Brigham and Women's Hospital
Founding Member, Mass General Brigham

Update in Dementia and Alzheimer's Disease

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- Dementia and Behavioral Neuroscience Fellowship at UCLA
- Professor of Neurology at HMS
- Director of Clinical Trials, Center for Alzheimer Research and Treatment at BWH
  - Clinical focus: Alzheimer's disease and related disorders
  - Research focus: AD clinical trials, multi-modal imaging, neuropsychiatric symptoms, and instrumental activities of daily living

Disclosures

- Research salary support for serving as site principal investigator for trials sponsored by:
  - Eisai Inc. and Eli Lilly and Company
- Consultant for Ono Pharma USA, Inc.

Objectives

- Discuss the current recommended diagnostic assessments of Alzheimer's disease (cognitive, imaging, and fluid markers)
- Discuss management of Alzheimer's disease (Components of management, FDA-approved treatments, lifestyle modifications, supplements)

Dementia Diagnostic Criteria

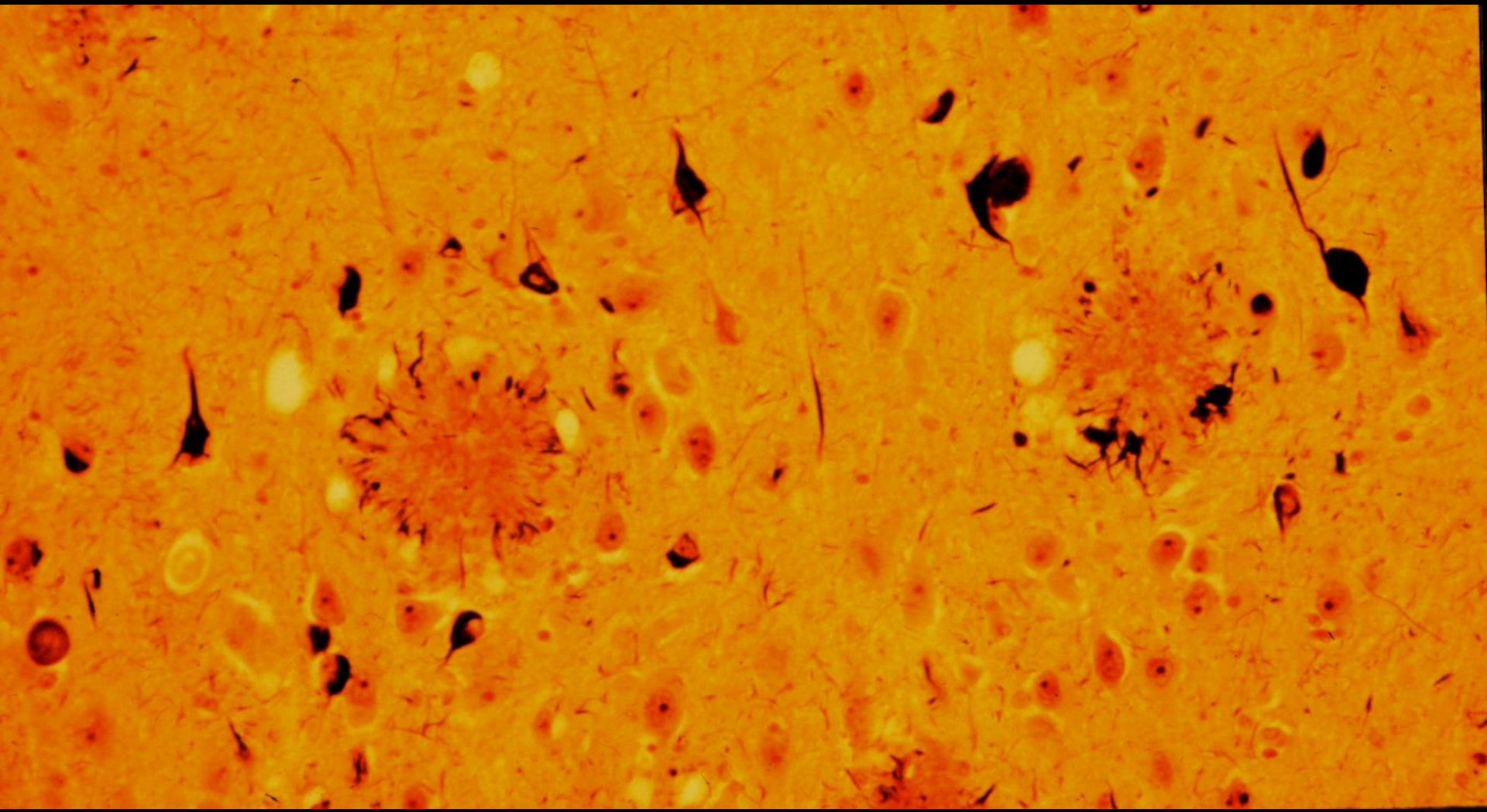
- Dementia is a chronic progressive syndrome consisting of cognitive, behavioral, and functional dysfunction
- Symptoms interfere with daily functioning
- Represents a decline from previous abilities
- Not explained by delirium or primary psychiatric condition
- Cognitive impairment is assessed by history (patient/caregiver) and exam ("bedside" or neuropsychological testing)
- Cognitive or behavioral impairment of 2 or more domains: memory, attention/executive function, visuospatial function, language, behavior

McKhann et al. *Alzheimers Dement* 2011

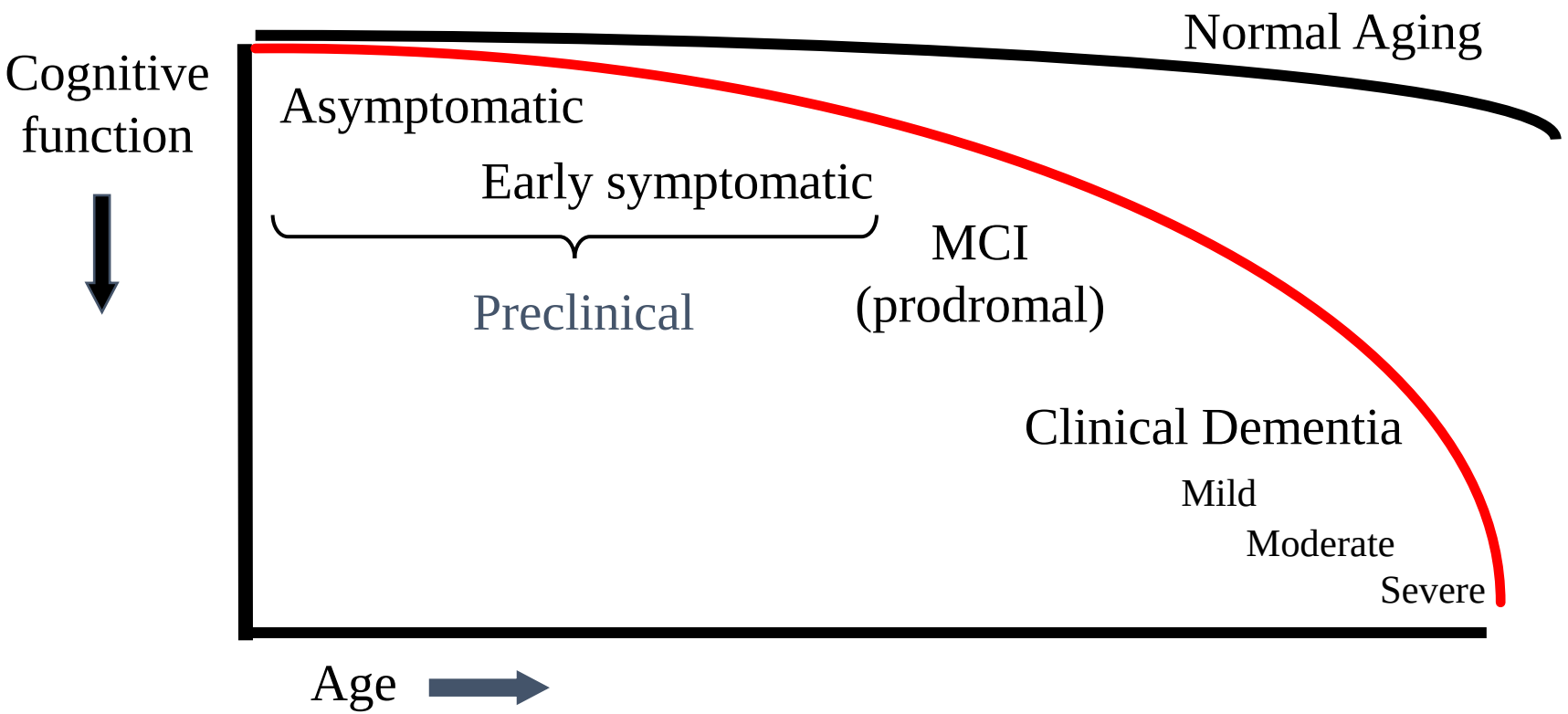
Alzheimer's Disease

- Most common cause of dementia
- Typical onset in early 70's
- Progressive neurodegenerative disease
  - Insidious clinical progression over years
  - Typically begins with impaired short-term memory, sense of direction, and praxis
  - Eventually affects general cognition, behavior, and daily functioning
- Nearly 7 million people in U.S. carry a diagnosis of AD dementia (Alzheimer's Association 2024)
  - 20 million more at risk over next 30 years
  - Prevalence doubles every 5 years
  - Cost estimates: > $350 billion/year
  - 1.5x more prevalent in Hispanics, 2x in African Americans

Alzheimer's Disease Pathology



Alzheimer's Disease Trajectory



Modified from Sperling et al. *Alzheimers Dement* 2011

Case Study—Joe: Initial Evaluation

- PCP: Annual visit
- Joe is a 66-year-old man who is seen alone
- Retired special-education teacher and later information technology specialist
- Reported decline in recent memory
- No relevant past medical history or family history
- Cognitive screening
  - Mini-Cog: 3/5 (-2 recall)
  - AD8: 3
- Referred to specialist

Mini-Cog™

Instructions for Administration & Scoring

ID: _____ Date: _____

Step 1: Three Word Registration

Look directly at person and say, "Please listen carefully. I am going to say three words that I want you to repeat back to me now and try to remember. The words are [select a list of words from the versions below]. Please say them for me now." If the person is unable to repeat the words after three attempts, move on to Step 2 (clock drawing).

The following and other word lists have been used in one or more clinical studies.[1-3] For repeated administrations, use of an alternative word list is recommended.

Version 1	Version 2	Version 3	Version 4	Version 5	Version 6
Banana	Leader	Village	River	Captain	Daughter
Sunrise	Season	Kitchen	Nation	Garden	Heaven
Chair	Table	Baby	Finger	Picture	Mountain

Step 2: Clock Drawing

Say: "Next, I want you to draw a clock for me. First, put in all of the numbers where they go." When that is completed, say: "Now, set the hands to 10 past 11."

Use preprinted circle (see next page) for this exercise. Repeat instructions as needed as this is not a memory test. Move to Step 3 if the clock is not complete within three minutes.

Step 3: Three Word Recall

Ask the person to recall the three words you stated in Step 1. Say: "What were the three words I asked you to remember?" Record the word list version number and the person's answers below.

Word List Version: ____ Person's Answers: _____ _____ _____

Scoring

Word Recall: _____ (0-3 points)	1 point for each word spontaneously recalled without cueing.
Clock Draw: _____ (0 or 2 points)	Normal clock = 2 points. A normal clock has all numbers placed in the correct sequence and approximately correct position (e.g., 12, 3, 6 and 9 are in anchor positions) with no missing or duplicate numbers. Hands are pointing to the 11 and 2 (11:10). Hand length is not scored. Inability or refusal to draw a clock (abnormal) = 0 points.
Total Score: _____ (0-5 points)	Total score = Word Recall score + Clock Draw score. A cut point of <3 on the Mini-Cog™ has been validated for dementia screening, but many individuals with clinically meaningful cognitive impairment will score higher. When greater sensitivity is desired, a cut point of <4 is recommended as it may indicate a need for further evaluation of cognitive status.

Tam et al.
JAGS 2018

AD8 Dementia Screening Interview

Patient ID#:_____
CS ID#:_____
Date:_____

Remember, "Yes, a change" indicates that there has been a change in the last several years caused by cognitive (thinking and memory) problems.	YES, A change	NO, No change	N/A, Don't know
1. Problems with judgment (e.g., problems making decisions, bad financial decisions, problems with thinking)			
2. Less interest in hobbies/activities			
3. Repeats the same things over and over (questions, stories, or statements)			
4. Trouble learning how to use a tool, appliance, or gadget (e.g., VCR, computer, microwave, remote control)			
5. Forgets correct month or year			
6. Trouble handling complicated financial affairs (e.g., balancing checkbook, income taxes, paying bills)			
7. Trouble remembering appointments			
8. **Daily** problems with thinking and/or memory			
TOTAL AD8 SCORE			

Score ≥ 2 cut-off for cognitive impairment

Galvin et al.
Neurology 2005

Case Study: Specialist History

- Neurologist evaluation
- 66-year-old right-handed man with 18 years of education, seen with wife
- 2-year history of gradual onset and progression of decline in recent memory
  - Repeating himself
  - Forgetting details of recent events
  - Forgetting his schedule for the day
  - Misplacing items
  - Mild difficulties with learning new information
- Remote memory remains intact

Case Study: Specialist History

- Mild difficulties with sense of direction in unfamiliar environments
- Mild word-findings difficulties without paraphasic errors
- Mild difficulties with calculations
- Difficulties making connections and integrating ideas
- Mild difficulties with organization and planning, especially when multiple steps are involved
- Issues with working memory

Case Study: Specialist History

- Recent mild situational anxiety and depressive symptoms when he thinks about his cognitive deficits
- 6-7 years of insomnia (taking diphenhydramine)
- Instrumental activities of daily living are mildly impaired
  - Not as efficient in completing tasks
  - Difficulties preparing meals due to difficulties keeping track of multiple steps
  - Mild difficulties calculating tips
  - Mild difficulties shopping even when he uses a list
- Still very intellectually active—runs a men's group, takes piano lessons, reads books
- Exercises 3/week and has a healthy diet

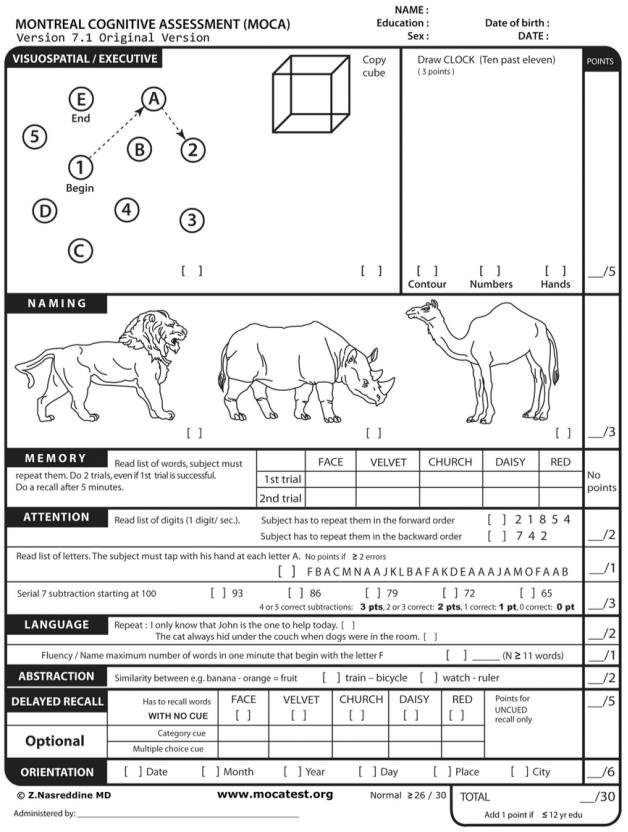
Case Study: Specialist Exam

- General physical exam and neurological exam unremarkable
- Cognitive exam:
  - MoCA 22/30
  - -1 Trails, -1 copy of cube, -1 clock (incorrect hand placement), -1 serial 7's, -3 delayed recall (+1 with multiple choice cues), -1 orientation
- Diagnosis: Mild cognitive impairment, amnestic, multiple domain

Screening Cognitive Assessments

- Variety of cognitive assessments typically used in primary care or specialist settings

MoCA	Montreal Cognitive Assessment
MMSE	Mini-Mental State Examination
AMTS	Abbreviated Mental Test Score
MSQ	Mental Status Questionnaire
SPMSQ	Short Portable Mental Status Questionnaire
6CIT	Six-item Cognitive Impairment Test
GPCOG	General Practitioner Assessment of Cognition
AD8	Eight-item Interview to Differentiate Aging and Dementia
Mini-Cog	Three-item Recall Test and Clock Drawing Test

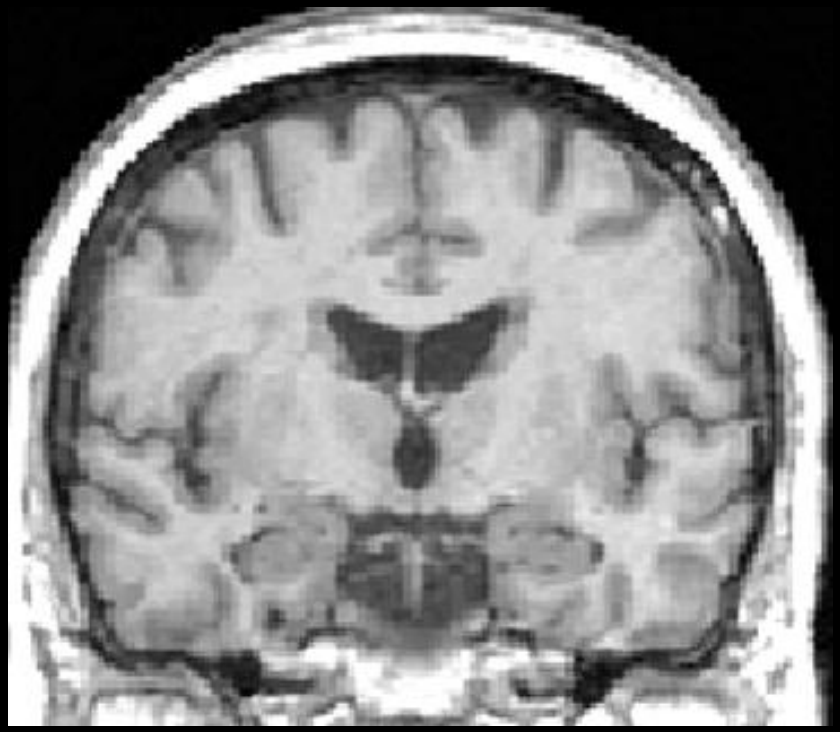


Ghadiri-Sani et al. *Clin Pract.* 2014; Janssen et al. *BMC Fam Pract*. 2017; Smith et al. *Can J Psychiatry* 2007

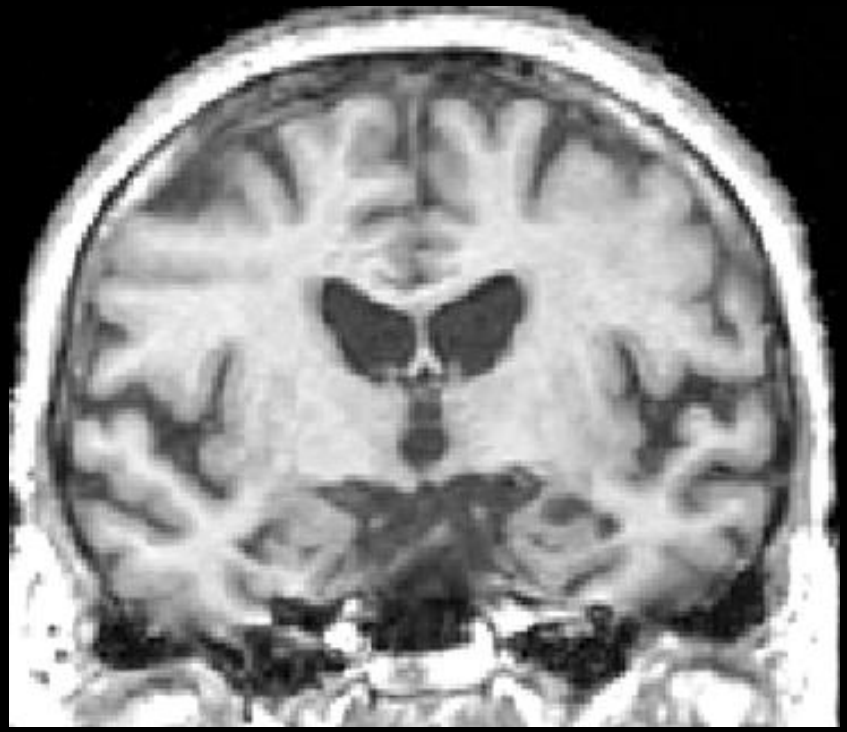
Case Study: Specialist Diagnostic Assessments

- Laboratory assessment for reversible causes of cognitive impairment: Normal vitamin B12, TSH (lipids, CBC, electrolytes)
- MRI of the brain: Mild-moderate bilateral parietal atrophy, minimal bilateral frontal atrophy, mild bilateral hippocampal atrophy, and mild-moderate small vessel ischemic disease. No strokes, hemorrhages or masses

Structural Magnetic Resonance Imaging (MRI) in AD: Atrophy



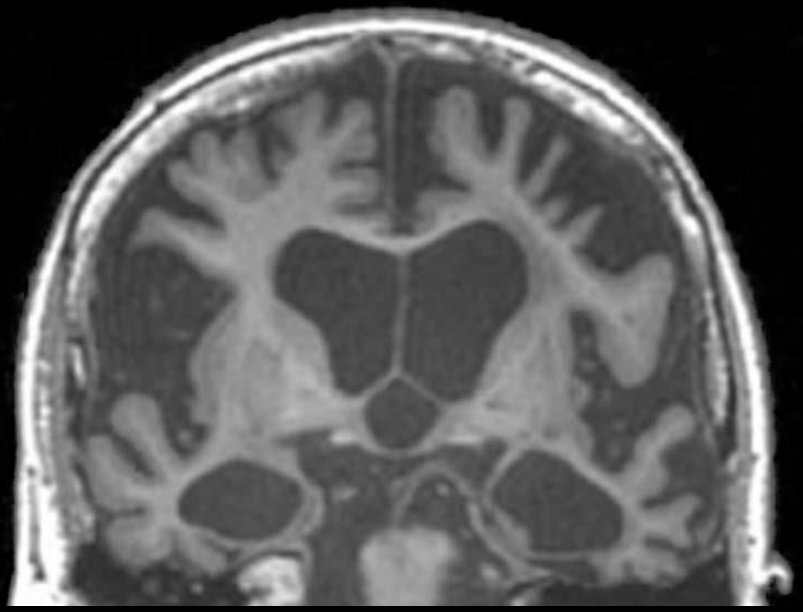
Normal older individual
(age = 77)



Patient with mild AD dementia
(age = 77)

Images courtesy of Reisa Sperling, MD

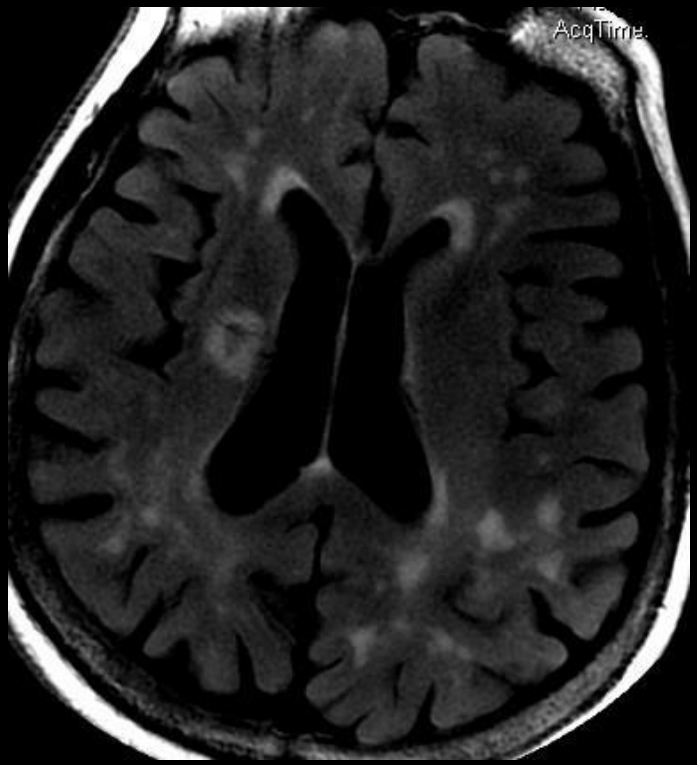
Structural MRI in AD: Atrophy

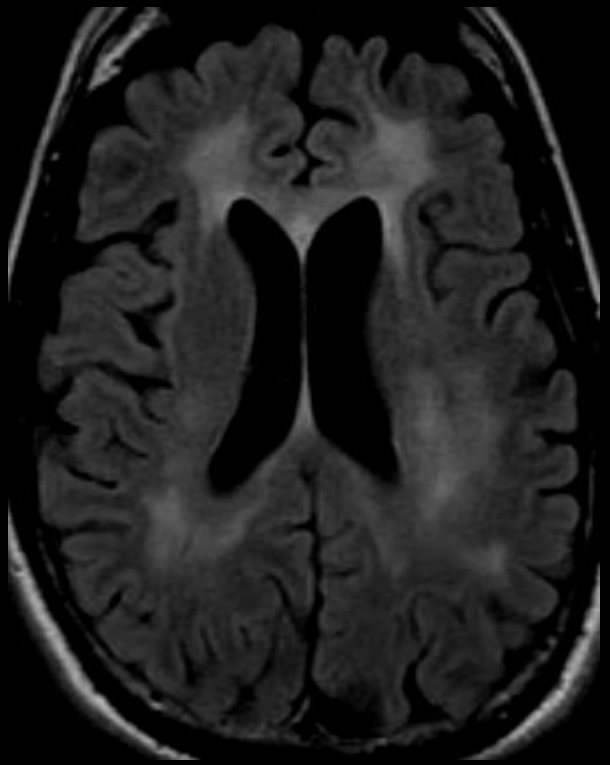


Patient with severe AD dementia
(age = 86)

Image courtesy of Gad Marshall, MD

Structural MRI: Cerebrovascular disease





Images courtesy of Scott McGinnis, MD

Case Study: Additional Diagnostic Assessments

- Neuropsychological testing:
  - Premorbid intelligence in the superior range
  - MMSE 26/30, Blessed Dementia Scale 3, CDR global 0.5, sum of boxes 2.5
  - Attention average to impaired
  - Executive function average to impaired (average to impaired working memory, average phonemic verbal fluency, impaired semantic verbal fluency, impaired divided attention, average abstract reasoning, and impaired visual planning)
  - Non-contextual verbal memory impaired for encoding and retrieval and low average to impaired for storage
  - Naming average
  - Visuospatial function average to impaired
  - Questionnaires of mood: no significant depression or anxiety
- Underlying pathology: Likely a combination of Alzheimer's disease and cerebrovascular disease

Assessing Global Functioning and ADL

- Clinical Dementia Rating (CDR)
  - Interview caregiver and patient
  - 6 domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, personal care
- Weintraub ADL
  - Interview caregiver
  - 7 domains: self-care activities, household care, employment and recreation, shopping and money, travel, communication, social responsibilities
- Lawton and Brody scale, Functional Activities Questionnaire (FAQ)
  - Interview caregiver to assess IADL

Morris *Neurology* 1993; Weintraub *J Am Geriatr Soc* 2004; Lawton et al. *Gerontologist*. 1969; Pfeffer et al. *J Gerontol.* 1982

Assessing Mood and Neuropsychiatric Symptoms

- Depression
  - Patient Health Questionnaire 9 (PHQ-9)
  - Geriatric Depression Scale (GDS)
- Anxiety
  - Geriatric Anxiety Inventory (GAI)
  - Generalized Anxiety Disorder 7 (GAD-7)
- Neuropsychiatric symptoms
  - Neuropsychiatric Inventory Questionnaire (NPI-Q)
  - Mild Behavioral Impairment Checklist (MBI-C)

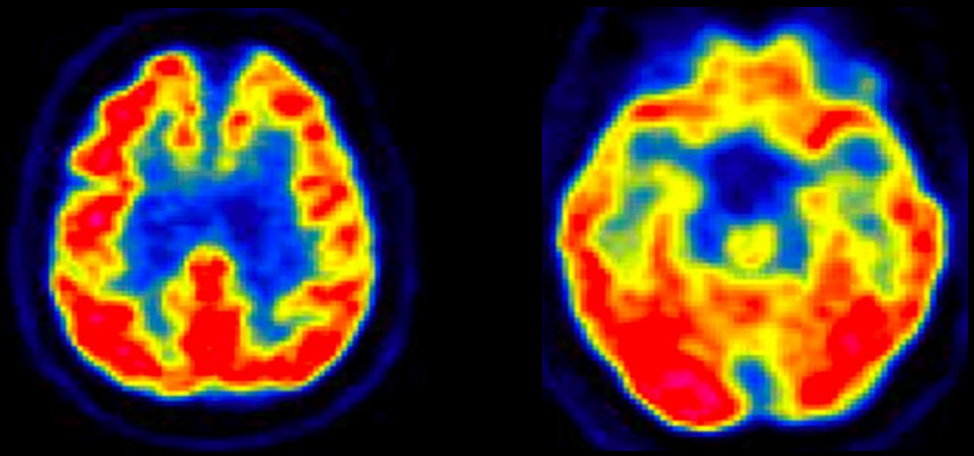
Kroenke et al. *J Gen Intern Med* 2001; Yesavage et al. *J Psychiatr Res* 1982; Pachana et al. *Int Psychogeriatr* 2007; Spitzer et al. *Arch Intern Med* 2006; Kaufer et al. *J Neuropsychiatry Clin Neurosci* 2000; Ismail *J Alzheimers Dis* 2017

Case Study: Additional Diagnostic Assessments

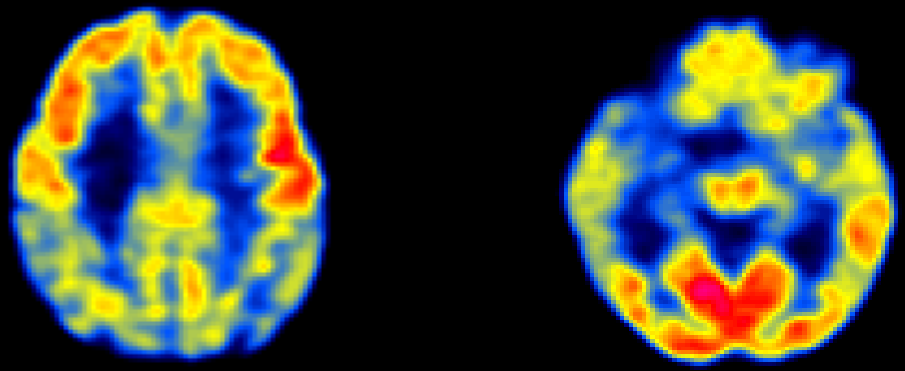
- Considered obtaining FDG PET
  - Declined by patient and wife
- Considered performing lumbar puncture or obtaining amyloid PET
  - Florbetapir PET: elevated amyloid across 4 cortical regions
  - Consistent with underlying Alzheimer's disease pathology

18F-Fluorodeoxyglocuse Positron Emission Tomography (FDG-PET) in AD

Normal older individual

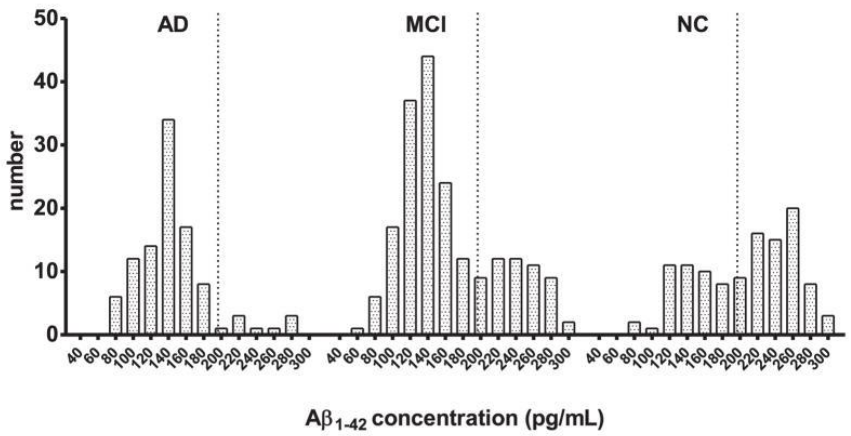


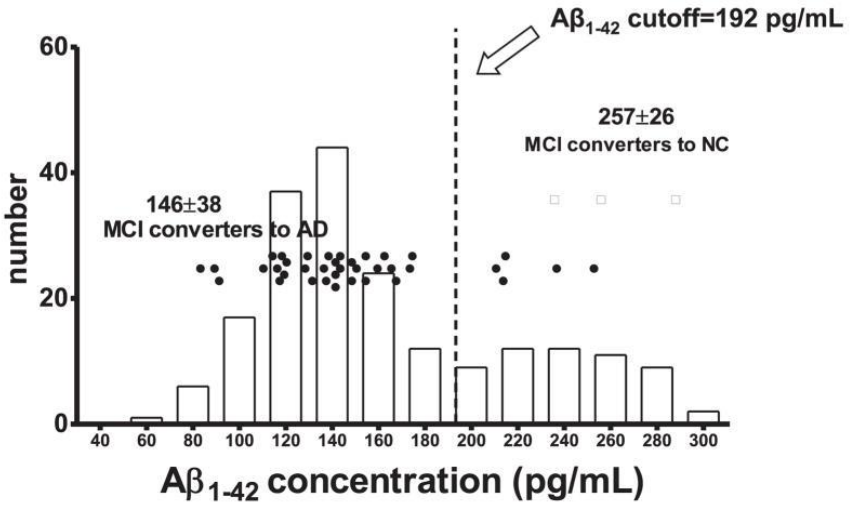
AD dementia



Johnson et al. *Cold Spring Harb Perspect Med* 2012

CSF Biomarker Signature of AD





- $A\beta_{1-42}$ < 192 pg/ml
  (sensitivity 96%, specificity 77%)
- Total tau > 93 pg/ml
  (sensitivity 70%, specificity 92%)
- Phospho-tau > 23 pg/ml
  (sensitivity 68%, specificity 73%)
- Total tau / $A\beta_{1-42}$ > 0.39
  (sensitivity 86%, specificity 85%)
- Phospho-tau / $A\beta_{1-42}$ > 0.10
  (sensitivity 91%, specificity 71%)

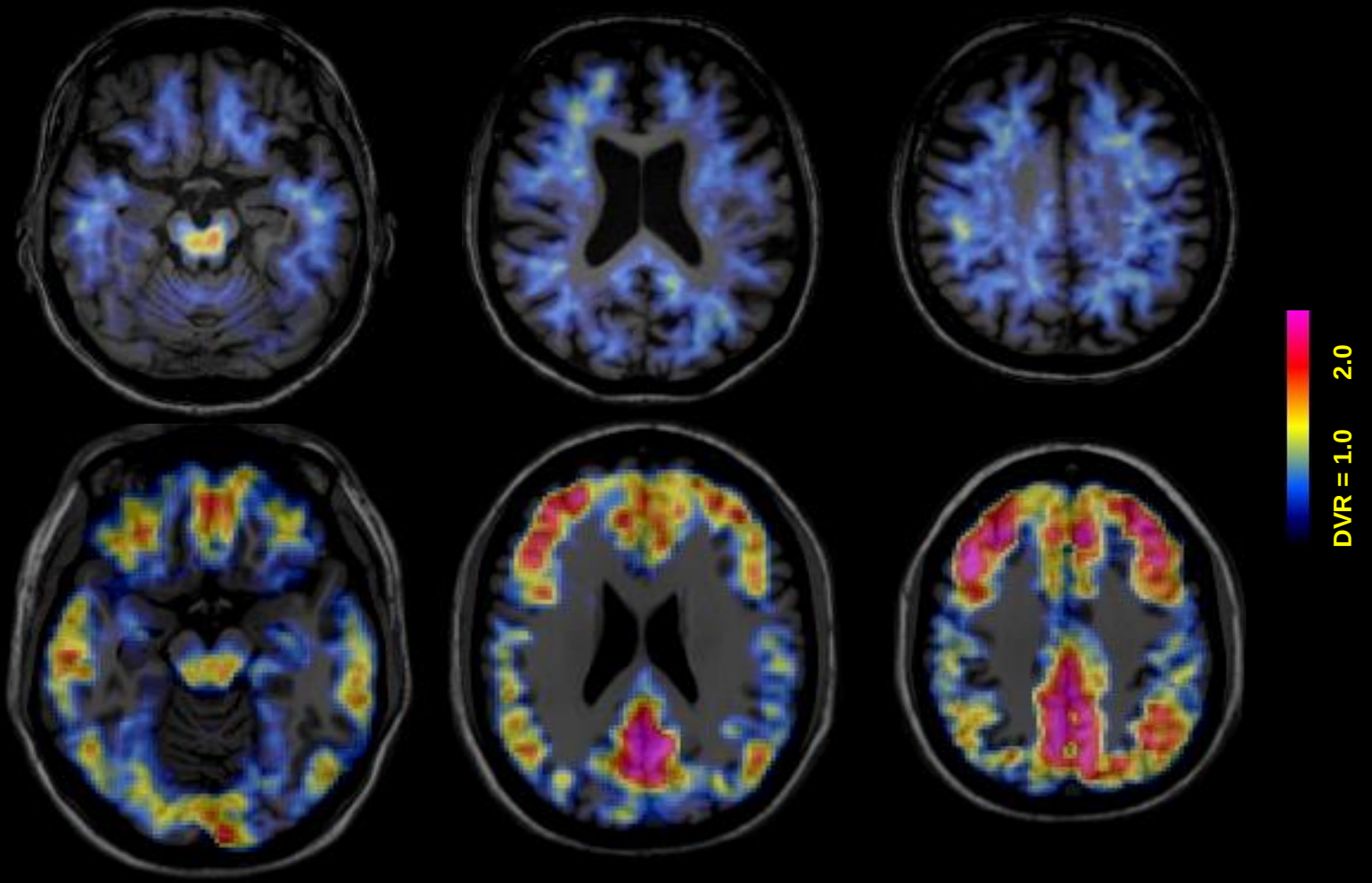
- CSF $A\beta_{1-42}$ / $A\beta_{1-40}$ FDA approved May 2022
  - Covered by Medicare and private insurance

Shaw et al. *Ann Neurol* 2009

Amyloid Imaging
^{11}C PiB-PET (Pittsburgh compound B)

Normal older individual

AD dementia

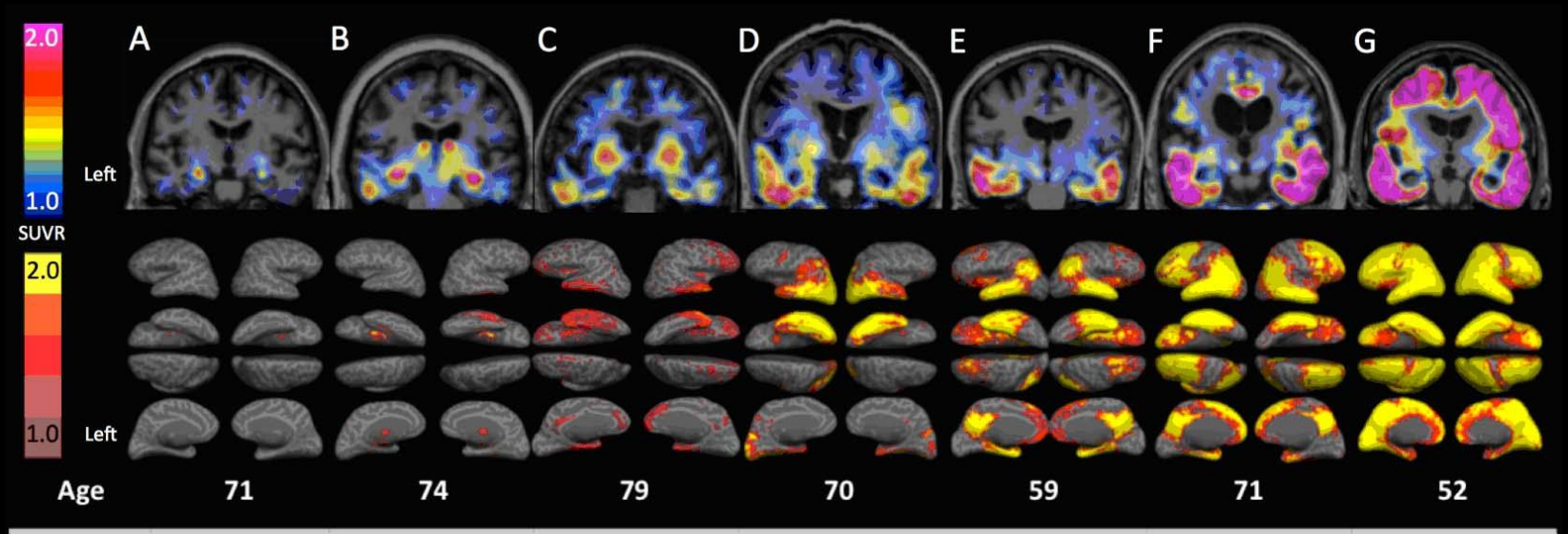


Images courtesy of Keith Johnson, MD

Amyloid imaging: F-18 agents

- Longer half-life than PiB (~2 hrs vs. 20 min)
  - More practical for clinical use
- Florbetapir (Amyvid™, ^{18}F-AV-45)
  - Widely used in clinical trials
  - Approved by FDA for detecting amyloid *in vivo* in symptomatic patients in April, 2012
  - Visual rating training for radiologists available
- Flutemetamol (Vizamyl™, ^{18}F-GE067)
  - Approved by FDA October, 2013
- Florbetaben (Neuroceq™, ^{18}F-BAY94-9172)
  - Approved by FDA March, 2014
- IDEAS (Imaging Dementia—Evidence for Amyloid Scanning) (Rabinovici 2019)
  - Improved diagnostic accuracy, management
  - Covered by Medicare as of October 2023

Flortaucipir PET Tau imaging



MMSE	30	30	29	27	26	23	11
PiB (DVR)	Low (1.0)	High (1.2)	High (1.8)	High (1.5)	High (1.7)	High (1.5)	High (1.5)
Dx	CN	CN	CN	MCI	MCI	AD	AD
PET Braak	0, I-II	III-IV	III-IV	III-IV	III-IV	V-VI	V-VI

- Flortaucipir (Tauvid™) approved by FDA May 2020; not covered by Medicare

Johnson et al. *Ann Neurol* 2016

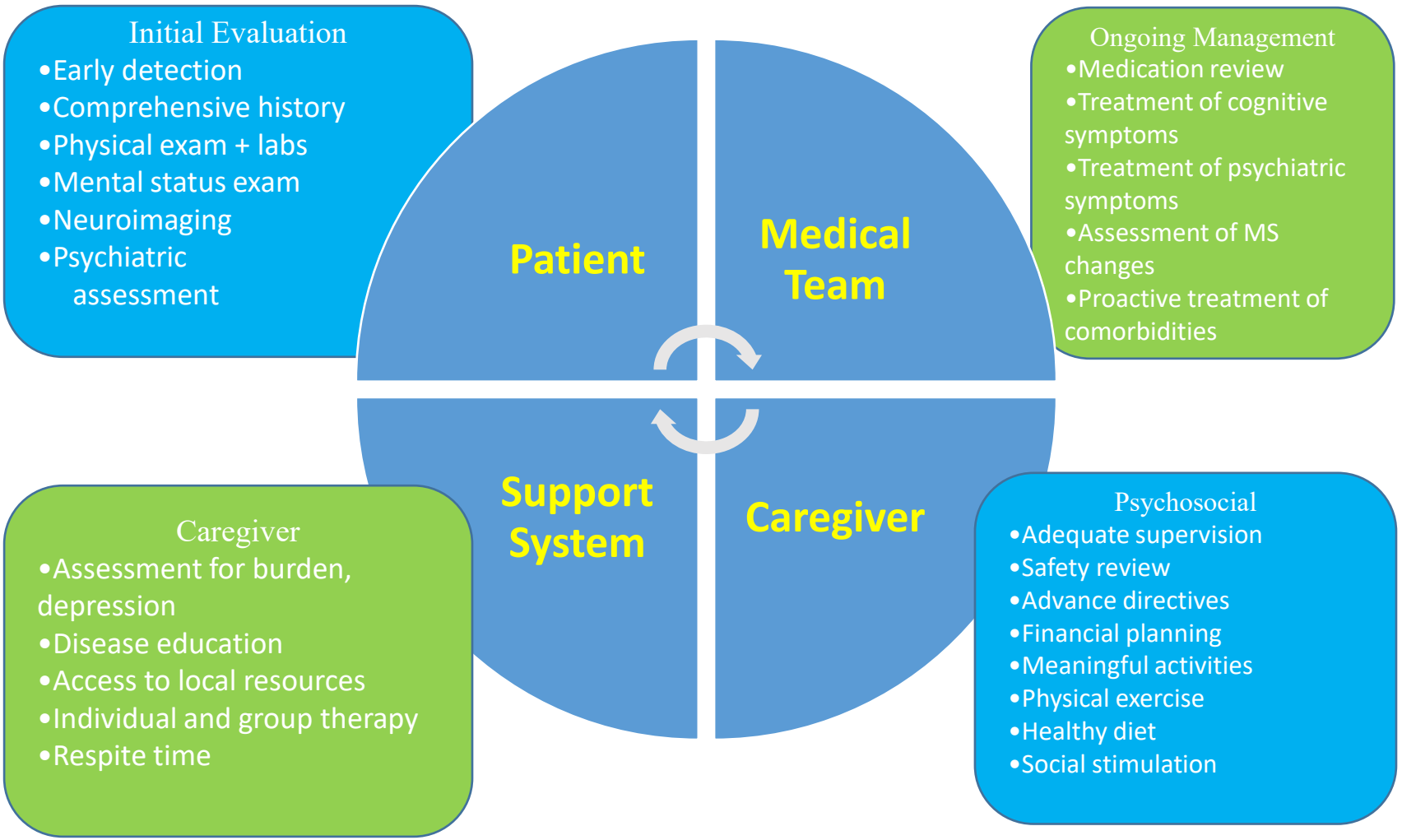
Dementia Diagnostic Assessments: Summary

- "Bedside" assessment
  - Brief: Mini-Cog, AD8
  - Intermediate: MoCA, MMSE, SLUMS, Blessed
  - Long: ACE, CERAD, CDR
  - Physical exam: Parkinsonism, localizing features, motor neuron disease features
- Neuropsychological testing
- CSF (routine, $A\beta_{1-42}$, tau, 14-3-3), plasma p-tau217*, blood (B12, TSH, CBC, electrolytes, LFTs), urinalysis
- Brain imaging
  - Brain Structure: MRI (CT)
  - Brain Function: FDG-PET (SPECT)
  - Molecular imaging of pathology: Amyloid and tau PET imaging
- Genetic testing (family history suggestive of autosomal dominant inheritance: PS1, PS2, APP)
- EEG, EMG/NCS

Case Study: Management

- Recommended discontinuing diphenhydramine
- Discussed medication options
  - Patient and wife elected to hold off on a cholinesterase inhibitor
  - Considered lecanemab or donanemab, which received traditional/full approval by the FDA for MCI and mild AD dementia in 2023 and 2024
- Recommended aggressive control of vascular risk factors
- Recommended designating healthcare proxy and durable power of attorney
- Counseled about observational research studies and clinical trials
  - Patient and wife expressed interest

Multiple Components of Dementia Management



Courtesy of the Alzheimer's Association

FDA Approved Medications for Alzheimer's Disease

tacrine (Cognex®)	donepezil (Aricept®)	rivastigmine (Exelon®)	galantamine (Razadyne®)	memantine (Namenda®)	aducanumab (Aduhelm®)	lecanemab (Leqembi®)	Donanemab (Kisunla®)

- **Cholinesterase-inhibitors (ChE-I's):** donepezil, rivastigmine, galantamine, tacrine* (no longer clinically used)
  - All FDA approved for treatment of mild to moderate AD dementia
  - Donepezil also FDA approved for treatment of severe AD dementia (2006)
  - Galantamine available as a generic since 2009; donepezil, rivastigmine since 2010
- **NMDA (glutamate) receptor antagonist:** memantine
  - FDA approved for treatment of moderate to severe AD dementia (generic 2015)

* Accelerated approval (not traditional/full approval); withdrawn from market 2024

AD Dementia Medications: Symptomatic Benefit

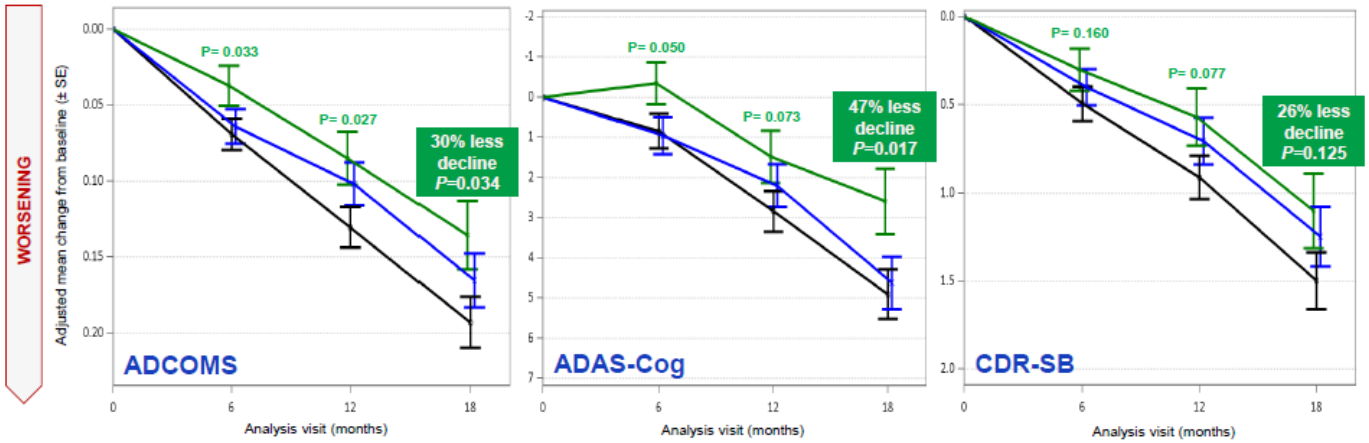
- ChE-I's and Memantine: shown in multiple randomized, double-blind, placebo-controlled trials of AD dementia to provide *modest* but *clinically significant* improvements for *groups* of participants
  - Daily functioning, cognition, neuropsychiatric symptoms, caregiver burden (and potentially saving money)
- Individual results vary
  - Highly variable effects across time between and *within* individuals

Treatment of other dementias

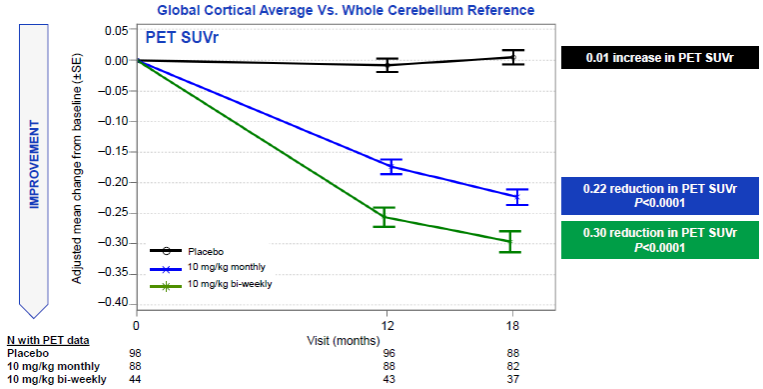
- Rivastigmine FDA approved for treatment of Parkinson's disease with dementia (PDD) since 2007
  - Off-label use of all ChE-I's for PDD and dementia with Lewy bodies (DLB)
- There is no FDA approved drug for treatment of vascular dementia (VaD)
  - ChE-I's are used off label for VaD or mixed AD/VaD dementia based on a positive donepezil trial (Roman 2005) and a positive and a partially positive galantamine trial (Erkinjuntti 2002, Auchus 2007)
- No FDA approved drug for frontotemporal dementia (FTD)

Lecanemab (BAN2401) phase 2b

Anti-amyloid monoclonal antibody, MCI / mild AD dementia



N with data	0 mo.	6 mo.	12 mo.	18 mo.
Placebo	238	216	187	160
10 mg/kg monthly	246	208	165	146
10 mg/kg bi-weekly	152	130	93	79



N with PET data			
Placebo	98	96	88
10 mg/kg monthly	88	88	82
10 mg/kg bi-weekly	44	43	37

* FDA granted accelerated approval based on phase 2b on 1/6/23

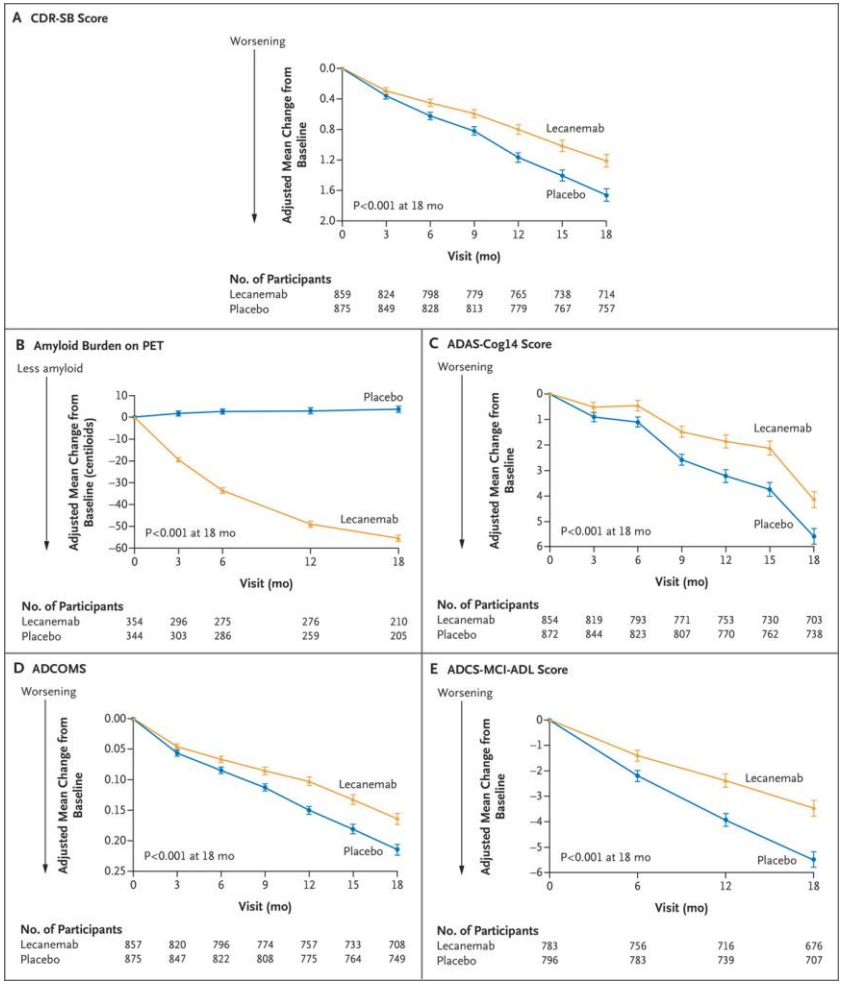
Swanson et al. *Alzheimers Res Ther* 2021

Clarity AD: Lecanemab Phase 3 Trial

- MCI or mild AD dementia
- 1795 participants recruited across 245 sites
- MMSE 22-30
- CDR global 0.5-1
- Impaired memory (age-adjusted score on Logical Memory delayed recall)
- Positive biomarker for amyloid: amyloid PET or t-tau/Aβ CSF
- MRI exclusions: >4 microhemorrhages; single macrohemorrhage (≥1 cm); area of superficial siderosis
- Allowed anticoagulation (about 5% of participants)
- Lecanemab vs. placebo 1:1, 18-month treatment
- Infusions of 10 mg/kg every 2 weeks

van Dyck et al. *N Engl J Med* 2022

Clarity AD: Main Results



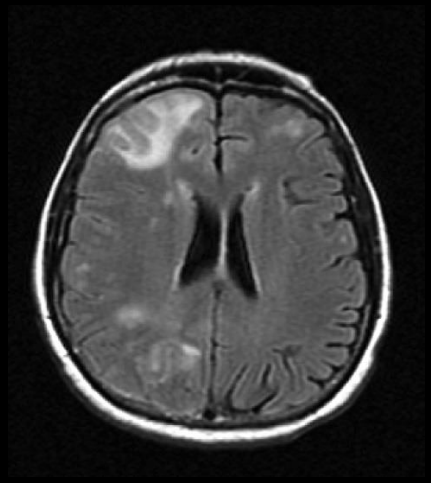
Adverse Events:

- Infusion reaction in 26.4% on Lecanemab vs. 7.4% on placebo
- ARIA-E in 12.6% on Lecanemab (higher in ApoE ε4 carriers) vs. 1.7% on placebo
- ARIA-H (mostly microhemorrhages) in 17.3% on Lecanemab vs. 9.0 on placebo (isolated ARIA-H without ARIA-E 8.9% on Lecanemab vs. 7.8% on placebo)
- Macrohemorrhages in 0.6% on Lecanemab vs. 0.1% on placebo (when anticoagulated 2.4% vs. 0%)
- Higher ARIA rate in APOE4 carriers
- FDA granted full/traditional approval on 7/6/23

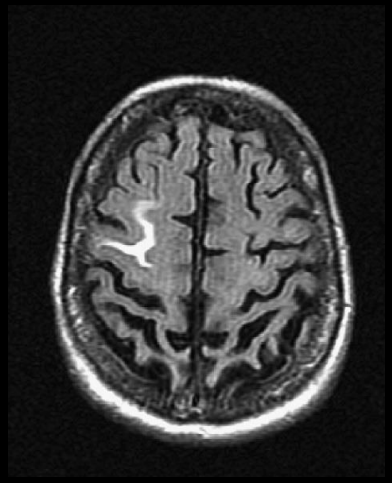
van Dyck et al. *N Engl J Med* 2022

Amyloid-Related Imaging Abnormalities (ARIA)

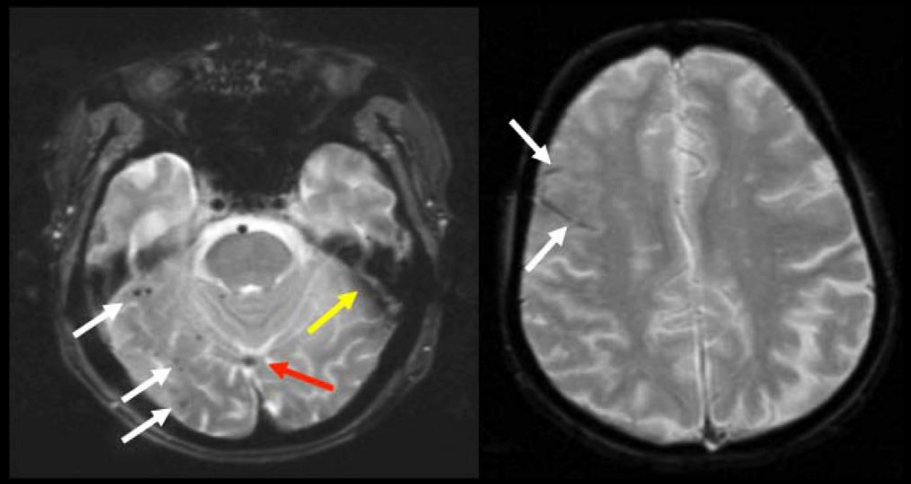
Vasogenic Edema



Sulcal Effusion



Microhemorrhages and Superficial Siderosis



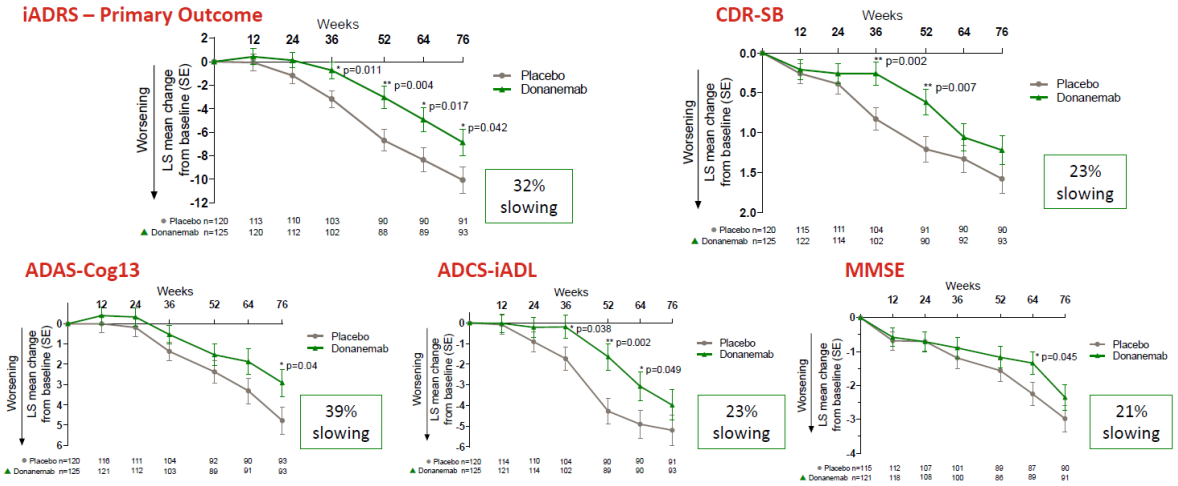
Sperling et al. *Alzheimers Dement* 2011

Societal Impact of lecanemab (Leqembi)

- The first disease modifying therapy for AD to receive FDA full/traditional approval
- Cost (drug only): $26,500/year
- Medicare is covering the drug in the clinical setting (80%)
  - Requires a registry with minimal dataset but not participation in a clinical trial
- Arguably, our healthcare system is not ready to cope with the challenges and demands of a drug like lecanemab
  - Equitable access
  - Determination of amyloid status for eligibility
  - APOE testing for risk stratification
  - Infusions every 2 weeks
  - Multiple MRI scans to monitor for ARIA
  - Specialists to determine eligibility, administer drug, and monitor for adverse events

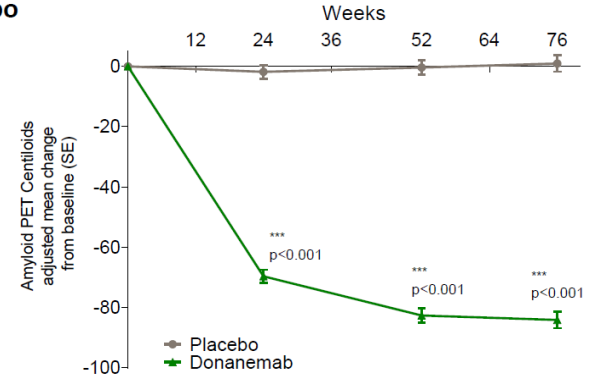
Trailblazer (Donanemab) Phase 2 Trial Results: Clinical Outcomes

Anti-amyloid monoclonal antibody, MCI / mild AD dementia



* Inclusion of participants based on both elevated amyloid and intermediate tau

Treatment with donanemab reduced amyloid plaque by 85 Centiloids at 76 weeks compared with placebo



Placebo n= Donanemab n=	112 121	111 115	91 92	91 90
Donanemab 'amyloid negative' <24.1 CL, n (%)		46 (40%)	55 (60%)	61 (68%)

	LS Mean Change Δ (SE) Donanemab vs. Placebo
W24	-67.83 (3.16)
W52	-82.30 (3.41)
W76	-85.06 (3.87)

40% of donanemab-treated participants reached amyloid negative levels by 24 weeks

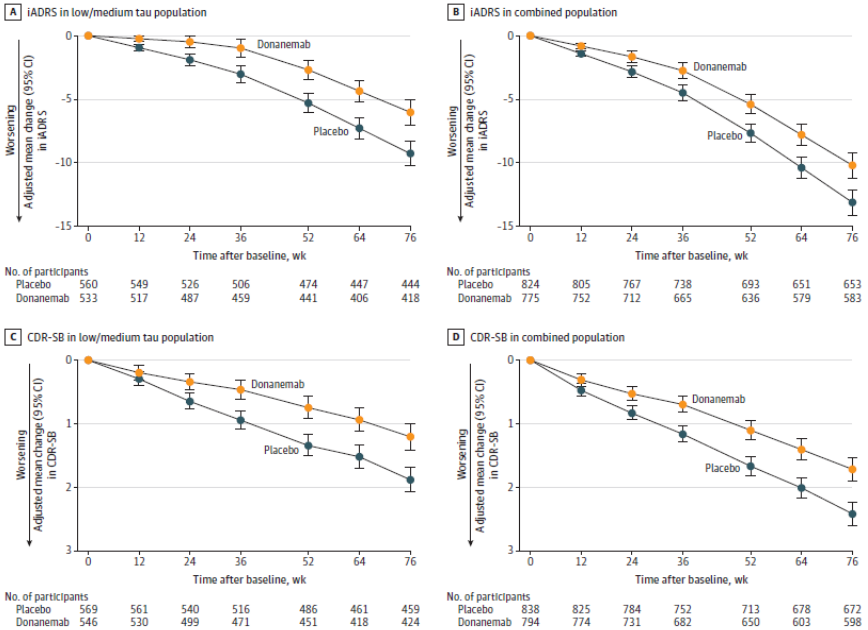
Mintun et al. *N Engl J Med* 2021

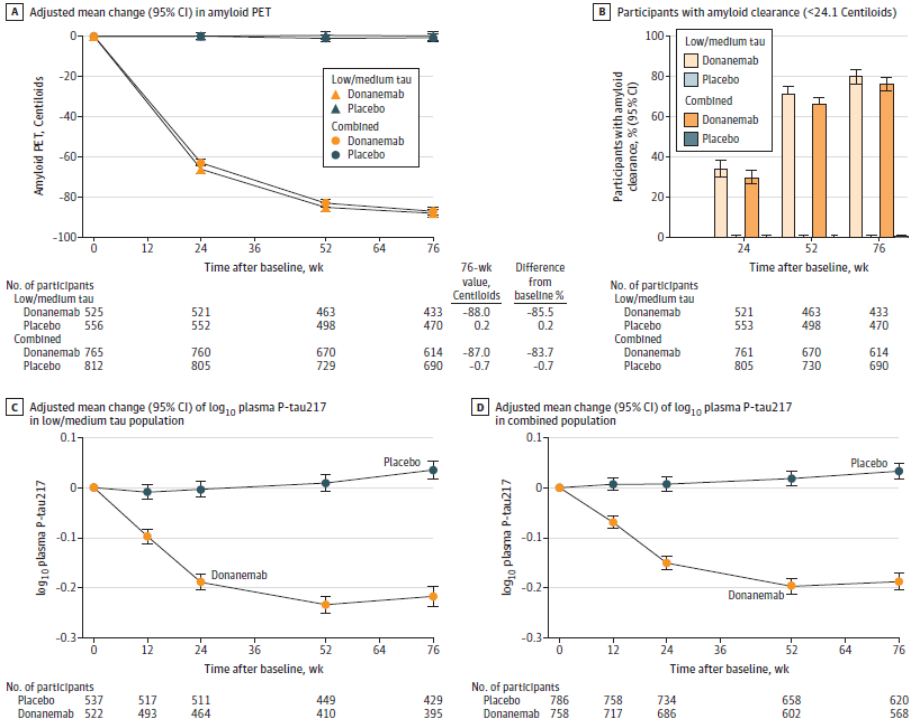
Trailblazer-ALZ 2 (Donanemab) Phase 3 Trial Results

- MCI / mild AD dementia, elevated amyloid (primary analyses in participants with low/medium tau, n=1182)
- Completed April 2023, results reported 5/3/23
- Significant slowing of clinical decline over 18 months
  - 35% slowing on iADRS
  - 37% CDR-SB, 40% ADCS-IADL, 32% ADAS-Cog 13
- Results were attenuated but still significant when including participants with high (combined) tau (n=1736)
- 34% amyloid negative by 6 months, 80% by 18 months
- Adverse events:
  - ARIA-E 24% (symptomatic in 6.1%, serious in 1.6%)
  - ARIA-H (mostly microhemorrhages or superficial siderosis) 31.4% on drug vs. 13.6% on placebo (isolated ARIA-H without ARIA-E 12.7% on drug vs. 12.4% on placebo)
  - Macrohemorrhages in 0.4% on Donanemab vs. 0.2% on placebo
  - Infusion reactions in 8.7% (most mild-moderate) on drug vs. 0.5 on placebo

Sims et al. *JAMA* 2023

Trailblazer-ALZ 2: Clinical and Biomarker Outcomes





* FDA granted full/traditional approval on 7/2/24

- Trailbalzer-ALZ 6: modified titration reduced ARIA-E rate from 24% to 14%

Sims et al. *JAMA* 2023

Lifestyle Modifications

- Mediterranean diet (Scarmeas 2006, Féart 2009)
  - High in vegetables, legumes, fruits, nuts, cereals, fish, olive oil
  - Low in saturated fats
  - Reduces risk of developing AD dementia and slows cognitive decline
- Physical exercise (Larson 2006, Scarmeas 2009)
  - Aerobic exercise 3 or more times per week or vigorous exercise 1 hour per week reduces risk of progressing from MCI to AD dementia
- Cognitive training (ACTIVE, Ball 2002, Willis 2006, Rebok 2014)
  - Reduced decline in reasoning, processing speed, IADL

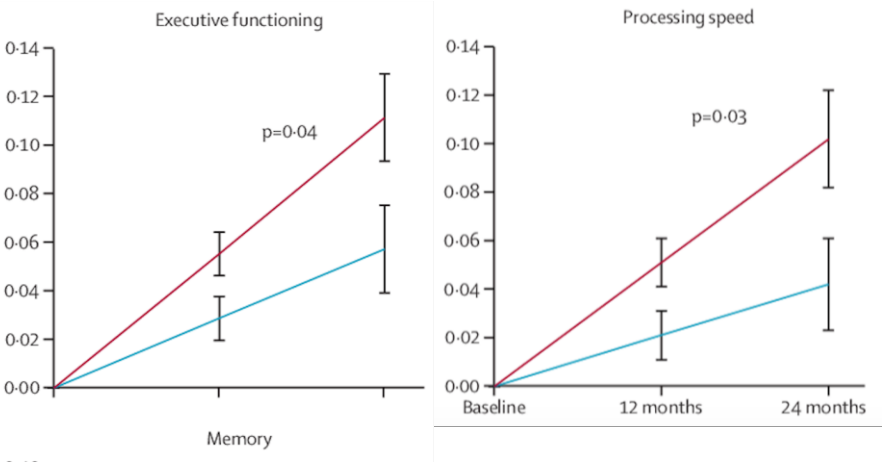
Lifestyle Modifications: Hypertension Treatment

- SPRINT MIND trial (Williamson 2019)
- RCT in cognitively normal older adults (age 68)
  - Intensive control: SBP <120 (n=4,278)
  - Standard control: SBP <140 (n=4,285)
  - Median intervention period: 3.3 years
  - Median f/u period: 5.1 years
- Primary Outcome: progression to dementia
  - HR 0.83 (95% CI, 0.67-1.04)
- Secondary Outcome: progression to MCI
  - HR 0.81 (95% CI, 0.69-0.95)

Lifestyle Modifications: Multi-domain

- Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER study) (Ngandu 2015)
  - 2-year multidomain lifestyle intervention trial
  - 1260 individuals aged 60-77 years and at risk for dementia
  - Randomized 1:1 to receive extra intervention

Interventions
Nutrition
Exercise
Cognitive training
Management of vascular risk factors



Findings from this large, long-term, randomized controlled trial suggest that a multidomain intervention could modestly improve or maintain cognitive functioning in at-risk elderly people from the general population

- US Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk (US POINTER)
  - 2000 participants aged 60-79 years
  - Launched 2019

Nutraceuticals / Supplements

- Antioxidants (Sano 1997, Petersen 2005, Galasko 2012, Dysken 2014)
  - Vitamin E (high doses) modest benefit in treating mild to severe AD dementia (not in MCI); prevention trial ongoing
  - Vitamin C, Alpha lipoic acid, Coenzyme-Q10 ineffective in biomarker trial in AD dementia
- Cocoa extract / Multivitamin (Baker 2022)
  - Multivitamin modestly effective; cocoa ineffective in cognitively normal older adults
- Ginkgo biloba (DeKosky 2008, Vellas 2012)
  - Ineffective in preventing dementia (in cognitively normal older adults, subjective cognitive decline, and MCI)
- Omega 3 fatty acids / fish oil (DHA) (Quinn 2010, Sydenham 2012)
  - Multiple studies: ineffective in preventing cognitive decline or dementia or treating AD dementia
- Folic acid/vitamin B6/vitamin B12 (Aisen 2008)
  - Ineffective in treating AD dementia
- Huperzine, a naturally occurring ChE-I (Rafii 2011)
  - Ineffective in treating AD dementia

Dementia Management: Summary

- Dementia management consists of medications, psychosocial support, and caregiver support
- There is a limited number of FDA approved medications for AD at the stage of dementia and more recently MCI
- Lifestyle modifications can help prevent or slow existing symptoms
- Supplements have been mostly unhelpful

Participating in AD research

- Two major types of research studies
  - Randomized clinical trials (drug trials)
  - Observational (natural history) studies
- Research is an option that allows participants to be proactive, take some control of their future, and contribute to finding a cure for AD
- Observational studies are a nice way to engage in research and contribute for individuals who are not ready to jump into a clinical trial

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Questions?

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