CME CAST

Diagnosing AD Early with SDM and Culturally Sensitive Care

This activity is supported by an educational grant from Lilly

This activity may include discussions of products or devices that are not currently labeled for use by the FDA.

The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational uses (any uses not approved by the FDA) of products or devices.

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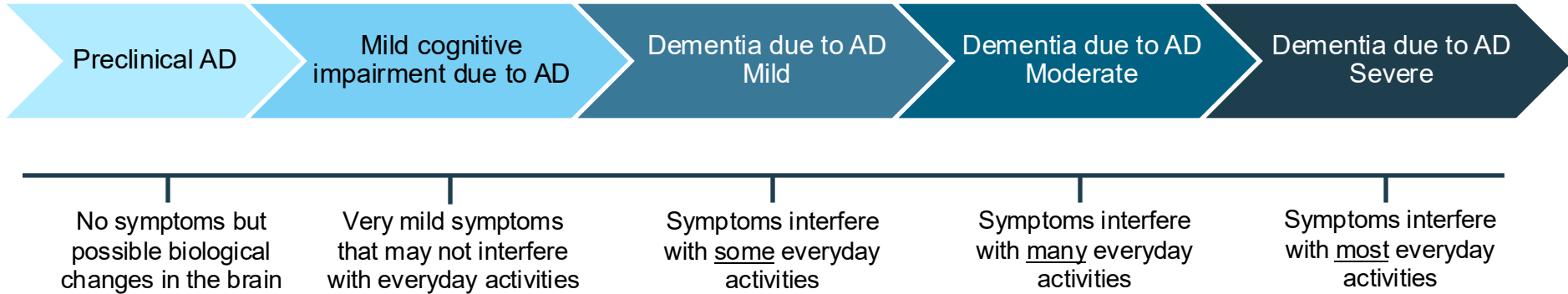Department of Neurology
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Learning Objectives

1. Utilize current and emerging diagnostic tools in diverse populations for detection of Alzheimer's disease (AD) early in the disease course

2. Integrate culturally sensitive patient and caregiver education strategies to improve shared decision-making (SDM) on brain health and/or AD management with patients

3. Implement multidisciplinary team (MDT) care when managing patients with AD
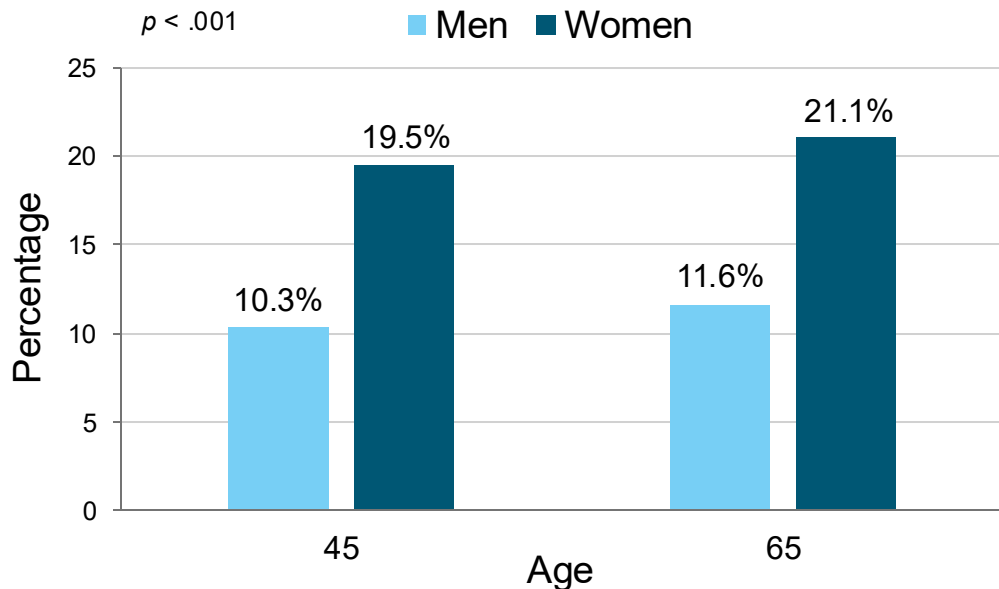
Continuum of Alzheimer's Disease

Preclinical AD	Mild cognitive impairment due to AD	Dementia due to AD Mild	Dementia due to AD Moderate	Dementia due to AD Severe
No symptoms but possible biological changes in the brain	Very mild symptoms that may not interfere with everyday activities	Symptoms interfere with <u>some</u> everyday activities	Symptoms interfere with <u>many</u> everyday activities	Symptoms interfere with <u>most</u> everyday activities

2024 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2024;20(5):3708-3821.

CME OUTFITTERS

Impact of AD on Different Communities

Estimated Lifetime Risk for AD, by Sex, at Age 45 and 65
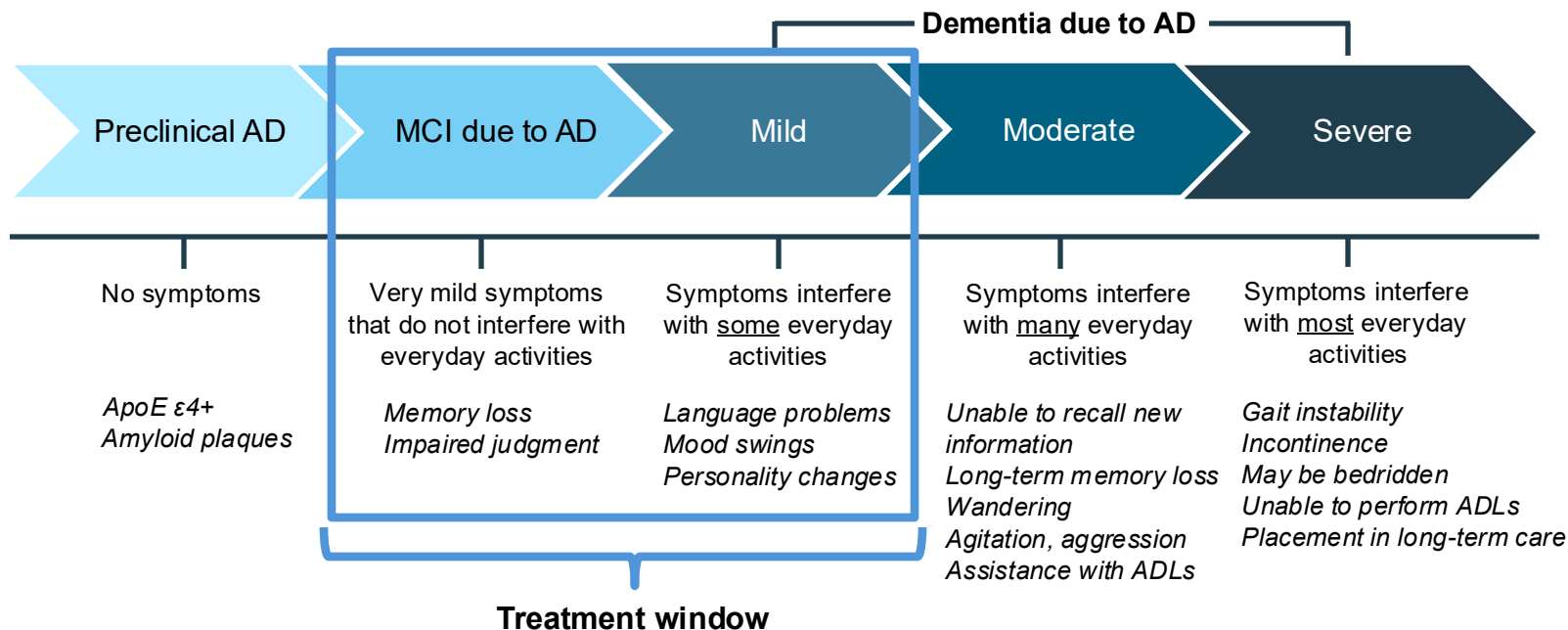**Gender-Specific Risk of Dementia and AD**

p < .001

■ Men ■ Women

[Bar chart showing Percentage vs Age]

- Age 45: Men 10.3%, Women 19.5%
- Age 65: Men 11.6%, Women 21.1%

Y-axis: Percentage (0, 5, 10, 15, 20, 25)
X-axis: Age (45, 65)

- Incidence of AD is almost **2x** higher in older **African American** individuals
- Risk of AD in **Hispanic/Latino** individuals is **1.5x** greater
- **AIAN** individuals are at higher risk of AD compared with White or Asian American populations
  - Approximately **one third** of AIAN elders will develop AD and related dementias

AIAN = American Indian, Alaska Native

Lim AC, et al. *Commun Med (Lond)*. 2023;3(1):101. Alzheimer's disease facts and figures. *Alzheimers Dement*. 2024;20(5):3708-3821.
Chene G, et al. *Alzheimers Dement*. 2015;11(3):310-320. Matthews KA, et al. *Alzheimers Dement*. 2019;15(1):17-24.

CME OUTFITTERS

Symptoms and Stages of AD

Dementia due to AD

Preclinical AD	MCI due to AD	Mild	Moderate	Severe

No symptoms

ApoE ε4+
Amyloid plaques

Very mild symptoms that do not interfere with everyday activities

Memory loss
Impaired judgment

Symptoms interfere with <u>some</u> everyday activities

Language problems
Mood swings
Personality changes

Symptoms interfere with <u>many</u> everyday activities

Unable to recall new information
Long-term memory loss
Wandering
Agitation, aggression
Assistance with ADLs

Symptoms interfere with <u>most</u> everyday activities

Gait instability
Incontinence
May be bedridden
Unable to perform ADLs
Placement in long-term care

Treatment window

Cognitive Screening Instruments: Not a Substitute for Complete Diagnostic Workup Evaluation

Screening Tool	Approximate Time to Administer and Details
Mini-Mental State Examination (MMSE)	10 minutes Widely used and reliable tool for detecting dementia
Mini-Cog	3–5 minutes Widely used and reports have been positive
Montreal Cognitive Assessment (MoCA)	10 minutes Relatively simple Brief test that helps health professionals quickly determine if a person has declining cognitive function
Saint Louis University Mental Status (SLUMS) Exam	7 minutes 1-item Alzheimer's screening test that is especially good at identifying people with milder cognitive problems that don't yet rise to the level of dementia
General Practitioner Assessment of Cognition (GPCOG)	4 minutes to administer the patient assessment 2 minutes to interview the caregiver
AD8 Informant Interview (not a test)	3 minutes to complete

Reiss AB, et al. *AIMS Public Health*. 2022;9(4):661-689. Myrberg K, et al. Clin *Linguist Phonet*. 2019;34:652-670. Mini-cog. Dementia Care Website. 2021. https://dementiacare.com.my/abc-of-dementia/quick-screening-test-for-dementia/. Montreal Cognitive Assessment (MoCA) test. 2024. https://mocatest.com. SLU Website. 2024. https://www.slu.edu/medicine/internal-medicine/geriatric-medicine/aging-successfully/assessment-tools/mental-status-exam.php. General Practitioner Assessment of Cognition Website. 2016. http://gpcog.com.au/. Galvin J and Zweig Y. Hartford Institute for Geriatric Nursing (HIGN) Website. 2021. https://hign.org/consultgeri/try-this-series/ad8-washington-university-dementia-screening-test.

Cross-Cultural Applicability

- Montreal Cognitive Assessment (MoCA)
  - Widely used to screen for mild cognitive impairment (MCI)
- While there are many available versions, the cross-cultural validity of the assessment has not been explored sufficiently

Clinical Discussion

- Highlights the necessity for cross-cultural considerations
- Recognize it as a screening tool and not a diagnostic tool
- Suggest making appropriate cutoffs and point adjustments for education

Nasreddine ZS, et al. *J Am Geriatr Soc*. 2005;53(4):695-699.
O'Driscoll C, Shaikh M. *J Alzheimers Dis*. 2017;58(3):789-801.

Bio-Hermes Study: Predictive Power of Biomarkers in Diverse Populations

Total Population · **Non-Hispanic White** · **Non-Hispanic Black** · **Hispanic**

Legend: — P-tau181 — P-tau217 — Aβ42/Aβ40 Ratio
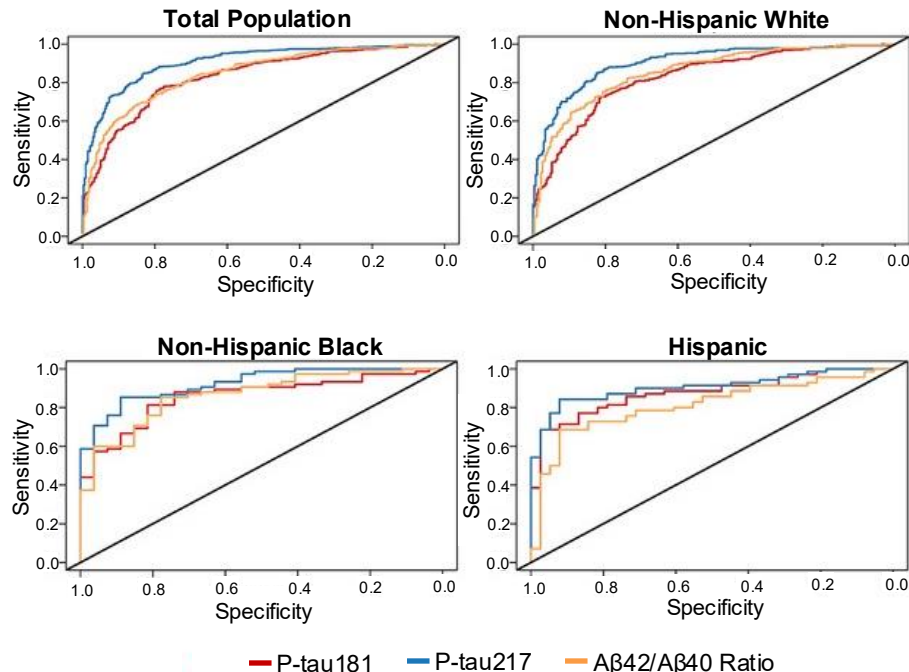
Results

- Blood-based biomarkers (BBBs) predict brain amyloid positivity in a community-based population in all groups
- **Demographic and biomarker differences associated with ethnicity and race may influence screen failure rates**

Clinical Discussion

- BBBs are very good for identifying persons with amyloid plaques in the brain with or without symptoms of disease and for persons of all racial and ethnic backgrounds
- **May help identify patients who may benefit from treatment**
- **Room to develop other technologies based on differences**

Receiver operating characteristic curve used for prediction of brain positron emission tomography or cerebrospinal fluid amyloid positivity adjusted for age and ApoE ε4 status with imputed values

Aβ = amyloid beta; p-tau = phosphorylated tau

Mohs RC, et al. *Alzheimers Dement.* 2024;20(4):2752-2765.

CLARITY AD: Impact of Lecanemab

Change in CDR-SB Score (Range, 0-18)

Difference in least-squares mean change, -0.45 (95% CI, -0.67 to -0.23)

N = 1,795
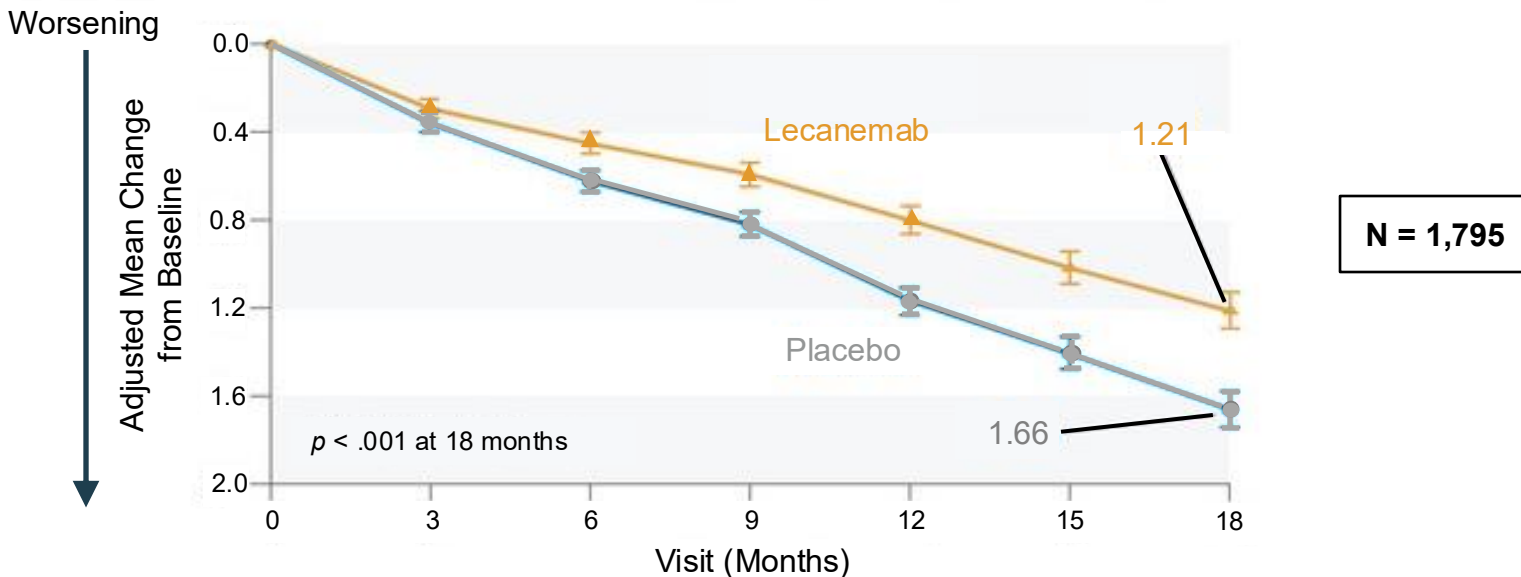
Change in score on the Clinical Dementia Rating–Sum of Boxes (CDR-SB) from baseline
CI = confidence interval
van Dyck CH. *N Engl J Med*. 2023;388(1):9-21.

TRAILBLAZER-ALZ 2: Impact of Donanemab

iADRS in Low/Medium Tau Population

Worsening — Adjusted Mean Change (95% CI) in iADRS

Donanemab

Placebo

$p < .001$

Time After Baseline (Weeks)

iADRS in Combined Population

Worsening — Adjusted Mean Change (95% CI) in iADRS

Donanemab

Placebo

$p < .001$

Time After Baseline (Weeks)

CDR-SB in Low/Medium Tau Population

Worsening — Adjusted Mean Change (95% CI) in CDR-SB

Donanemab

Placebo

$p < .001$

Time After Baseline (Weeks)

CDR-SB in Combined Population

Worsening — Adjusted Mean Change (95% CI) in CDR-SB

Donanemab

Placebo

$p < .001$

Time After Baseline (Weeks)

N = 1,736*

*Participants were randomized in a 1:1 ratio to receive donanemab (n = 860) or placebo (n = 876) intravenously every 4 weeks for 72 weeks

iADRS = integrated AD Rating Scale
Sims JR, et al. *JAMA*. 2023;330(6):512-527.

Monitoring for ARIA-H and ARIA-E

ARIA-H

- Characterized by microhemorrhages and superficial siderosis

ARIA-E

- Characterized by edema and effusion
- Dose dependent: higher incidence in those receiving higher doses of anti-Aβ immunotherapies

ARIA-E = amyloid-related imaging abnormalities characterized by edema/effusion; ARIA-H = ARIA characterized by microhemorrhages and superficial siderosis
Roytman M, et al. *AJR Am J Roentgenol.* 2023;220(4):562-574.

Team-Based Approach for the Management of Alzheimer's Disease
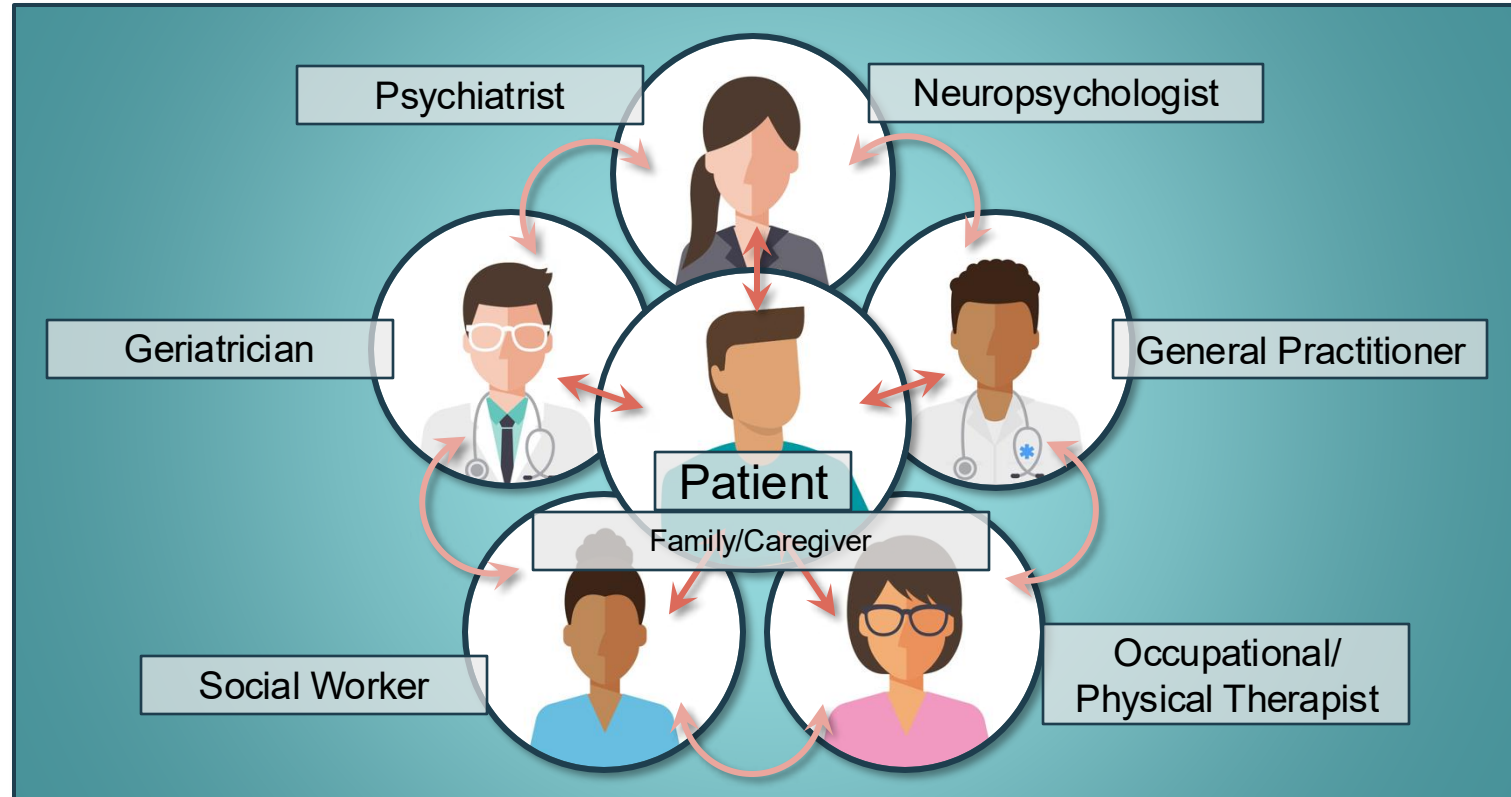
SMART Goals
Specific, Measurable, Attainable, Relevant, Timely

- Utilize simple cognitive screening tools (e.g., MoCA) while keeping in mind time constraints and advantages and limitations in diverse populations
- Talk to your colleagues about identifying and characterizing cognitive and functional symptoms leading to a syndromic diagnosis
- Provide culturally sensitive education for patients and caregivers to improve health literacy, communication, and shared decision-making about treatments that are most effective in early stages of illness
- Consistently initiate conversations with patients and their families to destigmatize "thinking change" and normalize "normal aging"
- Collaborate with the multidisciplinary team to provide care for patients with AD and support for their caregivers

Other Activities in This Series Include…

CMEO BriefCase — *Discussions on Brain Health and Cognitive Concerns*

CMEO BriefCase — *Diagnosis of AD and Treatment with SDM*

https://www.cmeoutfitters.com/practice/alzheimers-disease-hub/

Suggested Reading

1. Alzheimer's disease facts and figures. *Alzheimers Dement*. 2024;20(5):3708-3821.

2. Chene G, Beiser A, Au R, Preis SR, Wolf PA, Dufouil C, et al. Gender and incidence of dementia in the Framingham Heart Study from mid-adult life. *Alzheimers Dement.* 2015;11(3): 310-20.

3. Chin NA, Dinsmore D, Gonzales T, et al. Alzheimer's disease - anti-amyloid medications, early detection, and screening. *N Engl J Med*. 2024;390(10):e22.

4. Fontanella RA, Ghosh P, Pesapane A, et al. Tirzepatide prevents neurodegeneration through multiple molecular pathways. *J Transl Med*. 2024;22(1):114.

5. Galvin J, Zweig Y. The AD8: The Washington University Dementia Screening Test. https://hign.org/consultgeri/try-this-series/ad8-washington-university-dementia-screening-test. 2023. Accessed December 23, 2024.

6. General Practitioner Assessment of Cognition (GPCOG). http://gpcog.com.au/. 2016. Accessed December 24, 2024.

7. Giannisis A, Al-Grety A, Carlsson H, et al. Plasma apolipoprotein E levels, isoform composition, and dimer profile in relation to plasma lipids in racially diverse patients with Alzheimer's disease and mild cognitive impairment. *Alzheimers Res Ther*. 2023;15(1):160.

8. Kopp KO, Glotfelty EJ, Ki Y, Greig NH. Glucagon-like peptide-1 (GLP-1) receptor agonists and neuroinflammation: implications for neurodegenerative disease treatment. *Pharmacol Res*. 2022;186:106550.

9. Lim AC, Barnes LL, Weissberger GH, et al. Quantification of race/ethnicity representation in Alzheimer's disease neuroimaging research in the USA: a systematic review. *Commun Med (Lond)*. 2023;3(1):101.

10. Matthews KA, Xu W, Gaglioti AH, et al. Racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015-2060) in adults aged ≥65 years. *Alzheimers Dement*. 2019;15(1):17-24.

11. Mielke MM, Fowler NR. Alzheimer disease blood biomarkers: considerations for population-level use. *Nat Rev Neurol*. 2024;20(8):495-504.

Suggested Reading

12. Mini-Cog. ABC of dementia: quick screening test for dementia. https://dementiacare.com.my/abc-of-dementia/quick-screening-test-for-dementia/. 2021. Accessed December 24, 2024.

13. Mohs RC, Beauregard D, Dwyer J, et al. The Bio-Hermes Study: biomarker database developed to investigate blood-based and digital biomarkers in community-based, diverse populations clinically screened for Alzheimer's disease. *Alzheimers Dement*. 2024;20(4):2752-2765.

14. Montreal Cognitive Assessment (MoCA). https://mocatest.com. 2022. Accessed December 24, 2024.

15. Myrberg K, Hydén LC, Samuelsson C. The mini-mental state examination (MMSE) from a language perspective: an analysis of test interaction. *Clin Linguist Phonet*. 2019;34:652-670.

16. Palmqvist S, Tideman P, Mattsson-Carlgren N, et al. Blood biomarkers to detect Alzheimer disease in primary care and secondary care. *JAMA*. 2024;332(15):1245-1257.

17. Quiroz YT, Solis M, Aranda MP, et al. Addressing the disparities in dementia risk, early detection and care in Latino populations: highlights from the second Latinos & Alzheimer's Symposium. *Alzheimers Dement*. 2022;18(9):1677-1686.

18. Ramanan VK, Graff-Radford J, Syrjanen J, et al. Association of plasma biomarkers of Alzheimer disease with cognition and medical comorbidities in a biracial cohort. *Neurology*. 2023;101(14):e1402-e1411.

19. Reiss AB, de Levante Raphael D, Chin NA, Sinha V. The physician's Alzheimer's disease management guide: early detection and diagnosis of cognitive impairment, Alzheimer's disease and related dementia. *AIMS Public Health*. 2022;9(4):661-689.

20. Roytman M, Mashriqi F, Al-Tawil K, et al. Amyloid-related imaging abnormalities: an update. *AJR Am J Roentgenol*. 2023;220(4):562-574.

21. Simons RL, Ong ML, Lei MK, et al. Racial discrimination during middle age predicts higher serum phosphorylated tau and neurofilament light chain levels a decade later: a study of aging black Americans. *Alzheimers Dement*. 2024;20(5):3485-3494.

22. Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA*. 2023;330(6):512-527.

Suggested Reading

23. Saint Louis University (SLU) Mental Status Exam. https://www.slu.edu/medicine/internal-medicine/geriatric-medicine/aging-successfully/assessment-tools/mental-status-exam.php. 2024. Accessed December 24, 2024.

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25. Sofer T, Kurniansyah N, Granot-Hershkovitz E, et al. A polygenic risk score for Alzheimer's disease constructed using APOE-region variants has stronger association than APOE alleles with mild cognitive impairment in Hispanic/Latino adults in the U.S. *Alzheimers Res Ther*. 2023;15(1):146.

26. Suchy-Dicey A, Howard B, Longstreth WT Jr, Reiman EM, Buchwald D. APOE genotype, hippocampus, and cognitive markers of Alzheimer's disease in American Indians: data from the Strong Heart Study. *Alzheimers Dement*. 2022;18(12):2518-2526.

27. Suchy-Dicey AM, Longstreth WT Jr, Rhoads K, et al. Plasma biomarkers of Alzheimer's disease and related dementias in American Indians: the Strong Heart Study. *Alzheimers Dement*. 2024;20(3):2072-2079.

28. Targum SD, Fosdick L, Drake KE, et al. Effect of age on clinical trial outcome in participants with probable Alzheimer's disease. *J Alzheimers Dis*. 2021;82(3):1243-1257.

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31. Wessels AM, Dennehy EB, Dowsett SA, Dickson SP, Hendrix SB. Meaningful clinical changes in Alzheimer disease measured with the iADRS and illustrated using the donanemab TRAILBLAZER-ALZ study findings. *Neurol Clin Pract*. 2023;13(2):e200127.