Early Detection, Dementia, MCI, and Alzheimer's Biomarkers

Julie Bynum, MD MPH

October 29, 2026

ADRD Coordinating Center Fall Mtg

Presenter

Julie Bynum, MD, MPH

Margaret Terpenning Collegiate Professor of Internal Medicine,
Division of Geriatric & Palliative Medicine
Director, Center to Accelerate Population Research in Alzheimer's (CAPRA)
University of Michigan Medical School

Funding Sources

P30 AG066582 (NIA/NIH)
U54 AG090084 (NIA/NIH)
P30 AG024824 (NIA/NIH)
R01 AG079226 (NIA/NIH)
R01 AG087243 (NIA/NIH)
RF1 AG083768 (NIA/NIH)
R01 AG087073 (NIA/NIH)
and Michigan DHHS

Change Beginning January 2027

Dr. Jeffery L. Mandel Chair in Healthy Aging
Director, Center for Geroscience & Healthy Aging
Director, Division of Geriatrics & Palliative Care
Director, Healthy Aging Clinic
Professor, Department of Medicine
Professor, Department of Family Medicine & Community Health
University of Minnesota Medical School

No Conflicts to Disclose

Outline for Today's Presentation

- **Goal:** Provide basic context for social science consumers of new research and for those interested in conducting research in this space
  - Understand Cognitive Impairment & Dementia and when it is caused by Alzheimer's Disease
  - Movement toward earlier detection of "dementia" and role of blood-based biomarkers driven by anti-amyloid monoclonal antibodies (mAB) treatment options
  - Understand relationship between amyloid deposition and symptoms of cognitive impairment
  - Early detection and screening considerations
  - What is happening today in clinics



Clinical Case

- Your mother is 82 years old and lives independently in the house you grew up in. She needs help with heavy housework and is slowing down but does well enough. She sometimes has trouble finding words like her friends.
- She calls you in the evening to talk about her doctor visit today.

What are you thinking if the doctor says she has:

- Normal cognitive aging
- Mild cognitive impairment
- Early dementia
- Alzheimer’s disease

Clinical Case of Everyone’s Mom

Our next questions

- What do those words mean?
- Is the assessment correct?
- Is there anything we should do to make sure it is correct?
- What does this mean for her future?
- Is there anything to keep her as good as she is today?

Where do we find these answers?



What Do Those Words Mean?

Alzheimer's Disease
- A biological cause of dementia
- American and European scientific communities define this differently

This is where it gets interesting and confusing!

Normal Cognitive Aging
- All physiological systems age.
- NOT a disease or pathological.
- Characterized by slower retrieval of information and multitasking.

Mild Cognitive Impairment
- Measurable cognitive decline that does not impair daily function and is not caused by other things (like depression, medications).
- Typically impacts a single cognitive domain.
- Considered "prodromal" to dementia.

Early Dementia
- "Dementia" is measurable cognitive decline in multiple domains serious enough to impair function and is not caused by other things (like depression, medications)
- "Early" refers to severity of impairment (impacting work, perhaps iADLs).
- Is a disease state.
- Multitude of potential biological causes.

Path to a Diagnosis in Neurodegenerative Cognitive Disorders

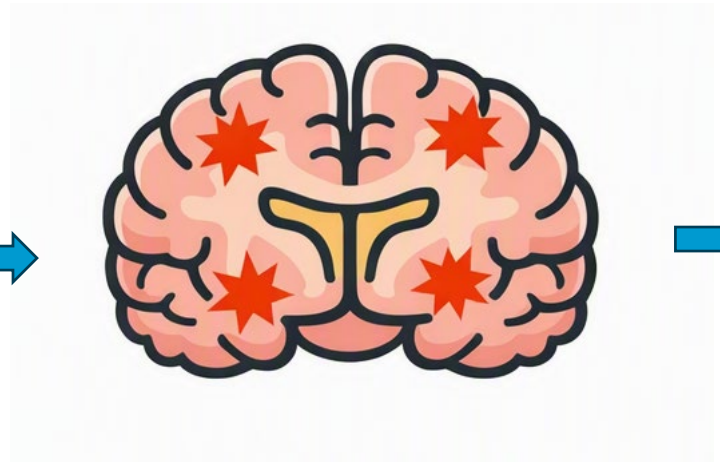
- Vascular, Alzheimer's disease, Lewy Body, Frontotemporal, LATE -



Hit to Brain

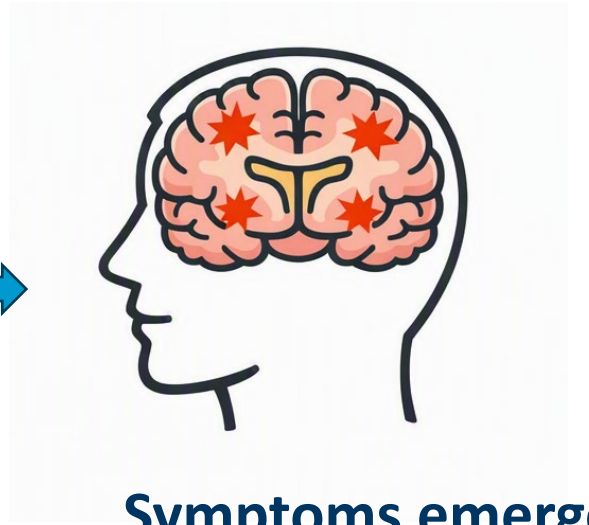
Ischemic injury

Protein Deposition
- Amyloid-beta
- Tau
- Alpha-synuclein
- TDP-43



Hits accumulate over time



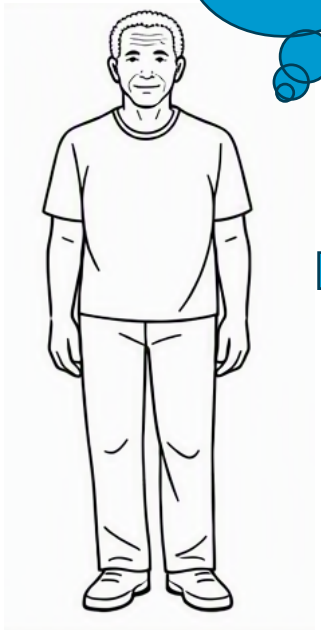


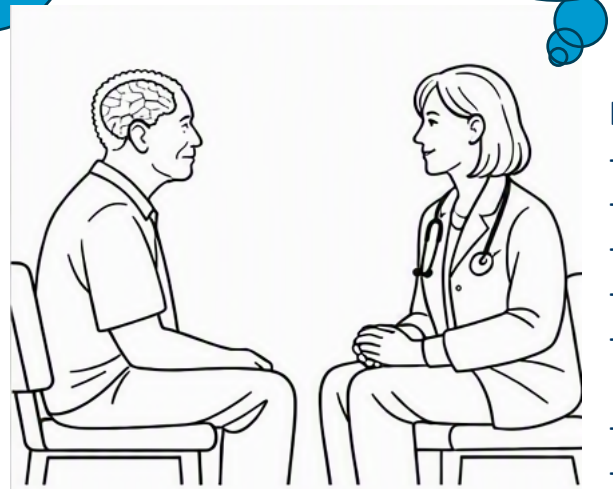
Symptoms emerge

Disease State
- Vascular Dementia
- Alzheimer's Dementia
- Frontotemporal Dementia
- Lewy Body Dementia
- LATE

Path to a Diagnosis as Experienced by a Person

My thinking and memory are not so good anymore





Yes it is, so what do we need to evaluate?

Primary Care to Patient

1. Let's determine if cognition is objectively abnormal
2. Then if yes, figure out why

Differential Diagnosis

- depression/anxiety
- medications
- acute illness/delirium
- head injury
- structural lesion in brain
- substance use disorder
- early sign of a dementia

I think this is early dementia. Let's figure out the cause



More history & testing

Possible Specialty Referral

Diagnostic Label

Vascular Dementia
Alzheimer's Dementia
Frontotemporal Dementia
Lewy Body Dementia
LATE

Getting a Diagnosis

This pathway is ineffective and takes too long due to numerous **barriers** at all levels

Potential Barriers

- Patient symptom recognition
- Stigma
- Tools for cognitive assessment
- Clinician expertise
- Complex clinical syndrome not measurable by a test
- Clinician expertise
- Communication of diagnosis
- Adverse consequences of label (autonomy, insurance)

Research on Barriers to Diagnosis

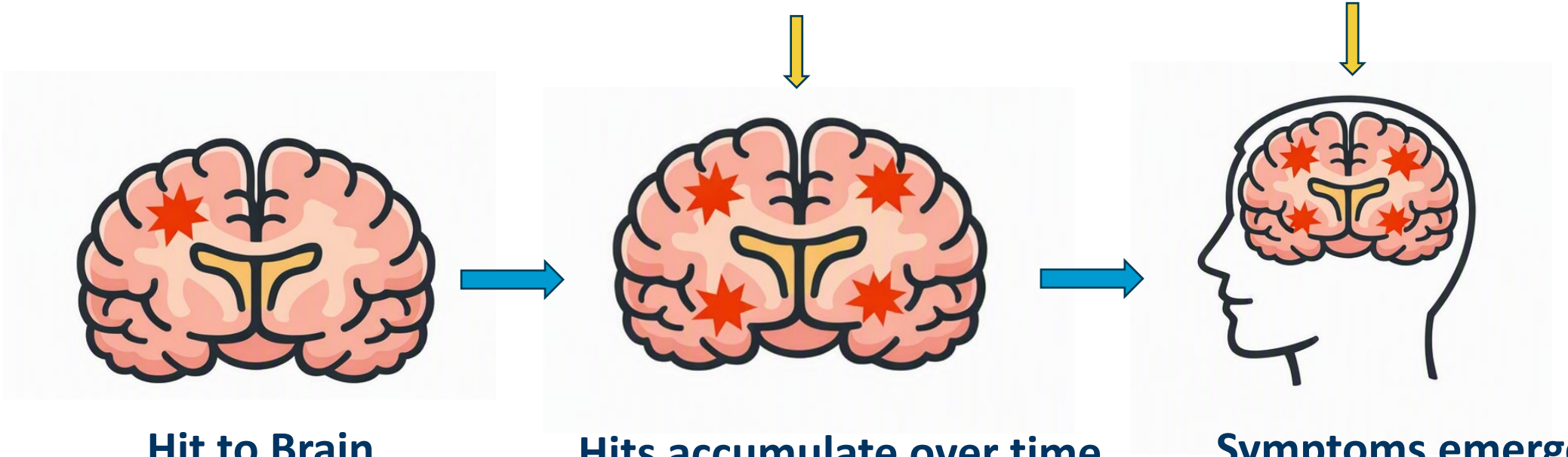
Conceptual Process of Diagnosis

National Academy of Medicine (2014)

Robust Research on Barriers to Diagnosis in Dementia

The Tricky Bit: When on the Path Does Diagnostic Label of Alzheimer's Disease Apply?

When "Alzheimer's Disease" label is applied



Hit to Brain

Hits accumulate over time

Alzheimer's Association Workgroup definition of Alzheimer's Disease is based on the biological presence of proteins

Jack et al. *Alzheimer's Dement*. 2024; 20: 5143–5169.

Symptoms emerge

International Working Group (IWG) definition of Alzheimer's Disease is based on symptoms along with the biology

Dubois et al. *JAMA Neurology*. 2026; 81: 1304-1311.

Clinical Case

- Your mother is 82 years old and lives independently in the house you grew up in. She needs help with heavy housework and is slowing down but does well enough. She sometimes has trouble finding words as do her friends.
- She calls you in the evening to talk about her doctor visit today.

What are you thinking if the doctor says she has:

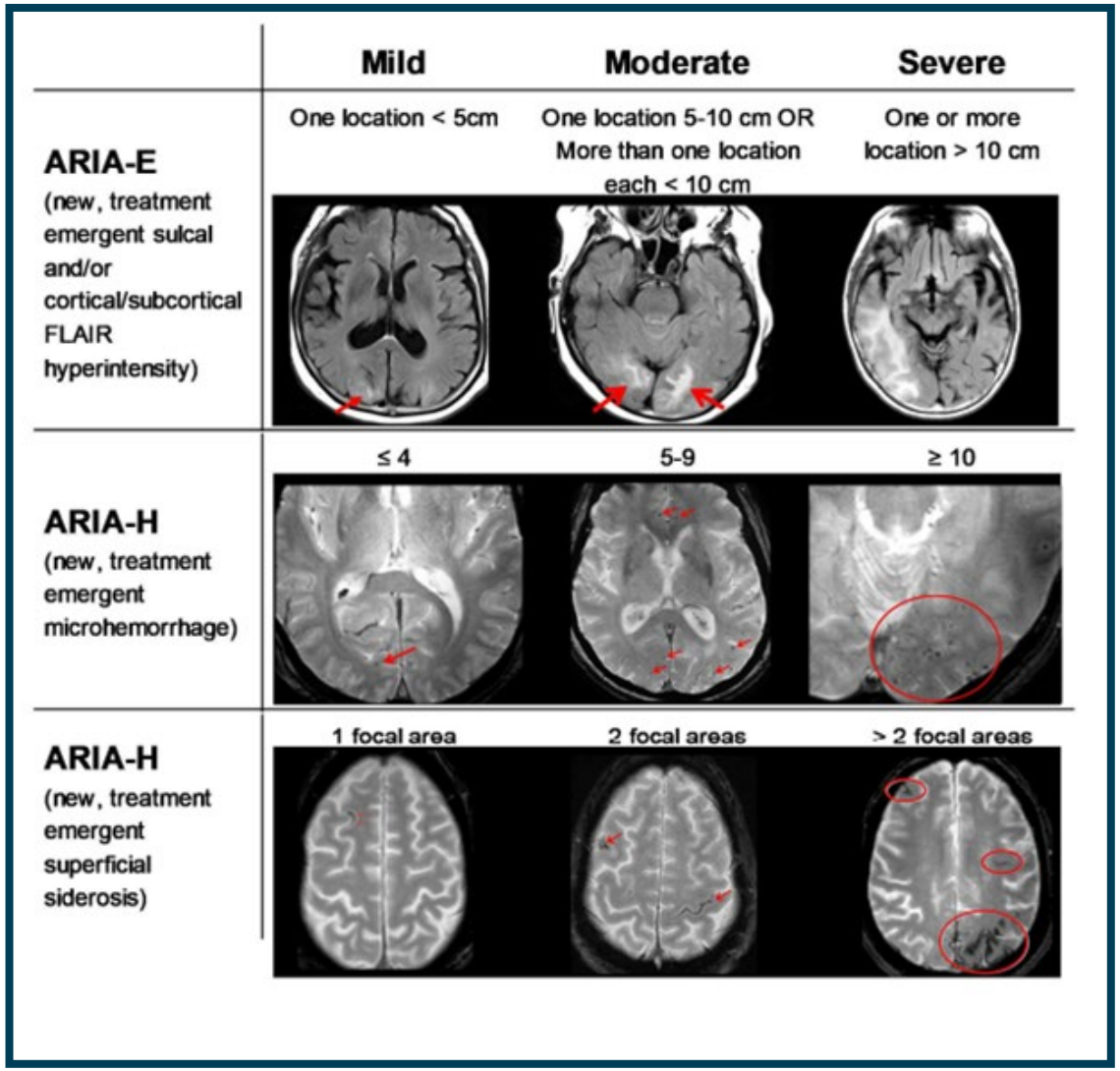
- Normal cognitive aging
- Mild cognitive impairment
- Early dementia
- Alzheimer’s disease

Anti-amyloid monoclonal antibodies (mAB) treatment options

Mechanism of action: Removal of amyloid deposition from the brain

Target Pop’n: Older adults with symptoms (MCI/early dementia)

Amyloid Related Imaging Abnormalities (ARIAs)



Questions I would have if I were considering treatment:

- What if I have a need for anti-coagulation (like acute stroke or heart attack)?

- If treated at my current age with no symptoms (which is not indicated right now), what does having ARIA mean for longterm cognition if I was one of the people who was not going to get dementia?

Cogswell et al., AJNR (2024)

Relationship Amyloid in Brain with Cognitive Impairment

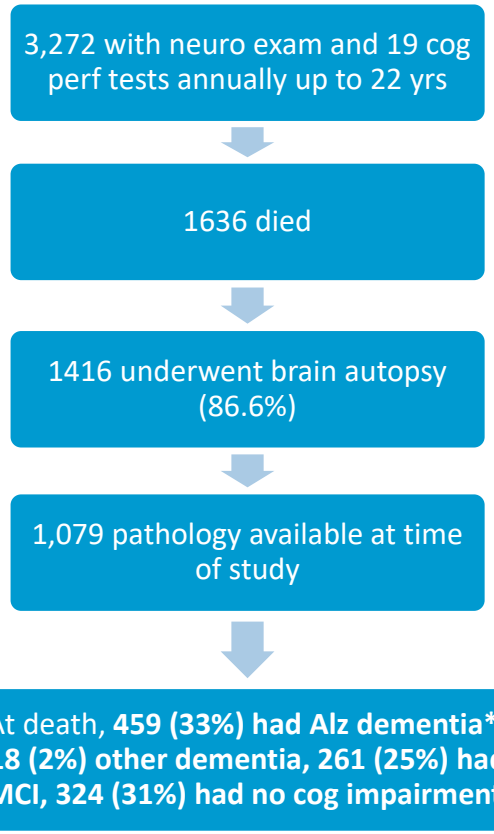
- Approx 1/3 of Cognitively normal (no MCI or dementia rigorously followed annually) at death meet criteria for neuropathological Alzheimer's Disease
  - Bennett DA, Schneider JA, Arvanitakis Z, et al. Neuropathology of older persons without cognitive impairment from two community-based studies. Neurology. 2006;66(12):1837–1844.
- Amount of amyloid correlation with symptoms in life is complex with low specificity. Location & presence of other findings are important.
  - Nelson PT, Alafuzoff I, Bigio EH, et al. Correlation of Alzheimer disease neuropathologic changes with cognitive status: a review of the literature. Journal of Neuropathology & Experimental Neurology. 2012;71(5):362–381.
- The tau mediates the relationship between Aβ and cognition
  - Bennett DA, Schneider JA, Wilson RS, Bienias JL, Arnold SE. Neurofibrillary tangles mediate the association of amyloid load with clinical Alzheimer disease and level of cognitive function. Archives of Neurology. 2004;61(3):378–384.

How Much of Clinical AD is Due to AD Pathology?

Two studies from Rush Alzheimer's Disease Center

Boyle et al., Ann Neuro, 2018

Title: Person-Specific Contribution of Neuropathologies to Cognitive Loss in Old Age



Participant means:
Age at death 89
Yrs followed 8
Female 69%
Yrs educ 16

Results at autopsy

- 94% (N=1017) at least 1 neuropathology
- 65% AD; 35% TDP 43; 36% macroinfarcts; 30% microinfarcts; and mod to sev: CAA 36%, atherosclerosis 33%, arteriosclerosis 31%; 13% Lewy bodies, and 10% hippocampal sclerosis
- Multiple pathologies common
  - **78% 2+, 58% 3+, 35% 4+, 17% 5+**
  - AD rarely appeared alone (9%)
- 236 combinations of pathologies recorded with no single combination present in more than 6% of sample.

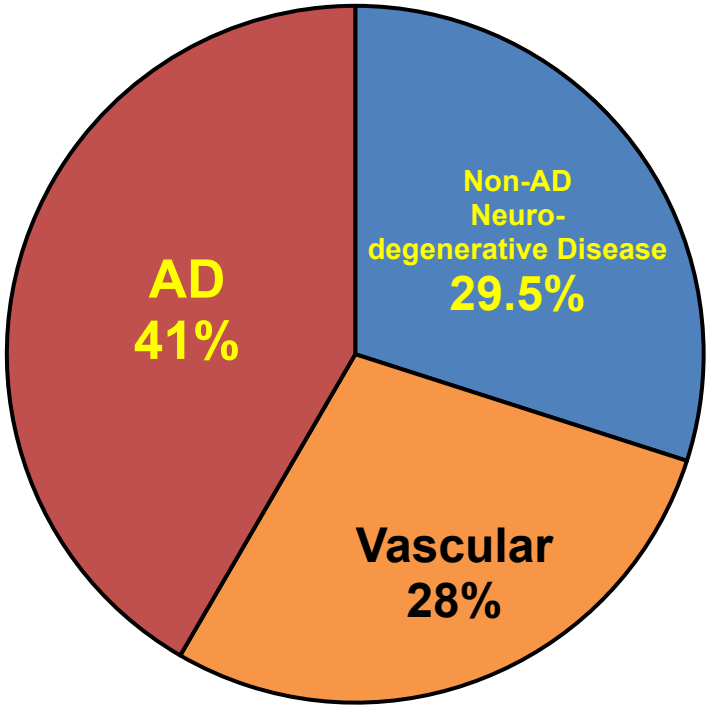
*in this study nearly all clinical cases of dementia were labeled Alzheimer's dementia

How Much of Clinical AD is Due to AD Pathology?

Boyle et al., Annals of Neurology, 2019

Good Review: Schnieder J. Neuropathology of Dementia Disorders. Continuum. 2022. 28(3):834-851

Title: Attributable Risk of Alzheimer's Dementia attributed to Age-related Neuropathologies



AD

Non AD Neurodegenerative Disease

- Lewy Bodies
- Hippocampal Sclerosis
- TDP-43 Pathology

Vascular

- Macroscopic Infarcts
- Cerebral Amyloid Angiopathy
- Atherosclerosis
- Arteriosclerosis

Attributable risk (%) derived from statistical modeling
Same cohort 1 yr later so slightly larger (N=1,161)

Other Results

- Cases remain unattributed to known pathology
  - 80% with known pathologies driven by the 8 pathologies
  - If include cases not attributed to any pathology, the fraction drops to 65%
- Prior studies suggested AD pathology drives 65% of cases but importance of mixed and other pathologies recognized
- "The present findings suggest that Alzheimer's dementia is a syndrome of multiple and heterogeneous processes and highlight the urgent need for therapeutic interventions that address the remarkable neuropathological heterogeneity underlying Alzheimer's dementia."

Biomarkers for Detection of Neurodegenerative Disease



Different types of biomarkers

- Fluid
  - Cerebrospinal fluid (lumbar puncture)
  - Blood (simple phlebotomy)
- Imaging
  - PET (for proteins)
  - MRI (structural)

Biomarkers for Alzheimer's disease

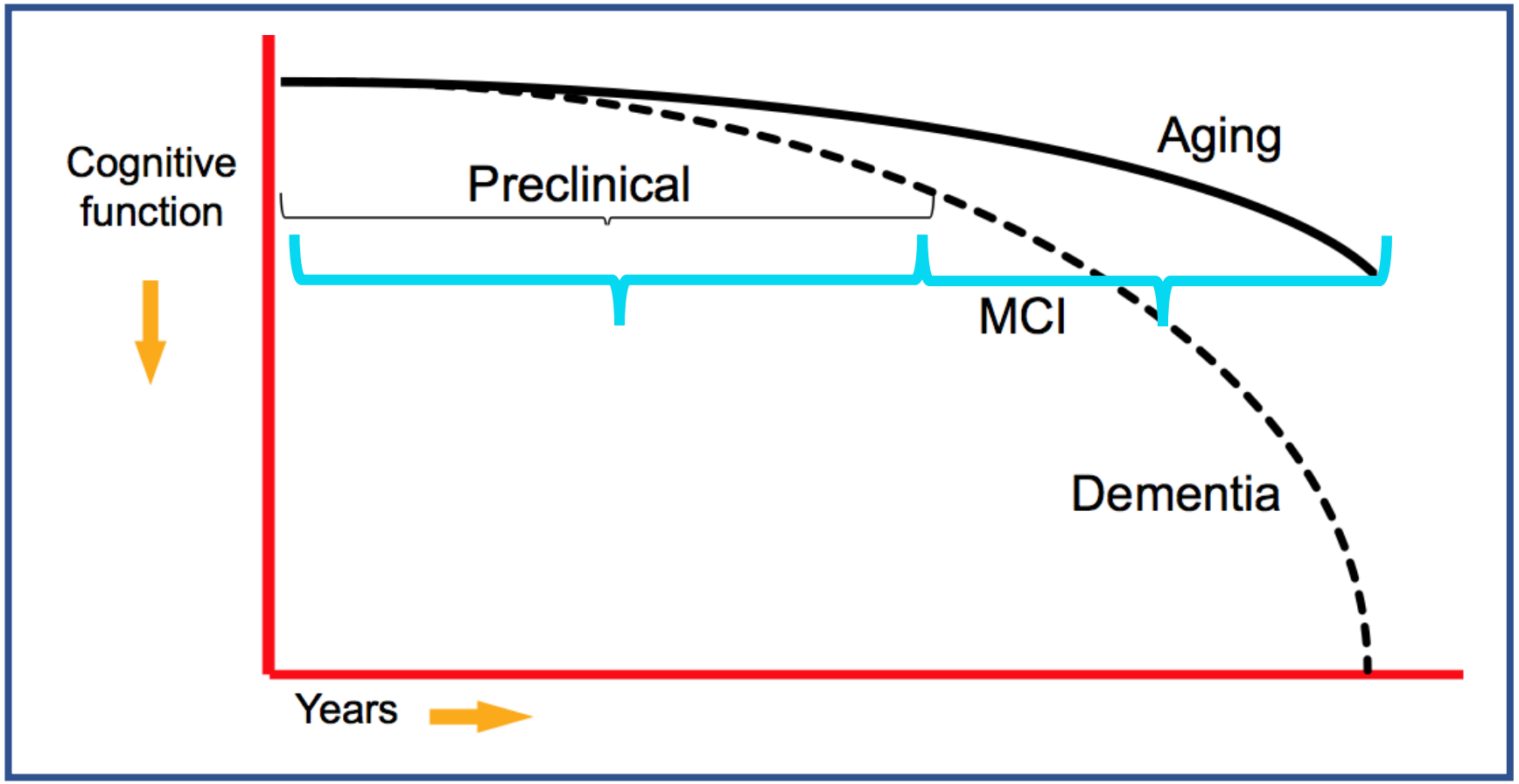
- AD specific (**p-tau217**)

Use of Biomarkers

- **Diagnosis**
- Monitoring Treatment Response

Early Detection of Alzheimer's Disease





Albert et al, Alzheimers Dement (2011)

Current Clinical Guidelines on Blood Based Biomarker for Alzheimer's

Use only in specialty settings for people who have symptoms

Palmqvist S et al. Alzheimer's Association clinical practice guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings. *Alzheimers Dement*. 2025;21(7):e70535. doi:10.1002/alz.70535

Rapidly Changing Landscape of BBB

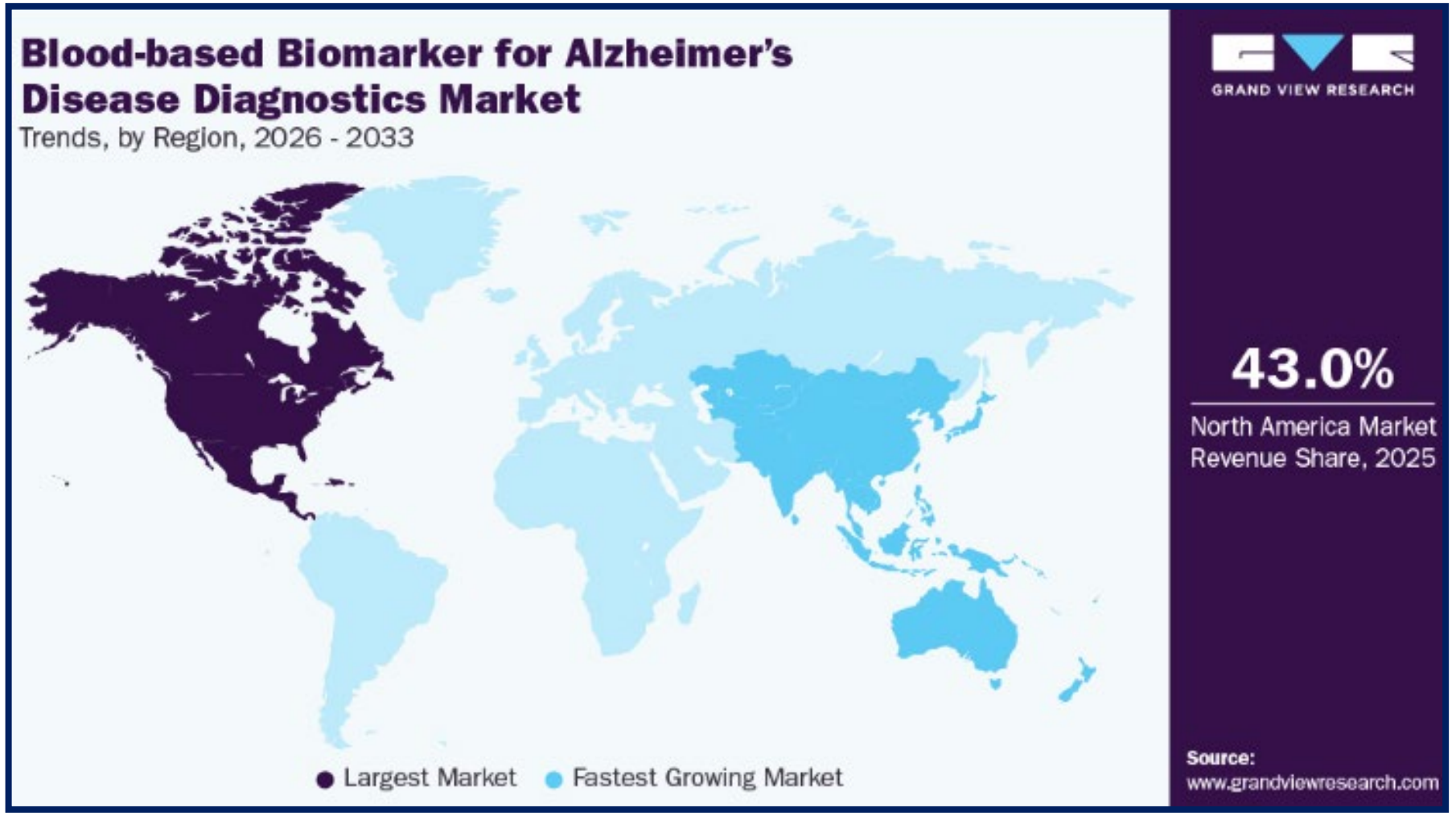
News

Roche receives FDA clearance for Elecsys® pTau217, advancing Alzheimer's disease assessment across primary and specialty care

August 24, 2026

https://diagnostics.roche.com/us/en/news-listing/2026/fda-elecsys-ptau217-alzheimers-blood-test.html

North America is the Largest Market for Blood-Based Biomarkers (BBB)



https://www.grandviewresearch.com/industry-analysis/blood-based-biomarker-alzheimers-disease-diagnostics-market-report

Early Detection of Amyloid Deposition in Preclinical Phase: Predictive Performance of Biomarkers for Dementia Onset

- **Amyloid biomarkers (PET, CSF) are strong at ruling out near-term decline but weak at predicting it in a given individual.** Prior probability is critically important for performance.
- Subjective Cognitive Decline progression to MCI or Dementia & CSF or PET Biomarkers for AD
  - Amyloid alone has a negative result carries a **high negative predictive value (~95%) and modest positive predictive value (~28%)** over typical follow-up periods of several years.

Rostamzadeh. 2022.

- In cognitively normal progression to dementia PET amyloid alone NS 3-5yrs, tau needed for prediction

Ossenkoppele. 2022.

- In cognitively normal progression to dementia using PET amyloid alone 10yrs and lifetime weak 65-74, tau needed for prediction

Jack. 2025.

- p-Tau217 BBB trial showing highest level of p-Tau217 associated with 38% absolute risk of progression cog impairment (MCI/dementia) over 5 years

Buckley. 2026.

Editorials: Schindler. 2026 & Devi. 2026.

Criteria for When Consider a Screening Program

Wilson and Jungner criteria

- **Important health problem**
- **Recognizable latent or early stage**
- **Natural history is adequately understood**
- **Suitable test or examination exists.**
- **Test is acceptable to the population**
- **Accepted treatment exists**
- **Agreement on whom to treat**
- **Capacity for diagnosis/treatment**
- **Cost is economically balanced**

Additional Criteria

- **RCT evidence** of mortality/morbidity benefit
- **Benefits weighed explicitly against harms**

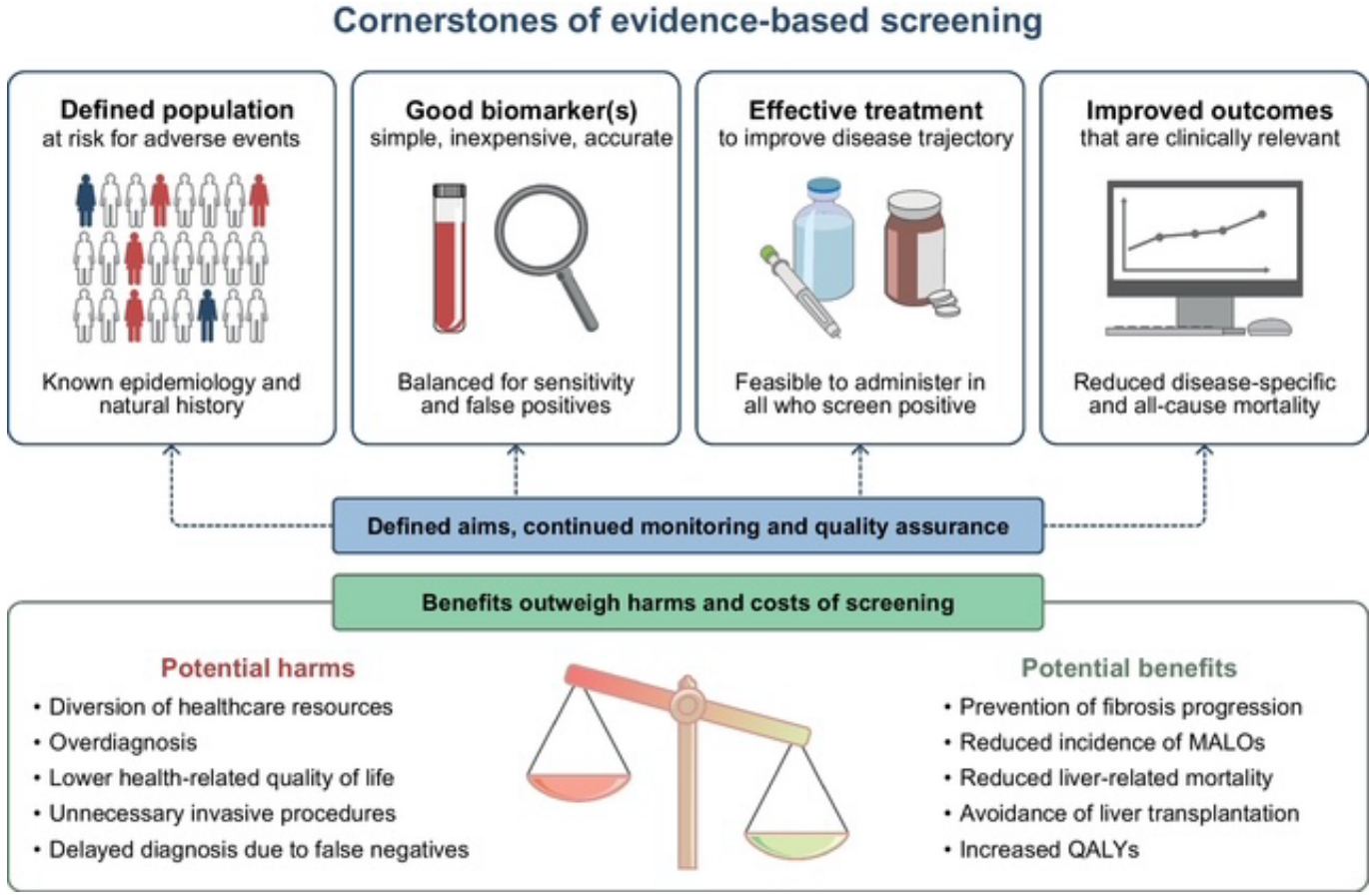
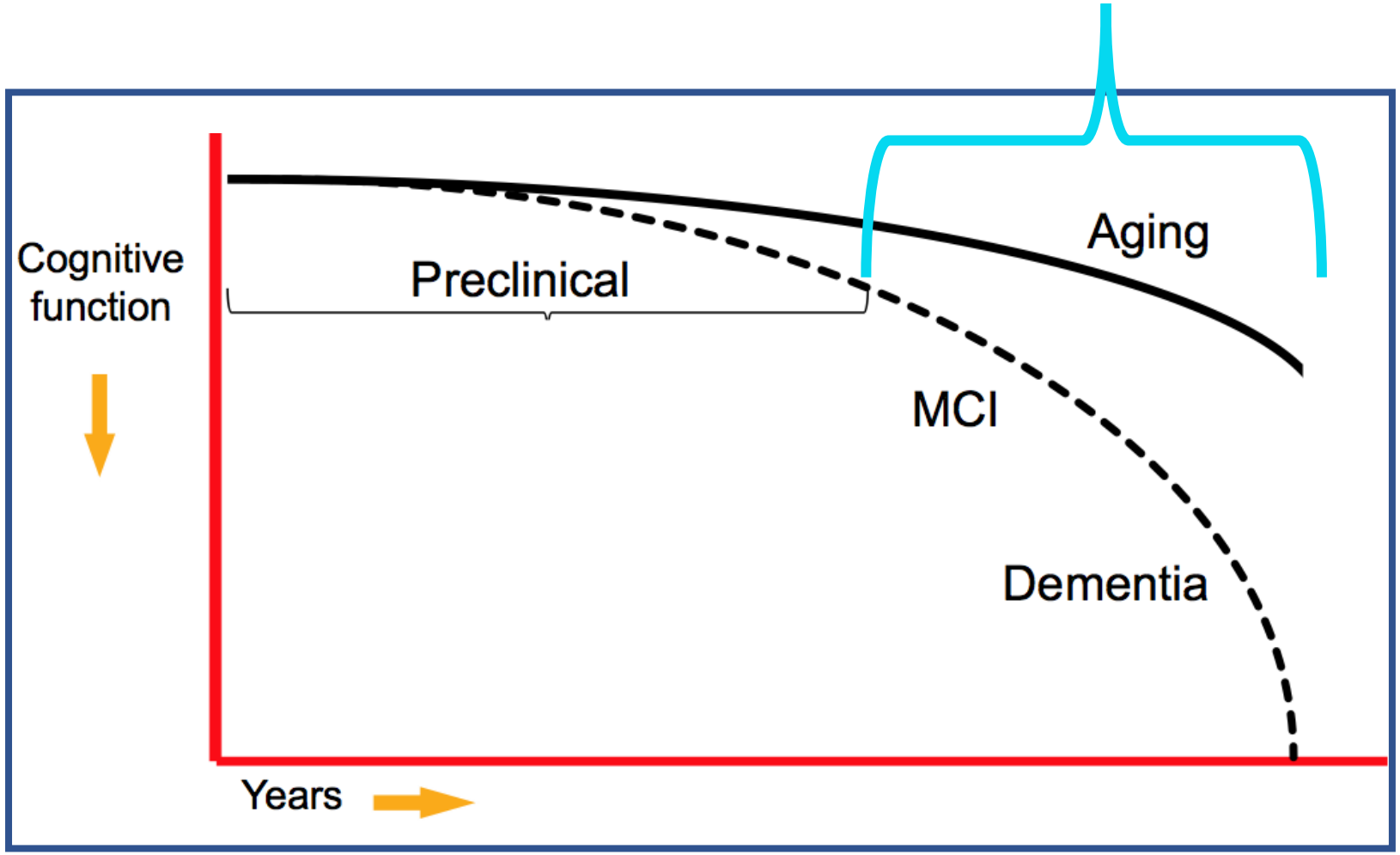


Figure From: Screening and diagnosis of liver disease in diabetes: a guide and evidence-based assessment.Diabetologia. 2026.

Early Detection of Cognitive Impairment





Albert et al, Alzheimers Dement (2011)

How can we detect people earlier in symptomatic phase?

- Increase public knowledge
- Reduce Stigma
- Increase benefit vs harms tuat results from disease labeling
- Streamline and improve accuracy of cognitive testing for clinics
  - Digital Tools

    Products already in use: CANTAB is FDA-cleared and in clinical use. Cognivue, Cogstate, cCOG, NIH Toolbox, and UCSF TabCAT are also available.
- Provide adequate to specialist support
- A note of caution about subjective cog complaints. Associated with objective cognitive impairment younger, higher educated but not others

Screening for Dementia?

USPSTF:

- 2025 Update Pending
- 2020, 2014, 2003 ”I” inconclusive

Recent Review in mAB era applying

Wilson-Jungner Criteria concluded screening* is not justified, citing:

- limited specialist capacity
- cost
- modest efficacy of current treatments
- side effects of current treatments
- few long-term data

*screening for cog impairment not biomarker

Chatanaka MK et al. Critical Reviews in Clinical Laboratory Sciences. 2025.

Risks and Benefits of Screening for Dementia in Primary Care (IU CHOICE) Trial

RCT: 4005 (7,724 evaluated) primary care pts screen vs no screening. 3416 included, If Mini-Cog + referred to specialty eval

12 mo Outcomes:

No health or utilization benefit

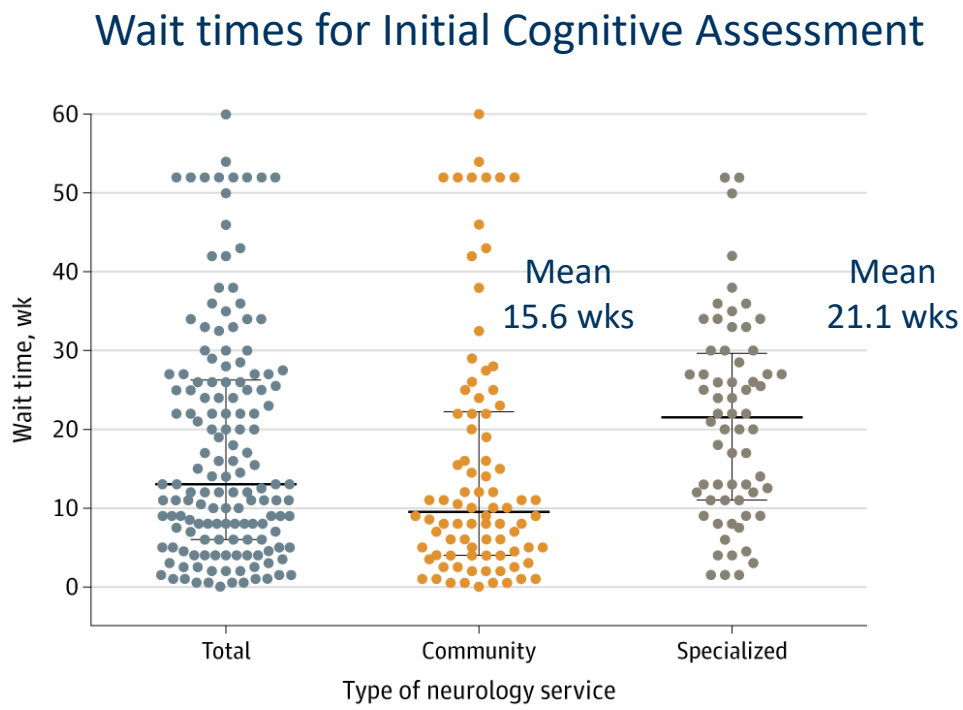
- 134 screened + (7.7%)
- Among screen +, 88 (66%) refused diagnostic work up

Fowler NR et al. Journal of the American Geriatrics Society. 2020.

VA QI Project similar design N=8342
26% failed screen, 72% refused eval

McCarten et al. Journal of the American Geriatrics Society. 2012.

Real World Practice



Knox. JAMA Netw Open. Oct 21 2026;9(10):e2639836.

- Currently, per report from clinically active colleague experts, quite frequently seeing asymptomatic people in their clinics who have had blood biomarker or PET scans and no cognitive testing. The anecdotes are worrying.
  - Care not aligned with current evidence or guideline
  - Access to treatment for people eligible is low and further reduced by these referrals

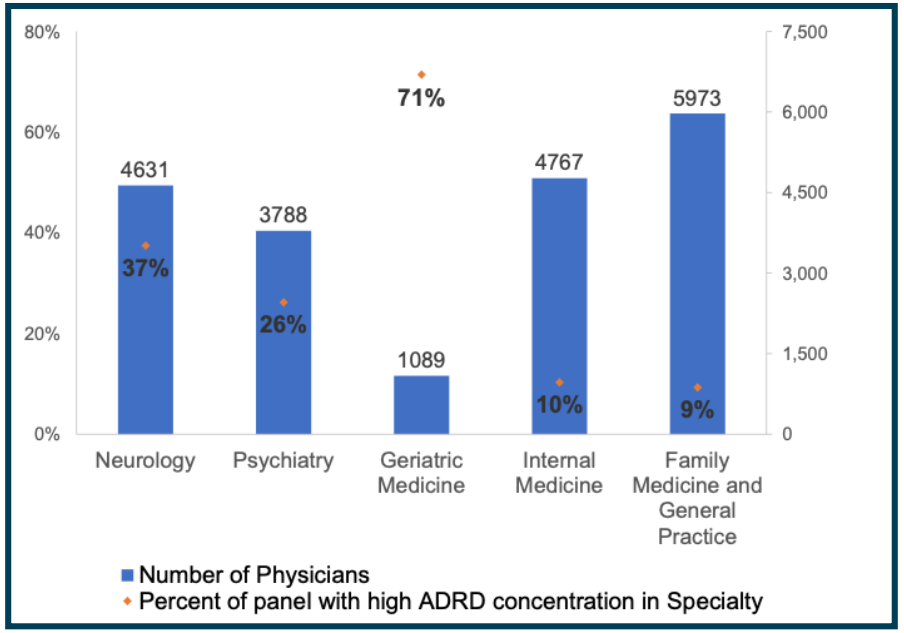
Getting a Diagnosis

This pathway is ineffective and takes too long due to numerous **barriers** at all levels

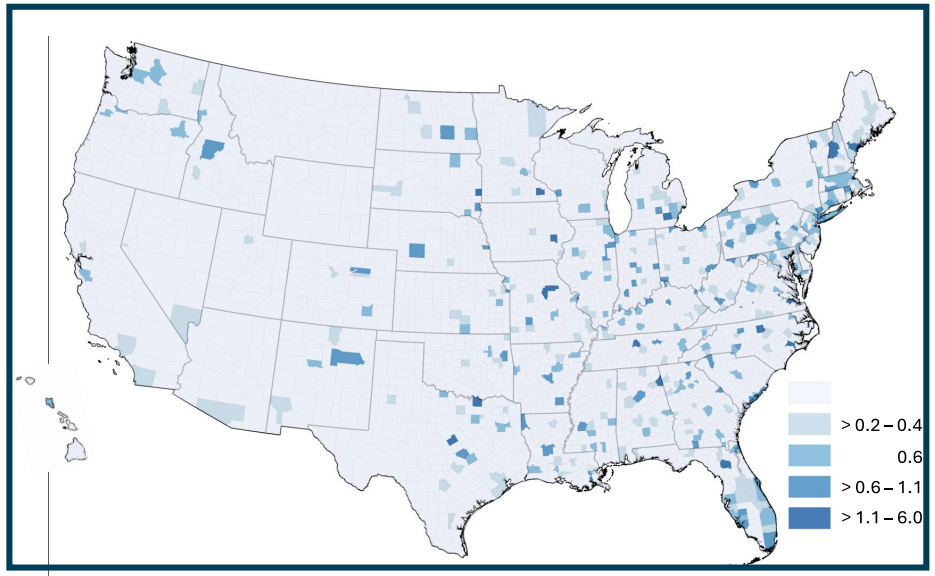
- Patient symptom recognition
- Stigma
- Tools for cognitive assessment
- Clinician expertise
- Complex clinical syndrome not measurable by a test
- Clinician expertise
- Communication of diagnosis
- Adverse consequences of label (autonomy, insurance)

Physician Specialties who Concentrate on Dementia Patients (defined by >25% of Medicare panel with dementia)

A minority of Medicare-billing neurologists (37%) and psychiatrists (26%) concentrate their practice on care of people with dementia



More than 96% of the neurologists, psychiatrists, geriatric medicine, and geriatric psychiatry physicians who concentrate their practice on ADRD are in urban areas.



Bynum, Unpublished work

Summary

Clarity about the words related to dementia used by clinicians, researchers, and advertisements to the public is needed

Use of blood-based biomarkers (BBB) for neurodegenerative disease including AD and other condition will continue to increase

AD neuropathology is one piece of the biological puzzle. Complexity necessitates humility about what happens next.

Research on economic implications of early detection needs to incorporate knowledge of the evolving basic and clinical science and the uncertainties and disagreements in the ADRD field

Bibliography

Bennett DA, Schneider JA, Arvanitakis Z, et al. Neuropathology of older persons without cognitive impairment from two community-based studies. Neurology. 2006;66(12):1837–1844.

Bennett DA, Schneider JA, Wilson RS, Bienias JL, Arnold SE. Neurofibrillary tangles mediate the association of amyloid load with clinical Alzheimer disease and level of cognitive function. Archives of Neurology. 2004;61(3):378–384.

Buckley RF, Townsend DL, Birkenbihl CJ, et al. Prognostic Value of Blood-Based P-Tau217 Levels for Progression to Cognitive Impairment. *JAMA.* 2026;336(11):950–959. doi:10.1001/jama.2026.12556

Cao Q, Tan C-C, Xu W, et al. The Prevalence of Dementia: A Systematic Review and Meta-Analysis. *Journal of Alzheimer's Disease*. 2020;73(3):1157-1166.

Chan JYC, Yau STY, Kwok TCY, Tsoi KKF. Diagnostic performance of digital cognitive tests for the identification of MCI and dementia: A systematic review. Ageing Res Rev. 2021 Dec;72:101506.

Chatanaka MK, Pascual Lorén M, Diamandis EP. Is screening for Alzheimer's disease ready for prime time? Ask Wilson and Jungner. Crit Rev Clin Lab Sci. 2025 Dec;62(8):631-645.

Ding Z, Lee TL, Chan AS. Digital Cognitive Biomarker for Mild Cognitive Impairments and Dementia: A Systematic Review. J Clin Med. 2022 Jul 19;11(14):4191.

Dou X, Lenzen S, Connelly LB, Lin R. Generational Differences in Age-Specific Dementia Prevalence Rates. *JAMA Netw Open.* 2025;8(6):e2513384.

Dubois B, Villain N, Schneider L, et al. Alzheimer Disease as a Clinical-Biological Construct—An International Working Group Recommendation. *JAMA Neurol.* 2024;81(12):1304–1311.

Fowler NR, Perkins A, Gao A, Sachs G, Boustani MA. Risks and benefits of screening for dementia in primary care: the IU CHOICE Trial. J Am Ger Soc. 2020;68:535-543.

Fowler NR, Perkins AJ, Gao S, Bakas T, Head KJ, Higbie A, Baucco C, Callahan CM, Williams-Farrelly MM, Boustani MA. Benefits and Harms of Dementia Screening for Family Members of Older Adults: A Randomized Clinical Trial. JAMA Intern Med. 2026 Jun 1;186(6):689-700.

Grande, G., Valletta, M., Rizzuto, D. *et al.* Blood-based biomarkers of Alzheimer's disease and incident dementia in the community. *Nat Med* 31, 2027–2035 (2025).

Jack CR, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimer's Dement. 2024; 20: 5143–5169.

Jack C Hu M, Wiste H et al. Lifetime and 10-year absolute risk of cognitive impairment in relation to amyloid PET severity: a retrospective, longitudinal cohort study. The Lancet Neurology, 24, 1016-1025

Manly JJ, Jones RN, Langa KM, et al. Estimating the Prevalence of Dementia and Mild Cognitive Impairment in the US: The 2016 Health and Retirement Study Harmonized Cognitive Assessment Protocol Project. *JAMA Neurol.* 2022;79(12):1242–1249.

Nelson PT, Alafuzoff I, Bigio EH, et al. Correlation of Alzheimer disease neuropathologic changes with cognitive status: a review of the literature. Journal of Neuropathology & Experimental Neurology. 2012;71(5):362–381.

Ossenkoppele, R., Pichet Binette, A., Groot, C. *et al.* Amyloid and tau PET-positive cognitively unimpaired individuals are at high risk for future cognitive decline. *Nat Med* 28, 2381–2387 (2022).

Palmqvist S, Whitson HE, Allen LA, Suarez-Calvet M, Galasko D, Karikari TK, Okrahvi HR, Paczynski M, Schindler SE, Teunissen CE, Zetterberg H, Carrillo MC, Edelmayer RM, Mahinrad S, McAteer MB, Kahale LA, Pahlke S, Tampi MP. Alzheimer's Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings. Alzheimers Dement. 2025 Jul;21(7):e70535. doi: 10.1002/alz.70535.

Rostamzadeh A, Bohr L, Wagner M, Baethge C, Jessen F. Progression of Subjective Cognitive Decline to MCI or Dementia in Relation to Biomarkers for Alzheimer Disease: A Meta-analysis. Neurology. 2022 Oct 25;99(17):e1866-e1874.

Schindler SE, Wolk DA. Predicting Risk of Cognitive Impairment With Alzheimer Disease Blood Biomarkers. *JAMA.* 2026;336(11):923–925. doi:10.1001/jama.2026.13322

Schnieder J. Neuropathology of Dementia Disorders. Continuum. 2022. 28(3):834-851

US Preventive Services Task Force. Screening for Cognitive Impairment in Older Adults: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2020;323(8):757–763.

Zetterberg H, Schott JM. Objectifying Subjective Cognitive Decline: The Prognostic Role of Alzheimer Biomarkers. Neurology. 2022 Oct 24;99(17):735-736.

Prior Probability of Dementia and MCI by Age

Age (years)	Dementia	MCI	References
50–59	0.3%	—	[1]
60–64	~1–2%	6.7% (95% CI 3.4–12.7)	[1-2]
65–69	~2–3%	8.4% (5.2–13.4)	[1-2]
70–74	~3–5%	10.1% (7.5–13.5)	[1-2]
75–79	~5%	14.8% (10.1–21.1)	[1-2]
80–84	~15% (80–89)	25.2% (16.5–36.5)	[1-2]
85+	~30–33%	5–25% (DSM-5 range by 85)	[4-5]
90–99	35.7%	—	[1]
≥100	65.9%	—	[1]

Population prevalence, which serves as the pretest probability, rises steeply with age.

In community samples, dementia roughly **doubles every 5 yrs**:

1–3% at 60–74,

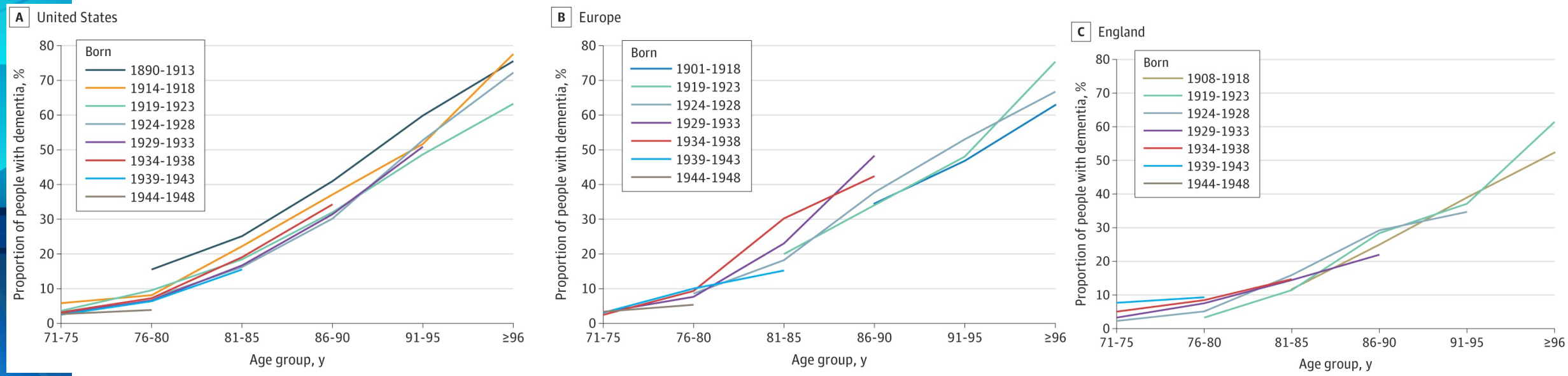
5% at 70–79,

15% at 80–89, and

35% at 90–99. [1]

MCI rises from about **7% at 60–64 to 25% at 80–84**.

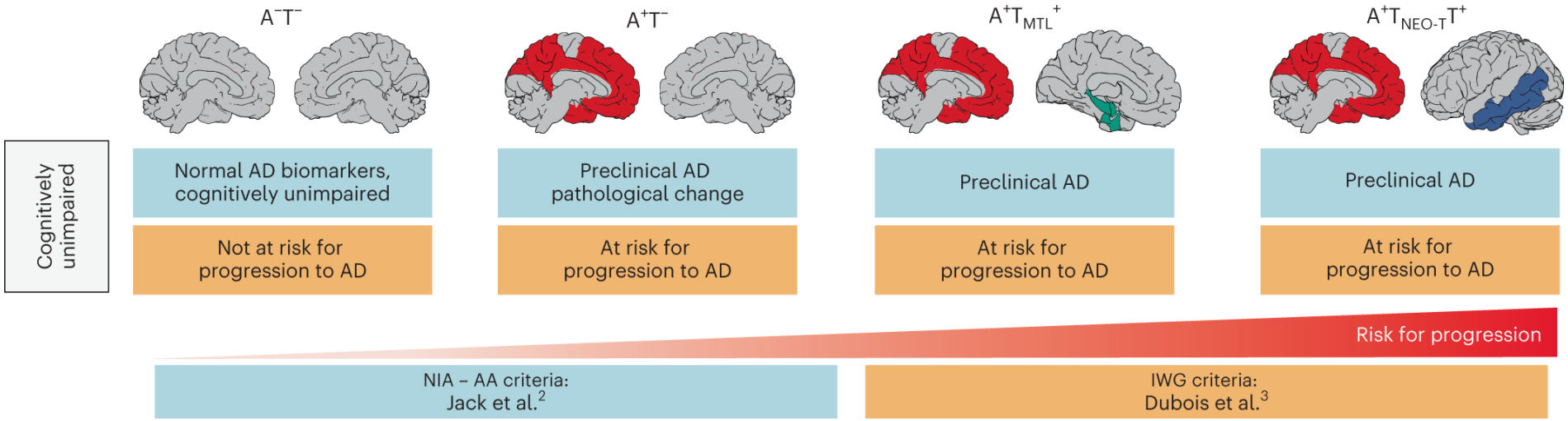
Figure 1: Generational Differences in Age-Specific Dementia Prevalence Rates



This cross-sectional study used data from 1994 to 2021 from the United States Health and Retirement Study (HRS), from 2004 to 2020 from the Survey of Health, Ageing and Retirement in Europe (SHARE), and from 2002 to 2019 from the English Longitudinal Study of Ageing (ELSA).

Dou X et al. JAMA Network Open. 2025. 2025;8;(6):e2513384.

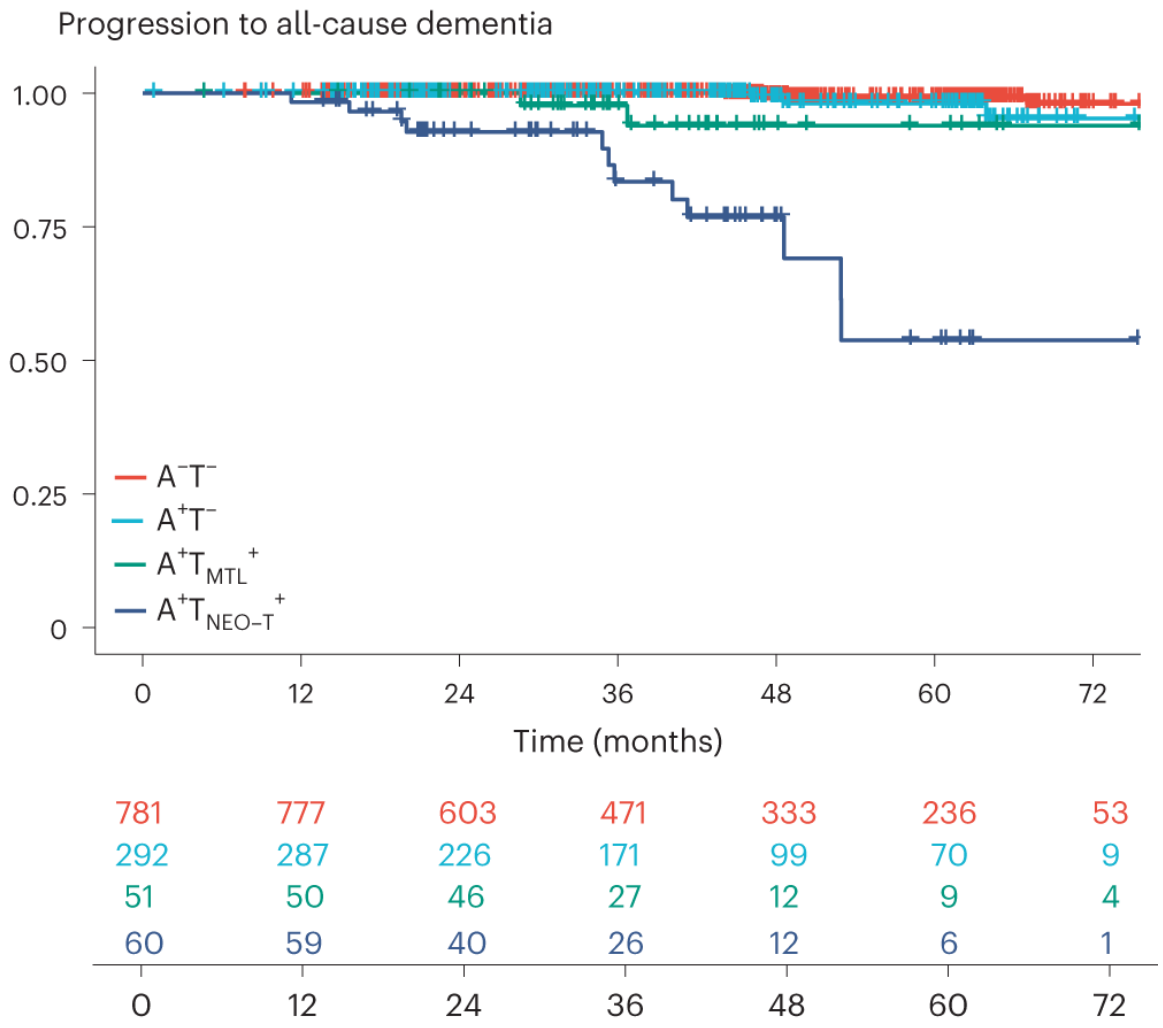
Prediction of amyloid +/- tau PET biomarkers of future dementia or MCI in people with normal cognition (3-5 yr risk)



Differences in the nomenclature of cognitively unimpaired individuals with (⁺) or without (−) in vivo biomarker evidence of Aβ (A) and tau (T) pathology in the NIA-AA versus IWG criteria for AD. Note that for the IWG criteria, the presumed 'risk for progression' level rises when both A and T biomarkers are positive.

Ossenkoppele, R., Pichet Binette, A., Groot, C. *et al.* Amyloid and tau PET-positive cognitively unimpaired individuals are at high risk for future cognitive decline. *Nat Med* **28**, 2381–2387 (2022).

Prediction of amyloid +/- tau PET biomarkers of future dementia or MCI in people with normal cognition (3-5 yr risk)



Progression to all-cause dementia (3-5 years)	
	HR (95% CI), P
A^-T^-	ref
A^+T^-	1.58 (0.46–5.4), P = 0.47
$A^+T_{MTL}^+$	6.22 (1.44–26.8), P = 0.01
$A^+T_{NEO-T}^+$	41.26 (16.70–102), P < 0.001

Ossenkoppele *et al*. *Nat Med* **28**, 2381–2387 (2022)

Centiloids of amyloid by PET prediction by age Dementia (MCI looks the same) lifetime and 10-year

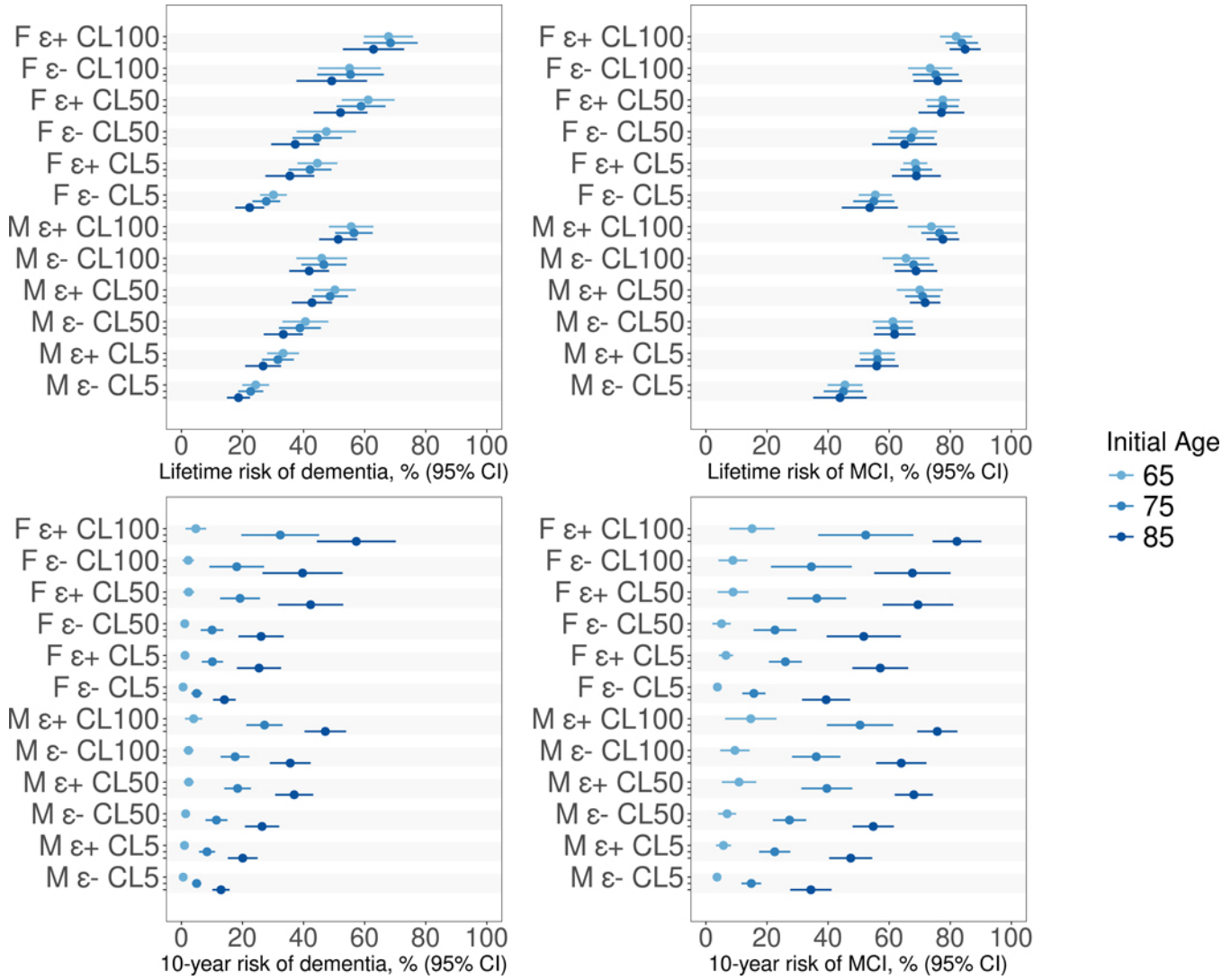


Figure 3:. Lifetime and 10-year absolute risks of MCI and dementia for individuals alive and cognitively unimpaired, by PET centiloid value, sex, *APOE* ε4 status, and starting age 95% CI bars are shown. MCI=mild cognitive impairment.

Jack Lancet Neurol. 2025 Dec;24(12):1016–1025

Continuous Amyloid PET Centiloids & Risk Dementia or MCI

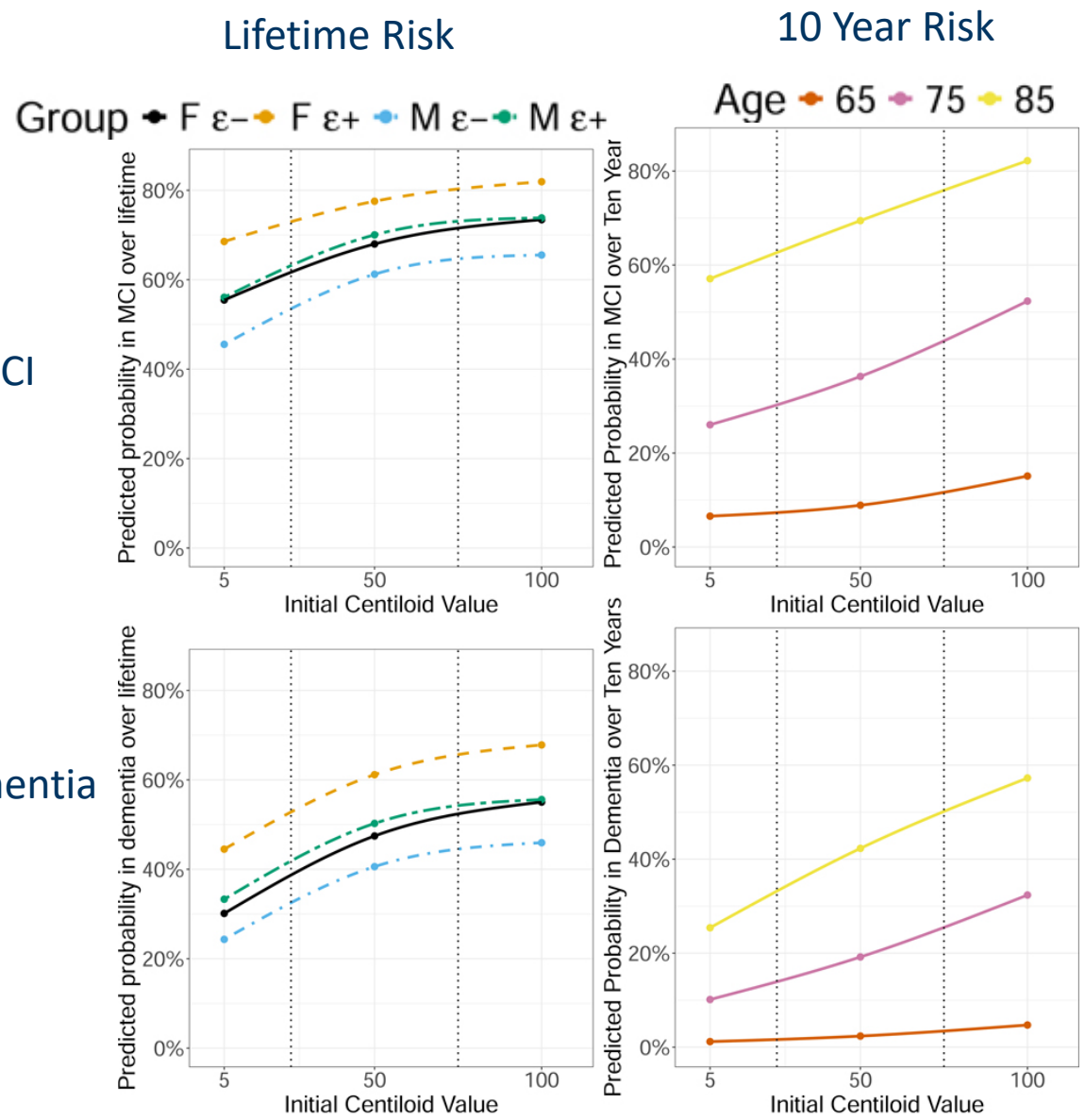


Figure 2:. Lifetime and 10-year absolute risks of MCI and dementia as a function of continuous amyloid PET centiloid value

Both lifetime absolute risk plots for MCI and dementia show four lifetime risk curves for the four sex and *APOE* ε4 status (carrier vs non-carrier) groups given at a starting age of 65years. Both 10-year absolute risk plots for MCI and dementia show three 10-year absolute risk curves for each starting age for a female *APOE* ε4 carrier. Vertical dotted lines indicate centiloid values 25 and 75 for reference.

Jack Lancet Neurol. 2025 Dec;24(12):1016–1025

What does it mean to have a “Disease” based on BBB?

- 50+ year-old male
- He has family history of AD and was ordered blood-based biomarker of AD to assess risk. He does not have any memory problems, and no cognitive testing was performed.
- Blood based biomarker came back as “indeterminate” (14% of blood-based biomarker came back as indeterminate, Galasko D. et al., JAD 2022)
- “I wish I had never gotten tested”

Application of Biomarkers



- "Best Biomarker Test"
  - 90% sensitivity 90% specificity
- 50+ year-old male
  - No family history of Alzheimer's disease
  - Having trouble with recalling names, but no other symptoms and normal testing
  - Biomarker test was "positive"

Considering Prior Probability of AD

- 50+ year-old male
  - No family history of Alzheimer's disease
  - Having trouble with recalling names, but no other symptoms and normal testing
  - Biomarker test was "positive"
  - Prevalence of AD in < 65 is ~ 4 % (prior probability)

Careful Application of Biomarkers

- 50+ year-old male
  - "Best Biomarker Test" 90% sensitivity 90% specificity
  - No family history of Alzheimer's disease
  - Having trouble with recalling names, but no other symptoms and normal testing
  - Prevalence of AD in < 65 is ~ 4 %
  - Negative predictive value ~ 99% (triage)

Careful Application of Biomarkers

- 50+ year-old male
  - "Best Biomarker Test" 90% sensitivity 90% specificity
  - No family history of Alzheimer's disease
  - Having trouble with recalling names, but no other symptoms and normal testing
  - Biomarker test was "positive"
  - Prevalence of AD in < 65 is ~ 4 %
  - Positive Predictive Value ~ 27%