Brain Health through the Lifespan

Jay B. Lusk, MD, MBA
Assistant Professor of Neurology
Assistant Professor of Medicine
Assistant Professor of Health Economics, Systems, and Policy



Why Brain Health, Why Now



57 million

People living with dementia

WHO estimate for 2021



~10 million

New cases every year

A growing global burden



Up to 45%

Potentially preventable or delayable

By addressing modifiable factors

WHO dementia estimates; Livingston et al. Lancet Commission, 2024

A Life-Course Framework



Early life

Build reserve

Education and learning
Cognitive enrichment
Supportive environments

Midlife

Reduce exposure

Blood pressure, glucose, lipids
Obesity and inactivity
Hearing, tobacco and alcohol

Later life

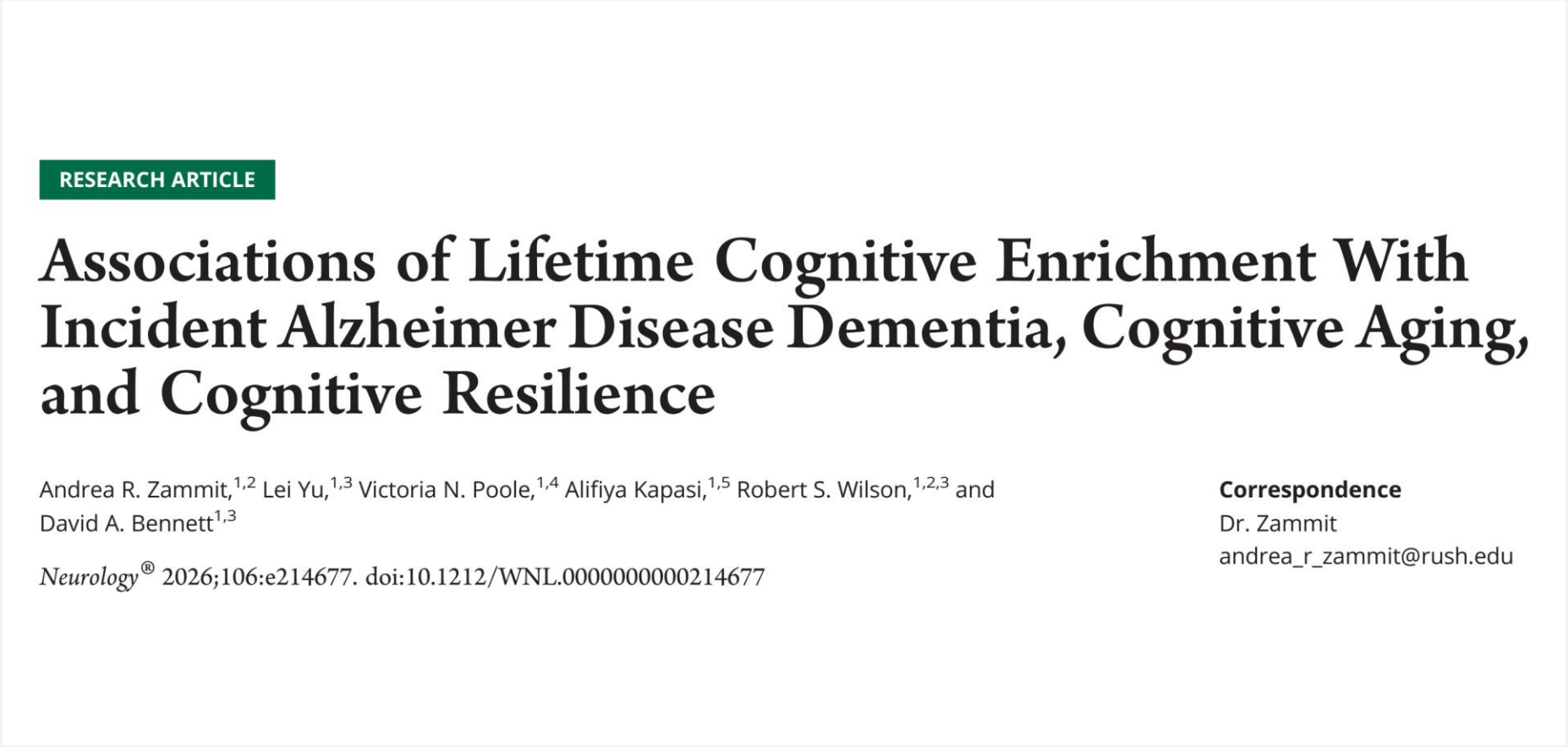
Preserve function

Social and physical activity
Vision and hearing care
Cardiometabolic management

Across life Sleep • Cleaner air • Head injury prevention • Stroke prevention

WHO life-course framework; Livingston et al. Lancet Commission, 2024

Lifetime Cognitive Enrichment



RESEARCH ARTICLE

Associations of Lifetime Cognitive Enrichment With Incident Alzheimer Disease Dementia, Cognitive Aging, and Cognitive Resilience

Andrea R. Zammit,[1,2] Lei Yu,[1,3] Victoria N. Poole,[1,4] Alifiya Kapasi,[1,5] Robert S. Wilson,[1,2,3] and David A. Bennett[1,3]

Correspondence
Dr. Zammit
andrea_r_zammit@rush.edu

Neurology® 2026;106:e214677. doi:10.1212/WNL.0000000000214677

Longitudinal observational evidence; enrichment spans the entire lifespan.

Early Life Foundations

38%

lower hazard of Alzheimer dementia
per 1-unit higher lifetime
cognitive enrichment score



Education and access to learning are brain health policy

Zammit et al. Neurology, 2026. Observational cohort

Midlife Is the Leverage Point

Vascular and metabolic health shape cognitive aging

Decades of exposure

Physical activity and healthier glucose levels in midlife are associated with slower later cognitive decline.

Different settings

214,251 adults across 14 countries and regions: risk-factor prevalence varies substantially.

Different vulnerability

In a study of >17,000 adults, some risk factors had stronger cognitive associations in women.

Observational evidence: Nichols et al.; Fitzhugh et al.; midlife cardiovascular studies, 2026

Midlife Cardiovascular Health

Received: 2 December 2025 | Revised: 26 May 2026 | Accepted: 15 June 2026

DOI: 10.1002/bsa3.70096

Alzheimer's & Dementia
Behavior & Socioeconomics of Aging

RESEARCH ARTICLE

Longitudinal association between midlife cardiovascular health and cognitive change in a bi-ethnic cohort

Janette Vazquez[1] | Rebecca Bernal[1] | Luis A. Aguirre[1] | Jesus D. Melgarejo[2,3,4] | Gladys Maestre[2,3,4] | Sudha Seshadri[1,5,6] | Helen P. Hazuda[1,7] | Chen-Pin Wang[1,8] | Claudia L. Satizabal[1,5,6,8]

Physical activity and glucose control are linked to later cognitive trajectories.

Risk Priorities Vary by Country



The Lancet Healthy Longevity

Date: June 2026

Article: 100867

Volume: Volume 7, Issue 6

View accessibility

Research article ● Open access Under a Creative Commons license ↗ Get rights and content ↗

Articles

Differences in the prevalence and patterns of dementia risk factors across 14 countries and regions: a harmonised cross-national analysis

Emma Nichols PhD [a b *], Zachary J Kunicki PhD [d *], Michael Markot MPH [a], Drystan Phillips MA [a], Jenny Wilkens MPH [a], Prof Alden L Gross PhD [e f], Prof Jinkook Lee PhD [a c] Show more

View PDF Download full issue Cite Add to Mendeley Share 10.1016/j.lanhl.2026.100867 ↗

Article Recommended articles Cited by (2) Metrics

214,251 adults across 14 countries and regions.

Sex Differences in Risk and Cognition

Fitzhugh and Pa *Biology of Sex Differences* (2026) 17:110
https://doi.org/10.1186/s13293-026-00908-7

Biology of Sex Differences

RESEARCH Open Access

Sex differences in modifiable risk factors of dementia and their associations with cognition

Megan C. Fitzhugh[1,2] and Judy Pa[1,2*]

17,182 participants; risk prevalence and cognitive associations differ by sex.

The Original FINGER Trial



The Lancet

Date: 6–12 June 2015

Pages: 2255-2263

Volume: Volume 385, Issue 9984

Research article ● Full text access Get rights and content ↗

Articles

A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

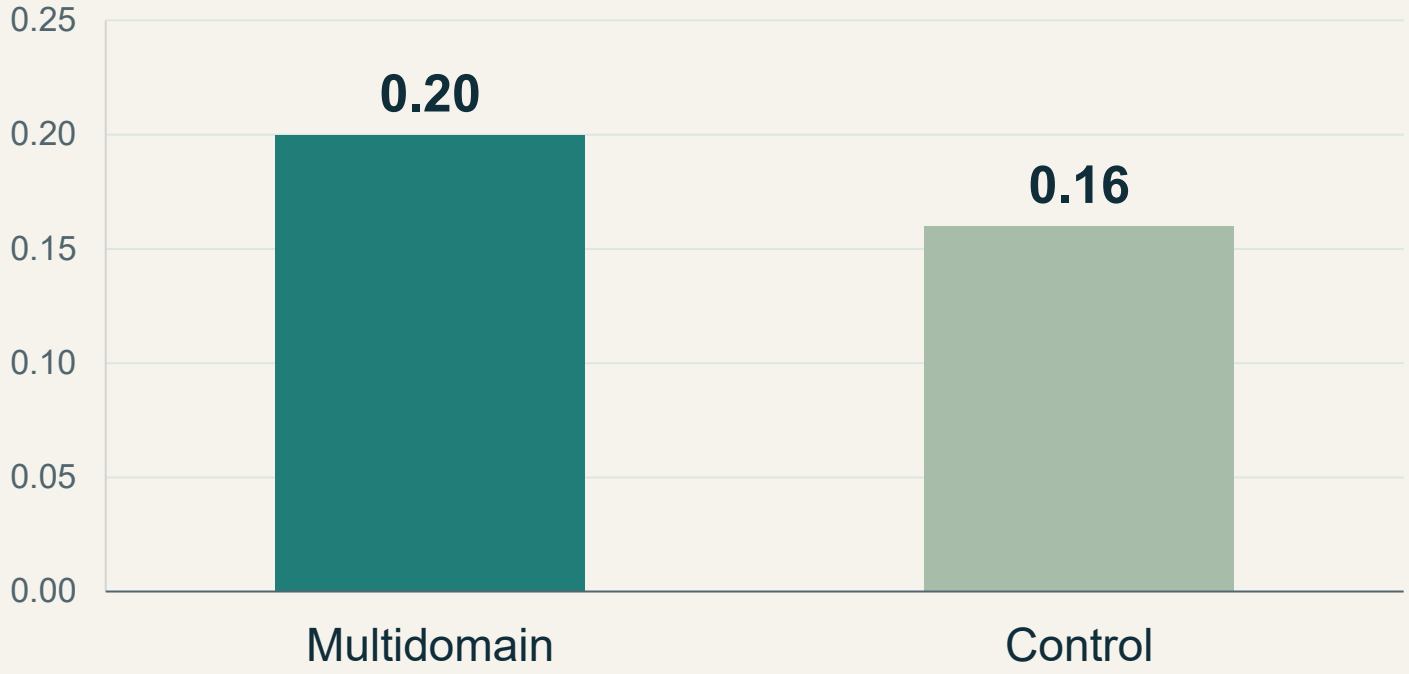
Tiia Ngandu PhD [a c], Jenni Lehtisalo MSc [a], Alina Solomon PhD [c d f], Esko Levälahti MSc [a], Satu Ahtiluoto MD [a], Prof Riitta Antikainen PhD [g h i], Prof Lars Bäckman PhD [f], Tuomo Hänninen PhD [j], Prof Antti Jula PhD [a], Prof Tiina Laatikainen PhD [a e], Jaana Lindström PhD [a], Francesca Mangialasche PhD [f], Teemu Paajanen MA Psy [l], Satu Pajala PhD [b], Prof Markku Peltonen PhD [a], Prof Rainer Rauramaa PhD [k m], Anna Stigsdotter-Neely PhD [n], Prof Timo Strandberg PhD [g o], Prof Jaakko Tuomilehto PhD [a p q r s], Prof Hilkka Soininen PhD [d j]...Prof Miia Kivipelto PhD [a c d f] Show more

View PDF Download full issue Cite Add to Mendeley Share 10.1016/S0140-6736(15)60461-5 ↗

Two years of multidomain intervention in at-risk older adults.

The FINGER Model

Change in cognitive composite over 2 years (z score)



~25%

greater cognitive improvement

Dietary counseling
Exercise
Cognitive training
Vascular risk monitoring

Ngandu et al. Lancet, 2015

US POINTER

Research

JAMA | Original Investigation

Structured vs Self-Guided Multidomain Lifestyle Interventions for Global Cognitive Function

The US POINTER Randomized Clinical Trial

Laura D. Baker, PhD; Mark A. Espeland, PhD; Rachel A. Whitmer, PhD; Heather M. Snyder, PhD; Xiaoyan Leng, MD, PhD; Laura Lovato, MS; Kathryn V. Papp, PhD; Melissa Yu, MD; Miia Kivipelto, MD, PhD; Ashley S. Alexander, MHSA; Susan Antkowiak, BS; Maryjo Cleveland, MD; Claire Day, BSW; Richard Elbein, MS; Sarah Tomaszewski Farias, PhD; Deborah Felton, BS; Katelyn R. Garcia, MS; Darren R. Gitelman, MD; Sarah Graef, DC; Marjorie Howard, MSPH; Jeffrey Katula, PhD; Katherine Lambert, BA; Olivia Matongo, MPH; Anne Marie McDonald, MEd, MBA; Valory Pavlik, PhD; Rema Raman, PhD; Stephen Salloway, MD, MS; Christy Tangney, PhD; Jennifer Ventrelle, MS; Sharon Wilmoth, BA; Benjamin J. Willliams, MD, PhD; Rena Wing, PhD; Nancy Woolard; Maria C. Carrillo, PhD

US POINTER: Design

2,111

adults aged 60–79
Five US sites, two years

Sedentary lifestyle, suboptimal diet
and at least two additional risk criteria

Structured

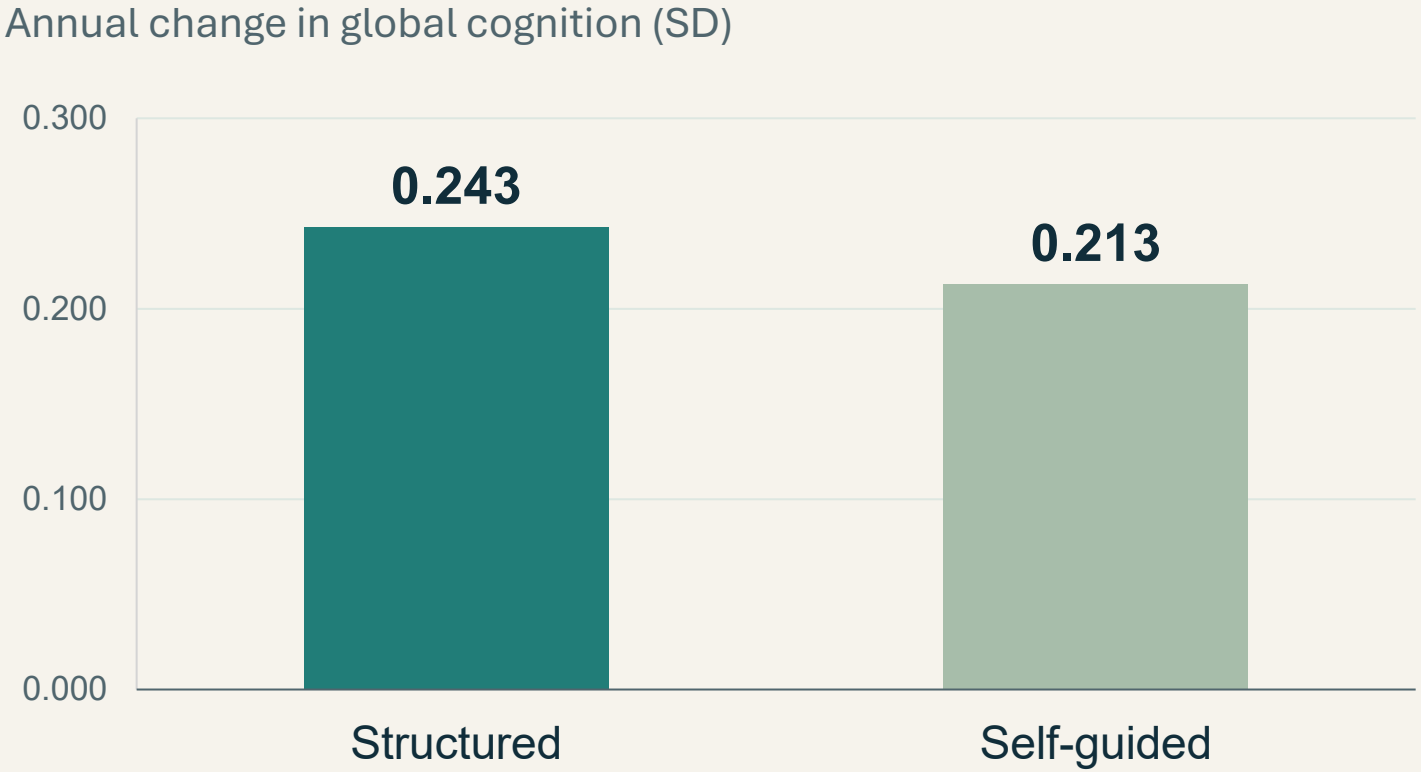
Higher intensity, coaching and accountability

Self-guided

Lower intensity, participant-led change

Both: activity, nutrition, cognitive and social challenge, health monitoring

US POINTER: Results



+0.029

SD/year adjusted difference
95% CI 0.008–0.050

Consistent across key subgroups
Larger benefit with lower baseline cognition

US POINTER: Takeaways



Support adds benefit

Both groups improved, but the structured program improved more.



Interpret carefully

Cognitive change is not dementia incidence.



Deliver at scale

Make coaching and accountability affordable and accessible.

Baker, Espeland et al. JAMA, 2025

LatAm-FINGERS



The Lancet

Date: 1–7 August 2026

Pages: 417-429

Volume: Volume 408, Issue 10553

View accessibility information

Research article ● Full text access Get rights and content ↗

Articles

Multidomain lifestyle intervention for the prevention of cognitive decline in at-risk older adults in Latin America (LatAm-FINGERS): a single-blind, multicentre, randomised controlled trial

Dr Lucia Crivelli PhD [a] * ✉, Claudia Kimie Suemoto MD [d e f], Ana Luisa Sosa PhD [g], Francisco Lopera MD [h †], David Aguillón PhD [h], Ricardo Francisco Allegri PhD [a], Prof Ricardo Nitrini MD [i], Ismael Luis Calandri MD [a j], Lina Velilla-Jiménez MSc [h], Prof Mônica Sanches Yassuda PhD [i k], Natalia Acosta-Baena PhD [h], Rosa María Salinas PhD [g], Ana Charamelo MSc [l], Carolina Delgado Derio MD [m], Daisy Miguelina Acosta MD [n], Jorge Mario León-Salas MD [o], Lissette Duque-Peñailillo MD [s], María Isabel Cusicanqui MD [t v], Nilton Custodio PhD [w], Adriana Anchia-Alfaro MD [o]... Valeria Contreras Show more

View PDF Download full issue Cite Add to Mendeley Share

10.1016/S0140-6736(26)01278-X ↗

A culturally adapted multidomain intervention across 11 countries.

World-Wide FINGERS: The Global Network

70+

countries with research teams

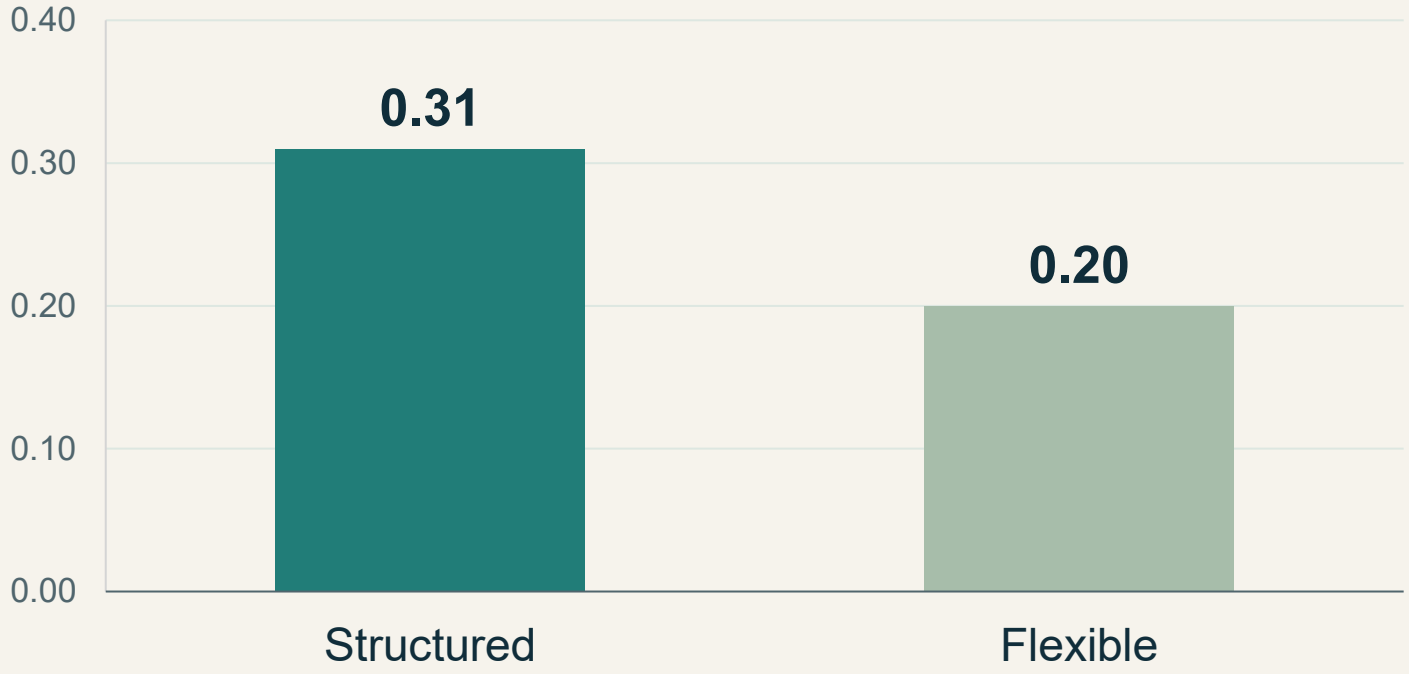
25+

completed trials
A similar number underway or planned



LatAm-FINGERS Results

Annual change in global cognition (SD)



55%

greater annual improvement
0.11 SD/year difference
95% CI 0.06–0.15

1,065 participants
11 countries
2 years

Crivelli et al. Lancet, 2026; AAIC 2026, London

Mixed Results Elsewhere in the Network

Trial	Primary finding	Interpretation
MAPT, France	No significant primary cognitive benefit	Some earlier subgroup signals
preDIVA, Netherlands	No overall dementia reduction	Later pooled analysis found no responder subgroup
AgeWell.de, Germany	No overall global cognitive benefit	Secondary and subgroup findings remain exploratory

Population, intervention intensity and comparator matter.
Subgroup signals require confirmation.

MAPT / preDIVA pooled analysis, 2025; AgeWell.de, 2024

Next Step: Lifestyle Plus Drug

PROTECT-Cog

Multidomain lifestyle
Structured coaching
or structured-lite support

+

Metabolic therapy
A GLP-1 agonist
or similar metabolism-targeting drug

evoke and evoke+: GLP-1RA as a dementia treatment



The Lancet

Date: 30 May–5 June 2026

Pages: 2167-2179

Volume: Volume 407, Issue 10544

Research article ● Open access Under a Creative Commons license ↗ Get rights and content ↗

Articles

Efficacy and safety of oral semaglutide 14 mg (flexible dose) in early-stage symptomatic Alzheimer's disease (evoke and evoke+): two phase 3, randomised, placebo-controlled trials

Prof Jeffrey L Cummings MD [a], Prof Alireza Atri MD [b c d], Prof Mary Sano PhD [e], Prof Henrik Zetterberg MD [f g h i j k l], Prof Philip Scheltens MD [m n], Filip Knop MD [o], Peter Johannsen MD [o], Christian A Wichmann MSc [o], Rikke Mortensen Abschneider PhD [o], Teresa Leon MD [o *], Prof Howard H Feldman M [p]

Show more

View PDF Download full issue Cite Add to Mendeley Share

10.1016/S0140-6736(26)00459-9 ↗

Treatment in symptomatic Alzheimer disease did not demonstrate clinical efficacy.

GLP-1s: Prevention Versus Treatment

Treatment

3,808

amyloid-positive adults with
MCI or mild Alzheimer dementia

Oral semaglutide did not slow CDR-SB progression at 104 weeks

Prevention

An earlier window?

Can metabolic therapy add benefit before symptomatic disease?

PROTECT-Cog will test the hypothesis

evoke / evoke+, Lancet, 2026; PROTECT-Cog announcement

WHO Guidelines, Second Edition

A broader prevention framework



Expanded scope

Sleep, stroke, head injury, vision, HIV, air pollution, hormone therapy and multidomain interventions.



Sensory care

Hearing aids may be offered for possible dementia risk reduction in adults with hearing loss.



Treatment boundaries

Extra dementia benefit from intensive BP or glucose targets remains uncertain. Do not initiate menopausal hormone therapy solely for dementia prevention at age 65+.

WHO, July 2026. Guidance for adults without dementia, including MCI

Other Notable Recent Findings



Cognitive training

ACTIVE: speed training with boosters was associated with fewer claims-based dementia diagnoses over 20 years.



Vaccination

A Welsh natural experiment estimated 20% lower dementia probability after live zoster vaccination.



Environment

A Swedish 16-year cohort linked greener surroundings to lower dementia risk. Observational evidence.



Diagnostics

FDA cleared Roche’s Elecsys pTau217 assay in August 2026. Diagnostic progress is distinct from prevention.

Evidence types differ across these findings.

Cognitive Training: 20-Year Follow-up

Received: 13 October 2025 | Revised: 1 December 2025 | Accepted: 3 December 2025

DOI: 10.1002/trc2.70197

Alzheimer's & Dementia
Translational Research & Clinical Interventions

RESEARCH ARTICLE

Impact of cognitive training on claims-based diagnosed dementia over 20 years: evidence from the ACTIVE study

Norma B. Coe[1,2] | Katherine E. M. Miller[3] | Chuxuan Sun[1] | Elizabeth Taggert[4] | Alden L. Gross[5] | Richard N. Jones[6] | Cynthia Felix[7] | Marilyn S. Albert[8] | George W. Rebok[9] | Michael Marsiske[10] | Karlene K. Ball[11] | Sherry L. Willis[12]

Claims-based dementia outcomes from the ACTIVE trial follow-up.

Zoster Vaccination and Dementia



Article

A natural experiment on the effect of herpes zoster vaccination on dementia

https://doi.org/10.1038/s41586-025-08800-x

Received: 4 November 2023

Markus Eyting[1,2,3,9], Min Xie[1,4,9], Felix Michalik[1,4], Simon Heß[5], Seunghun Chung[1] & Pascal Geldsetzer[1,6,7,8]✉

Quasi-experimental study, one of several on this topic

Residential Greenspace and Dementia

Received: 8 May 2026 | Revised: 18 August 2026 | Accepted: 19 August 2026

DOI: 10.1002/alz.71835

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

RESEARCH ARTICLE

Precision residential greenspace, urban environmental exposures, and incident dementia among older adults in Sweden: A 16-year cohort study

Cecilia U. D. Stenfors[1,2] | Jing Wu[2] | Giulia Grande[2] | Andrei Pyko[3,4] | Mare Löhmus[3,4] | Göran Pershagen[3] | Debora Rizzuto[2]

A Swedish 16-year observational cohort although limited by residual confounding

Practical Brain Health Prescription

Move regularly and eat for heart health

Manage blood pressure, glucose and lipids

Treat hearing and vision loss

Stay socially and cognitively engaged

Avoid tobacco and limit alcohol

Protect sleep and prevent head injury



Structure and support make change easier to sustain

WHO risk-reduction guidance; multidomain intervention trials

Open Questions

01 Will cognitive gains translate into fewer dementia diagnoses?

02 Who benefits most, and how should prevention target risk?

03 How can health systems deliver structured support at scale?

04 Will lifestyle plus medication outperform either approach alone?

05 How should priorities adapt across countries and communities?

Conclusions

Brain health is a lifelong project

Structured lifestyle programs improve cognition
in diverse at-risk older populations.

WHO guidance supports action across the lifespan.
Long-term dementia prevention remains the key test.

Next: combination prevention and scalable support