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FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2025

U.S. POINTER STUDY SHOWS STRUCTURED LIFESTYLE PROGRAM TARGETING MULTIPLE RISK FACTORS IMPROVES COGNITION IN OLDER ADULTS AT RISK OF COGNITIVE DECLINE

Key Takeaways

- **Two lifestyle interventions in U.S. POINTER improved cognition in older adults at risk of cognitive decline. A structured intervention with more support and accountability showed greater improvement compared to a self-guided intervention.**
- **In a large, representative group of older adults at high risk for cognitive decline, multidomain lifestyle interventions were delivered with high adherence and safety.**
- **Cognitive benefits were consistent across age, sex, ethnicity, heart health status and apolipoprotein E-e4 genotype.**

TORONTO, July 28, 2025 — The Alzheimer's Association U.S. Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk ([U.S. POINTER](#)) — a two-year, multi-site clinical trial testing two different lifestyle interventions in a representative population of older adults at risk for cognitive decline and dementia — found that both interventions improved cognition in older adults at risk of cognitive decline. Trial participants in the structured (STR) intervention showed greater improvement on global cognition compared to the self-guided (SG) intervention, protecting cognition from normal age-related decline for up to two years. The STR intervention differed from the SG intervention in intensity, structure, accountability and support provided.

The results were reported for the first time today at the [Alzheimer's Association International Conference](#) (AAIC) 2025 in Toronto and online. "Effects Of Structured vs Self-Guided Multidomain Lifestyle Interventions for Global Cognitive Function: The U.S. POINTER Randomized Clinical Trial," was published in *The Journal of the American Medical Association (JAMA)* simultaneously with the report at AAIC 2025.

U.S. POINTER is the first large-scale, randomized controlled clinical trial to demonstrate that an accessible and sustainable healthy lifestyle intervention can protect cognitive function in diverse populations in communities across the United States.

"As the burden of dementia grows world-wide, U.S. POINTER affirms a vital public health message: healthy behavior has a powerful impact on brain health," said [Joanne Pike, DrPH](#), Alzheimer's Association president and CEO.

"This is a critical public health opportunity. The intervention was effective across a broad, representative group — regardless of sex, ethnicity, APOE genetic risk, or heart health status — demonstrating its applicability and scalability for communities across the country," said Pike. "The positive results of U.S. POINTER encourage us to look at the potential for a combination of a lifestyle program and drug treatment as the next frontier in our fight against cognitive decline and possibly dementia."

U.S. POINTER leadership acknowledges participants, their family members and study site staff for their unique and essential contributions: "You helped change what we know about brain health. Thanks to your dedication, time and support, U.S. POINTER delivered groundbreaking results. Your children, grandchildren and generations to come will benefit from the commitment you made."

Both interventions focused on physical exercise, nutrition, cognitive challenge and social engagement, and heart health monitoring, but differed in intensity, structure, accountability and support provided.

- *Structured lifestyle intervention.* Participants attended 38 facilitated peer team meetings over two years, and were provided with a prescribed activity program with measurable goals for: aerobic, resistance and stretching exercise; adherence to the MIND diet; cognitive challenge through BrainHQ training and other intellectual and social activities; and regular review of health metrics and goal-setting with a study clinician.
- *Self-guided lifestyle intervention.* Participants attended six peer team meetings to encourage self-selected lifestyle changes that best fit their needs and schedules. Study staff provided general encouragement without goal-directed coaching.

“The potential to improve cognition with fewer resources and lower participant burden is compelling. It highlights that while not everyone has the same access or ability to adhere to more intensive behavior interventions, even modest changes may protect the brain,” said [Laura D. Baker, Ph.D.](#), Professor of Gerontology and Geriatrics, and Internal Medicine, at Wake Forest University School of Medicine and Advocate Health, and U.S. POINTER principal investigator.

“These are the initial results. Over the coming weeks and months, study leadership will be exploring all of the data collected in the trial to paint an even more comprehensive picture of the U.S. POINTER intervention effects on brain health,” Baker said.

People with cognitive decline and dementia often have a variety of damaging changes in their brain. This means effective treatment will likely require a multi-pronged or combination strategy to address multiple disease mechanisms.

“Complex diseases like heart disease and cancer use combination treatment strategies tailored to individual characteristics. The next generation of treatments for diseases like Alzheimer’s will likely integrate drug and non-drug strategies. U.S. POINTER provides a strong foundation for such combination approaches,” said [Heather M. Snyder, Ph.D.](#), Alzheimer’s Association study primary investigator and senior vice president of medical and scientific relations.

“While these results are fascinating and extremely hopeful, how they are rolled out to the public — especially those at risk for Alzheimer’s and other diseases that cause dementia — needs to be handled with care and individual attention to tailor to the local environment,” said Snyder.

The Alzheimer’s Association has invested nearly \$50 million to lead this study to date, with additional support from the National Institute on Aging at the National Institutes of Health for add-on studies exploring imaging, vascular measures, sleep and gut microbiome-related health data. In addition to its investments to date, the Alzheimer’s Association will invest more than \$40 million over the next four years to continue to follow U.S. POINTER participants, and to bring U.S. POINTER interventions to communities across America.

U.S. POINTER is a phase 3, five-site, two-year, single-blind randomized clinical trial of two lifestyle interventions in older adults at risk for dementia. U.S. POINTER was developed to assess whether the results of the FINGER study [[Lancet](#), 6-6-15] generalize to a larger, more diverse U.S. population at risk for cognitive decline and dementia, using culturally adapted protocols. The primary aim was to compare the effects of two multimodal lifestyle interventions on global cognitive function in 2,000+ at-risk older adults. Secondary aims assessed intervention effects on specific cognitive domains, and potential differences based on baseline cognition, sex, age, APOE-e4 genotype, and cardiovascular risk.

The study was conducted at five geographically dispersed U.S. academic centers and health care systems in partnership with the Alzheimer's Association. Participant eligibility criteria were designed to enrich the risk of cognitive decline and included older age (60-79 years), sedentary lifestyle, suboptimal diet and cardiometabolic health, and family history of memory impairment. 2,111 participants were enrolled and randomized to STR (n=1,056) or SG (n=1,055). Mean age was 68.2 years, 68.9% were female, 30.8% were from ethnoracial minority groups. Seventy-eight percent (78%) reported a first-degree family history of memory loss, and 30% were APOE-e4 carriers. Retention was high, with 89% completing the final 2 year assessment.

At two years, there was a statistically significant intervention group difference on the primary outcome. Global cognitive composite scores (primary outcome) increased over time in both groups but the improvement over time was statistically significant for a greater benefit for the STR versus SG: 0.029 SD per year (95% CI, 0.008-0.050, $P=0.008$). For secondary outcomes, the increase in executive function z-score was greater in STR than SG by 0.037 SD per year (95% CI, 0.010-0.064). Processing speed showed a similar trend but was not statistically significant. There were no group differences in memory.

Looking ahead, the Association will build on the momentum of U.S. POINTER by launching several programs and initiatives, including:

- A personal brain health assessment tool.
- A virtual brain health training program for health care providers.
- A community recognition program for organizations championing brain health.
- A brain health roundtable that will unite leaders across health care, public health, community and corporate sectors to accelerate impact.

About AAIC

AAIC is the world's largest gathering of researchers from around the world focused on Alzheimer's and other diseases that cause dementia. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

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About the Alzheimer's Association

The Alzheimer's Association is a worldwide voluntary health organization dedicated to Alzheimer's care, support and research. Our mission is to lead the way to end Alzheimer's and all other dementia — by accelerating global research, driving risk reduction and early detection, and maximizing quality care and support. Our vision is a world without Alzheimer's and all other dementia®. Visit [alz.org](https://www.alz.org) or call +1 800.272.3900.

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U.S. POINTER: Topline Results of a Large Multisite Randomized Controlled Multidomain Lifestyle Intervention Trial

Abstract/Proposal #96524

Topic Selection: U.S. POINTER: Topline Results and Implications

Slot: 2-19-FRS-C: Monday, July 28, 2025: 2:00 PM-3:30 PM (Scheduled Time: 2:45 PM)

Background: The U.S. Study to Protect Brain Health through Lifestyle Intervention to Reduce Risk (U.S. POINTER) is a Phase 3, multicenter, 2-year, randomized controlled trial assessing the effects of two multidomain lifestyle interventions on cognition in older adults at risk for cognitive decline due to well-established factors such as sedentary behavior, suboptimal diet, and suboptimal cardiometabolic health. A key aim was to test the generalizability of the FINGER findings in a diverse, representative U.S. cohort. Interventions were modeled on FINGER, adapted to U.S. culture, and delivered in collaboration with community partners.

Method: Participants aged 60-79 years meeting pre-specified risk criteria for cognitive decline were randomized (1:1) at five sites to one of two intervention arms. Both arms targeted physical activity, nutrition, cognitive/social challenge and cardiometabolic risk management, but differed in intensity and accountability. The Structured arm (STR) included frequent peer team meetings, regular exercise, the MIND diet, BrainHQ cognitive training, social/cognitive challenge, and monthly blood pressure monitoring. The Self-Guided arm (SG) included fewer peer team meetings and general health education with support to encourage health behaviors. The primary outcome, assessed at baseline and every six months, was change in global cognition, measured using a composite score based on tests of executive function, episodic memory, and processing speed. Secondary outcomes included domain-specific cognitive scores, Clinical Dementia Rating-Sum of Boxes, functional ability, frailty, and intervention response by subgroups (e.g., APOE4 carriers).

Result: A total of 2,111 participants (mean age 68 ± 5 years, 69% female, 31% from minoritized ethnoracial groups) were randomized. Retention exceeded 94%, and intervention adherence remained high throughout the 2-year intervention period. Topline findings on intervention effects for primary and secondary outcomes will be presented. Additionally, two participants will share testimonials about their trial experiences.

Conclusion: U.S. POINTER, the largest lifestyle intervention trial globally, successfully met ambitious recruitment goals and engaged a diverse, at-risk cohort while maintaining high retention and participation rates. The topline results will provide pivotal evidence on the effectiveness of multidomain interventions to improve cognition or slow decline in older U.S. adults, with high potential to inform public health initiatives aimed at reducing Alzheimer's disease and related dementia risk.

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