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Important New Evidence Service

In partnership with The Centre for Medicines Optimisation at Keele University

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Study finds lowering blood pressure reduces dementia risk in people with hypertension

An open-label, cluster-randomised trial involving nearly 34,000 people aged ≥ 40 years with uncontrolled hypertension in rural China has found that an intervention involving antihypertensive medication titrated by a trained non-physician community health-care provider (to target BP <130/80 mmHg), alongside health coaching on lifestyle changes, reduced the risk of all-cause dementia (the primary outcome) by 15% over a 48-month period compared with usual care (risk ratio [RR] 0.85, p = 0.0035). Furthermore, cognitive impairment without dementia (CIND) was reduced by 16% (RR=0.84, p <0.0001). Systolic BP was reduced by 22.0 mm Hg and diastolic BP by 9.3 mm Hg in the intervention group compared to the usual care group.

The findings add to the evidence that optimising blood pressure control in people with hypertension may improve health outcomes.

Reference: He J, Zhao C, Zhong Z *et al.* Blood pressure reduction and all-cause dementia in people with uncontrolled hypertension: an open-label, blinded-endpoint, cluster-randomized trial. Nat Med (2025). https://doi.org/10.1038/s41591-025-03616-8

What do we know already?

- Currently, an estimated 982,000 people are living with dementia in the UK and by 2040 this figure is expected to rise to 1.4 million. The prevalence of dementia in people aged over 65 years was estimated at 7.1% in 2019 and projected to rise to 8.8% by 2040.
- Observational studies have found that untreated hypertension is associated with an increased risk of cognitive decline and dementia. However, the association is complex and not fully elucidated. A meta-analysis of seven population-based cohorts involving 17,286 older adults (mean age 75 years) showed a U-shaped relationship between systolic BP and dementia risk.
- The SPRINT-MIND randomised controlled trial (n = 9,361) found intensive antihypertensive treatment (systolic BP goal <120 mm Hg) was associated with a non-significant 17% reduction in adjudicated dementia compared with standard treatment (systolic BP goal <140 mm Hg) in people aged over 50 years with hypertension (systolic BP between 130 and 180 mm Hg at the screening visit) and high cardiovascular risk.
- An individual patient level meta-analysis that combined individual participant data from five large double-blind placebo-controlled trials found that blood pressure reduction (mean difference of 10/4 mmHg) was associated with a reduction of incident dementia compared with placebo. However, as a meta-analysis, there is potential bias in the combining of data from different trials. Differential attrition, and mortality or stroke rates in the different arms of the trials, combined with early stopping due to cardiovascular benefits, may have reduced the potential to identify incident dementia cases and to follow participants for a longer period.

What does this evidence add?

- The authors of this study report that it is one of the largest randomised controlled trials to assess whether blood pressure reduction can reduce dementia risk in real world primary care settings. They suggest that their intervention should be widely adopted and scaled up to reduce the global burden of dementia.
- The effectiveness of BP reduction on the risk of dementia was consistent across subgroups based on age, sex, education, history of cigarette smoking, body mass index, systolic BP, fasting plasma glucose and 10-year atherosclerotic cardiovascular disease risk (CVD) at baseline. Adverse events were comparable between the two groups, and serious adverse events were significantly lower in the intervention group compared with the usual care group.
- Although the study participants and research staff who collected blood pressure data were unmasked, research staff responsible for collecting cognitive outcome data were masked to the randomisation assignments. The final diagnosis of all-cause dementia or CIND was made by an expert adjudication panel blinded to the intervention assignment.

- A limitation of the study is that cases of mild cognitive impairment may not have been diagnosed at the beginning because baseline cognitive assessments were not performed.

Study details

Participants

- The China Rural Hypertension Control Project (CRHCP) was a cluster-randomised trial that included 33,995 people (mean age 63.3 years; 61% women) from 326 villages located at least 2 km apart from each other with a regular non-physician community health-care provider (NPCHP).
- Eligible residents were aged over 40 years with a mean untreated systolic BP ≥140 mm Hg and/or a diastolic BP ≥90 mm Hg (or ≥130 mm Hg and/or ≥80 mm Hg among those with clinical CVD, diabetes or chronic kidney disease) or a mean treated systolic BP ≥130 mm Hg and/or a diastolic BP ≥80 mm Hg, based on six measurements taken on two different days.

Intervention and comparator

- Villages were randomised 1:1 to the intervention group or usual care group using a random allocation sequence generated with SAS software and were stratified by province, county and township. The randomisation assignments were concealed until recruitment and baseline data collection were completed. Baseline characteristics were reported to be comparable between groups.
- In the intervention group, trained NPCHPs initiated and titrated antihypertensive medications according to a simple stepped-care protocol with the aim of achieving a systolic BP <130 mm Hg and a diastolic BP <80 mm Hg. NPCHPs also conducted health coaching for lifestyle modifications and medication adherence, and provided monitors and instructions to participants for home BP monitoring. Based on clinical guidelines, the study protocol recommended angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), and/or thiazide or thiazide-like diuretics as the first-line medication.
- In the usual care group, NPCHPs received training in standard BP measurement but not in protocol-based hypertension management. Participants in control villages had their BP managed at their usual healthcare settings by either NPCHPs or primary care physicians in township hospitals. They did not receive free home BP monitors or antihypertensive medications. However, participants in both groups had the same health insurance plan (the China New Rural Cooperative Medical Scheme) and received similar healthcare apart from BP management.

Outcomes

- The primary outcome was all cause dementia, and the main secondary outcome was CIND. The diagnostic criteria for all-cause dementia and CIND were adopted from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.

Results:

- A total of 15,972 (91.8%) in the intervention group and 15,072 (90.9%) participants in the usual care group were followed up for clinical outcomes at 48 months.
- In the intervention group, the mean systolic BP decreased from 157.0 at baseline to 127.6 mm Hg at 48 months, while diastolic BP decreased from 87.9 to 72.6 mm Hg. In the usual care group systolic BP decreased from 155.4 to 147.7 mm Hg, and diastolic BP decreased from 87.2 to 81.0 mm Hg over 48 months. The net reduction in systolic BP was 22.0 mm Hg (95% confidence interval [CI] 20.6 to 23.4; $p < 0.0001$) and that in diastolic BP was 9.3 mm Hg (95% CI 8.7 to 10.0; $p < 0.0001$) in the intervention group compared to usual care.
- A total of 67.7% of participants in the intervention group and 15.0% in the usual care group achieved an systolic BP <130 mm Hg and a diastolic BP <80 mm Hg at 48 months.
- At the 48-month follow-up visit, the primary outcome of all-cause adjudicated dementia was significantly lower in the intervention group than in the usual care group (668 participants in the intervention group and 734 participants in the usual care group, RR 0.85, 95% CI 0.76 to 0.95, $p = 0.0035$).
- The secondary outcome of CIND was also lower in the intervention group than the usual care group (2,506 participants in the intervention group and 2,808 participants in the usual care group, RR 0.84, 95% CI 0.80 to 0.87, $p < 0.0001$). The RR for the composite outcome of dementia or CIND was 0.84 (95% CI 0.81 to 0.87, $p < 0.0001$).
- Serious adverse events occurred less frequently in the intervention group than the usual care group (RR 0.94, 95% CI 0.91 to 0.98; $p = 0.0006$). There was no difference between the two groups in terms of injurious falls requiring medical care, symptomatic hypotension confirmed at a village doctor visit or syncope needing medical care. There were 1,269 deaths in the intervention group, and 1,392 deaths in the usual care group.
- A sensitivity analysis that adjusted for age, sex, education, smoking, major CVD history, antihypertensive medication use, BMI, SBP, low-density lipoprotein (LDL) cholesterol and fasting plasma glucose at baseline found the risk reduction for the primary and secondary outcomes associated with the intervention remained significant.

Level of evidence: Level 1 according to SORT criteria.

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