NEW PAPERS

The association between hypertension and Alzheimer's disease

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Hypertension affects an estimated 1.3 billion persons worldwide1 and is the leading cause of strokes and cerebrovascular disease2. There is good evidence that it increases risk of vascular dementia (VaD)3 and now emerging evidence is strongly indicating that hypertension is also an important risk factor both in mid- and latelife for Alzheimer's dementia, which makes up around 70% of all dementia cases. The lack of current effective treatment makes the targeting of modifiable risk factors such as hypertension all the more important. The 2024 Lancet Commission on Dementia highlighted that approximately 40% of dementia cases were potentially modifiable, through the targeting of these risk factors.

Research Connecting Hypertension and Dementia

Our recent research has begun to uncover the critical relationship between high blood pressure and dementia. In a 2019 meta-analysis, our team found a clear link between mid-life hypertension and Alzheimer's disease (AD), with stage 1 hypertension (systolic blood pressure [SBP] >140 mmHg) associated with an 18% increased risk of AD, and stage 2 hypertension (>160 mmHg) linked to a 25% increased risk4. In 2020, another metaanalysis confirmed that mid-life hypertension increased the risk of all-cause dementia by 19% to 55%5.

However, the relationship between late-life hypertension and dementia remains more complex. Longitudinal studies on older adults have shown mixed results, with some suggesting a neutral or even protective effect of high blood

pressure in later years. This disparity highlights the importance of understanding how treatment status affects dementia risk.

New evidence on Untreated versus Treated Hypertension

Our recent research (2023–2024)6,7 has provided clearer answers regarding hypertension's role in dementia. In two individual-participant data (IPD) meta-analyses, involving 34,519 participants aged 60 and over from 15 countries, our team found that untreated hypertension was associated with a significantly increased risk of both dementia (+42%) and Alzheimer's disease (+36%) compared to individuals without a history of hypertension. However, individuals who had their hypertension treated exhibited no elevated risk for dementia or AD. In fact, those treated for hypertension had a substantially lower risk of dementia (-26%) and AD (-42%) compared to untreated individuals. These findings held true across different age groups, including those in their 70s and 80s, underscoring the importance of blood pressure management even in older populations.

Interestingly, the study also included underrepresented populations from countries like Nigeria and the Republic of Congo. The results showed no significant moderating effects based on race or sex, suggesting that effective blood pressure treatment could be equally beneficial across diverse populations.

While the studies were observational and subject to confounding factors, the results are consistent with findings from clinical trials, including a 2022







meta-analysis of five randomized controlled trials, which found that antihypertensive treatment reduced dementia risk by 13%8. These findings also align with the 2024 Lancet Commission report, which highlighted that untreated hypertension increases dementia risk by 20%9.

The Path Forward

Despite its high prevalence, hypertension remains underappreciated as a risk factor for dementia. Traditionally, high blood pressure has been primarily associated with heart disease and stroke, with limited public awareness of its connection to cognitive decline. This lack of awareness is one of the key challenges in improving hypertension diagnosis and treatment, particularly as hypertension is often considered a "normal" part of aging, especially in the elderly.

In a <u>recent survey</u> of Australians attending an outpatient clinic, dementia was the second most feared disease, having been listed as the primary worry for 29.3% of respondents, compared to only 7.3% and 3.7% who replied with "coronary heart disease" and "cerebrovascular disease" respectively. We anticipate that this greater concern for dementia diagnosis compared to heart disease or kidney impairment is similar around the globe. The growing evidence base connecting high blood pressure and dementia will change the way that patients see blood pressure and may modify the way they think about risk of non-detection and non-compliance with treatment.

As of 2022, nearly 50% of people with hypertension in Australia are undiagnosed, while a further 18% have their condition under control but inadequately treated. Among those over 65 years old, the rates are even more alarming: 34% have been diagnosed with hypertension, but 39% have poorly controlled blood pressure. Alarmingly, the rates of high blood pressure in the community have worsened, rising from 21.5% in 2011-12 to 23.3% in 2022. Improving public understanding of the relationship between hypertension and dementia will be a crucial step in addressing the burgeoning public health crisis of aging and cognitive decline.

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References

- 1. World Health Organization (WHO). Global Report on Hypertension. 2023.
- 2. Murray CJL, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet [online serial]. Elsevier; 2020;396:1223-1249. Accessed at: https://doi.org/10.1016/ S0140-6736(20)30752-2.
- 3. Emdin CA, Rothwell PM, Salimi-Khorshidi G, et al. Blood Pressure and Risk of Vascular Dementia: Evidence From a Primary Care Registry and a Cohort Study of Transient Ischemic Attack and Stroke. Stroke. United States; 2016;47:1429-1435.
- 4. Lennon MJ, Makkar SR, Crawford JD, Sachdev PS. Midlife Hypertension and Alzheimer's Disease: A Systematic Review and Meta-Analysis. J Alzheimers Dis. Netherlands; 2019;71:307-316.
- 5. Ou Y-N, Tan C-C, Shen X-N, et al. Blood Pressure and Risks of Cognitive Impairment and Dementia. Hypertension [online serial]. American Heart Association; 2020;76:217-225. Accessed at: https://doi.org/10.1161/ HYPERTENSIONAHA.120.14993.
- 6. Lennon MJ, Lam BCP, Lipnicki DM, et al. Use of Antihypertensives, Blood Pressure, and Estimated Risk of Dementia in Late Life: An Individual Participant Data Meta-Analysis. JAMA Netw Open [online serial]. 2023;6:e2333353-e2333353. Accessed at: https://doi. org/10.1001/jamanetworkopen.2023.33353.
- 7. Lennon MJ, Lipnicki DM, Lam BCP, et al. Blood Pressure, Antihypertensive Use, and Late-Life Alzheimer and Non-Alzheimer Dementia Risk: An Individual Participant Data Meta-Analysis. Neurology. United States; 2024;103:e209715.
- 8. Peters R, Xu Y, Fitzgerald O, et al. Blood pressure lowering and prevention of dementia: an individual patient data meta-analysis. Eur Heart J. Epub 2022.:1-11.
- 9. Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet</ em> standing Commission. Lancet [online serial]. Elsevier; 2024;404:572-628. Accessed at: https://doi.org/10.1016/ 50140-6736(24)01296-0.





