DEMENTIA Care Aware

Early detection. Better care.

Understanding the New Diagnostics and Treatments in Alzheimer's Disease

Presenter:
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Assistant Professor
Department of Neurology, UCSF

PACE

Partners for Advancing Clinical Education

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Dr. Anna H. Chodos, faculty for this educational activity, has the following relevant financial relationships:

- Consultant, advisor, or speaker for Novo Nordisk

Dr. Lawren VandeVrede, faculty for this educational activity, has the following relevant financial relationships:

- Site PI for clinical trial for Biogen

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Dementia Care Aware was established, funded and supported by the California Department of Health Care Services (DHCS) from 2022-2024. The contents of this webinar may not necessarily represent the official views or policies of the State of California.

Logistics

Please use the chat and Q&A functions to enter your questions throughout.

A recording and materials will be available on **dementiacareaware.org** at the end of this webinar.

CE/CME information will be available at the end of the hour.

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Today's speakers

Presenter
Lawren VandeVrede, MD, PhD
Assistant Professor
Memory and Aging Center
Department of Neurology

Moderator
Anna Chodos, MD, MPH
Executive Director
Dementia Care Aware

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Review: the cognitive health assessment

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Begin~ Detection: the Cognitive Health Assessment

Screen patients older than age 65 annually (who don't have a pre-existing diagnosis of dementia)

Part 1

Take a Brief Patient History

Part 2

Use Screening Tools

Part 3

Document Care Partner Information

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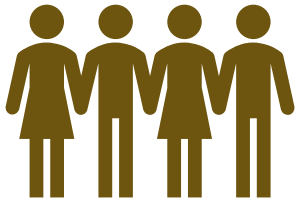
Next steps after a positive screen: a care pathway



Think about your population at risk and screen.

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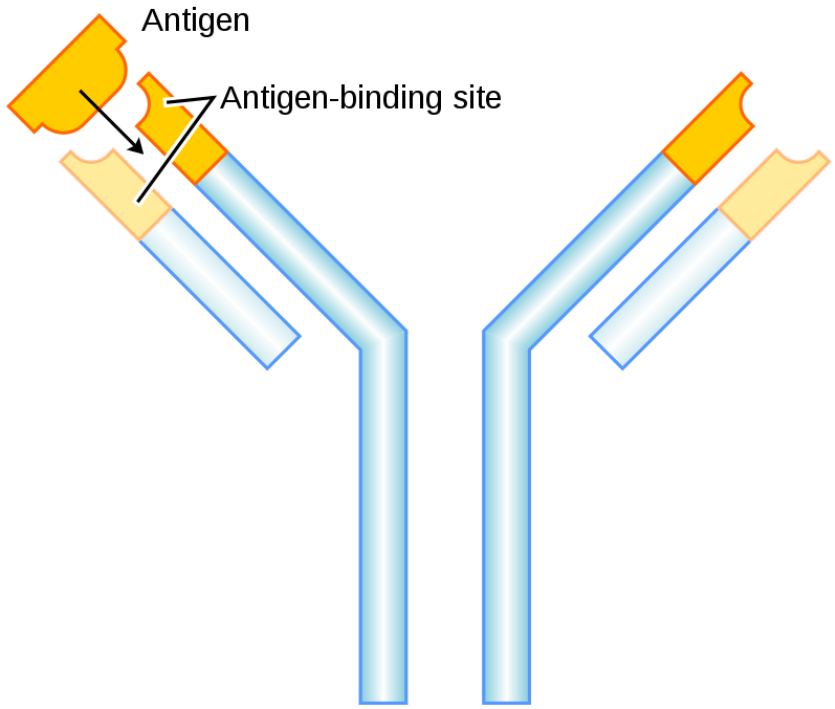
Learning Objectives

At the end of this session, learners will be able to:

1. Describe the pathophysiology of Alzheimer's disease.
2. List one way in which biomarkers are used to diagnose Alzheimer's disease.
3. Identify two criteria for disease-modifying treatments.
4. Discuss the risks of anti-amyloid treatments.



Today's presentation

Recent Advances in Alzheimer's Disease

1. AD Diagnosis: Clinical Symptoms ~ Biological Cause
2. AD Biomarkers: Multiple Modalities Available
3. AD Treatments: Clinically Implemented

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1. AD Diagnosis: Clinical Symptoms ~ Biological Cause

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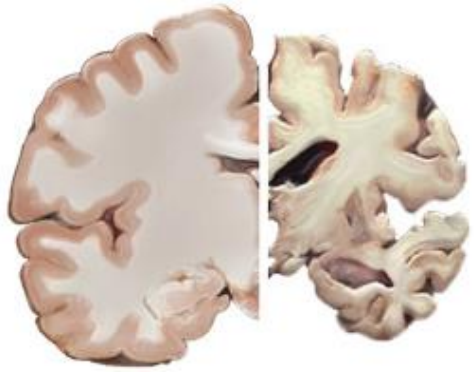
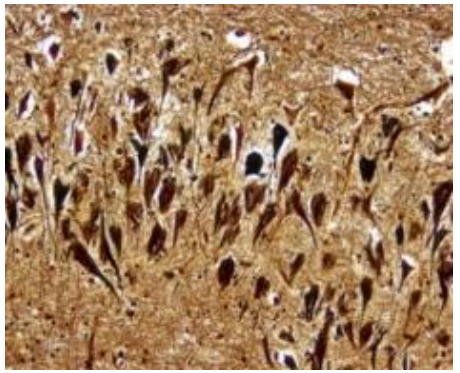
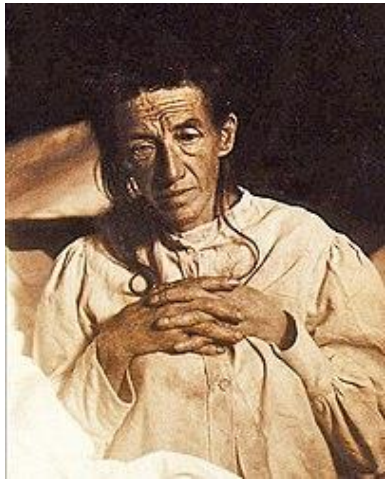
1906: Dr. Alzheimer's Discovery

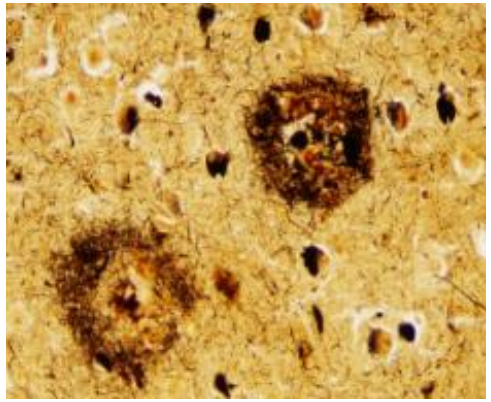


"The post-mortem showed an evenly atrophic brain…[t]he larger vascular tissues show arteriosclerotic change."



"Bielschowsky's silver method show very striking changes of the neurofibrils…[t]he cell itself disintegrate and only a tangle of fibrils indicates the place where a neuron was previously located."





"The glia have developed numerous fibers, moreover, many glial cells show adipose saccules."

"Distributed all over the cortex, but especially numerous in the upper layers, there are minute miliary foci which are caused by the deposition of a special substance in the cortex."

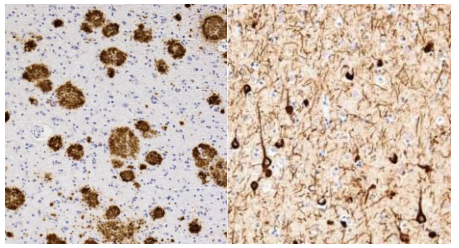
Alzheimer *Neurol Central* 1906

What is the difference between dementia and Alzheimer's disease?

Dementia is an umbrella term that refers to cognitive impairment that impairs function in everyday life. There are many causes of cognitive impairment, many stages of cognitive impairment (dementia is one), and many syndromes that present with cognitive impairment.

Cognitive Impairment

Alzheimer's disease (AD) is a specific brain disease defined by specific brain pathology (amyloid plaques and tau neurofibrillary tangles). AD is the most common cause of cognitive impairment in the elderly, though many patients with AD have other contributing conditions.



Amyloid Plaques | Tau Tangles

"Alzheimer's Disease"

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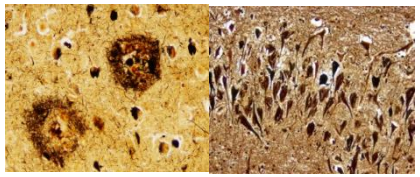
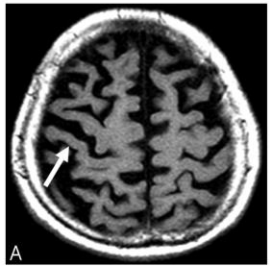
Symptom/Biological Relationship is Complex

Simple Model of AD:



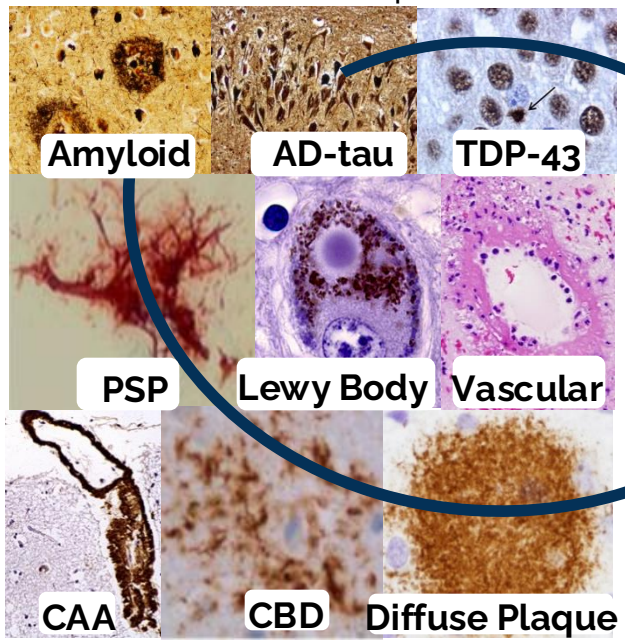
Amyloid/Tau



Neurodegeneration

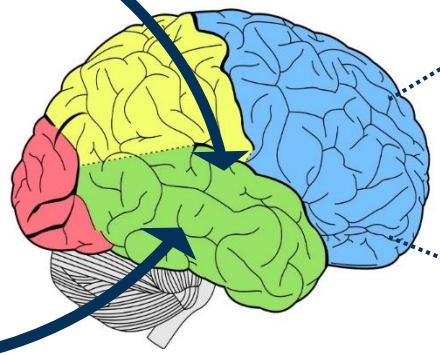
Dementia

Pathologic Changes
(often multiple)



Location
(often variable)

Individual Factors
(often diverse)



Genetics
Education
Age
Environment
Race

Syndrome
(often atypical)

AD-Related Syndromes
Late-Onset Amnestic
Early-Onset Amnestic
Corticobasal Syndrome
Frontal/Dysexecutive
Logopenic Aphasia
Posterior Cortical Atrophy

Syn-Related Syndromes
Parkinson's Disease
Dementia with Lewy Bodies
Multiple System Atrophy
Pure Autonomic Failure

Tau-Related Syndromes
Corticobasal Syndrome
Richardson's Syndrome
Non-fluent Aphasia Variant
Behavioral Variant of FTD

TDP-Related Syndromes
Behavioral Variant of FTD
Semantic Variant of PPA
Non-fluent Aphasia Variant
LATE

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Take-Home Points

- Alzheimer's clinical diagnosis is based on progressive and insidious onset of cognitive symptoms, which eventually impact daily function, with stages ranging from SCI to MCI and dementia (mild, moderate, severe).

- Biological diagnosis requires biomarker-confirmation of amyloid, whereas other biomarkers may inform biological stage/co-pathology.

- AD is one cause of symptoms, but co-pathology and non-AD causes are common, especially in younger patients and in atypical presentations.

- Remember to consider non-neurodegenerative causes of symptoms!

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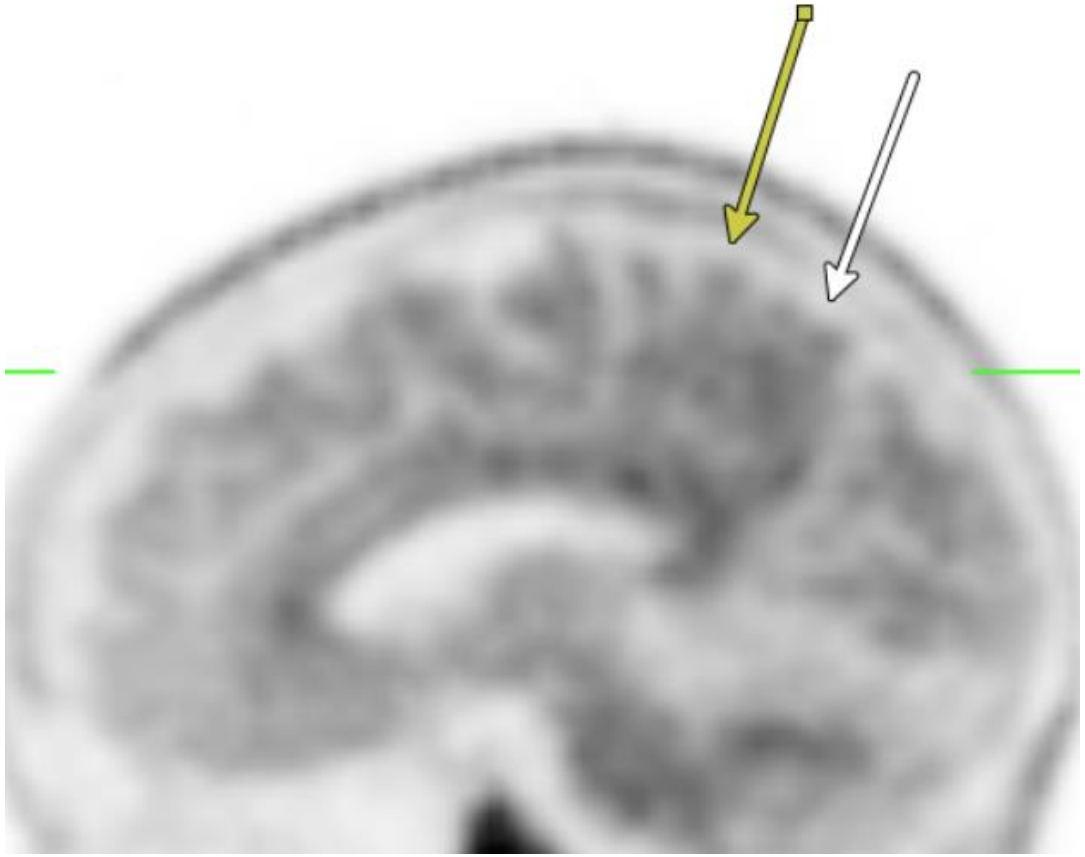

2. AD Biomarkers: Multiple Modalities Available

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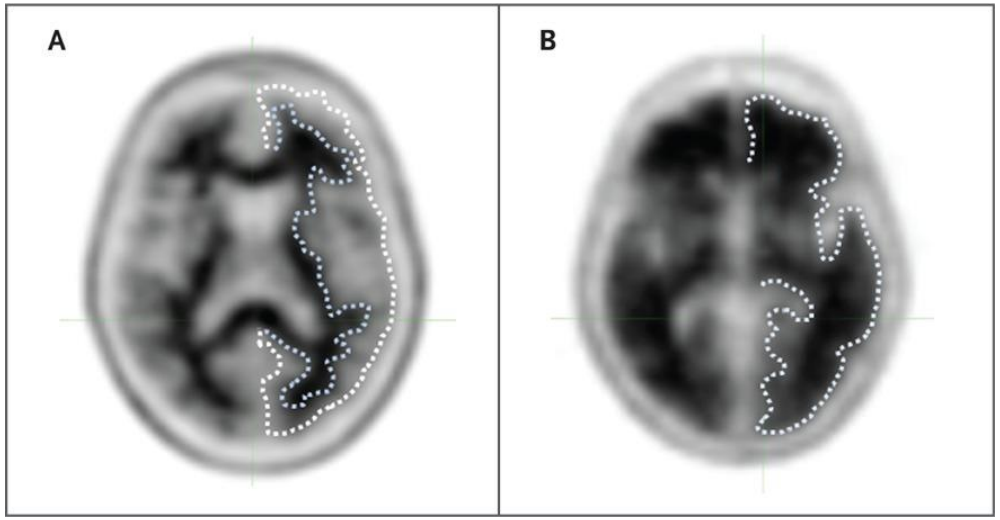
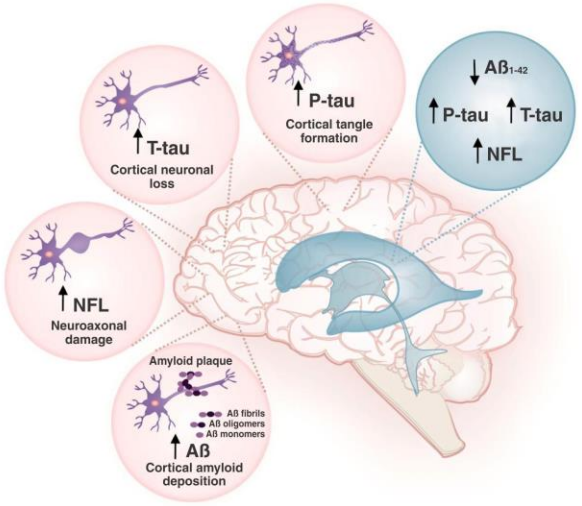
Alzheimer's Disease Biomarker Tests



PET



CSF

Blood

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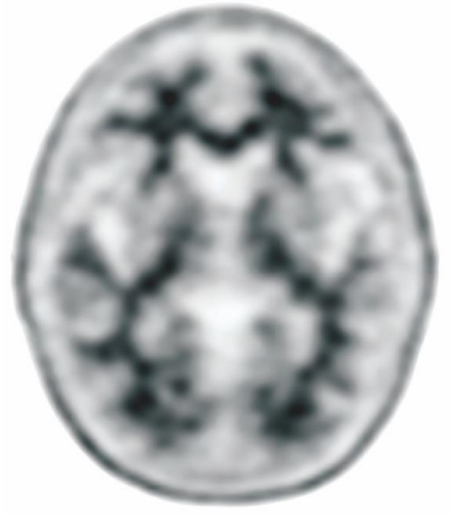
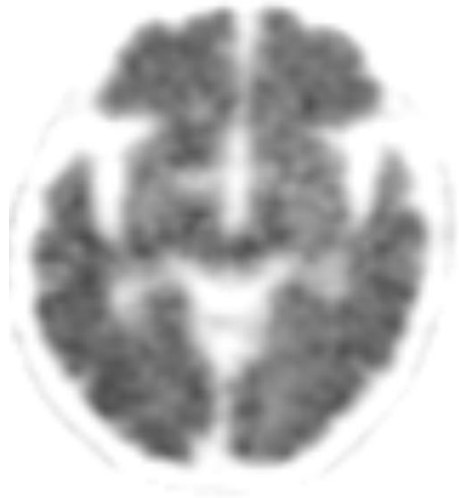
Amyloid PET

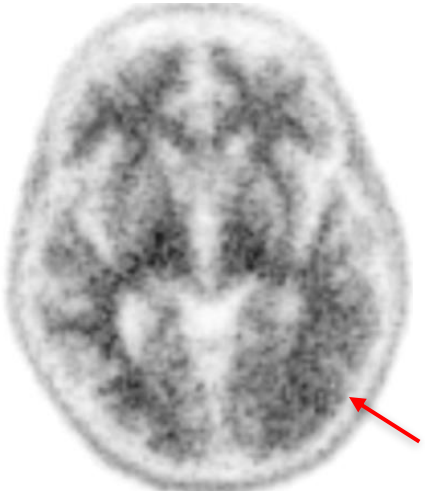
- **Procedure:** Patient is injected with a radiotracer that binds amyloid plaques and a PET scan images the radiotracer binding
- **Interpretation:** Visually read as "positive" or "negative"; though can be quantified as "centiloids"
- **Advantages:**
  - Visualizes the burden and distribution of amyloid plaques;
  - Can track amyloid plaque removal by anti-amyloid treatments;
  - Insurance coverage is clear for certain indications (CMS)
- **Drawbacks (non-modifiable):**
  - Requires expensive, specialized equipment and highly trained personnel not available at every center;
  - Requires a small amount of radioactivity;
  - Cost is typically ~$5,000/scan



Negative



Diffusely Positive



Focally Positive

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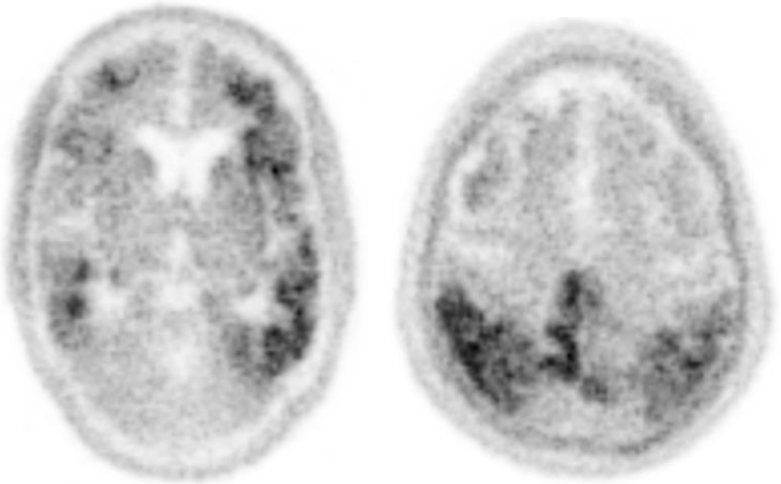
Tau PET

- **Procedure**: Patient is injected with a radiotracer that binds tau tangles and a PET scan images the radiotracer binding
- **Interpretation**: Visually read as "positive" or "negative"; though can be quantified (ongoing area of research)
- **Advantages**:
  - Visualizes the burden and distribution of tau tangles;
  - Location and amount of signal correlates with symptoms and disease severity
- **Drawbacks (non-modifiable)**:
  - Requires expensive, specialized equipment and highly trained personnel not available at every center;
  - Requires a small amount of radioactivity;
  - Insurance coverage is unclear in most cases and cost is typically ~$10,000/scan



Logopenic Variant | Posterior Cortical Atrophy

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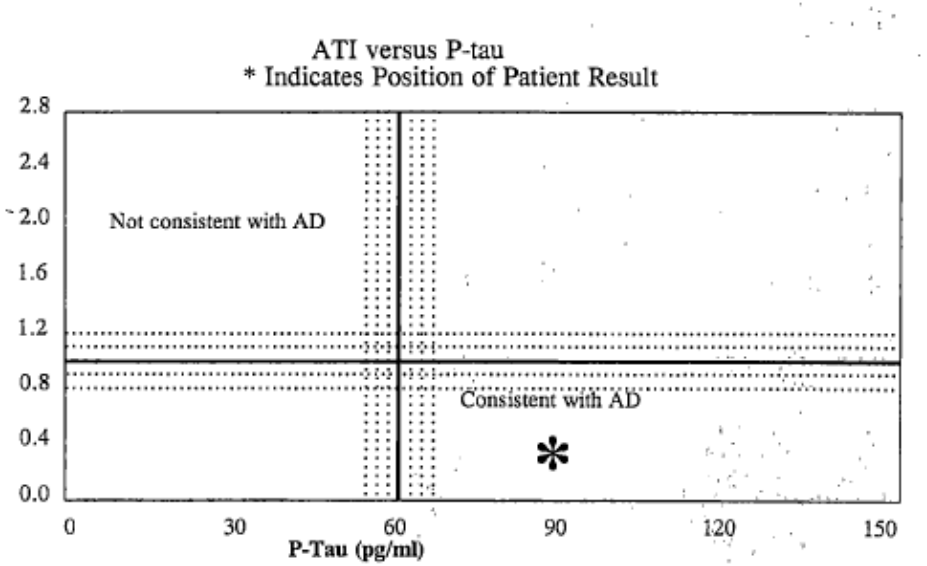
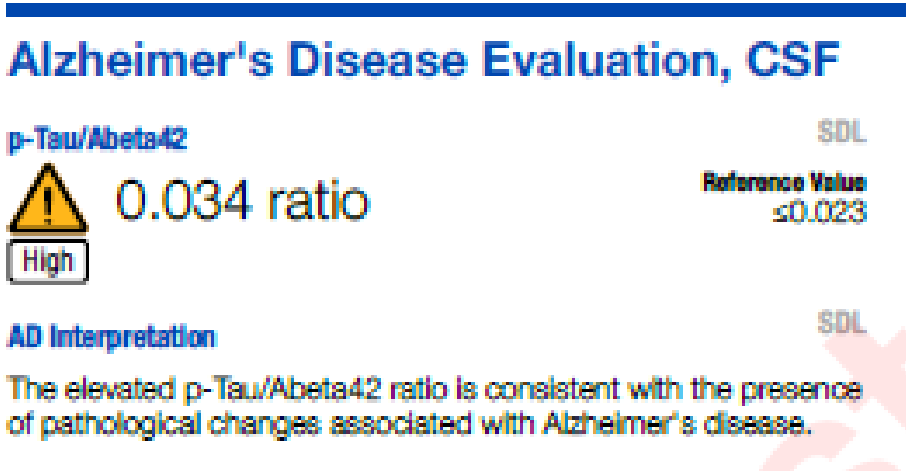
CSF Testing

- Procedure:
  - Patient undergoes a lumbar puncture (LP) to collect cerebrospinal fluid (CSF) and certain proteins related to plaques and tangles are measured
- Interpretation: Positive or negative (or intermediate) based on the cut-off value for a ratio; continuous values provided
- Advantages:
  - Tests for non-AD conditions can be performed;
  - Covered by most insurances for AD diagnosis
- Drawbacks (non-modifiable):
  - Barriers due to negative stigma around lumbar puncture and patient contraindications;
  - Time-consuming and expensive to set up clinics, frequently poorly reimbursed;
  - Occasionally unsuccessful, patients may have side effects.





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Blood-based Biomarkers

- Procedure:
  - Patient undergoes a blood draw and certain proteins related to plaques and tangles are measured
- Interpretation: Positive or negative (or intermediate) based on the cut-off value; continuous values provided
- Advantages:
  - More acceptable/accessible and less burdensome;
  - Less expensive than other modalities (with similar accuracies);
  - Blood work routine part of current medical paradigm
- Drawbacks (potentially modifiable/addressable):
  - Variability in the accuracy (difficult to parse for non-experts);
  - Lack of reimbursement or inconsistent reimbursement;
  - Certain peripheral factors impact test results (kidney and liver disease, extremes of BMI, motor neuron disease)

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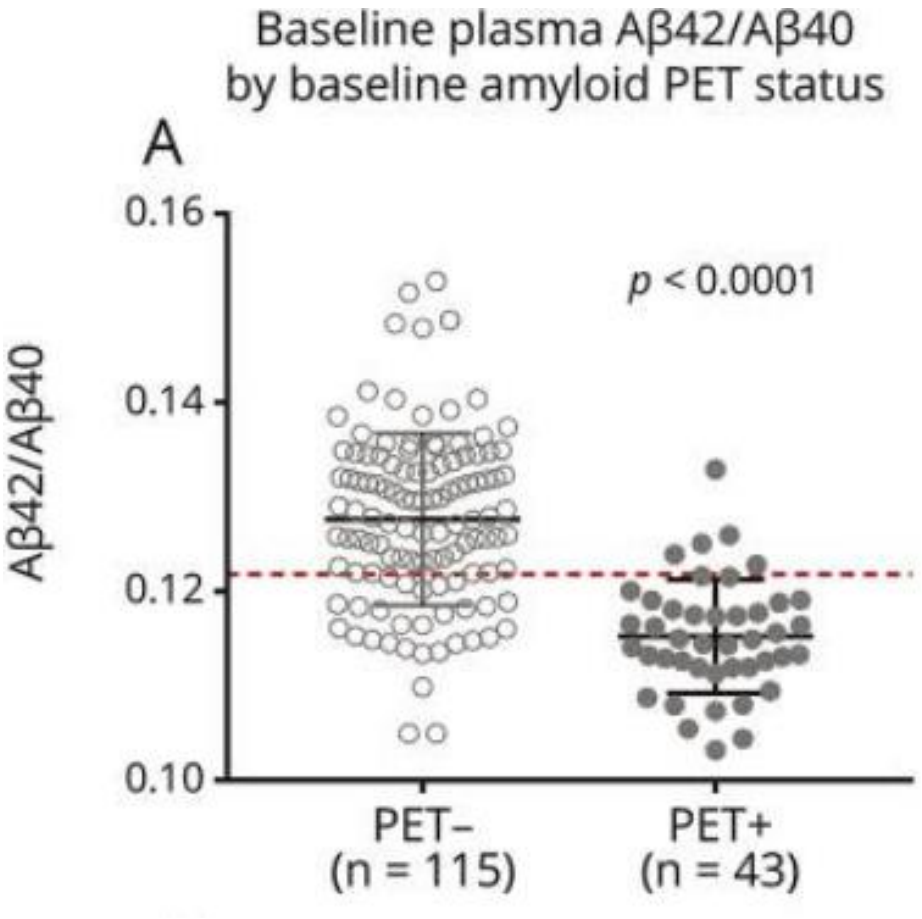
Multiple Modalities Permit An Individualized Approach

Patient-specific factors	Amyloid PET	CSF tests	Blood tests
Patient is very concerned about risks from radiation	↓	↑	↑
Patient has severe claustrophobia	↓	↑	↑
Patient lacks insurance coverage for biomarker testing and cost is a concern	↓	↓	↑
Patient is treated with anticoagulant medications	↑	↓	↑
Patient is very concerned about invasiveness or risks of lumbar puncture	↑	↓	↑
Patient has risk factors for a difficult lumbar puncture such as scoliosis, prior lumbar back surgery, or severe lumbar adiposity	↑	↓	↑
Patient's differential diagnosis includes non-AD conditions that can be evaluated for with CSF tests	↓	↑	↓
Patient is a candidate for AD-specific treatments and insurance requires CSF or amyloid PET for biomarker confirmation	↑	↑	↓
Patient can only access lower accuracy or poorly validated AD blood tests	↑	↑	↓
Patient has chronic kidney disease, liver cirrhosis, or prior myocardial infarction or stroke	↑	↑	↓

VandeVrede and Schindler, *Alzheimer's and Dementia 2024*

Aβ Ratios Are Clinically Available



- Sensitive to early amyloid accumulation
- Relatively specific to AD, but fold-change is not high
- May work better in earlier stages of disease (?)

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Schindler *Neurology* 2019

P-tau217 is Gold Standard BBM for AD

Plasma phosphorylated tau 217 and phosphorylated tau 181 as biomarkers in Alzheimer's disease and frontotemporal lobar degeneration: a retrospective diagnostic performance study

Elisabeth H Thijssen, Renaud La Joie*, Amelia Strom, Corrina Fonseca, Leonardo Iaccarino, Amy Wolf, Salvatore Spina, Isabel E Allen, Yann Cobigo, Hilary Heuer, Lawren VandeVrede, Nicholas K Proctor, Argentina Lario Lago, Suzanne Baker, Rajeev Sivasankaran, Agnieszka Kieloch, Arvind Kinhikar, Lili Yu, Marie-Anne Valentin, Andreas Jeromin, Henrik Zetterberg, Oskar Hansson, Niklas Mattsson-Carlgren, Danielle Graham, Kaj Blennow, Joel H Kramer, Lea T Grinberg, William W Seeley, Howard Rosen, Bradley F Boeve, Bruce L Miller, Charlotte E Teunissen, Gil D Rabinovici, Julio C Rojas, Jeffrey L Dage, Adam L Boxer, on behalf of the Advancing Research and Treatment for Frontotemporal Lobar Degeneration investigators†*

nature medicine

Article | Open access | Published: 21 February 2024

Highly accurate blood test for Alzheimer's disease is similar or superior to clinical cerebrospinal fluid tests

Nicolas R. Barthélemy, Gemma Salvadó, Suzanne E. Schindler, Yingxin He, Shorena Janelidze, Lyduine E. Collij, Benjamin Saef, Rachel L. Henson, Charles D. Chen, Brian A. Gordon, Yan Li, Renaud La Joie, Tammie L. S. Benzinger, John C. Morris, Niklas Mattsson-Carlgren, Sebastian Palmqvist, Rik Ossenkoppele, Gil D. Rabinovici, Erik Stomrud, Randall J. Bateman ✉ & Oskar Hansson ✉

JAMA Neurology | Original Investigation

Diagnostic Accuracy of a Plasma Phosphorylated Tau 217 Immunoassay for Alzheimer Disease Pathology

Nicholas J. Ashton, PhD; Wagner S. Brum; Guglielmo Di Molfetta, MSc; Andrea L. Benedet, PhD; Burak Arslan, MD; Erin Jonaitis, PhD; Rebecca E. Langhough, PhD; Karly Cody, PhD; Rachael Wilson, PhD; Cynthia M. Carlsson, PhD; Eugeen Vanmechelen, PhD; Laia Montoliu-Gaya, PhD; Juan Lantero-Rodriguez, PhD; Nesrine Rahmouni, MSc; Cecile Tissot, PhD; Jenna Stevenson, PhD; Stijn Servaes, PhD; Joseph Therriault, PhD; Tharick Pascoal, MD, PhD; Alberto Lleó, MD, PhD; Daniel Alcolea, MD, PhD; Juan Fortea, MD, PhD; Pedro Rosa-Neto, MD, PhD; Sterling Johnson, MD, PhD; Andreas Jeromin, PhD; Kaj Blennow, MD, PhD; Henrik Zetterberg, MD, PhD

JAMA Neurology | Original Investigation

Detection of Alzheimer Neuropathology in Alzheimer and Non-Alzheimer Clinical Syndromes With Blood-Based Biomarkers

Lawren VandeVrede, MD, PhD; Hanna Cho, MD, PhD; Mark Sanderson-Cimino, PhD; Fattin Wekselman, BS; Yann Cobigo, PhD; Maria Luisa Gorno-Tempini, MD; Hilary W. Heuer, PhD; Joel H. Kramer, PhD; Argentina Lario Lago, PhD; Dana Leichter, BS; Peter Ljubenkov, MD; Bruce L. Miller, MD; David C. Perry, MD; Gil D. Rabinovici, MD; Julio C. Rojas, MD, PhD; Howard J. Rosen, MD; Rowan Saloner, PhD; Adam Staffaroni, PhD; Gallen Triana-Baltzer, PhD; Salvatore Spina, MD, PhD; William W. Seeley, MD; Lea T. Grinberg, MD, PhD; Hartmuth C. Kolb, PhD; Renaud La Joie, PhD; Adam L. Boxer, MD, PhD

JAMA | Original Investigation

Blood Biomarkers to Detect Alzheimer Disease in Primary Care and Secondary Care

Sebastian Palmqvist, MD, PhD; Pontus Tideman, MSc; Niklas Mattsson-Carlgren, MD, PhD; Suzanne E. Schindler, MD, PhD; Ruben Smith, MD, PhD; Rik Ossenkoppele, PhD; Susanna Calling, MD, PhD; Tim West, PhD; Mark Monane, MD, MBA; Philip B. Verghese, PhD; Joel B. Braunstein, MD, MBA; Kaj Blennow, MD, PhD; Shorena Janelidze, PhD; Erik Stomrud, MD, PhD; Gemma Salvadó, PhD; Oskar Hansson, MD, PhD

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PrecivityAD2 (C2N): Mass Spec Assay

- PrecivityAD2 incorporates p-tau217/np-tau217 ratio and $A\beta_{42/40}$ ratio measured by LC-MS/MS and predicts amyloid PET positivity
- Highest diagnostic accuracy in head-to-head, comparable to CSF
- PrecivityAD2: $1450, with unclear insurance coverage due to lack of FDA approval or coverage determination. Financial assistance programs are available.
- Somewhat cumbersome to incorporate into clinical workflow due to kit requiring cold chain storage (though at home blood draw is available).

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Numerous P-tau217 Immunoassays

Fujirebio Lumipulse (G1200)

LabCorp

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Use a keyword, test name or number

Phosphorylated Tau 217 (pTau-217), Plasma

TEST: 484390 CPT: 83520

Print Share

Include LOINC® in print

MAYO CLINIC LABORATORIES

Phospho-Tau 217, Plasma

Test ID: PT217

Quest AD-Detect Phosphorylated tau217 (p-tau217), Plasma

Test code: 13825

Quanterix SiMoA (HD-X)

ALZpath Assay: p-Tau 217 Detection Made Simple

Expert Accelerator Lab Services:

Janssen Assay (p217+ tau): Validated Excellence at Your Fingertips

Roche Elecsys (cobas)

Roche

Products Health Topics Services

- The Elecsys® pTau217 plasma biomarker test is being developed as part of an ongoing partnership between Roche and Eli Lilly and Company
- Once approved, the test will aid healthcare providers in identifying amyloid pathology, a key feature of Alzheimer's disease

Appropriate Use for Clinical AD Biomarker Testing

Patients who are undergoing an evaluation who have objective evidence of cognitive impairment (recommend AGAINST testing patients with no symptoms):

1) In whom AD is considered a potential cause of cognitive impairment;

AND

2) biomarker testing is expected to affect diagnosis and/or management by:
   a) improving the accuracy of dementia diagnosis;
   b) and/or determining whether patients may be candidates for AD-specific treatments, such as anti-amyloid antibodies.

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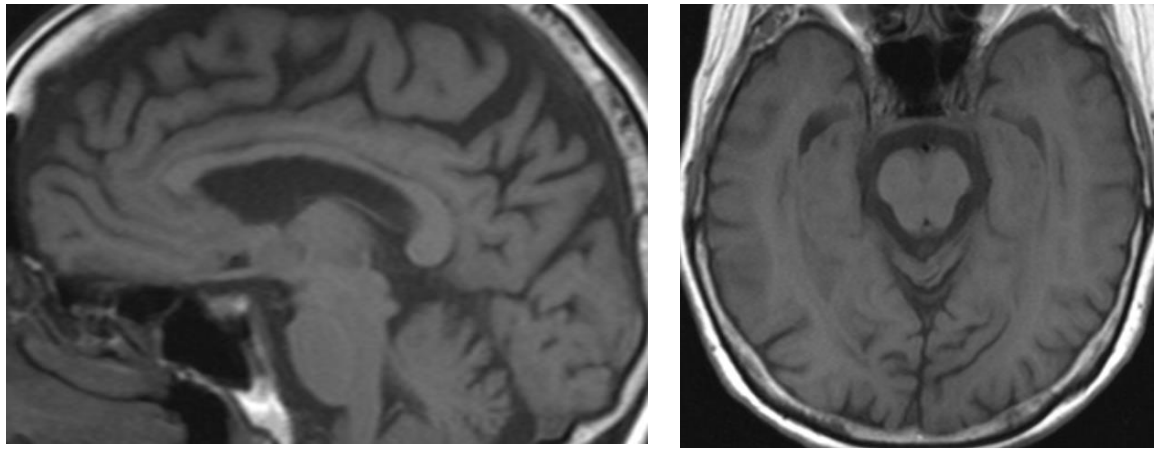
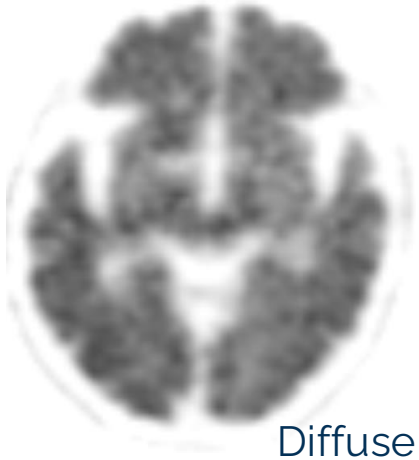
Triage Prior to PET

- 79-year-old woman with high cholesterol and prediabetes, presents with two years of progressive memory and navigation difficulty that have begun to interfere with her day-to-day functioning.
- Neurological exam was unremarkable. NPSY testing revealed trouble with delayed recall and visuospatial tasks; MMSE 25/30 (-3 delayed recall, -1 repetition, -1 pentagons).
- Diagnosis: mild dementia with high suspicion of AD pathology.



Brain MRI with mild precuneus and hippocampal atrophy with a mild burden of white matter disease.

BBM Testing:		
P-tau181	**2.77 pg/mL (RR <0.98)**	**High**
NfL	5.12 pg/mL (RR <7.64)	



Diffusely positive florbetapir PET.

OUTCOME: AD pathology was confirmed by PET scan after triage with BBM. Patient was approved for lecanemab and treatment was initiated.

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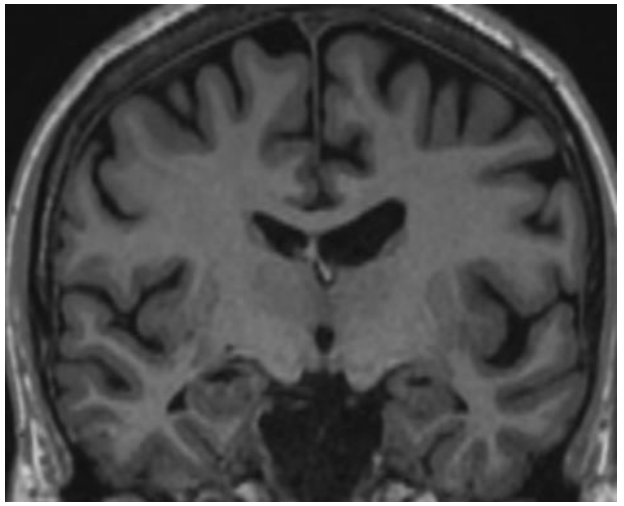
Atypical Presentations

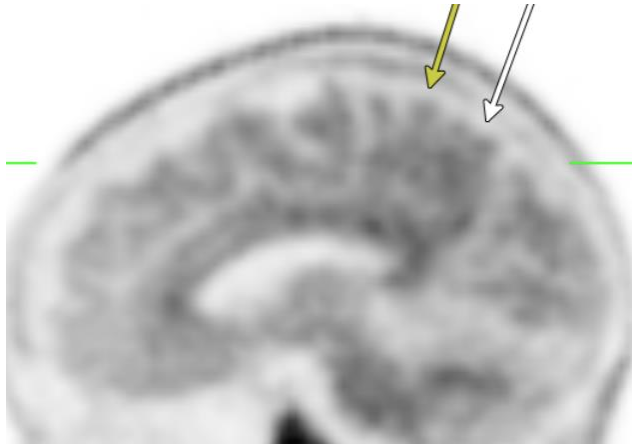
- 58-year-old woman with high blood pressure, fibromyalgia, chronic fatigue syndrome, IBS, PTSD, and anxiety, presenting for evaluation of two years of "brain fog."
- Neurological exam suggested a component of functional overlay. Neuropsychological testing found deficits in learning, memory, attention, and processing speed, MMSE 28/30.
- Diagnosis: MCI; BBM sent due to diagnostic uncertainty for AD.



Brain MRI with mild asymmetric atrophy, fairly reassuring for age.

BBM Testing:			
P-tau181	**1.47 pg/mL**	**(RR <0.98)**	**High**
NfL	3.47 pg/mL	(RR <3.78)	

OUTCOME: Positive p-tau181 warranted amyloid PET, which was positive. Patient was considered for disease-modifying treatment with lecanemab but ultimately declined.



Positive florbetapir PET.

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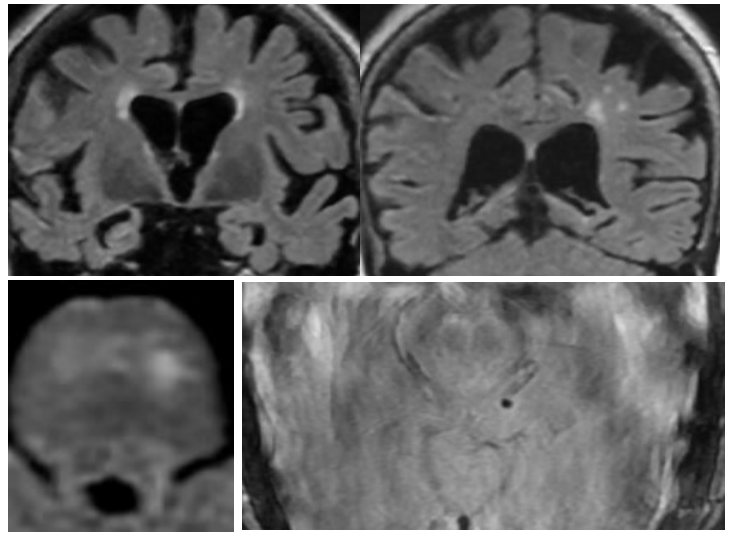
Diagnosis of Mixed Etiology Dementia

- 87-year-old woman with high blood pressure, high cholesterol, and hypothyroidism, presenting with cognitive changes for at least one year (likely longer).
- Neurological exam notable for difficulty mimicking complex hand gestures; NPSY testing revealed deficits in complex visuo-construction and recall, naming and generativity, and automatic sequencing, MMSE 22/30.
- Diagnosis: multi-domain moderate dementia with deficits in visuospatial and executive function, followed by memory.



Brain MRI with moderate hippocampal atrophy, white matter disease, and lobar microhemorrhage.

BBM Testing:		
P-tau181	0.49 pg/mL (RR <0.98)	
NfL	**58.6 pg/mL (RR <51.2)**	**High**

OUTCOME: Concordant negative AD biomarkers suggest non-AD etiology despite high clinical suspicion, working diagnosis is now multifactorial, includes vascular disease, LATE, and CAA.

Negative florbetapir PET.

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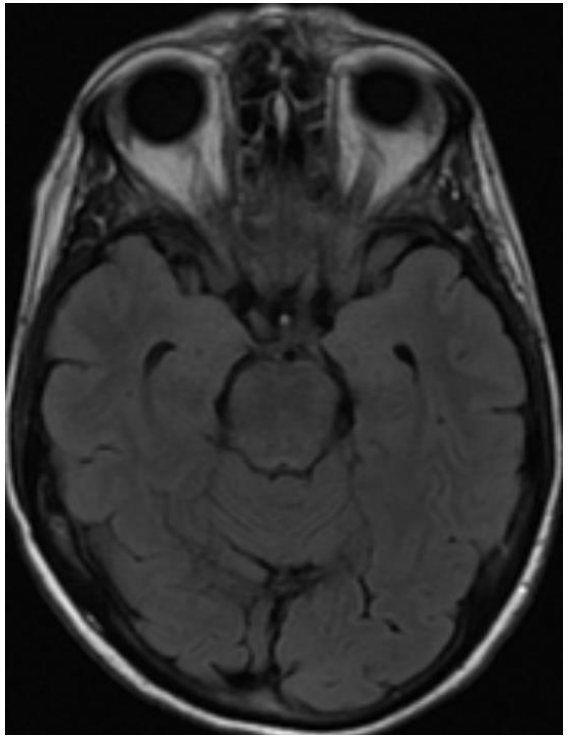
Lower Suspicion of Disease

- 69-year-old woman with insomnia, anxiety, and positive family history for AD, followed in clinic for five years of cognitive concerns after initial work-up with negative CSF testing for AD biomarkers in 2019. Reports worsening memory symptoms.
- Normal neurologic exam and average NPSY testing (thought to have high premorbid baseline due to educational attainment).
- Diagnosis: subjective cognitive impairment (SCI) with suspicion for neurodegenerative disease.



Reassuring MRI for age (perhaps mild hippocampal atrophy)

BBM Testing:		**2023**	**2024**
P-tau181	(RR <0.98)	0.59 pg/mL	0.49 pg/mL
NfL	(RR <7.64)	2.54 pg/mL	2.21 pg/mL

OUTCOME: Unambiguously negative tests provided reassurance that cognitive symptoms were unlikely to be due to AD (OSA later diagnosed).

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Take-Home Points

- Several biomarkers are clinically available to biologically diagnose AD
- CSF and amyloid PET have the longest history of use and clear coverage; tau PET shows promise (biologic staging?), not part of routine use yet
- Several blood-based AD biomarkers are clinically available (p-tau217 looks like the best), but availability, cost, and insurance coverage are moving targets, especially with a proliferation of tests

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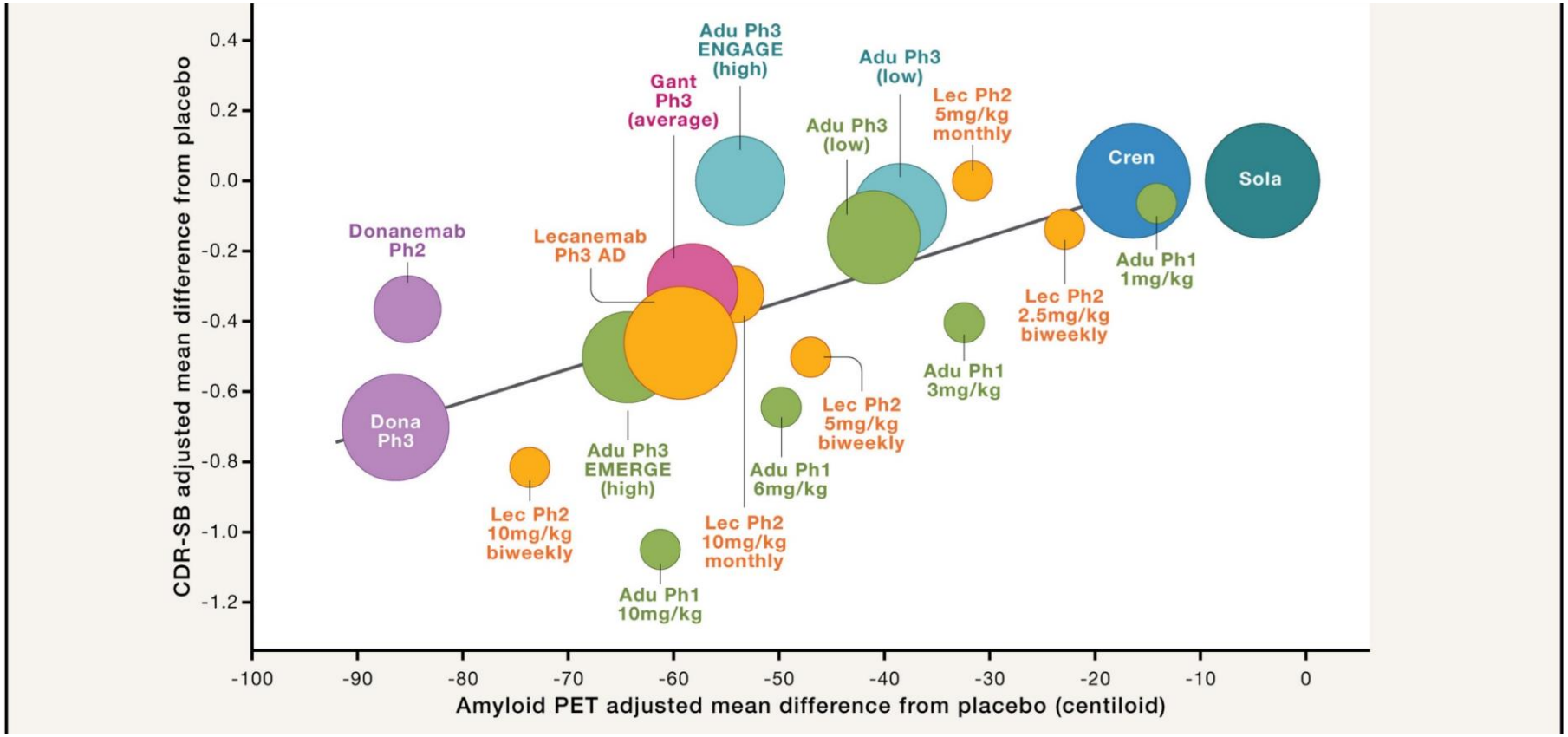

3. AD Treatments: Clinically Implemented

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2005-present: Amyloid Treatment Era

2005-2012 Bapineuzmab Ph2/3

2009-2017 Solaneuzemab Phase 3 (x3)

2012-present DIAN-TU

2001-2003: AN1792

2012-2021 Lecanemab Phase 2

2014-2023 Solaneuzemab Prevention Trial

2015-2019 Multiple Ph3 β-Secretase Trials

2015-2019 Aducanumab Ph3 (x2)

2016-2019 Crenezumab Ph3 (x2)

2017-2021 Donanemab Phase 2

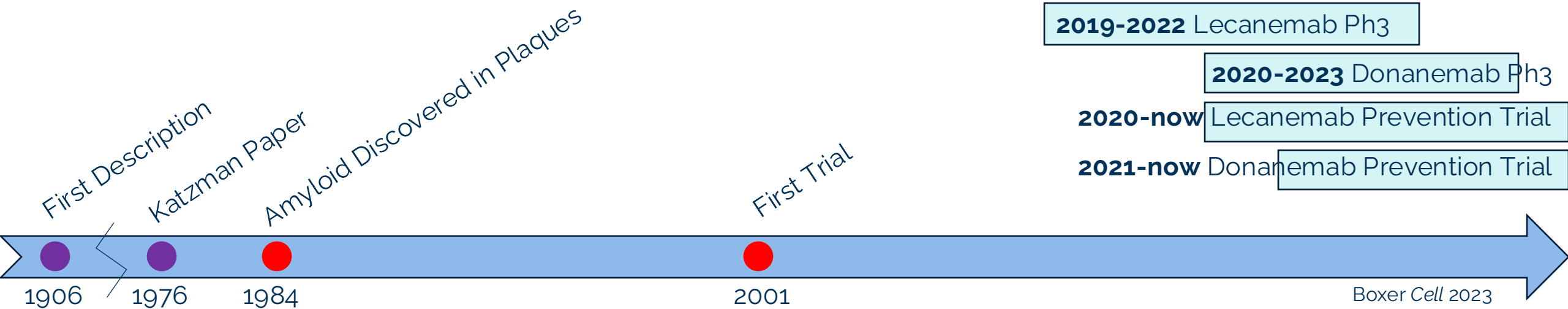
2018-2022 Gantenerumab Phase 3 (x2)

2019-2022 Lecanemab Ph3

2020-2023 Donanemab Ph3

2020-now Lecanemab Prevention Trial

2021-now Donanemab Prevention Trial



Boxer *Cell* 2023

2023/2024: Lecanemab & Donanemab

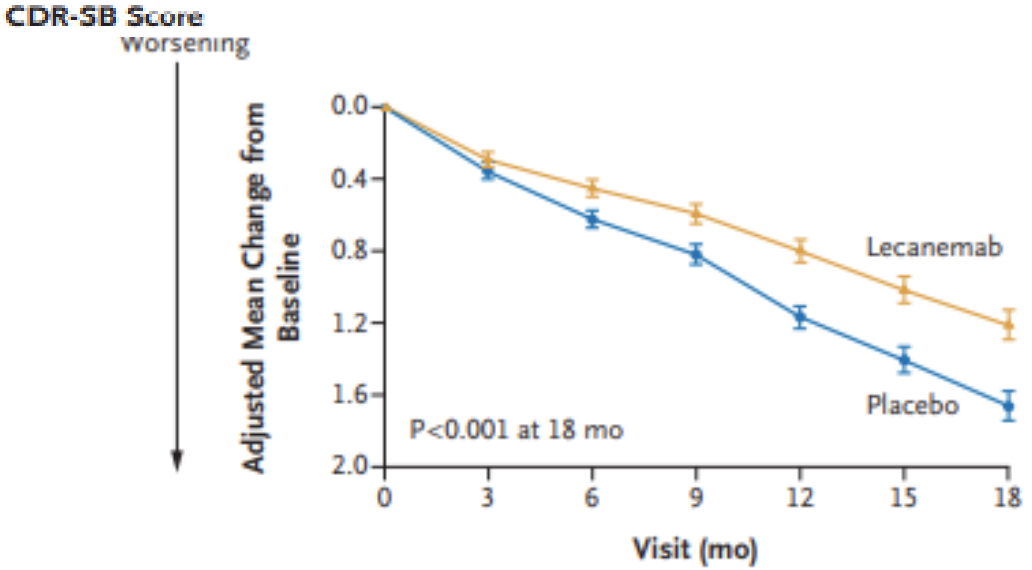
2019-2022 Lecanemab Ph3

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 5, 2023 VOL. 388 NO. 1

Lecanemab in Early Alzheimer's Disease

C.H. van Dyck, C.J. Swanson, P. Aisen, R.J. Bateman, C. Chen, M. Gee, M. Kanekiyo, D. Li, L. Reyderman, S. Cohen, L. Froelich, S. Katayama, M. Sabbagh, B. Vellas, D. Watson, S. Dhadda, M. Irizarry, L.D. Kramer, and T. Iwatsubo



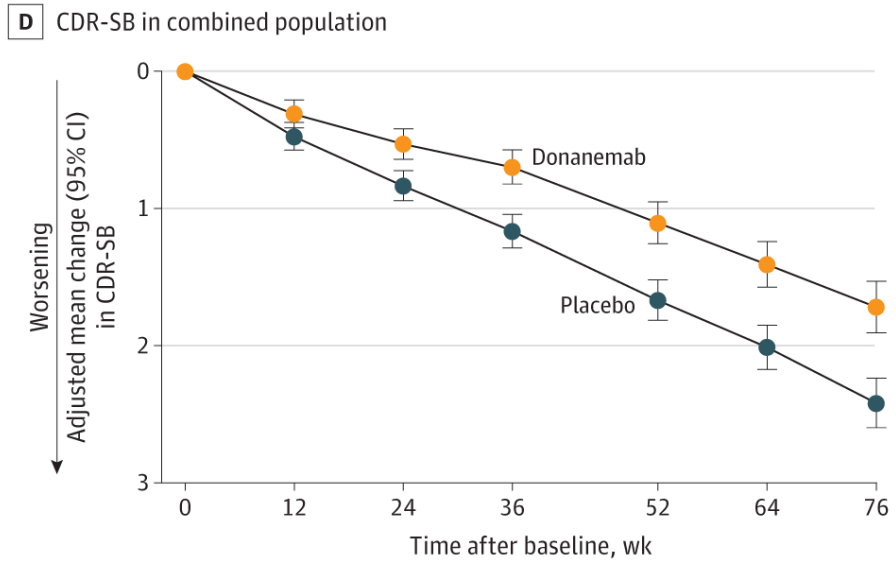
No. of Participants							
Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

2020-2023 Donanemab Ph3

JAMA | Original Investigation

Donanemab in Early Symptomatic Alzheimer Disease
The TRAILBLAZER-ALZ 2 Randomized Clinical Trial

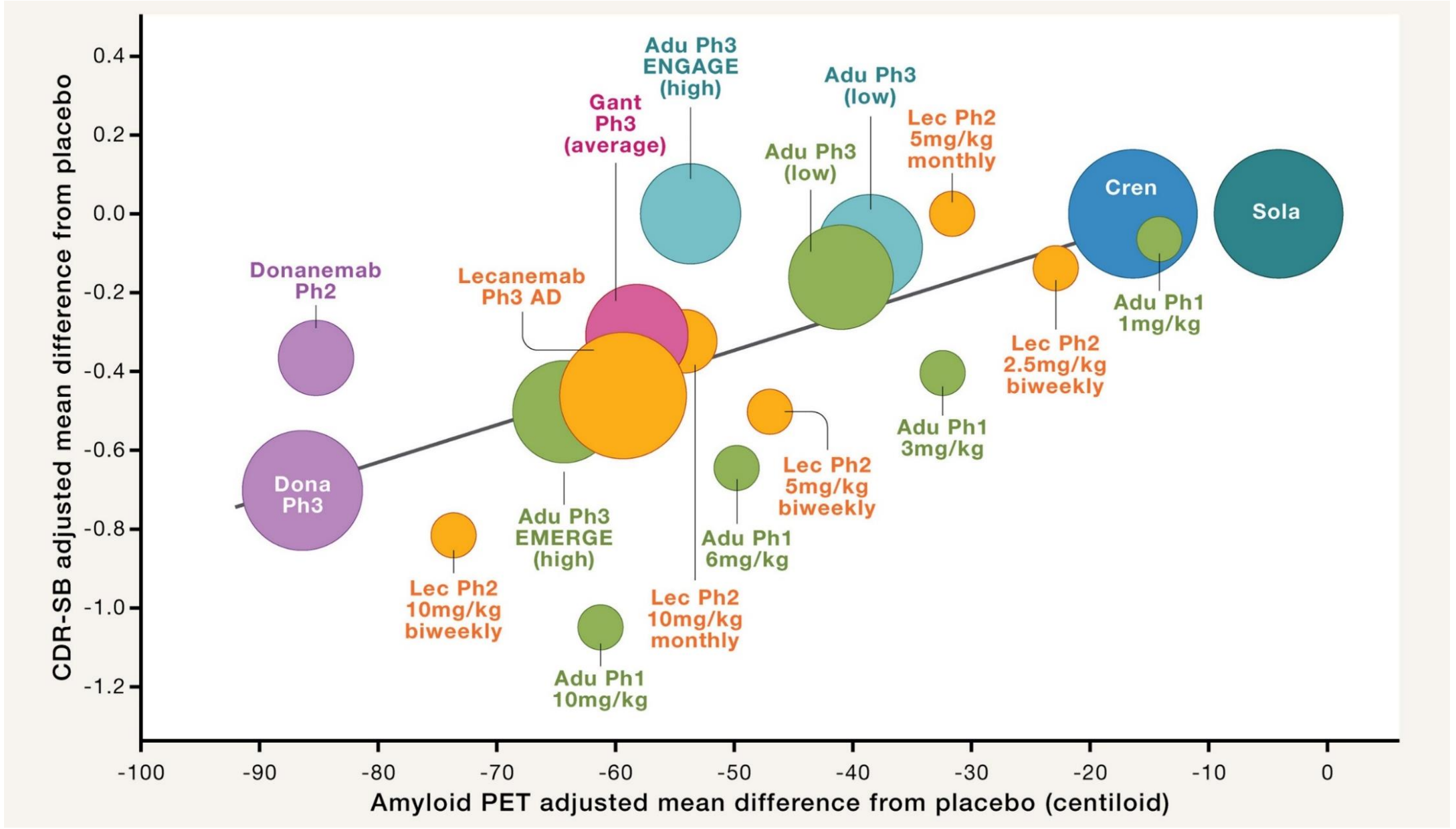
John R. Sims, MD; Jennifer A. Zimmer, MD; Cynthia D. Evans, PhD; Ming Lu, MD, MS, MPH; Paul Ardayfio, PhD; JonDavid Sparks, PhD; Alette M. Wessels, PhD; Sergey Shcherbinin, PhD; Hong Wang, PhD; Emel Serap Monkul Nery, MD; Emily C. Collins, PhD; Paul Solomon, PhD; Stephen Salloway, MD; Liana G. Apostolova, MD; Oskar Hansson, MD, PhD; Craig Ritchie, MD, PhD; Dawn A. Brooks, PhD; Mark Mintun, MD; Daniel M. Skovronsky, MD, PhD; for the TRAILBLAZER-ALZ 2 Investigators



No. of participants							
Placebo	838	825	784	752	713	678	672
Donanemab	794	774	731	682	650	603	598

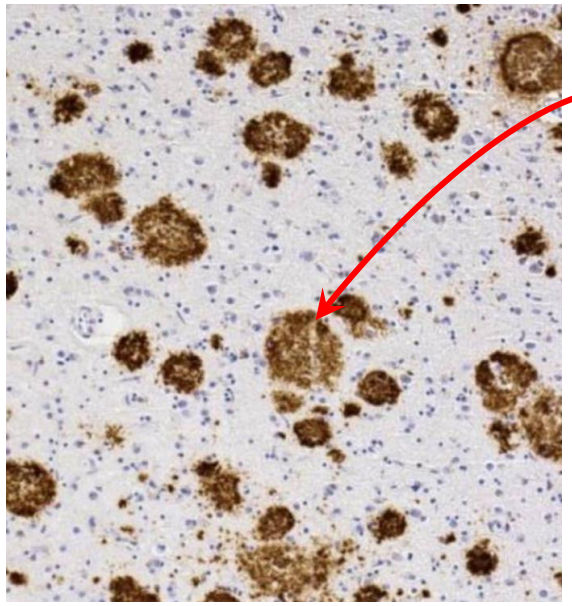
Van Dyck *NEJM* 2023; Sims *JAMA* 2023

Effect Size of Anti-Amyloid Treatment

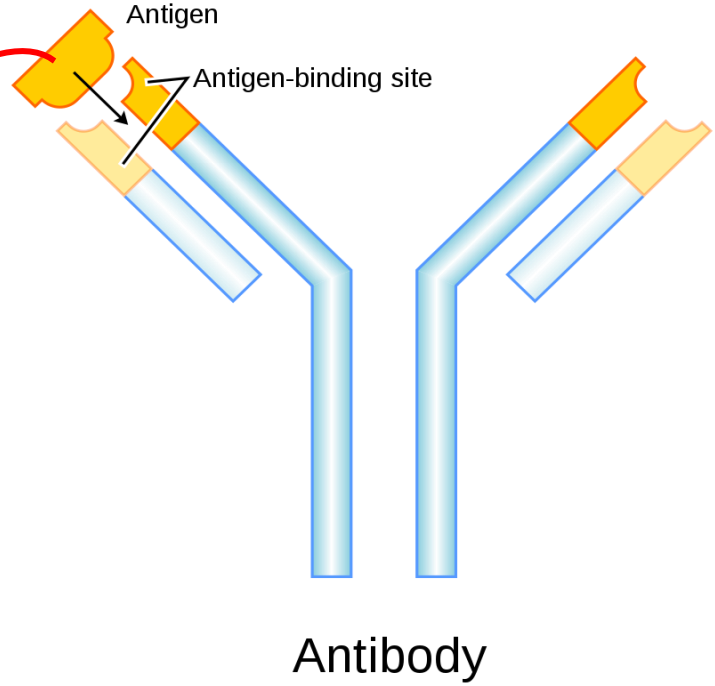


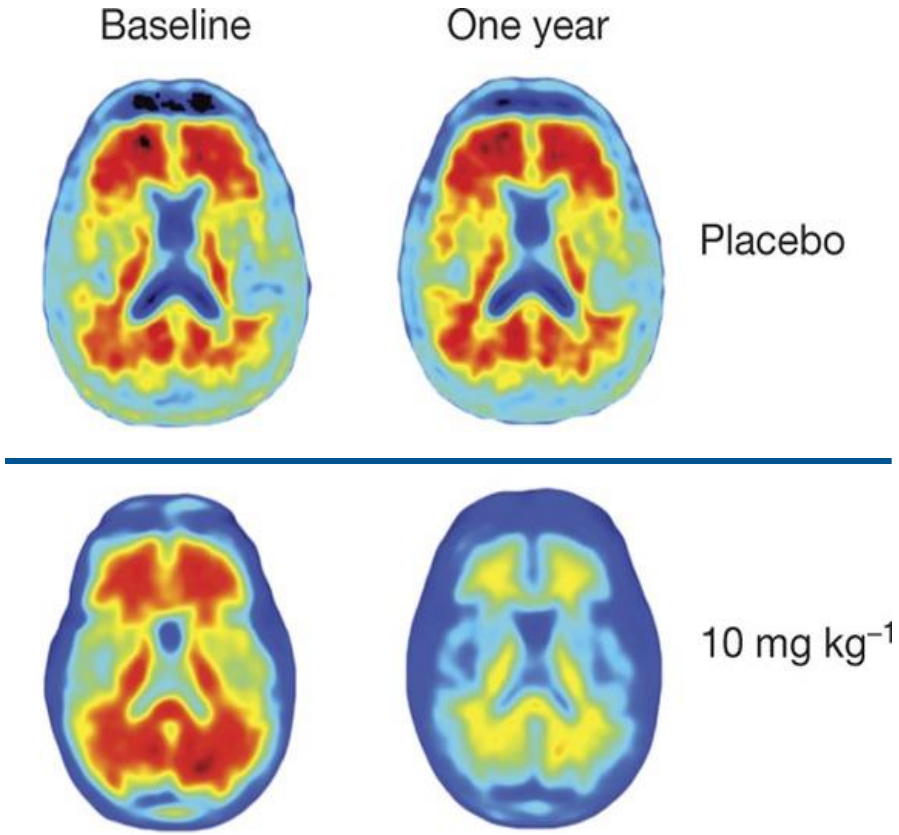
Boxer *Cell* 2023

Anti-Amyloid Antibodies: Introduction



Amyloid plaques





Antibodies that remove aggregated amyloid are considered “disease-modifying.”

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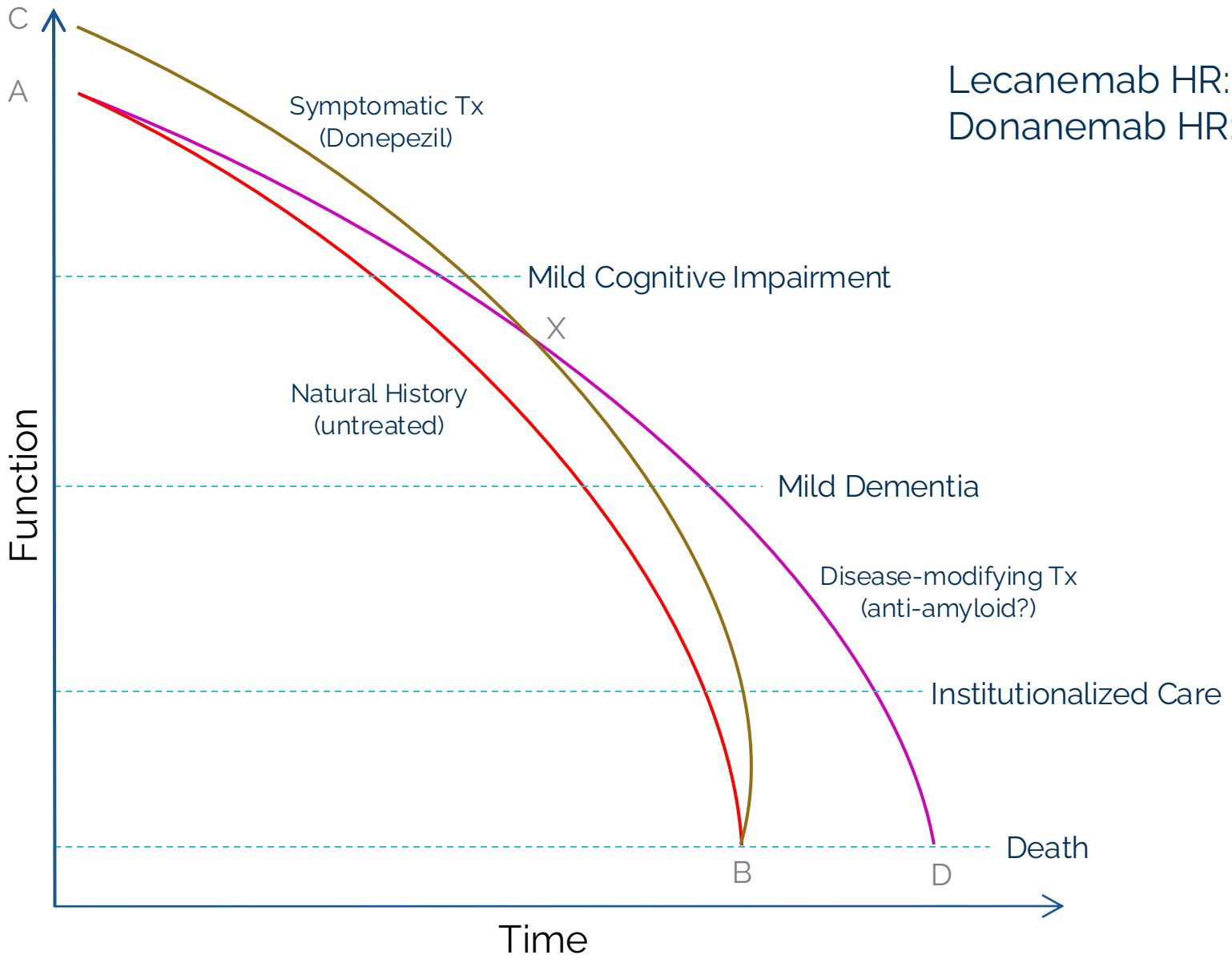
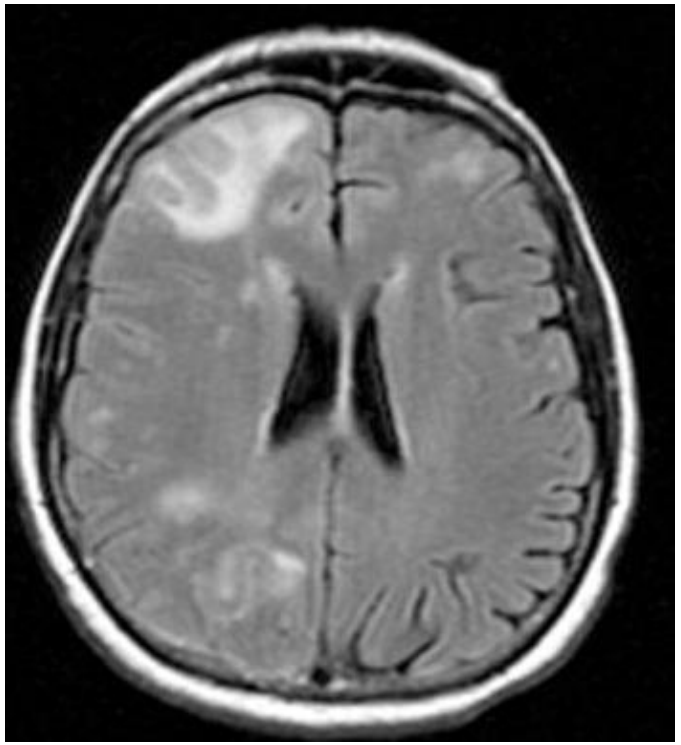
Disease-Modifying vs. Symptomatic Tx



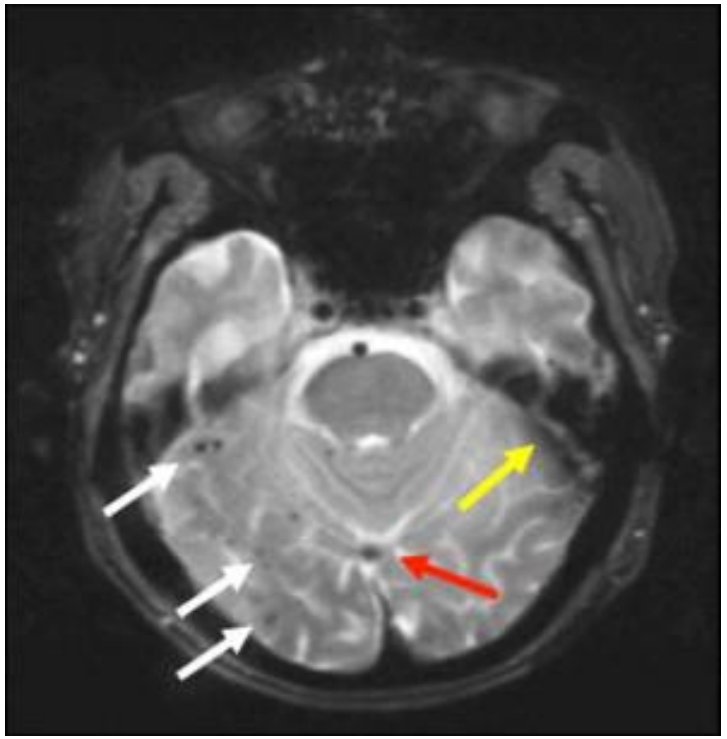
Lecanemab HR: 0.69
Donanemab HR: 0.61

ARIA: The Major Side Effect

ARIA stands for Amyloid Related Imaging Abnormalities.



ARIA-E (FLAIR)



ARIA-H (GRE)

- Associated with APOE4 (and CAA, biologic burden, and ???)
- Risk increased with AC, especially strong-clot busters like tPA (LETHAL)
- ARIA is common (~25%), severe symptoms are not (<1%)

White = ARIA-H
Red = Cerebral vein
Yellow = Edge artifact

ARIA refers to changes on MRI from vasogenic **e**dema (ARIA-E) and/or **h**emosiderin deposition (ARIA-H) in the context of anti-amyloid antibody treatment.

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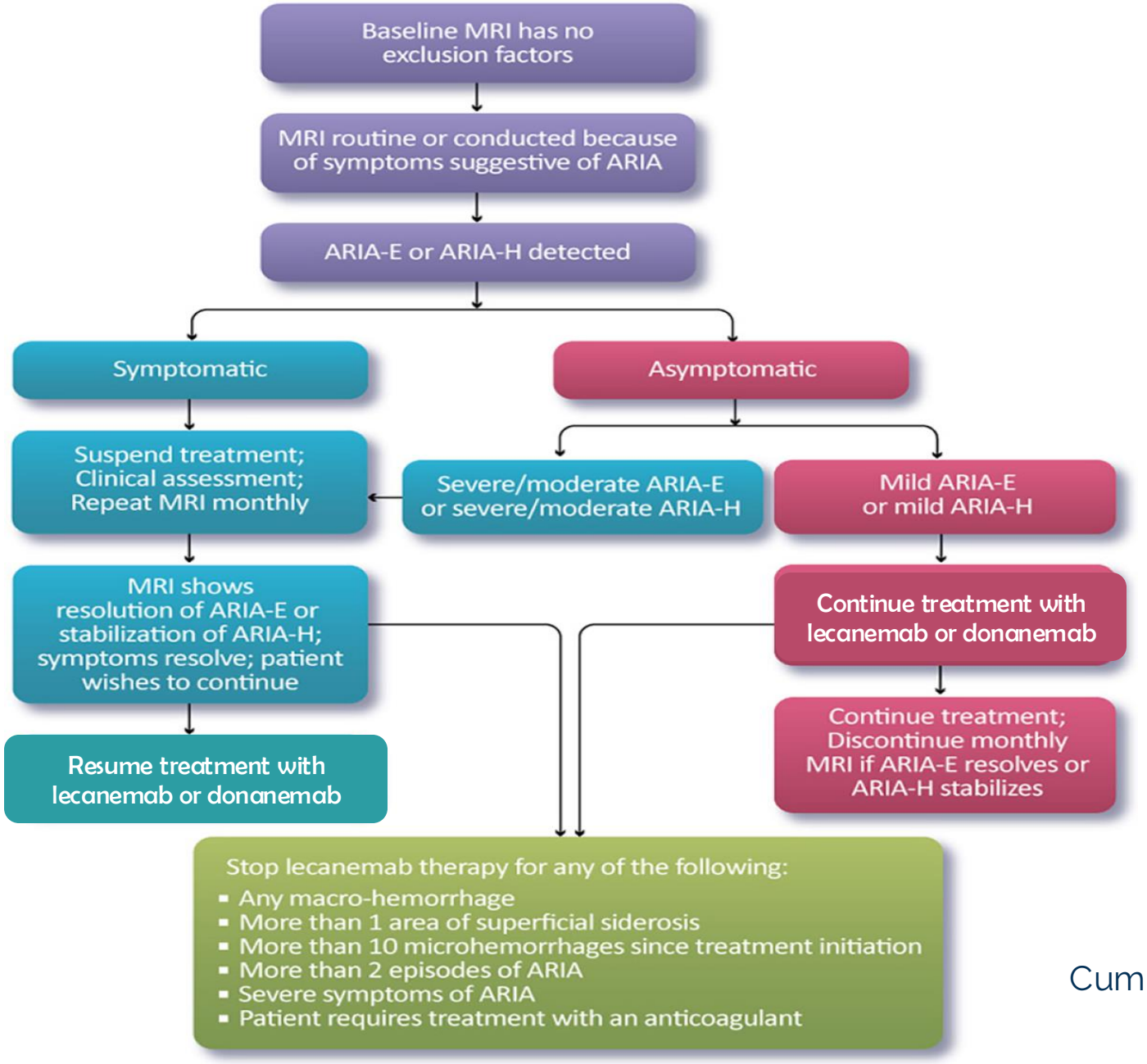
Sperling *Alz Dem* 2011

Manage ARIA w/ Treatment Pause



Cummings *J Prev Alz Dis* 2024

Appropriate Use Recommendations

- ✓MCI or mild dementia
- ✓MMSE 22-30
- ✓Amyloid positivity (CSF/PET, plasma?)
- ✓Concerning imaging findings: >4 microhemes, superficial siderosis, severe WMD, >2 lacunar infarcts, territorial infarct, prior ICH
- ✓APOE testing required to inform risk/benefit
- ✓Do not treat patients on anticoagulation

Appropriate Use Recommendations

University of California (UC) Anti-Amyloid Beta Antibody Infusion Protocol

Current Editors

Peter A. Ljubenkov, MD (corresponding author)
Lawren VandeVrede, MD, PhD
Melanie Stephens, PhD
Courtney Lane-Donovan, MD, PhD
Julio C. Rojas, MD, PhD
Adam Boxer, MD, PhD
Gil Rabinovici, MD

With Guidance from Current Members of the University of California Anti-Amyloid Antibody Infusion Working Group.

FREQUENTLY ASKED QUESTIONS (FAQ) ABOUT *APOE* TESTING

This FAQ sheet provides information for people with symptoms related to Alzheimer's disease who are considering *APOE* genetic testing.

What is the *APOE* gene?

The *APOE* gene is a set of instructions we all have inside of our DNA code. The *APOE* gene tells your body how to make a protein that interacts with fats in your blood. Everyone has two copies of *APOE* gene instructions in their DNA code, and their combination of copies is called a "genotype." *APOE* genotypes affect a person's lifetime risk for Alzheimer's disease. We do not completely understand why or how *APOE* affects this risk. The role of *APOE* is also not well understood for all racial or ethnic groups.

What are the versions of *APOE* and how do they affect Alzheimer's disease risk?

Informed Consent to Receive Anti-Amyloid Therapy at UCSF

What are lecanemab and donanemab?

Alzheimer's disease involves the buildup of amyloid protein plaques and tau protein tangles in the brain. Anti-amyloid drugs like **lecanemab** (marketed as LEQEMBI™) and **donanemab** (marketed as KISUNLA™) are antibodies (immune proteins) that help your immune system remove amyloid plaques. These drugs do not directly target tau tangles.

What are the potential benefits of lecanemab and donanemab?

Lecanemab and donanemab do not stop or cure Alzheimer's disease. On average, these drug **slows the rate of Alzheimer's progression by about 20-30%.** In other words, if someone takes one of these drugs for 18 months, they may experience a 5-6 month delay in symptom progression during that time.

Is the benefit of lecanemab or donanemab the same for everyone?

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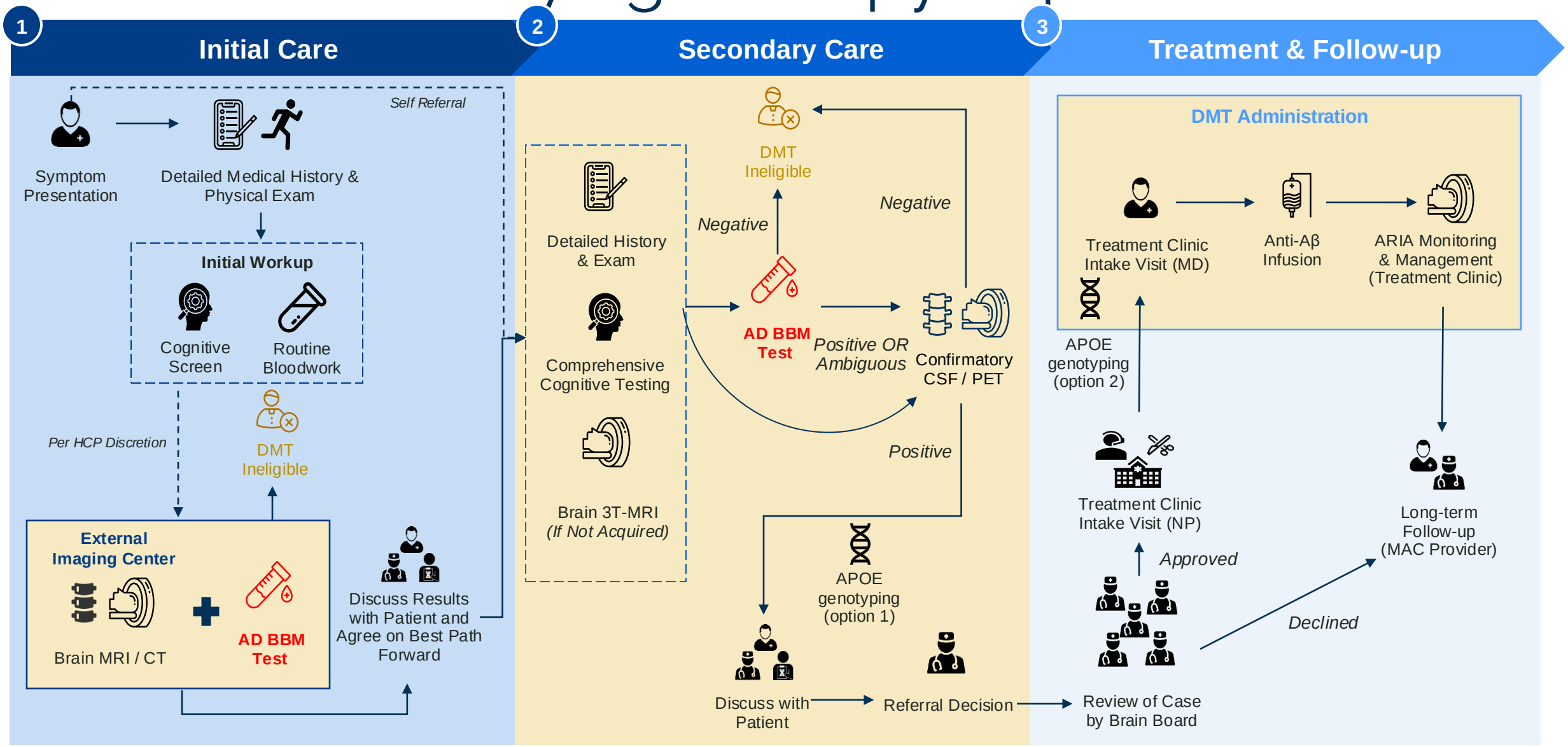
Disease-Modifying Therapy Implementation



Outstanding Questions about Amyloid DMTs

- What predicts a positive response to this intervention?
    - Tau Stage / Age / APOE / Sex / Syndrome / Co-pathology?
- How early or late in the disease is this approach effective?
- How long should we treat for? Can we stop and monitor?
- How can we better evaluate treatment response?
- How can we better monitor for and treat ARIA?
- Are combination therapies effective?

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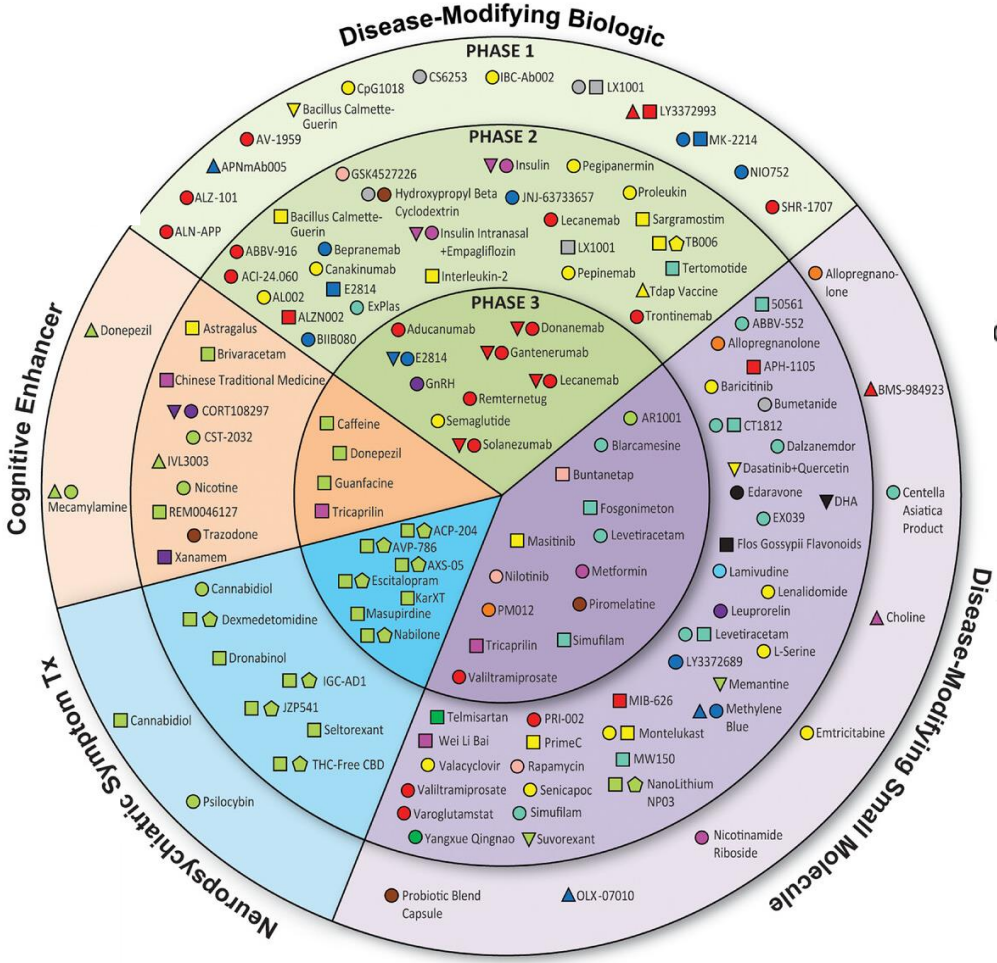
What is ALZ-NET?

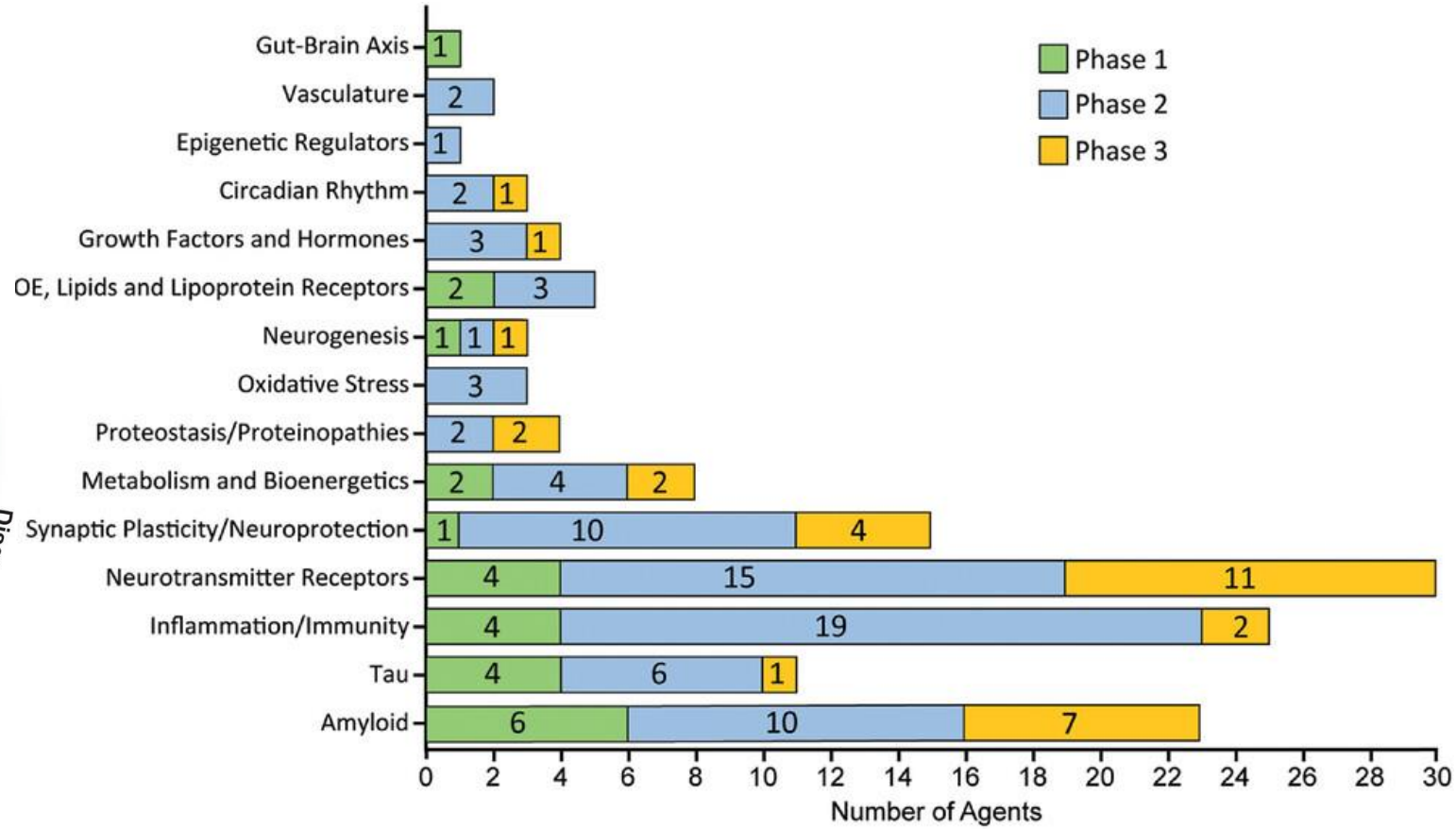
- Multi-site network that will **collect a minimum core set of regulatory-grade patient data** including diagnostic, treatment, measures of cognition, function and safety.
- **Archive and share de-identified data** including demographic, medical, neurologic, imaging, biomarker, genetic and biospecimens.
- Can **collaborate with affiliated studies** conducted by academia, industry, federal or ALZ-NET study teams.
- **Track health outcomes and resource utilization** of participants to inform clinical care

ALZ-NET DATA COLLECTION	SITE START-UP[1]	CASE REGISTRATION[2]	BASELINE[3]	FOLLOW-UP[3]
Participating Site Characteristics	x			
Site Investigator (*Prescribing Clinician*) Characteristics	x			
Informed Consent		x		
Eligibility Assessment		x		
Patient Demographics		x		
Concurrent Study Enrollment			x	x
Patient Characteristics			x	o
Medical History			x	x
Lifestyle Data			x	o
Vital Signs			x	x
Clinical Features of Co-pathology			x	x
Additional Measures (*Cognitive, Functional, and Behavioral*)			x	x
AD Diagnosis, Characteristics, and Biomarkers			x	x
Brain Imaging Clinical Data[4]			x	x
Brain Image(s) Transmission[5]			x	x
Concomitant Medications			x	x
AD Treatment and Dosing Log			x	x
MRI Assessment			x	x
Healthcare Encounters (*Hospitalizations and ER Visits*)			x	x
Adverse Events (AEs)			x	x
End of Participation (Death, Lost to Follow up, Consent Withdrawn) – *only if applicable*				x

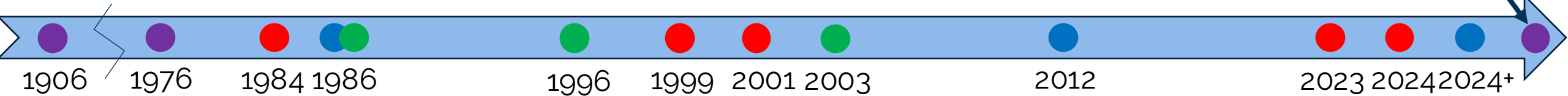
x = Required form o = Optional form

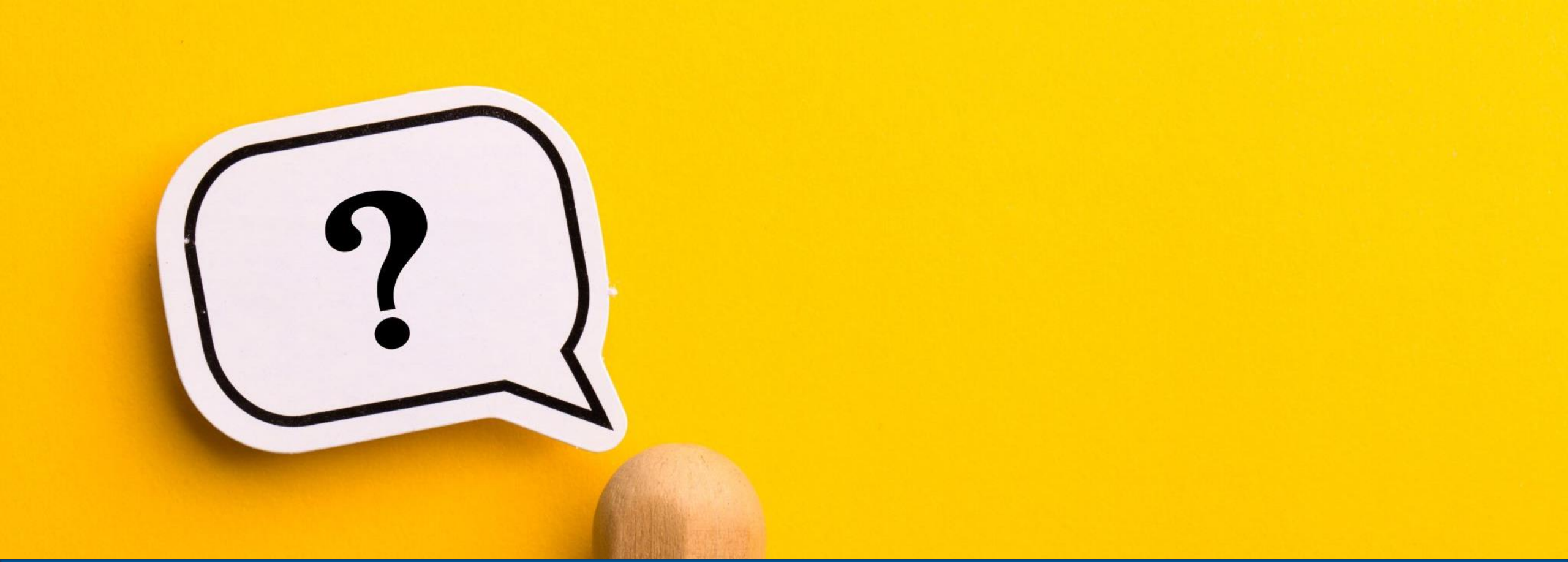
The Disease-Modifying Era Has Begun!





Combination Trials





Questions

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Training and support for providers and clinics

Education and Training:

- Core: CHA training
- More on-line training modules
- Bi-Monthly Webinars and Podcasts

Warmline:

1-800-933-1789

- A provider support and consultation service staffed by Dementia Care Aware experts

Practice change support:

- UCLA Alzheimer's and Dementia Care program
- Alzheimer's Association Health Systems team
- Implementation guide

dementiacareaware.org DCA@ucsf.edu

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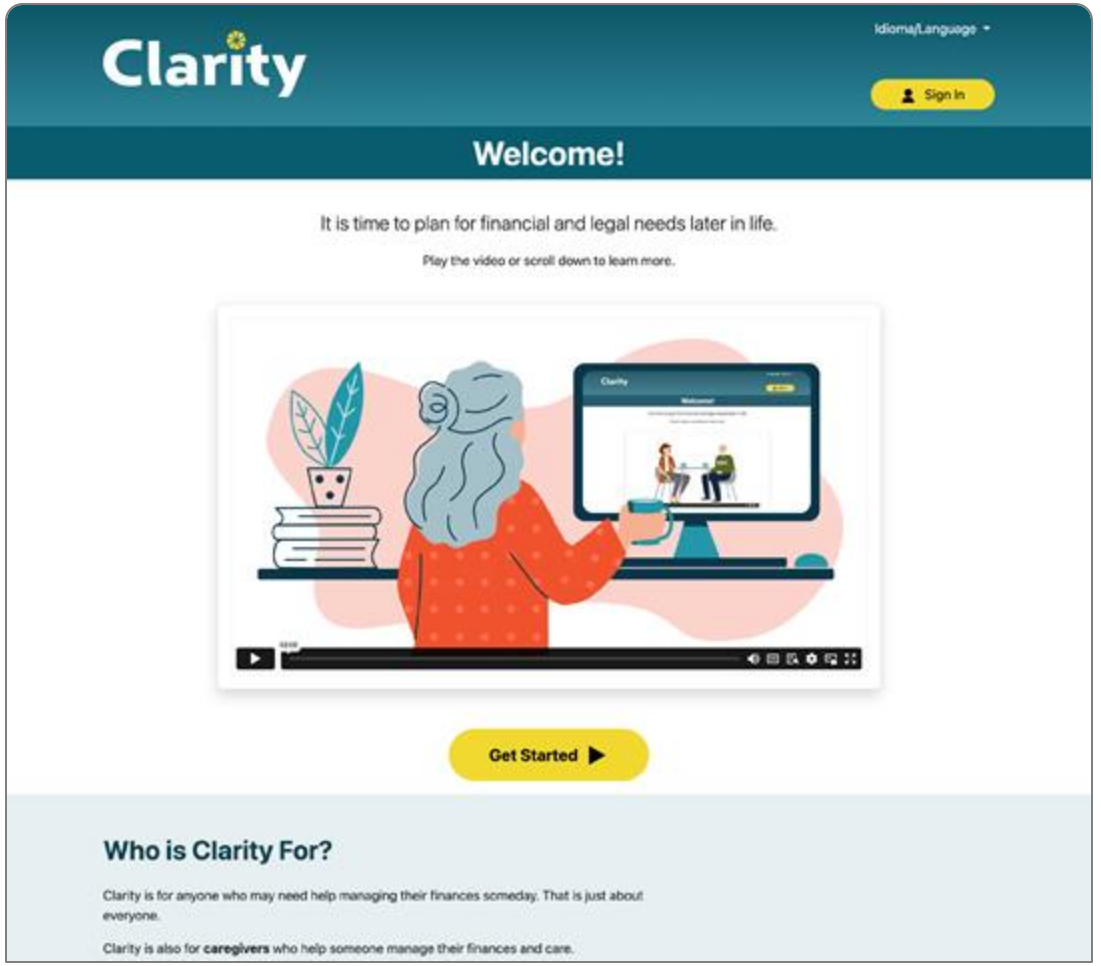
PlanforClarity.Org is a free tool for patients and caregivers to learn about legal and financial aspects of care planning.

NEW! Free tools, live training, & consults for health care teams!

Starting July 2025

Contact: peterselizabeth@uclawsf.edu



This project is supported by the AARP Foundation.