ORIGINAL RESEARCH

74. How is Hypertension Associated with the Risk of Dementia among Adults living in High-Income Countries: A Systematic Review and Meta-Analysis

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Background: Dementia is a major public health challenge in high-income countries (HICs). Hypertension is a modifiable risk factor for dementia, yet the timing of exposure and dementia subtype-specific associations remain uncertain. This meta-analysis quantifies the association between hypertension and dementia risk in HICs and examines life-course timing (midlife and late-life) and dementia subtypes.

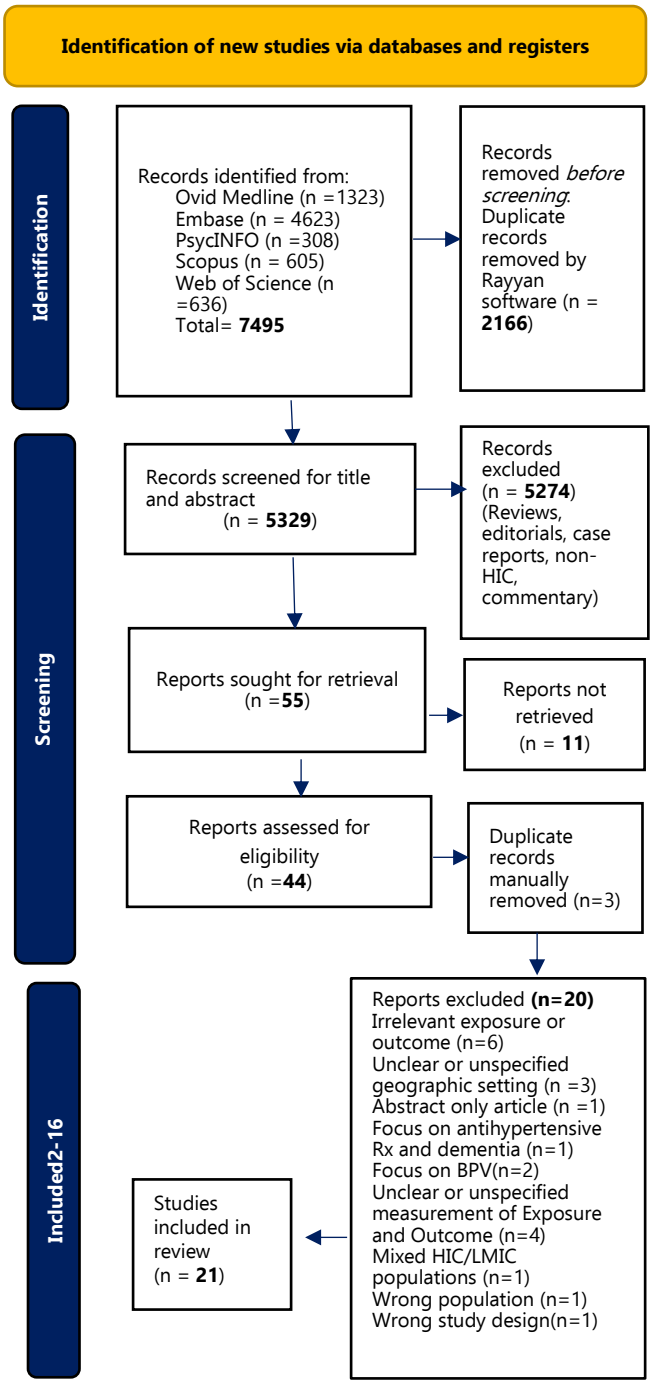
Methods: Systematic searches on OVID Medline, Embase, PsycINFO, Scopus and Web of Science (from inception to July 2025) identified 21 cohort studies. Four studies were meta- analyzed to quantify the association of midlife hypertension and all-cause dementia risk. The remaining studies were narratively synthesized using the SWiM guidelines. Screening and data extraction and analysis were done in accordance with PRISMA guidelines. Study quality was appraised with the JBI checklist; risk of bias was assessed with ROBINS-E and visualized using ROBVIS. Additionally, a Directed Acyclic Graph was constructed to map hypothesized causal pathways between hypertension and dementia, and to identify key confounders, particularly given the complex life-course interactions between these conditions.

Results: Twenty-one cohort studies, with sample size ranging from 1,462 to 848,505, follow-up between 8 to 37 years, and participant mean ages from 30-95 years. Study populations were largely homogeneous, consisting predominantly of white participants in Europe, the USA, and Australia, and Asian participants from Japan and Korea. Ethnic minority and socioeconomic status were not reported in the included studies. Single-country studies were conducted in the United Kingdom, USA, Finland, Norway, Sweden, Japan, South Korea,

and Australia. One multi-cohort study included seven cohorts across five countries (United States, Sweden, Germany, Netherlands, and Spain), and another study included two cohorts from two countries (Netherlands and Sweden). Meta-analysis of four studies showed midlife hypertension increases the risk of dementia by 63% (HR 1.63, 95%CI:1.37-1.89; I^2=0%). Narrative synthesis of the remaining 17 studies revealed that midlife hypertension is associated with dementia risk especially with vascular dementia (VaD). Heterogeneous findings were reported for late-life hypertension and dementia risk (null, inverse and U-shaped). Reverse nocturnal BP dipping increased dementia risk. Genetically elevated BP was found to be causal through Mendelian randomization. Evidence on antihypertensive therapy were mixed, with BP decline preceding dementia onset. Most studies had a moderate-to-serious the risk of bias due to confounding and exposure misclassification.

Conclusion: Midlife hypertension consistently increases dementia risk, making it a critical public health priority for reducing dementia burden in HICs. In contrast, late life hypertension-dementia associations are heterogeneous, reflecting complex life-course dynamics and highlighting evidence gaps that require further research.

Figure 1. PRISMA flowchart of reviewed literature



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