INPLASY

Effects of different antihypertensive drugs on fall risk in older people: a protocol for a systematic review and network meta-analysis

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ADMINISTRATIVE INFORMATION

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

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 3 June 2026 and was last updated on 3 June 2026.

INTRODUCTION

Review question / Objective To compare the effects of different antihypertensive drugs on fall risk in older adults (≥60 years) and to rank their safety using network meta-analysis.
PICOS:
Population: Adults aged ≥60 years with hypertension.
Intervention: Any antihypertensive drug (ACE inhibitors, calcium channel blockers, diuretics, beta-blockers, alpha-blockers, angiotensin II receptor blockers, nitrates, aliskiren).
Comparison: Placebo or another antihypertensive drug.
Outcome: Fall risk (incidence or odds ratio of falls).
Study design: Randomized controlled trials, cohort studies, case-control studies.

Rationale Falls are a leading cause of injury, hospitalization, and loss of independence in older adults. Several clinical guidelines have identified antihypertensive drugs as potential risk factors for falls due to their hemodynamic effects (e.g., orthostatic hypotension, dizziness). Despite these warnings, antihypertensive medications are widely prescribed in older populations to reduce cardiovascular events and mortality. However, the comparative safety of different antihypertensive drug classes with respect to fall risk remains poorly understood. Traditional pairwise meta-analyses cannot fully rank multiple interventions, and existing evidence is often conflicting, partly due to differences in study designs (randomized controlled trials vs. observational studies) and age distributions of participants. Therefore, a network meta-analysis that integrates direct and indirect comparisons is needed to provide a comprehensive ranking of fall risk associated with

various antihypertensive drugs. The findings will help clinicians make evidence-based decisions when selecting antihypertensive therapy in older adults, balancing cardiovascular benefits against fall-related harms.

Condition being studied Health condition of interest: Falls in older adults.
Background disease: Hypertension.
Falls are a common and serious health event among people aged 60 years and older. They can lead to fractures, head injuries, loss of independence, institutionalization, and increased mortality. Hypertension is a highly prevalent chronic condition in the older population, often requiring long-term antihypertensive drug therapy. While these medications reduce cardiovascular risk, some classes of antihypertensive drugs may increase fall risk through mechanisms such as orthostatic hypotension, dizziness, or muscle weakness. This systematic review and network meta-analysis investigates whether different antihypertensive drugs differentially affect fall risk in older hypertensive adults.

METHODS

Participant or population Adults aged ≥60 years with a diagnosis of hypertension (either documented in medical records or defined by study authors using standard criteria). No restrictions on sex, ethnicity, or setting (community-dwelling, hospital, or nursing home). Participants may have comorbidities, but studies focusing exclusively on secondary hypertension or specific conditions (e.g., pregnancy) will be excluded.

Intervention Any antihypertensive drug (e.g., ACE inhibitors, calcium channel blockers, diuretics, beta-blockers, alpha-blockers, angiotensin II receptor blockers, nitrates, aliskiren).

Comparator Placebo or another antihypertensive drug.

Study designs to be included Randomized controlled trials (RCTs), cohort studies, and case-control studies.

Eligibility criteria Inclusion:
Studies published in English or Chinese.
Full text available.
Exclusion:
Systematic reviews, reviews, conference abstracts, case reports, letters, books.
Duplicate publications.
Incomplete data that cannot be extracted.

Information sources We searched the following electronic databases from inception to March 2025: PubMed, Scopus, Web of Science, CINAHL, CNKI, VIP, and WanFang Data. No additional sources (e.g., trial registries, grey literature, or contact with authors) were used.

Main outcome(s) The primary outcome is fall risk, defined as the incidence of falls or the odds ratio (OR) of falls comparing different antihypertensive drugs or placebo. For each comparison, we extracted or calculated the OR with its 95% confidence interval (CI) from the original studies. In the network meta-analysis, the effect measure is the OR (95% CI). The ranking of antihypertensive drugs according to fall risk is based on the surface under the cumulative ranking curve (SUCRA). Timing of outcome assessment varies across studies (e.g., during follow-up periods of several months to years); no predefined time window was specified.

Quality assessment / Risk of bias analysis Two reviewers independently assessed the methodological quality of included studies. Disagreements were resolved by discussion or consultation with a third reviewer. For randomized controlled trials (RCTs), the Cochrane Risk of Bias tool (RoB 2.0) was used, and risk of bias graphs were generated using Review Manager 5.4. For cohort studies and case-control studies, the Newcastle-Ottawa Scale (NOS) was used, which evaluates selection, comparability, and outcome/exposure. The NOS has a maximum of 9 points; higher scores indicate better quality. No studies were excluded based solely on quality assessment results.

Strategy of data synthesis A network meta-analysis was conducted using a frequentist framework. Software used: R 4.2.2 and STATA 17.0. The effect measure for dichotomous outcomes (fall events) was the odds ratio (OR) with 95% confidence interval (CI). Heterogeneity was assessed using the I^2 statistic; an $I^2 > 50\%$ indicated substantial heterogeneity. Inconsistency between direct and indirect comparisons was evaluated using the node-splitting method. If no significant inconsistency was detected, a consistency model was applied. The ranking of antihypertensive drugs according to fall risk was based on the surface under the cumulative ranking curve (SUCRA). A SUCRA value closer to 1 indicated a higher fall risk. Pairwise comparisons were performed to determine statistical significance between specific drug pairs. Publication bias and small-study effects were

examined using comparison-adjusted funnel plots generated with STATA 17.0.

Subgroup analysis No subgroup analyses were planned or conducted.

Sensitivity analysis No sensitivity analyses were planned or conducted.

Country(ies) involved China.

Keywords Older people; Falls; Antihypertensive drugs; Systematic review; Network meta-analysis.

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