

Intensive blood pressure control reduces risk of mild cognitive impairment

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Significant reductions in the risk of mild cognitive impairment (MCI), and the combination of MCI and dementia, have been shown for the first time through aggressive lowering of systolic blood pressure in new

research results from the federally-funded SPRINT MIND Study reported at the Alzheimer's Association International Conference (AAIC) 2018 in Chicago.

"This is the first randomized clinical trial to demonstrate a reduction in new cases of MCI alone and the combined risk of MCI plus all-cause dementia," said Jeff D. Williamson, MD, MHS, Professor of Internal Medicine and Epidemiology and Chief, Section on Gerontology and Geriatric Medicine at Wake Forest School of Medicine. Williamson reported these results at AAIC 2018.

The results of this large-scale, long-term clinical trial provide the strongest evidence to date about reducing risk of MCI and dementia through the treatment of high [blood pressure](#), which is one of the leading causes of cardiovascular disease worldwide.

"This study shows more conclusively than ever before that there are things you can do—especially regarding cardiovascular disease risk factors—to reduce your risk of MCI and dementia," said Maria C. Carrillo, Ph.D., Alzheimer's Association Chief Science Officer. "To reduce new cases of MCI and dementia globally we must do everything we can—as professionals and individuals—to reduce blood pressure to the levels indicated in this study, which we know is beneficial to cardiovascular risk."

Carrillo pointed out that these results fit well with recent population data showing reductions in new cases of dementia in developed Western cultures. These lower rates of dementia may be occurring as these societies have begun to improve control of cardiovascular disease risk factors through medication management, reducing smoking, and greater awareness of healthy lifestyle.

"The future of reducing MCI and dementia could be in treating the

whole person with a combination of drugs and modifiable risk factor interventions—as we do now in heart disease," Carrillo suggested. "These new blood pressure findings raise our level of anticipation for the U.S. POINTER Study, which includes managing [cardiovascular disease risk](#) factors as part of the multi-component lifestyle intervention."

The Alzheimer's Association U.S. Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk (U.S. POINTER) is a two-year clinical trial funded by the Alzheimer's Association to evaluate whether lifestyle interventions can protect cognitive function in older adults at increased risk for cognitive decline. The interventions include physical exercise, nutritional counseling and modification, cognitive and social stimulation, and improved self-management of health status.

Intensive Blood Pressure Control Significantly Reduces New Cases of MCI, and Combined Risk of MCI and Dementia: SPRINT MIND Study

At AAIC 2018, Williamson and colleagues reported preliminary results related to risk of dementia and cognitive decline from the Systolic Blood Pressure Intervention Trial (SPRINT). SPRINT is a randomized clinical trial that compared two strategies for managing high blood pressure (hypertension) in older adults: an intensive strategy with a systolic blood pressure goal of less than 120 mm Hg versus a standard care strategy targeting a systolic blood pressure goal of less than 140 mm Hg. Previously, SPRINT demonstrated that more intensive blood pressure control reduced the risk for cardiovascular morbidity and mortality (NEJM, 11-26-15). SPRINT helped inform the 2017 American Heart Association and American College of Cardiology [high blood pressure](#) clinical guidelines.

SPRINT Memory and Cognition IN Decreased Hypertension (SPRINT MIND) examined whether treating to the lower blood pressure target reduces the risk of developing dementia and/or MCI, and reduces the

total volume of white matter lesions in the brain as shown by magnetic resonance imaging (MRI).

Study participants were 9,361 hypertensive older adults with increased cardiovascular risk (based on the Framingham risk score) but without diagnosed diabetes, dementia or prior stroke. Participant mean age was 67.9 years (35.6% women) and 8,626 (92.1%) completed at least one follow-up cognitive assessment. In SPRINT MIND, the primary outcome was incident probable dementia. Secondary outcomes included MCI and a composite outcome of MCI and/or probable dementia. Each outcome was adjudicated by an expert panel blinded to who was in each treatment group.

Recruitment for SPRINT began in October 2010. At one year, mean systolic blood pressure was 121.4 mmHg in the intensive-treatment group and 136.2 mmHg in the standard treatment group. Treatment was stopped in August 2015 due to cardiovascular disease (CVD) benefit after a median follow up of 3.26 years, but cognitive assessment continued until June 2018.

Intervention—According to *NEJM*, 11-26-15, "All major classes of antihypertensive agents were included in the formulary and were provided at no cost to the participants. SPRINT investigators could also prescribe other antihypertensive medications (not provided by the study). The protocol encouraged, but did not mandate, the use of drug classes with the strongest evidence for reduction in cardiovascular outcomes, including thiazide-type diuretics (encouraged as the first-line agent), loop diuretics (for participants with advanced chronic kidney disease), and beta-adrenergic blockers (for those with coronary artery disease)."

"Participants were seen monthly for the first 3 months and every 3 months thereafter. Medications for participants in the intensive-

treatment group were adjusted on a monthly basis to target a systolic blood pressure of less than 120 mm Hg. For participants in the standard-treatment group, medications were adjusted to target a systolic blood pressure of 135 to 139 mm Hg, and the dose was reduced if [systolic blood pressure](#) was less than 130 mm Hg on a single visit or less than 135 mm Hg on two consecutive visits. ... Lifestyle modification was encouraged as part of the management strategy."

In SPRINT MIND, the researchers found a statistically significant 19 percent lower rate of new cases of MCI ($p=0.01$) in the intensive blood pressure treatment group. The combined outcome of MCI plus probable all-cause dementia was 15 percent lower ($p=0.02$) in the intensive versus standard treatment group. There was a non-significant reduction in probable dementia alone ($HR=0.83$, $p=0.10$). Adverse events—According to NEJM, 11-26-15, "Serious adverse events occurred in 1793 participants in the intensive-treatment group (38.3%) and in 1736 participants in the standard-treatment group (37.1%) (hazard ratio with intensive treatment, 1.04; $P=0.25$). Serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or acute renal failure, but not injurious falls or bradycardia, occurred more frequently in the intensive-treatment group than in the standard-treatment group. Orthostatic hypotension as assessed during a clinic visit was significantly less common in the intensive-treatment group. A total of 220 participants in the intensive-treatment group (4.7%) and 118 participants in the standard-treatment group (2.5%) had serious adverse events that were classified as possibly or definitely related to the intervention (hazard ratio, 1.88; P

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