ALZHEIMER'S ASSOCIATION

AAIC 25

ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE®

JULY 27-31 > TORONTO, CANADA

AAIC Update, January 8, 2026

Sheena K Aurora, M.D.
Vice President Medical Affairs
Alzheimer's Association

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Scientific Sessions

148
Scientific Sessions

737
Podium Presentations

Topics included…

- Biological underpinnings of disease
- Learnings in recruitment and care science
- Diversification of the clinical trial pipeline
- Growing understanding of health disparities
- Treatment updates and growing understanding of treatment-related side effects
- Advances in tools for detection and diagnosis
- Growing understanding of contributions to risk across life
- AND MORE…

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News You Can Use

Risk Reduction and Healthy Habits

- Lead Pollution Linked To Memory Problems In Older Adults
- Walking, Lifestyle Changes May Slow Cognitive Decline in APOE4 Carriers
- US POINTER Results

Early Detection and Diagnosis

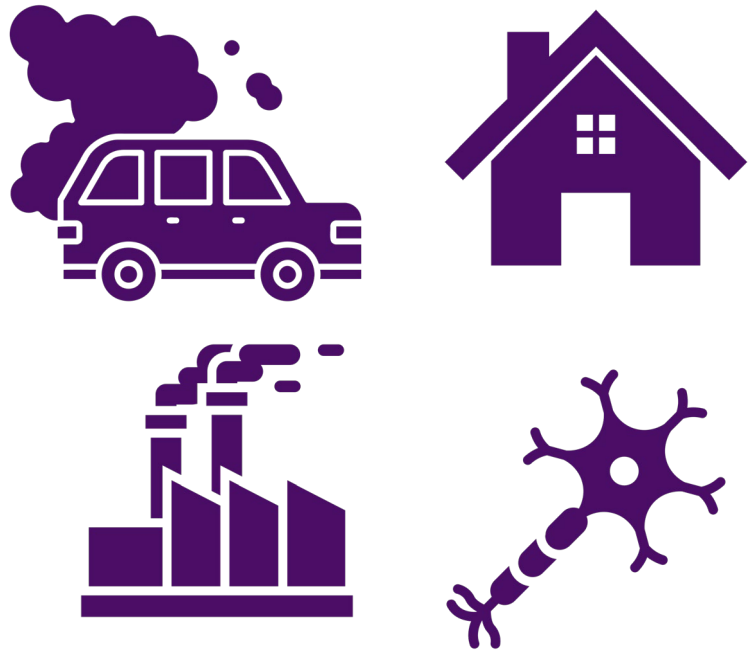
- Clinical Practice Guidelines – Blood-Based Biomarkers and Cognition

Treatment

- Combination of Common Cardiovascular Drugs May Protect the Brain
- Studies Provide First Real-World Results for Anti-Amyloid Alzheimer's Drugs

Decades-old Lead Pollution Linked To Memory Problems In Older Adults, Study Finds

- Historic levels of lead air pollution are associated with memory problems 50 years later
  - A study of more than 600,000 adults links early-life environmental lead exposure to memory problems later in life.
  - People who grew up in areas with moderate to extremely high atmospheric lead levels from 1960-1974 were 20% more likely to report memory problems as adults 50 years later.
- Living near lead-polluting sites may affect memory
- Lead exposure may leave a lasting molecular imprint on the brain, making it more vulnerable to age-related diseases, including Alzheimer's.



Eric Brown, M.D., MSc, et al. AAIC 2025 Poster
Kathryn C. Conlon, Ph.D., MPH, et al. AAIC 2025 Poster
Junkai Xie, Ph.D., et al. AAIC 2025 Poster

Walking, Lifestyle Changes May Slow Cognitive Decline in APOE4 Carriers

- Research from a 10-year Health ABC study shows walking and other lifestyle choices could be especially beneficial in helping to reduce cognitive decline for people with the APOE-e4 Alzheimer's risk gene variant
  - APOE4 is the strongest known genetic risk factor for late-onset Alzheimer's.
  - Black Americans had greater protection for overall cognition.
  - White females' cognition benefited more in processing & thinking speed.
- Overall, a healthy lifestyle can benefit even those at a greater risk of developing cognitive decline

1 What we set out to learn

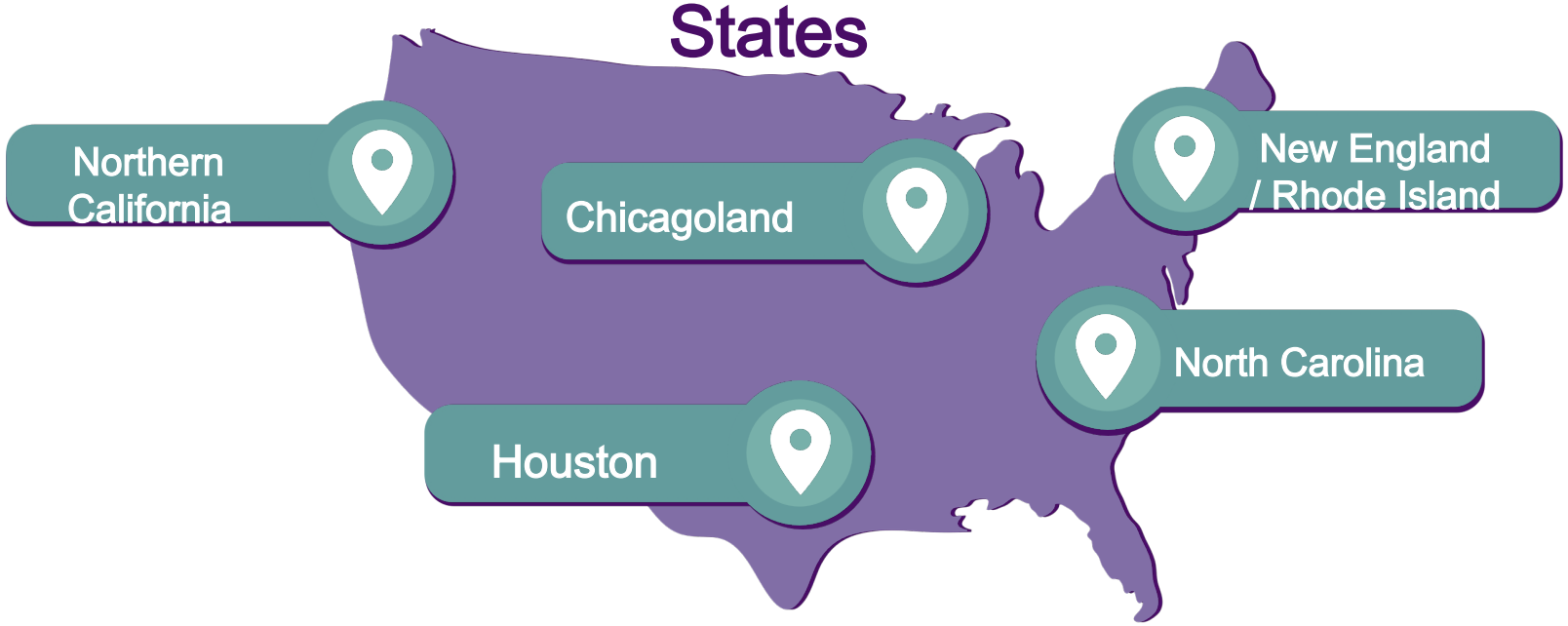
THE POINT OF POINTER

To understand whether lifestyle interventions can protect brain health and reduce risk of dementia in a large, diverse population of older adults in the United States—and whether varying levels of structure and support lead to different outcomes

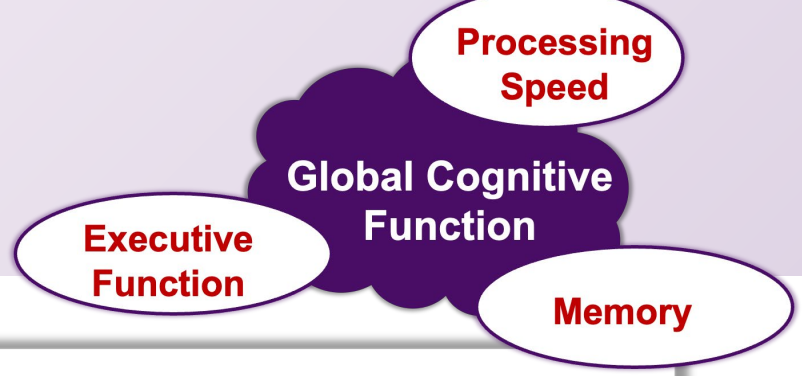
2 What we did

U.S. POINTER LOCATIONS

5 Sites Across the United States



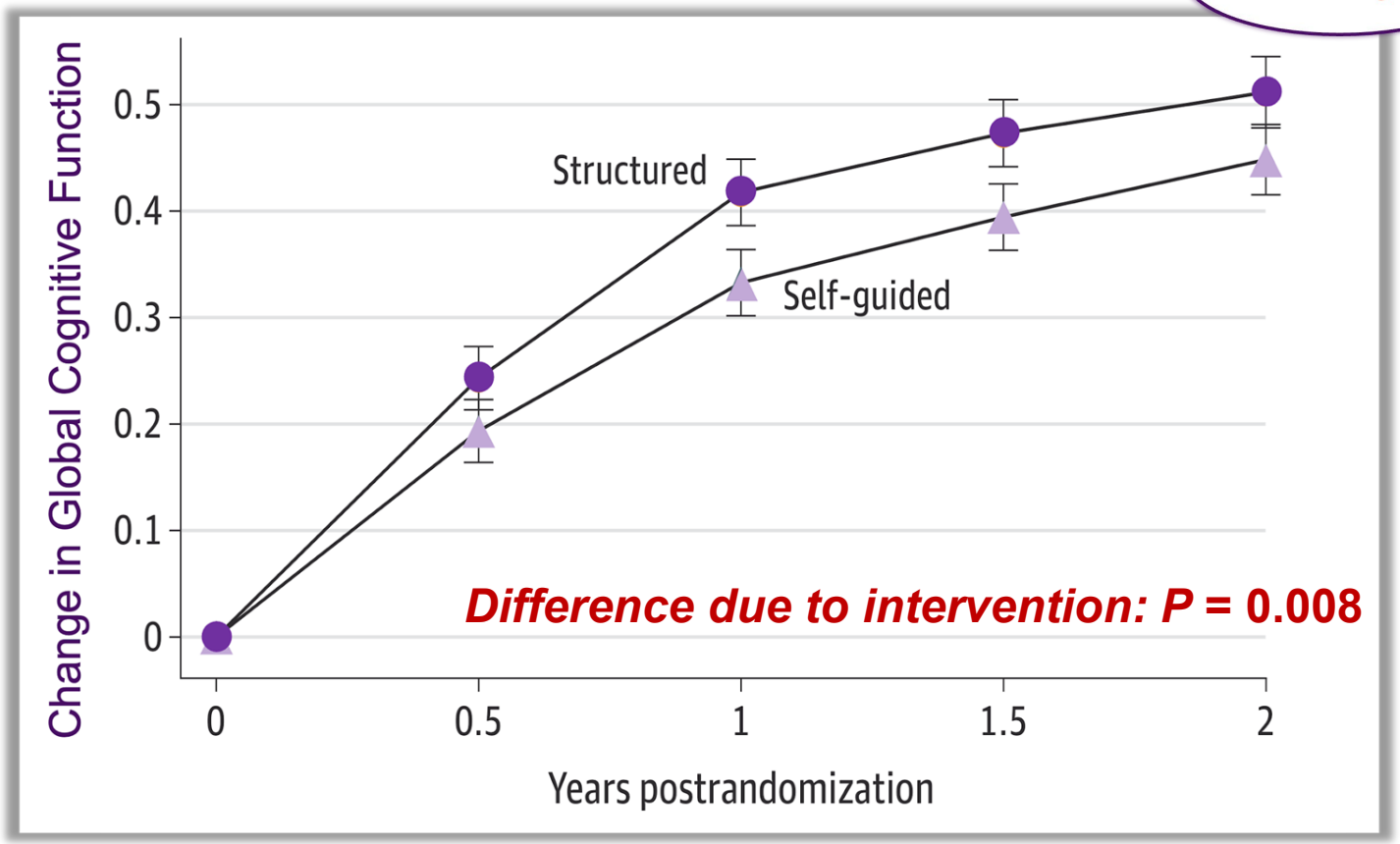
3 What we found



KEY TAKEAWAYS

1. Cognitive function improved over time for BOTH groups

2. **The Structured intervention had a significantly greater benefit**



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Clinical Practice Guidelines in Development

A collaboration between the Alzheimer's Association, guideline panels of clinical and subject-matter experts, partner organizations, and patient representatives are working to build clinical guidance that distills the best available evidence and translates it into clear and actionable recommendations for clinical practice.

Blood-Based Biomarkers in specialty care

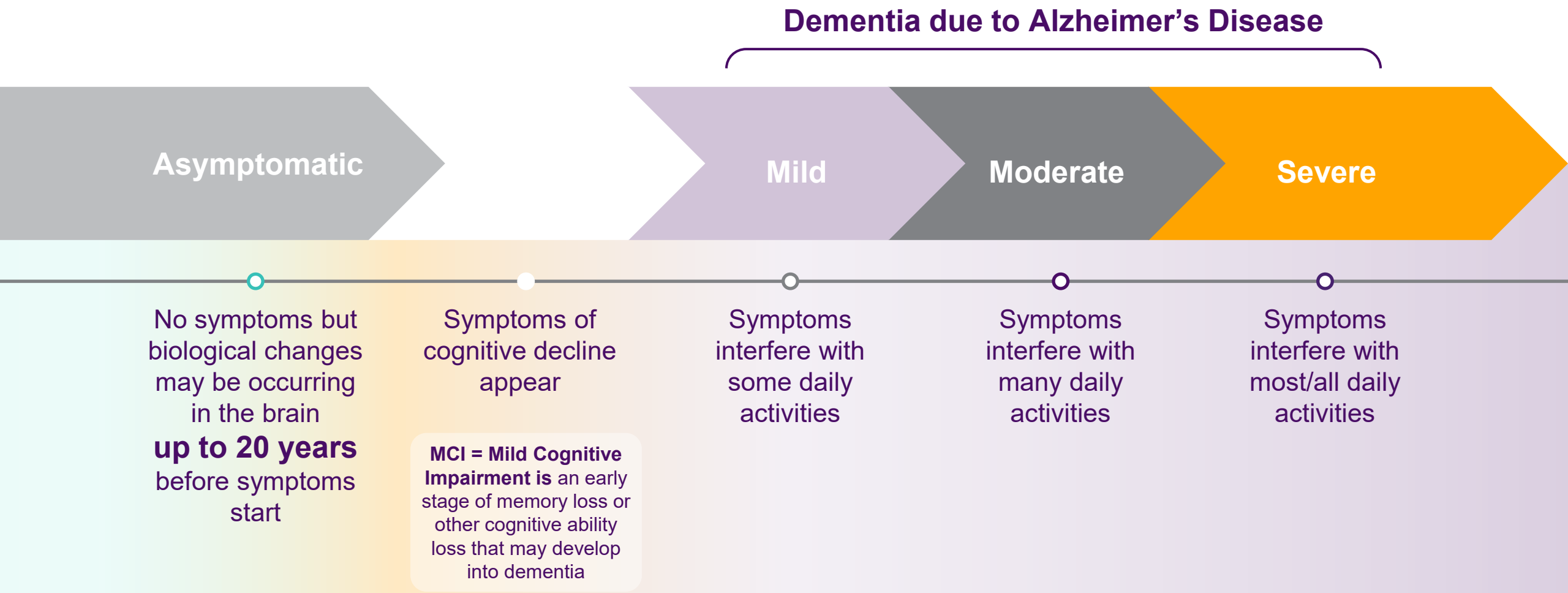
Can a BBM test be used as a **triaging test** for AD in the diagnostic work-up of patients with objective cognitive impairment in specialized care?

Can a BBM test be used as **a confirmatory test** for AD in specialty care settings?

Cognitive assessment tools for the detection of cognitive impairment in primary health care settings

In English- and Spanish-speaking adults aged 55+ in primary care, **which brief test should be used** for the early detection of cognitive impairment (including MCI and dementia)?

Alzheimer's Disease is a Continuum



Benefits of an Early and Accurate Diagnosis

Medical Benefits

- Access to current treatments
- An opportunity to participate in clinical trials
- A chance to prioritize health, including making lifestyle changes

Emotional and Social Benefits

- More time to plan for the future, access resources
- Time to plan end-of-life decisions

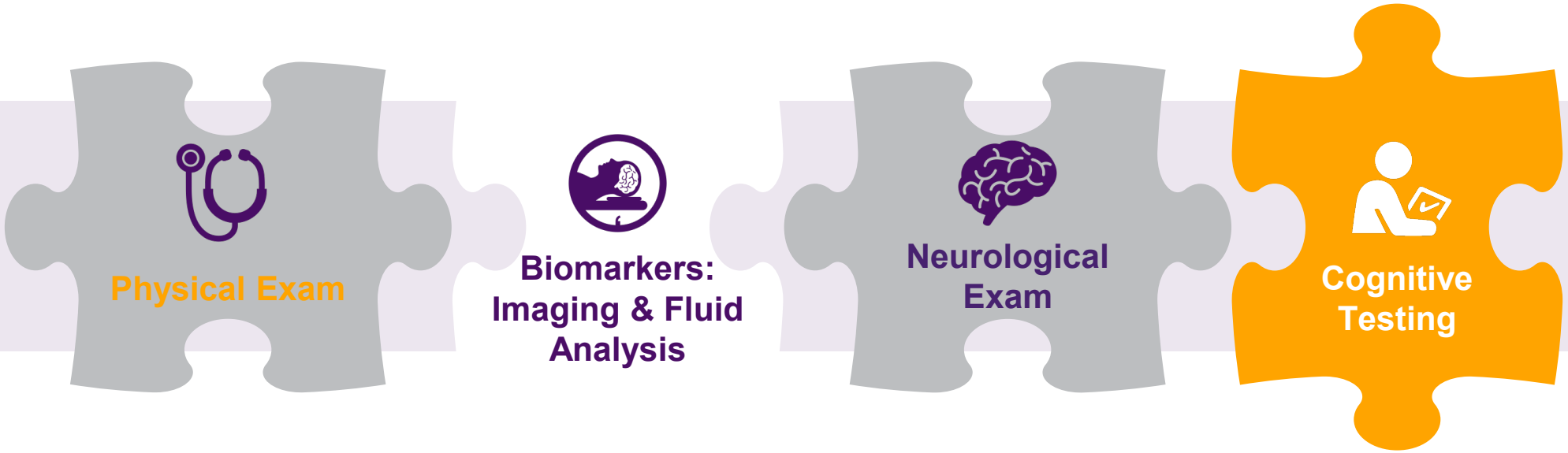
Financial Benefits

- Cost savings for families
- Cost savings for the U.S. government

How is Alzheimer's Currently Diagnosed?

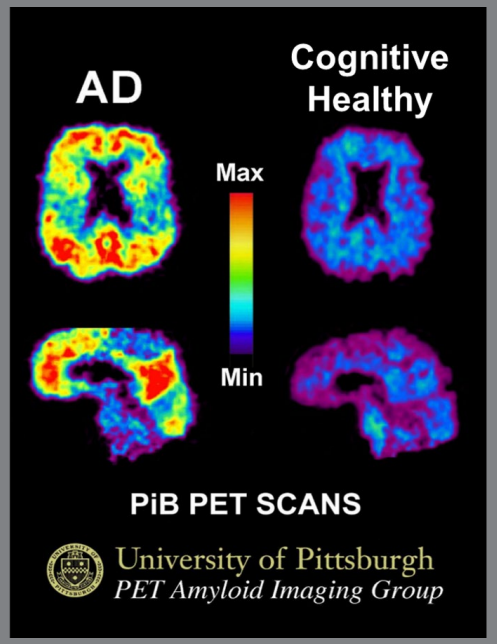
There is no single test that can determine if a person is living with Alzheimer's disease or another dementia.

Doctors use a combination of diagnostic tools combined with medical history to make an accurate diagnosis.



What is a Biomarker?

A biomarker is a biological marker that measures change.



Biomarkers are reliable predictors and indicators of disease and disease progression.

For example:

- Glucose is a biomarker for insulin resistance and diabetes.
- Cholesterol is a biomarker for heart disease

Uses of biomarkers in Alzheimer's disease include:

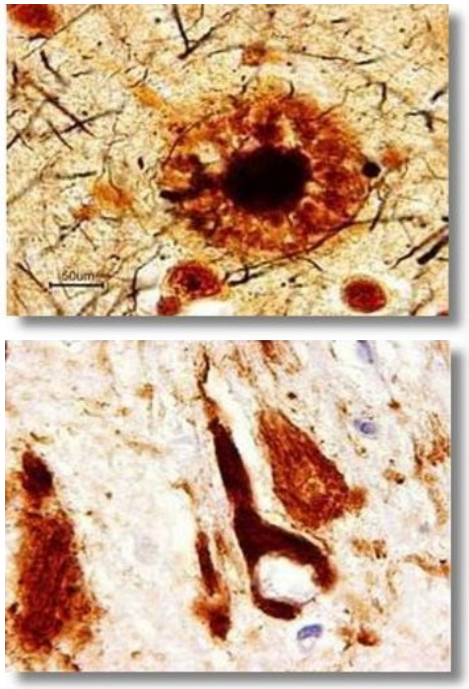
Diagnostic: used to determine diagnosis

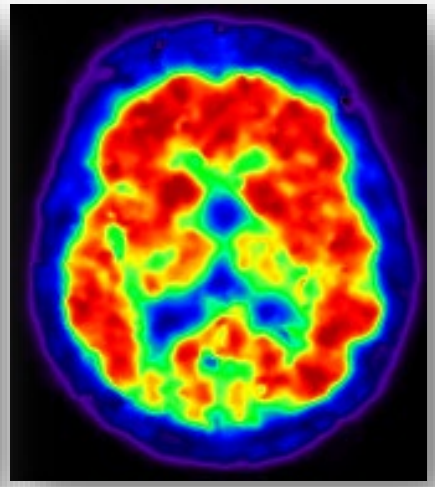
Enrichment: used to determine entry into a clinical trial

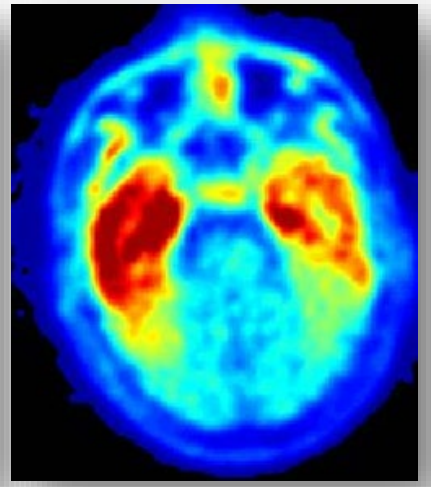
Prognostic: used to determine course of illness

Predictive: used to track outcomes and side effects of treatments

Biomarker Development for Hallmark Brain Changes







1906
Amyloid and Tau Pathology

Late 1990s
CSF Aβ, Tau, p-Tau

Mid-late 2000s
Amyloid PET

Mid-late 2010s
Tau PET

2020s
Plasma Aβ, Tau, p-Tau

Progress Toward a Blood Test

- Global race to develop blood-based biomarkers for Alzheimer's and other dementia
- More research is needed to validate amyloid beta and tau in blood by comparing to imaging and cognitive testing
- Blood-based biomarkers are making remarkable progress

Take home message:
While more research is needed, blood tests are sufficiently accurate to be **used by experts as** one piece of the **diagnostic workup** in specialty practice.
And soon will be in hands of primary care.

Blood Biomarkers on the Horizon

Tau	Amyloid-β	Neurodegeneration	Additional
pTau 217/npTau 217 pTau 181	Aβ 42/40	NfL	APOE Vitamin's TSH Folate Others

Markers listed are examples of what blood tests can measure that are currently available in the clinic today

- While progress is being made toward blood biomarker discovery, there are currently **two FDA-cleared** blood biomarkers for Alzheimer's *

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

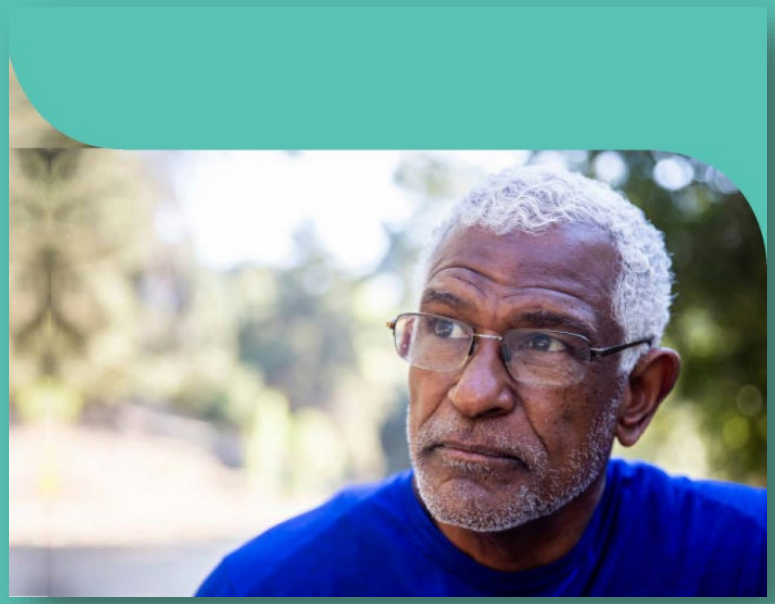
REVIEW ARTICLE

The Alzheimer's Association appropriate use recommendations for blood biomarkers in Alzheimer's disease

Oskar Hansson[1,2] | Rebecca M. Edelmayer[3] | Adam L. Boxer[4] | Maria C. Carrillo[3] | Michelle M. Mielke[5] | Gil D. Rabinovici[4] | Stephen Salloway[6] | Reisa Sperling[7] | Henrik Zetterberg[8,9,10,11,12] | Charlotte E. Teunissen[13]

*As of Sept 2024

The Right Test, For the Right Patient, at the Right Time



"Doc, I'm worried I have Alzheimer's disease. What testing do you recommend for me?"

Alzheimer's Association Clinical Practice Guidance

1

Building a library of clinical guidance: distilling best available evidence and translates it into clear, actionable recommendations for clinical practice.

2

Collaboration between the organization, guideline panels of clinical and subject-matter experts, partner organizations, and patient representatives.

3

A transparent guideline development framework and methodology is used to move the panel from the evidence to decisions (or recommendations).

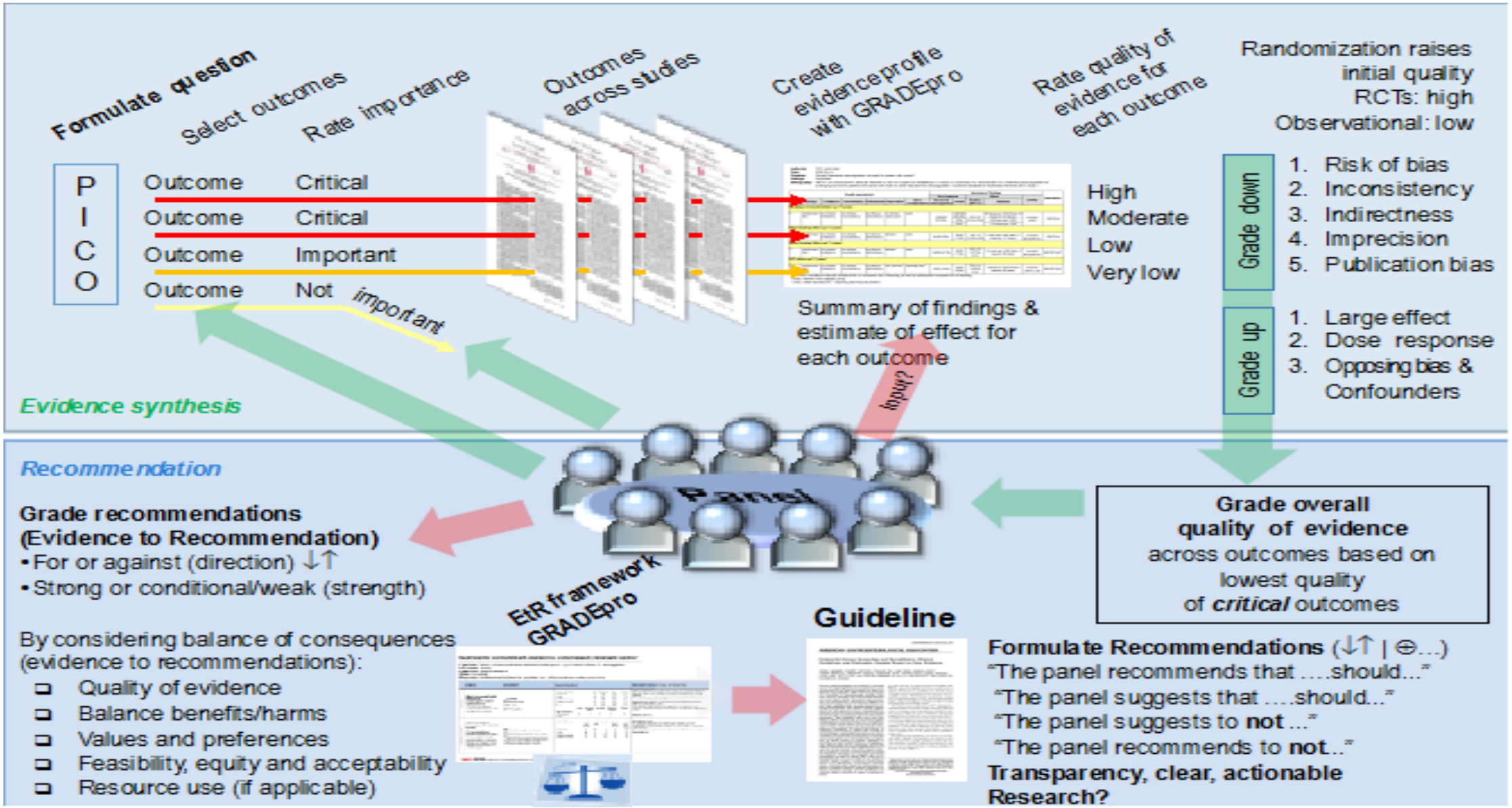
4

Upcoming topics include guidance on the use of:

- **Cognitive assessment tools**
- **Blood biomarker tests**

5

Deliverables will include peer-reviewed journal publications, clinical tools, and educational courses and presentations.


Formulate question
Select outcomes
Rate importance
Outcomes across studies
Create evidence profile with GRADEpro
Rate quality of evidence for each outcome
Randomization raises initial quality
RCTs: high
Observational: low
P
I
C
O
Outcome Critical
Outcome Critical
Outcome Important
Outcome Not important
Summary of findings & estimate of effect for each outcome
High
Moderate
Low
Very low
Grade down
1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias
Grade up
1. Large effect
2. Dose response
3. Opposing bias & Confounders
Evidence synthesis
Input?
Panel
Recommendation
Grade recommendations (Evidence to Recommendation)
• For or against (direction) ↓↑
• Strong or conditional/weak (strength)
By considering balance of consequences (evidence to recommendations):
Quality of evidence
Balance benefits/harms
Values and preferences
Feasibility, equity and acceptability
Resource use (if applicable)
EtR framework GRADEpro
Guideline
Grade overall quality of evidence across outcomes based on lowest quality of critical outcomes
Formulate Recommendations (↓↑ | ⊕...)
"The panel recommends that ....should..."
"The panel suggests that ....should..."
"The panel suggests to not ..."
"The panel recommends to not.."
Transparency, clear, actionable
Research?

Clinical question

- Can a BBM test be used as a **triaging test for AD** in the diagnostic work-up of patients with ***objective* cognitive impairment** who present for **specialized care** related to memory disorders?

- Can a BBM test be used as a **confirmatory test for AD** in the diagnostic work-up of patients with ***objective* cognitive impairment** who present for **specialized care** related to memory disorders?

Good Practice Statement

A BBM test should not be obtained before a comprehensive clinical evaluation by a healthcare professional, and test results should always be interpreted within the clinical context. The panel urges clinicians to consider the pre-test probability of AD pathology for each patient when deciding whether or not to use a BBM test.

Recommendations

- In patients with objective cognitive impairment presenting for specialized memory-care, the panel suggests using a high-sensitivity BBM test as a **triaging** test in the diagnostic workup of Alzheimer's disease **(Conditional recommendation, Low certainty evidence)**

- In patients with objective cognitive impairment presenting for specialized memory-care, the panel suggests using a high-sensitivity and high-specificity BBM test as a **confirmatory** test in the diagnostic workup of Alzheimer's disease **(Conditional recommendation, Low certainty evidence)**

Clinical thresholds

- Acceptable diagnostic test accuracy for triaging testing = at least 90% sensitivity and 75% specificity for a reference test (CSF AD biomarkers, amyloid PET, or AD neuropathology).

- Acceptable diagnostic test accuracy for confirmatory testing = at least 90% sensitivity and 90% specificity for a reference test (CSF AD biomarkers, amyloid PET, or AD neuropathology).

Remarks

- Host of situations where it would not be appropriate to provide a BBM test in specialized care.

- This includes:
  - Situations where patient does not want to know their amyloid status
  - Patients with:
    - obvious modifiable or temporary conditions that are likely to account for the patient's cognitive impairment
    - with limited life expectancy
    - history of conditions that can affect the brain and that may impact levels of a given BBM in ways that have not been well-studied
    - with medical conditions that may affect the levels of a given BBM

Clinical question

In **adults 55 years and older**, which test (i.e., 5-Cog, AD8, GPCOG, IQCODE, Mini-Cog, MIS, MoCA, QDRS, RUDAS, and SLUMS) should be used for the **early detection of cognitive impairment (including MCI and dementia)** in **primary care and ambulatory, outpatient settings**?

- US-based
- English or Spanish tests

Public Comments being Addressed

- Recommendation
  - Cognitive Screening Recommended
    - **Conditional for** SLUMS, AD8
- All informed by low-very low certainty evidence

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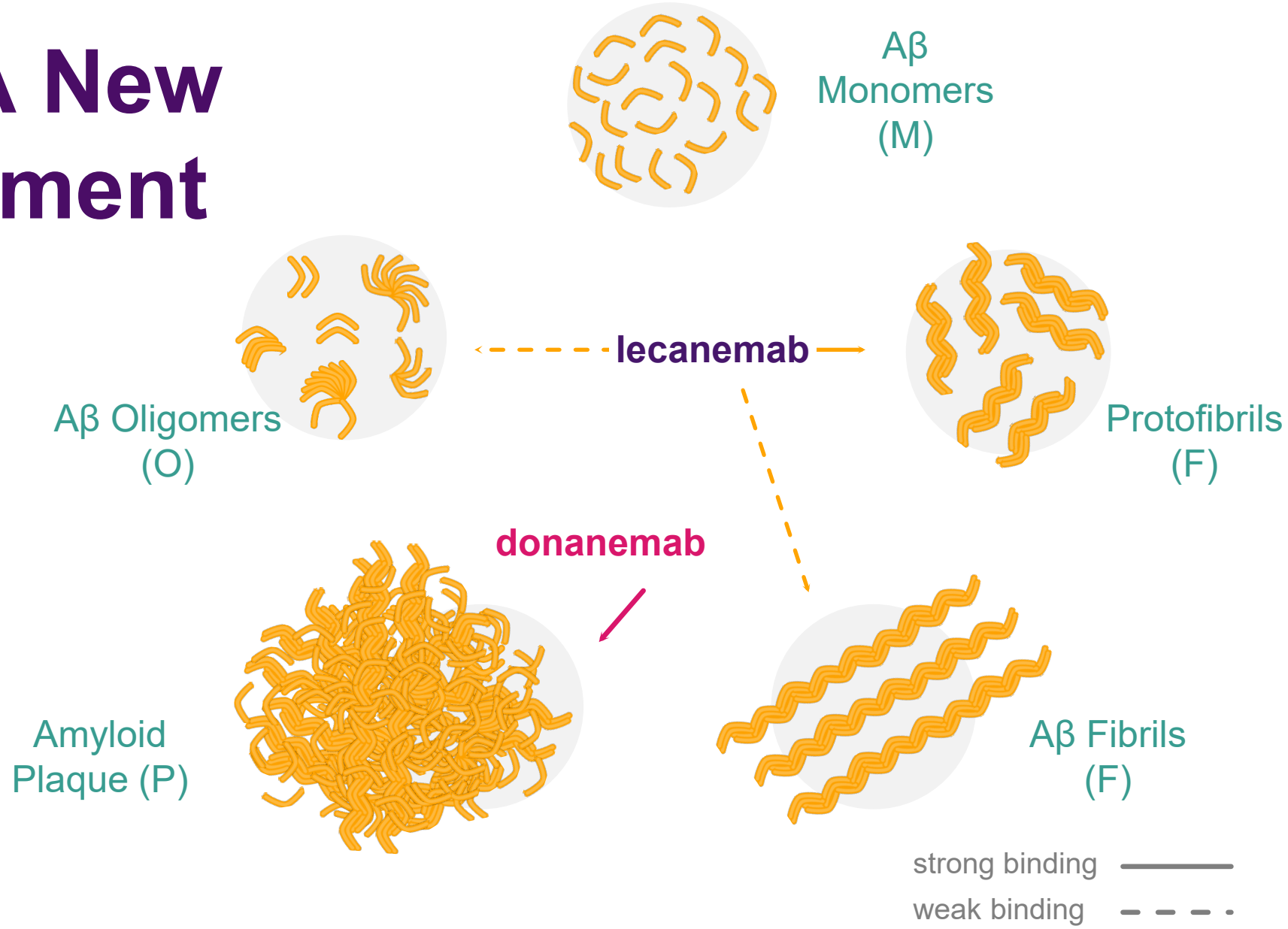
Deeper Dive: A New Phase of Treatment

lecanemab (Leqembi)
Approved in 2023
Targets Beta Amyloid

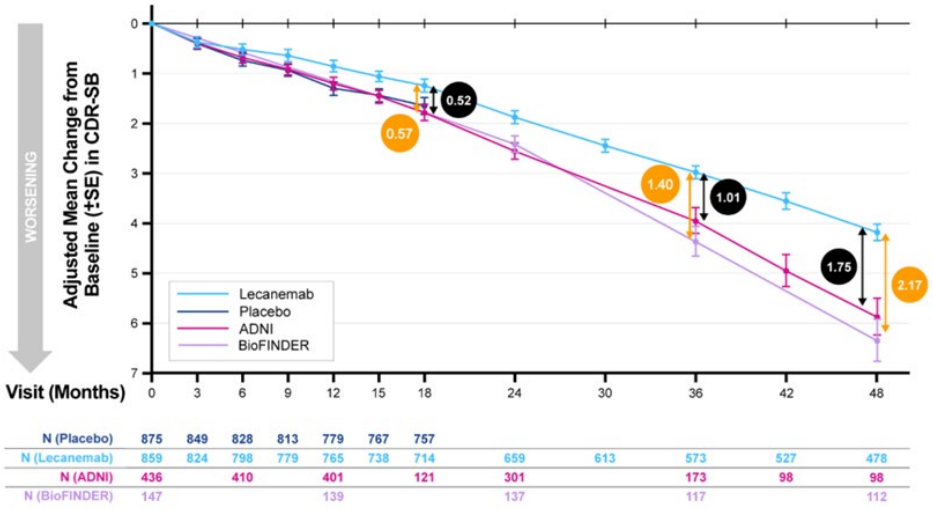
donanemab (Kisunla)
Approved in 2024
Targets Beta Amyloid



Long-Term Impact of Anti-Amyloid Therapies

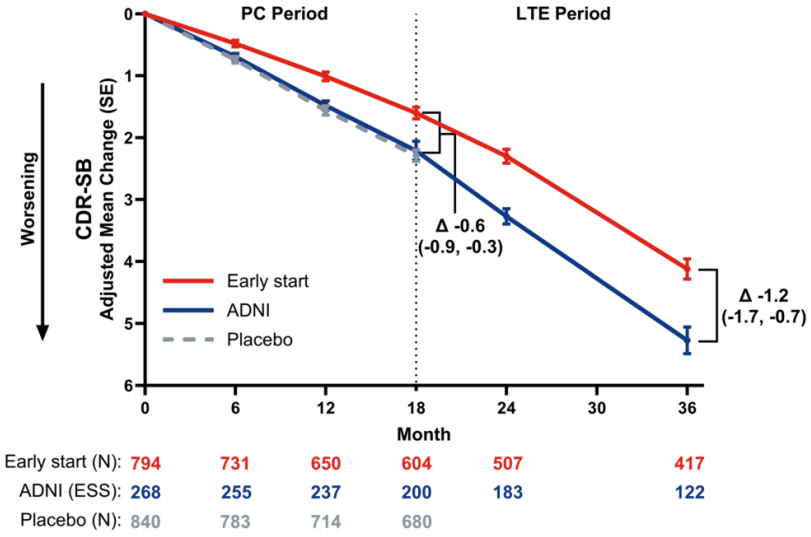
Lecanemab

- Four years of lecanemab therapy helped patients slow the progression of AD and remain in the early stages of AD longer.
- More than 50% of patients who started treatment in the earlier stages of AD continued to show improvement in clinical scores after four years of lecanemab therapy



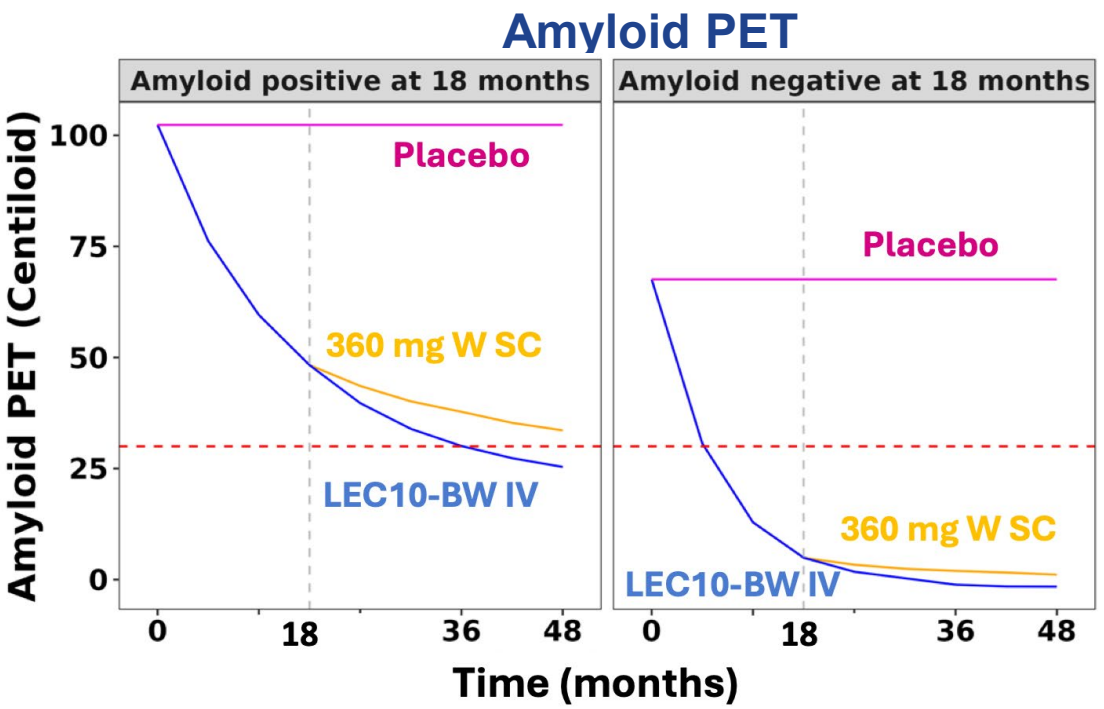
Donanemab

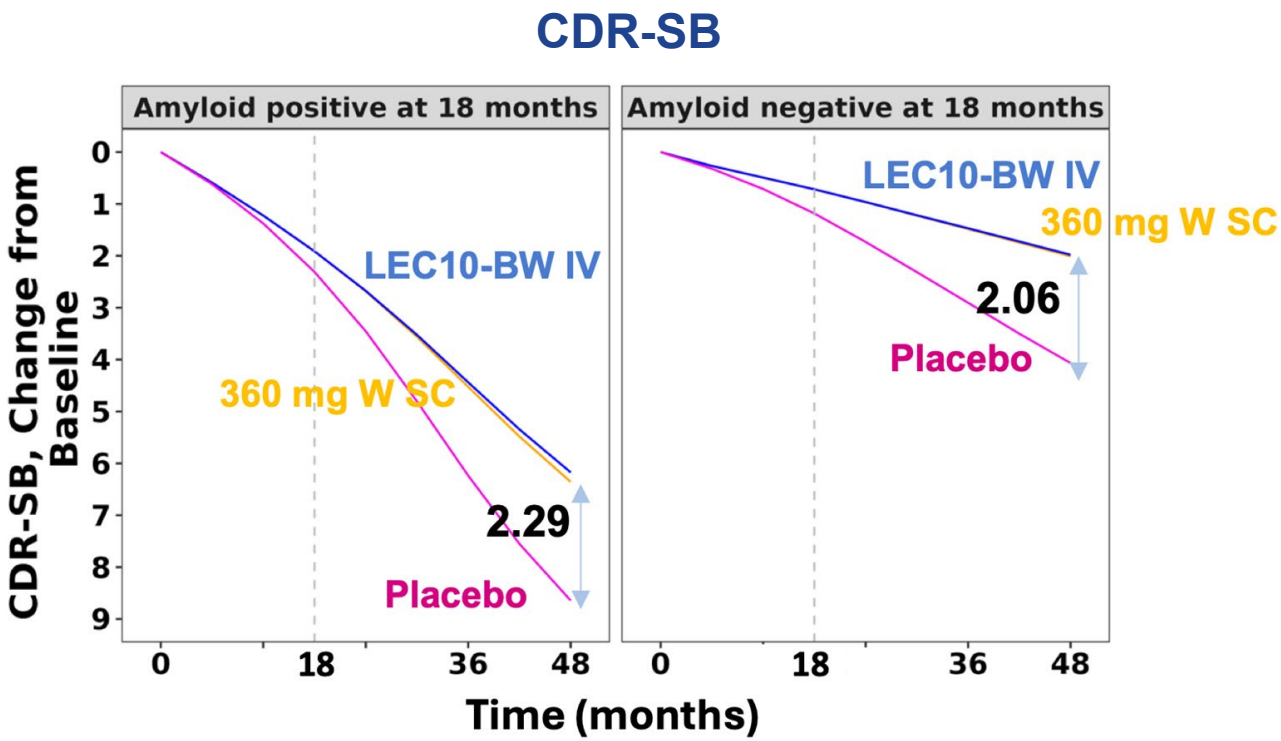
- Donanemab benefit continued to grow over 3 years compared to ADNI cohort.
- Early start donanemab group showed 27% reduced risk of progression to next stage of disease compared to delayed start donanemab group



Lecanemab 360 mg SC AI Weekly Maintenance Dosing Can be Initiated at 18 Months Irrespective of Amyloid Load

- Transitioning to weekly 360 mg SC AI maintenance dosing after 18 months is similar to continuing IV 10 mg/kg biweekly dose for maintaining amyloid reduction and clinical efficacy





CDR-SB = Clinical Dementia Rating scale Sum of Boxes. LEC10-BW = lecanemab 10 mg/kg biweekly. LEC10-M = lecanemab 10 mg/kg monthly. PET = positron emission tomography PD, pharmacodynamic. PK, pharmacokinetic. SC, subcutaneous.

Combination of Common Cardiovascular Drugs May Protect the Brain

- In a study of electronic health records of 4,500+ older adults, researchers found that taking a combination of medications to treat blood pressure, cholesterol levels, and diabetes may give individuals the cognition of someone 3 years younger and reduce dementia risk.
- Participants taking more than 2 vascular drugs showed fewer Alzheimer's brain changes.
- This study supports the idea that "What's good for the heart is good for the brain."

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AAIC FOR ALL

AAIC for All Attendees

In Person >450 Virtual >8,000

	Community Track	Clinician Track CME Credits
9:00 a.m. - 9:45 a.m.	AAIC 2025 In The Neighborhood	AAIC 2025 Highlights
9:45 a.m. - 10:00 a.m.	Break In Person Booths	
10:00 a.m. - 11:30 a.m.	AAIC 2025 Highlights	Clinical Practice Guidance And Resources
11:30 a.m. - 11:45 a.m.	Break	
11:45 a.m. - 1:00 p.m.	Plenary Session	

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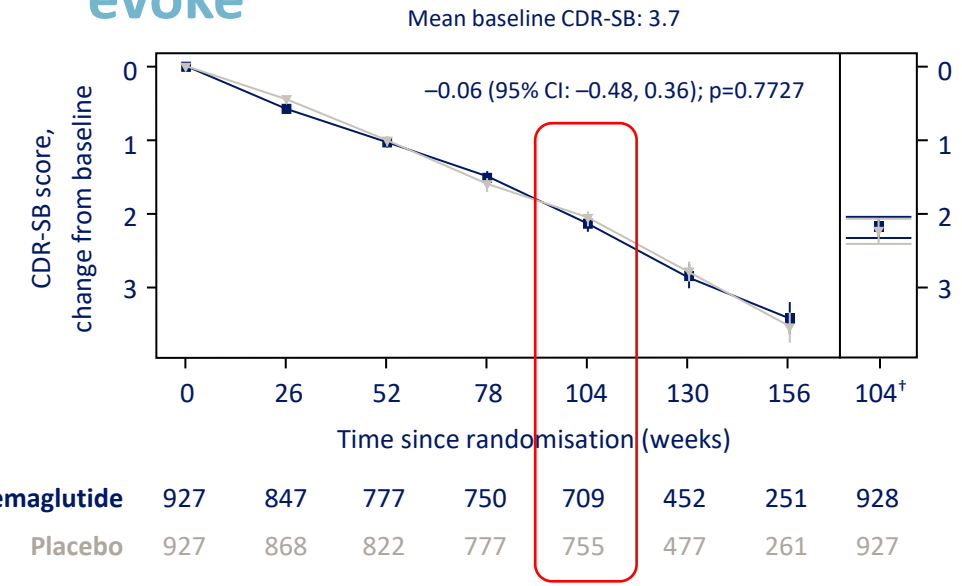
Oral semaglutide did not slow cognitive and functional decline in participants with early AD versus placebo in either trial

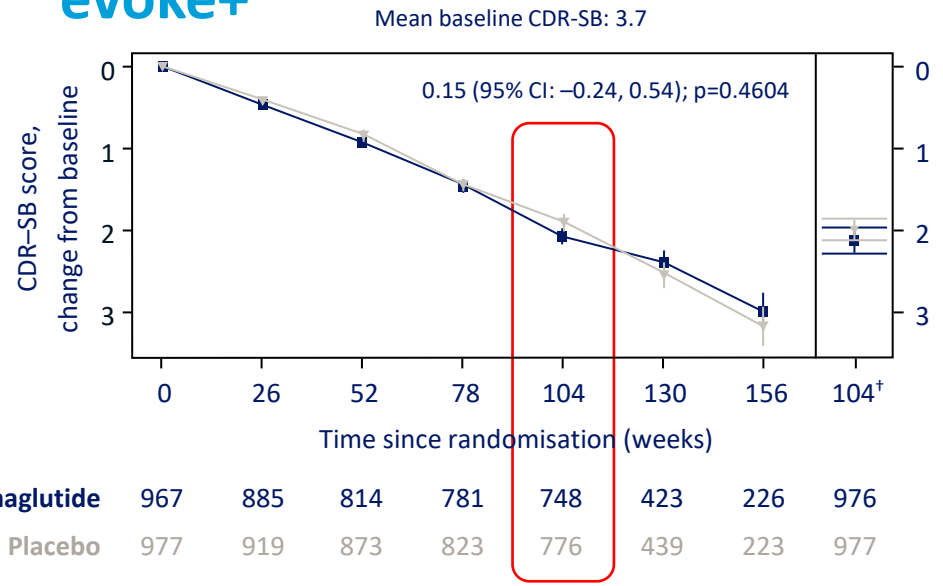
Change in CDR–SB score from baseline to week 104

evoke



Oral semaglutide	927	847	777	750	709	452	251	928
Placebo	927	868	822	777	755	477	261	927

evoke+



Oral semaglutide	967	885	814	781	748	423	226	976
Placebo	977	919	873	823	776	439	223	977

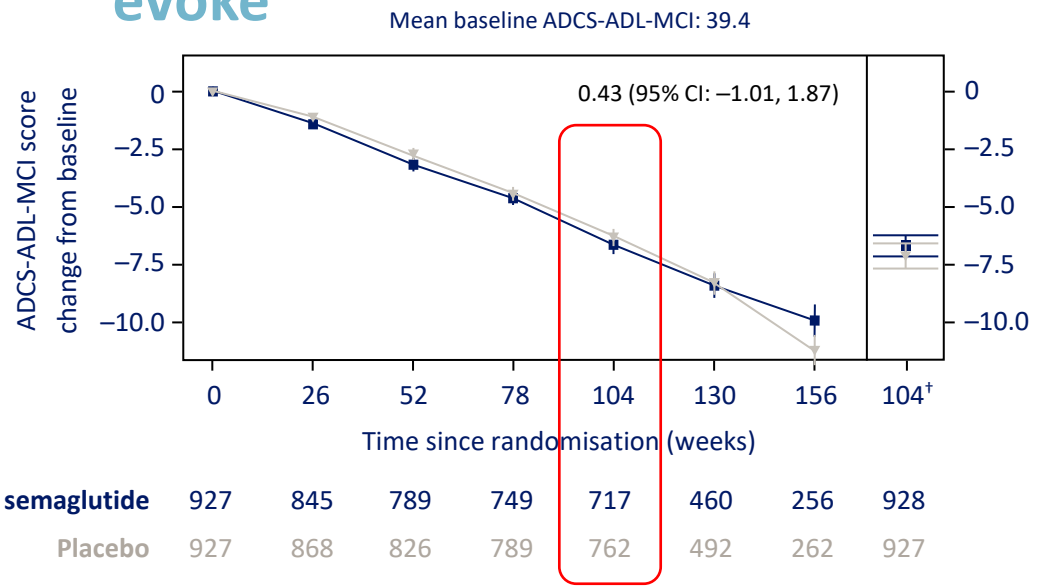
	Estimate†	95% CI	P-value
Oral semaglutide	2.2		
Placebo	2.2		
Oral semaglutide – Placebo	–0.06	–0.48 ; 0.36	0.7727

	Estimate†	95% CI	P-value
Oral semaglutide	2.1		
Placebo	2.0		
Oral semaglutide – Placebo	0.15	–0.24 ; 0.54	0.4604

†Data are for the treatment policy estimand. Error bars are mean +/- standard error of the mean.
AD, Alzheimer's disease; CDR-SB, Clinical Dementia Rating–Sum of Boxes; CI, confidence interval.

Oral semaglutide did not slow functional decline in participants with early AD versus placebo in either trial
Change in ADCS-ADL-MCI score from baseline to week 104

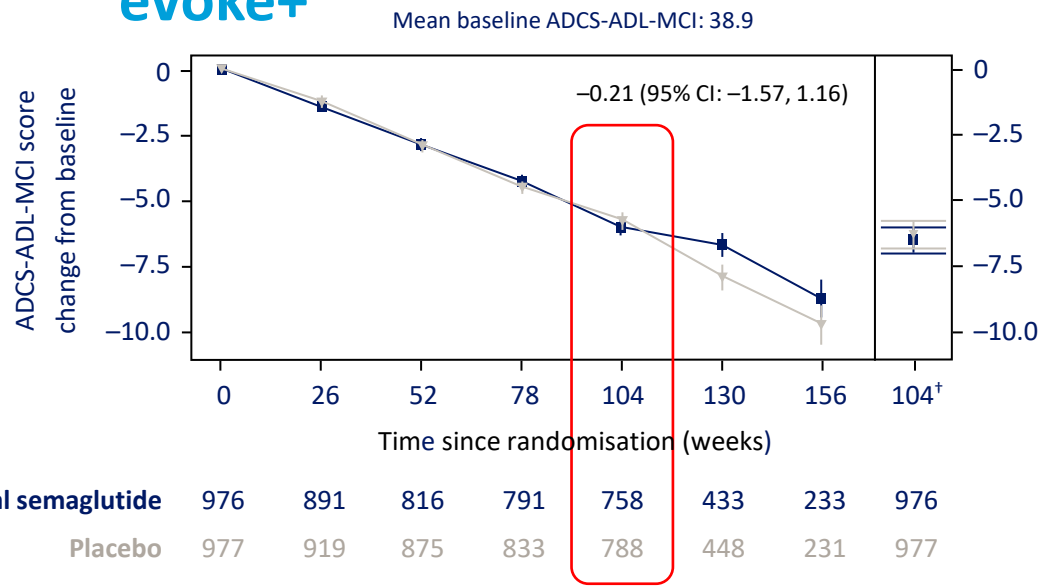
evoke



Oral semaglutide	927	845	789	749	717	460	256	928
Placebo	927	868	826	789	762	492	262	927

	Estimate†	95% CI
Oral semaglutide	–6.6	
Placebo	–7.1	
Oral semaglutide – Placebo	0.43	–1.01; 1.87

evoke+



Oral semaglutide	976	891	816	791	758	433	233	976
Placebo	977	919	875	833	788	448	231	977

	Estimate†	95% CI
Oral semaglutide	–6.5	
Placebo	–6.3	
Oral semaglutide – Placebo	–0.21	–1.57; 1.16

†Data are for the treatment policy estimand. Error bars are mean +/- standard error of the mean.
AD, Alzheimer's disease; ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study Activities of Daily Living Scale for mild cognitive impairment; CI, confidence interval.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AAIC 26
SAVE THE DATE
JULY 12-16 ANNUAL CONFERENCE > LONDON, UNITED KINGDOM, AND ONLINE
July 10-11 Educational Workshops and Preconferences
July 12-15 Exhibits
alz.org/AAIC

Q&A

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