Yang. INPLASY protocol 202590008. doi:10.37766/inplasy2025.9.0008 Downloaded from https://inplasy.com/inplasy-2025-9-0008/

INPLASY

Relationship between lead exposure and different types of hypertension : systematic review and dose-response meta-analysis

INPLASY202590008

doi: 10.37766/inplasy2025.9.0008

Received: 3 September 2025

Published: 3 September 2025

Yang, PL.

Corresponding author:
Peilin Yang

15561579858@163.com

Author Affiliation:
Heilongjiang University of Chinese Medicine.

ADMINISTRATIVE INFORMATION

Support - This work was supported by Shanxi Health Committee Foundation Project (2024057) and Fundamental Research Program of Shanxi Province (202403021222432).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590008

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 4 September 2025 and was last updated on 4 September 2025.

INTRODUCTION

Review question / Objective Hypertension, one of the most prevalent chronic non-communicable diseases worldwide, is a major risk factor for cardiovascular diseases, stroke, kidney disease, and other serious health conditions, imposing a substantial burden on public health systems. According to the World Health Organization, the global prevalence of hypertension continues to rise, with a trend toward younger onset ages. Its pathogenesis is complex, involving interactions among genetic, environmental, and lifestyle factors. In recent years, the relationship between environmental pollutant exposure and hypertension has gained increasing research attention. Among these pollutants, lead, a ubiquitous environmental toxicant, has drawn significant scientific interest due to its potential adverse effects on the cardiovascular system.

Lead is a heavy metal with neurotoxic and hematotoxic properties, which can enter the human body through various pathways such as air, water, food, and soil. Chronic accumulation may cause damage to multiple organ systems. Previous epidemiological studies have suggested a potential association between lead exposure and increased blood pressure or hypertension risk, yet the strength of this association remains controversial. Some studies have reported significant positive correlations between biomarkers of lead exposure—such as blood lead and bone lead—and hypertension, while others have failed to observe a clear relationship. These discrepancies may stem from variations in baseline population characteristics (e.g., geographic region, age, genetic background), exposure assessment methods (e.g., blood lead vs. bone lead), study design (e.g., cross-sectional vs. cohort studies), and the extent of confounding control. Furthermore, it remains unclear whether a dose-response relationship exists between lead

exposure and hypertension, and whether this relationship varies across hypertension subtypes—such as essential hypertension, resistant hypertension, and hypertension during pregnancy—has not yet been conclusively established.

Systematic reviews and meta-analyses serve as essential methods for synthesizing existing research evidence. They enhance statistical power by quantitatively combining results from multiple independent studies, reduce random errors inherent in individual studies, and facilitate the exploration of heterogeneity sources, thereby providing more robust evidence for scientific questions. Although several meta-analyses have examined the association between lead exposure and hypertension, most have not thoroughly examined variations across subgroups (e.g., geographic region, study design, hypertension subtype). Moreover, a systematic assessment of the dose-response relationship remains limited, particularly in elucidating the quantitative association between different levels of lead exposure and hypertension risk.

Based on the aforementioned research background, this study aims to comprehensively evaluate the association between lead exposure and different types of hypertension through systematic literature search and inclusion, using systematic review and dose-response meta-analysis methods. It further seeks to explore subgroup differences across various populations, study designs, and exposure characteristics. Additionally, by conducting dose-response analysis, the study intends to clarify the quantitative relationship between lead exposure levels and the risk of hypertension onset. The findings will provide scientific evidence for elucidating the role of lead exposure in the pathogenesis of hypertension and for developing targeted public health intervention strategies.

Condition being studied The initial search yielded 5170 articles. Through careful review of the titles, abstracts, and full texts, and by strictly adhering to the inclusion and exclusion criteria, a total of 24 studies were ultimately included in the analysis.

METHODS

Participant or population The study population comprised 181,500 adults drawn from the general population across multiple countries (China, South Korea, the United States, the Netherlands, and others). Participants included both environmentally and occupationally lead-exposed individuals, without restriction to any specific disease status at baseline. The primary outcome of interest was incident hypertension, analyzed across several subtypes—essential, resistant, gestational, menopausal, and uncontrolled hypertension.

Intervention Intervention (Exposure)
Environmental or occupational lead exposure, quantified by biomarkers:
• Blood lead (recent exposure)
• Bone lead (cumulative/long-term exposure).

Comparator No.

Study designs to be included To address this, we conducted subgroup analyses based on geographic region, study design (cross-sectional, cohort, case-control), exposure biomarker (blood lead vs.bone lead). Hypertension subtype (essential, resistant, gestational, uncontrolled, menopausal) and whether to adjust the influencing factors.

Eligibility criteria Exposure : blood lead, urine lead, bone lead
Diseases : hypertension (primary, secondary, special, such as Resistant Hypertension, pregnancy-induced hypertension)
Study : cross-sectional, cohort, case-control
Outcome : relative risk (RR) OR hazard ratio (HR) OR odds ratio (OR).

Information sources We conducted a computer assisted search of the following databases : PubMed, Embase, Cochrane, Scopus and Web of Science. The search focused on studies related to the
correlation between lead exposure and
Hypertension. The search spanned from the inception of each database to June 9, 2025.

Main outcome(s) Primary outcome: incident hypertension (overall and by subtype: essential, resistant, gestational, menopausal, and uncontrolled hypertension).

Quality assessment / Risk of bias analysis Two reviewers independently appraised study quality using validated tools:
• Newcastle-Ottawa Scale (NOS) for cohort and case–control studies
• JBI Critical Appraisal Checklist for cross-sectional studies
Discrepancies were resolved by discussion. All studies were rated and the scores are reported in Supplementary Tables S8–S10 and Supplementary Figures 1–3; no study was excluded on the grounds of quality alone.

Yang. INPLASY protocol 202590008. doi:10.37766/inplasy2025.9.0008 Downloaded from https://inplasy.com/inplasy-2025-9-0008/

Strategy of data synthesis The extracted data were subjected to meta-analysis using STATA 18.0 software. The specific procedures were as follows:
Effect-size selection: The odds ratio (OR) was chosen as the summary measure, with 95 % confidence intervals (CIs) computed for each study.
Heterogeneity evaluation: Between-study heterogeneity was assessed with the Q-test (P-value) and I^2 statistic. When $P > 0.10$ and $I^2 \leq 50$ %, heterogeneity was judged low and a fixed-effect model (FE) was applied; otherwise ($P \leq 0.10$ or $I^2 > 50$ %), a random-effects model (RE) was employed.
Assessment of publication bias: Funnel plots and Egger's regression test were used to detect potential publication bias in studies examining the relationship between lead exposure and hypertension.
Sensitivity analysis: A leave-one-out sensitivity analysis was conducted to evaluate the robustness of the pooled effect estimates.
Meta-regression and subgroup analyses: Univariate and multivariate meta-regression, together with predefined subgroup analyses (by country, study design, exposure biomarker, hypertension subtype, and covariate adjustment), were performed to explore sources of heterogeneity and their impact on the pooled results.

Subgroup analysis Subgroup analyses were performed to investigate potential sources of heterogeneity and to assess the stability of the lead–hypertension association across different contexts. We stratified studies by (1) geographic region (South Korea, USA, China, Netherlands), (2) study design (cross-sectional, cohort, case–control), (3) exposure biomarker (blood lead vs bone lead), (4) hypertension subtype (essential, resistant, gestational, menopausal, uncontrolled), (5) adjustment status for major confounders (alcohol, smoking, BMI, physical activity). Random-effects models were applied within each stratum, and between-subgroup differences were formally tested using meta-regression.

Sensitivity analysis To assess the robustness of the pooled estimate, we performed a leave-one-out sensitivity analysis using STATA 18.0. Each of the 24 studies was sequentially excluded, and the meta-analysis was repeated with the remaining studies. Across all iterations, the pooled OR for the association between lead exposure and hypertension remained stable (range 1.19–1.37), and the 95 % confidence interval never crossed the null value. No single study exerted undue influence on the overall result, confirming the reliability of our findings.

Country(ies) involved China.

Keywords Lead exposure; Hypertension; Meta-analysis; Systematic review; Dose-response relationship; Risk factor.

Contributions of each author
Author 1 - Peilin Yang.
Email: 15561579858@163.com

Yang. INPLASY protocol 202590008. doi:10.37766/inplasy2025.9.0008 Downloaded from https://inplasy.com/inplasy-2025-9-0008/