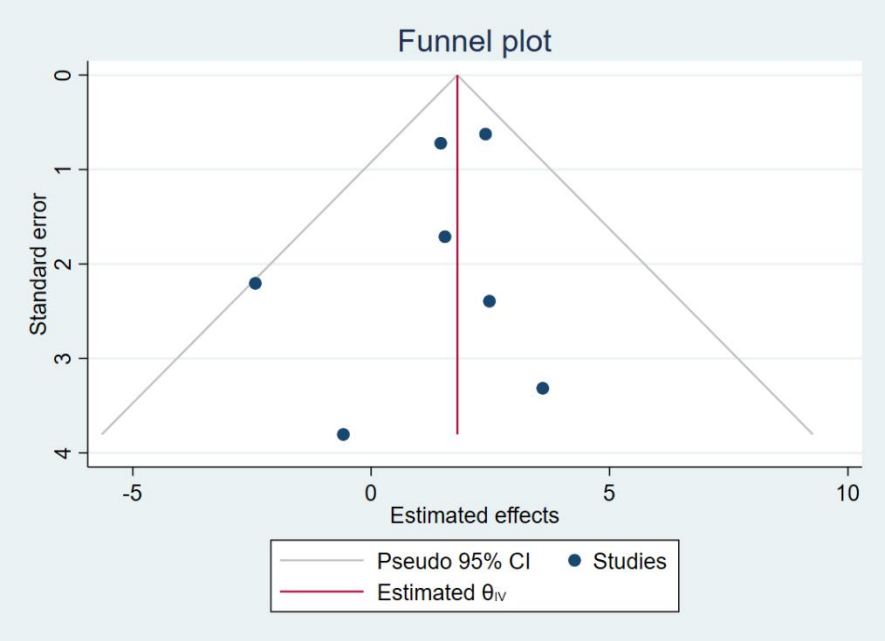

Figure S14. Funnel plot analysis in the meta-analysis of the association between long-term exposure to $PM_{2.5}$ and DBP.

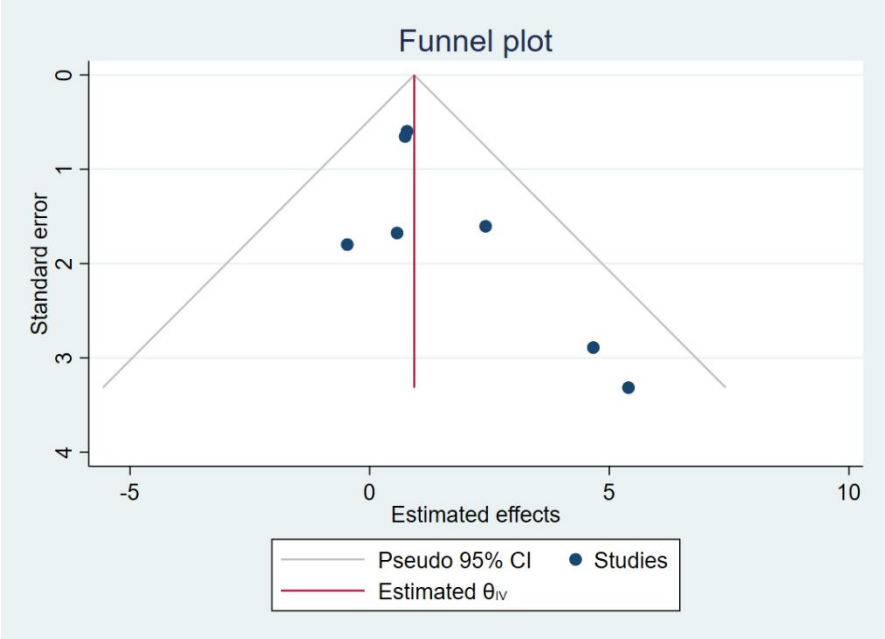

Figure S15. Funnel plot analysis in the meta-analysis of the association between long-term exposure to PM_{10} and SBP.

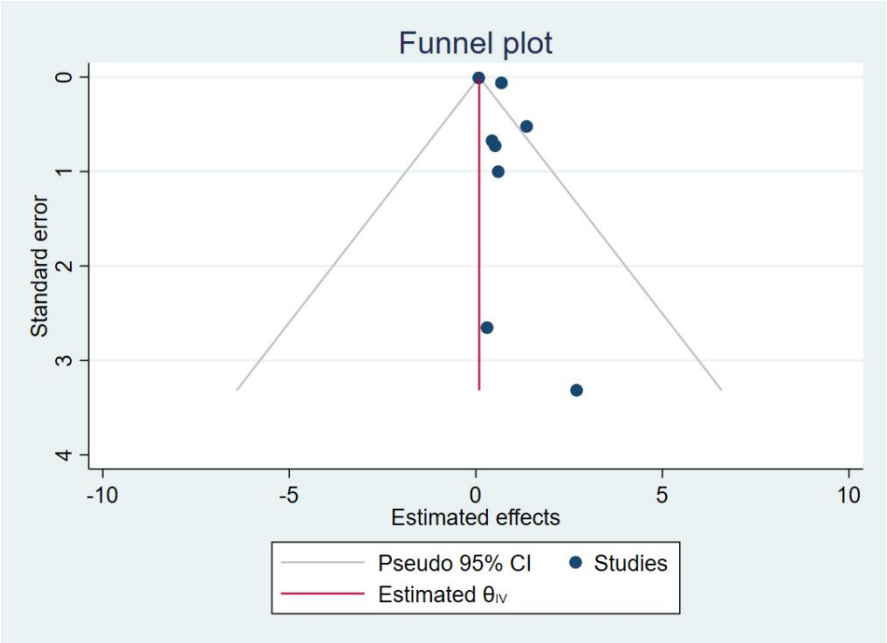

Figure S16. Funnel plot analysis in the meta-analysis of the association between long-term exposure to PM_{10} and DBP.

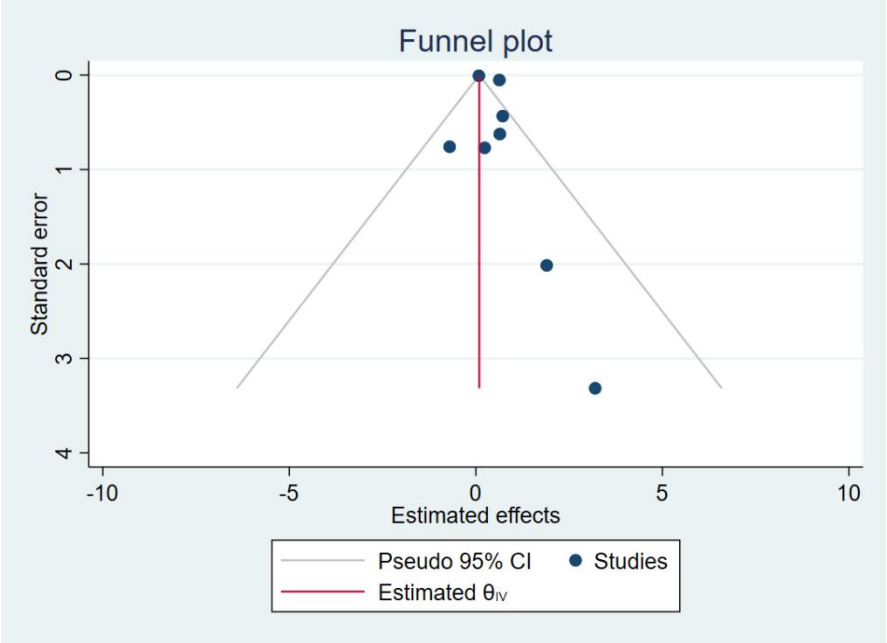

Figure S17. Funnel plot analysis in the meta-analysis of the association between long-term exposure to NO_2 and SBP.

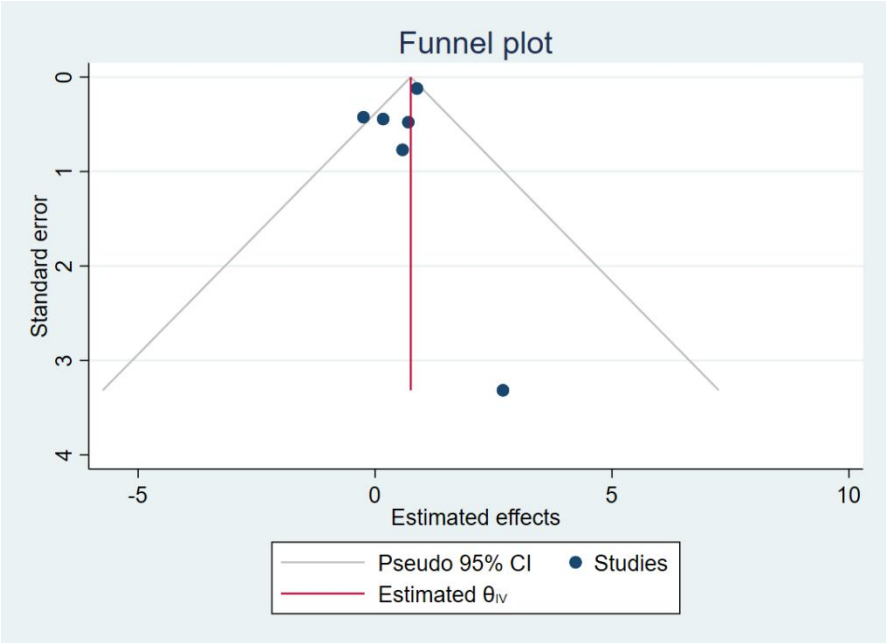

Figure S18. Funnel plot analysis in the meta-analysis of the association between long-term exposure to NO_2 and DBP.