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Use the QR code on the right or the link below to fill out the short pre-presentation survey before the presentation begins.

https://wh1.snapsurveys.com/s.asp?k=164407330154
Updates in Managing Mild Cognitive Impairment & Alzheimer’s Disease: The Role of the Primary Care Clinician

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VALLEJO, CA
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Austin Ulrich, PharmD, Editorial Support, and Michael Hanak, MD, Reviewer, disclosed no relevant financial relationship or interest with a proprietary entity producing, marketing, reselling or distributing health care goods or services.

All relevant financial relationships have been mitigated.
This CME activity includes discussion about uses of medications outside of their approved labeling.
## Learning Objectives

Participants in this presentation will be able to...

<table>
<thead>
<tr>
<th>Task</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify correct diagnostic criteria</td>
<td>Identify correct diagnostic criteria for mild cognitive impairment (MCI) and Alzheimer’s disease (AD) based on current guideline recommendations.</td>
</tr>
<tr>
<td>Design appropriate and effective treatment plans</td>
<td>Design appropriate and effective treatment plans for patients with MCI and AD and refer to a specialist when necessary.</td>
</tr>
<tr>
<td>Describe advances in testing and treatment for AD</td>
<td>Describe advances in testing and treatment for AD that may impact dementia care.</td>
</tr>
</tbody>
</table>
Overview of AD

• A progressive brain disease that worsens over time; the disease process is thought to begin 20 years prior to noticeable symptoms\(^1\)

• Results in a loss of neurons affecting cognitive function, causing neurologic symptoms such as impairment of activities of daily life, dementia, and ultimately, death\(^1\)

• Hallmark pathology is accumulation of beta-amyloid plaques surrounding neurons, as well as tau proteins inside neurons\(^1\)

Overview of AD (cont)

• The most common cause of dementia, with an estimated 60%-80% of dementia cases resulting from AD\(^1\)

• 50% of AD cases are “mixed,” demonstrating pathology and symptoms related to another dementia type in addition to AD\(^1\)

Disease Course

The AD Continuum

![Disease Course Diagram](image)

Note: components are not equal in duration, even though the arrows are equal in size.

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Overview of MCI

- Considered the second “phase” of AD, characterized by subtle cognitive and memory impairment that is usually noticeable only to the patient, family members, and friends.
- Symptoms occur as a result of losing the ability to compensate for destruction of neurons caused by AD.
- Presence of biomarker evidence indicating neurologic changes.

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Disease Burden of AD in the United States

Millions of people
- Ages 65-74
- Ages 75-84
- Ages 85+

Year
- 2020
- 2030
- 2040
- 2050
- 2060

Legend:
- 6.1
- 8.5
- 11.2
- 12.7
- 13.8

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MCI and AD - The PCP’s Role

Alzheimer’s Association Survey of PCPs in 2020

• 50% believed the medical profession is unprepared to meet the expected increase in demand for providing care for AD and other dementias

• More than half responded that there are not enough specialists to receive referrals for AD

• Fewer than half have pursued additional training in dementia care since medical school and residency (mainly due to limited access or availability)

• 40% learned how to manage patients with AD largely through clinical experience

MCI and AD - The PCP’s Role (cont)

Alzheimer’s Association Survey of PCPs in 2020

• 53% field questions about AD or dementia from patients 65 or older or their family members every few days; 19% receive these questions daily
• 27% are only sometimes or never comfortable answering patient questions about AD
• 32% make specialist referrals for their dementia patients at least once a month
• 82% feel they are on the front lines of providing dementia care

MCI and AD - The PCP’s Role

- Cognitive assessment
- Screening, testing, and diagnosis
- Disease management
- Refer to specialists when necessary

“[There] is a shortage of specialty physicians to provide care for the large and increasing numbers of people with Alzheimer’s dementia in the United States. As a result, the responsibility for their medical care rests mainly with primary care …”
Case Scenario

• KB is an 82-year-old female who presents to her PCP for a routine annual wellness visit (AWV). She has a history of hypertension and a family history of dementia. She presents with her husband who usually accompanies her to appointments.

• Her routine labs are within normal limits, and her blood pressure today is 118/70.

• Her husband reports cognitive difficulties for KB that have worsened over the past year, but this is only noticeable to those who know KB well.

• She does not have trouble with most daily activities but has stopped driving and balancing her checkbook because she is “concerned she’ll make a mistake.”

How would you evaluate this patient for cognitive impairment during the AWV?
Cognitive Assessment in Primary Care

- Cognitive assessment is a component of AWVs for Medicare
- However, less than half of PCPs have a standard protocol to assess for cognitive impairment
- Detecting cognitive impairment can occur with regular patient and caregiver interactions convenient to primary care settings
- Several validated screening tools are available to objectively assess for cognitive impairment

Clinicians should routinely screen patients at risk for Alzheimer’s disease with a validated cognitive assessment tool.
# Cognitive Assessment Tools for Primary Care

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Number of Items</th>
<th>Time to Complete (minutes)</th>
<th>Patient or Informant</th>
<th>Shortened Version?</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE (Mini-Mental State Examination)</td>
<td>30</td>
<td>5-10</td>
<td>Patient</td>
<td>Yes</td>
</tr>
<tr>
<td>MoCA (Montreal Cognitive Assessment)</td>
<td>12</td>
<td>10</td>
<td>Patient</td>
<td>Yes</td>
</tr>
<tr>
<td>Mini-Cog (Mini Cognitive Assessment Instrument)</td>
<td>3 item recall with clock drawing</td>
<td>2-3</td>
<td>Patient</td>
<td>Yes</td>
</tr>
<tr>
<td>AD8</td>
<td>8</td>
<td>2-3</td>
<td>Informant</td>
<td>No</td>
</tr>
<tr>
<td>IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly)</td>
<td>16 or 26</td>
<td>10</td>
<td>Informant</td>
<td>No</td>
</tr>
</tbody>
</table>

One approach to cognitive screening in primary care

<table>
<thead>
<tr>
<th>SCREENING VISIT</th>
<th>10 WARNING SIGNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generally due to concerns about cognition or function, noted by Patient, Family Member or Physician</td>
<td>1. Memory loss disrupts daily life</td>
</tr>
<tr>
<td><strong>History</strong></td>
<td>2. Challenges in planning or problem solving</td>
</tr>
<tr>
<td>Changes in cognition and/or function</td>
<td>3. Difficulty completing familiar tasks</td>
</tr>
<tr>
<td>Ask about 10 Warning Signs</td>
<td>4. Confusion with time or place</td>
</tr>
<tr>
<td><strong>Conduct Cognitive Screen</strong></td>
<td>5. Trouble understanding visual images or spatial relationships</td>
</tr>
<tr>
<td>Assess for Red Flags</td>
<td>6. Problems with words</td>
</tr>
<tr>
<td>Mini-Cog ≤3</td>
<td>7. Misplacing items and inability to retrace steps</td>
</tr>
<tr>
<td><strong>Optimal</strong></td>
<td>8. Decreased or poor judgment</td>
</tr>
<tr>
<td>Conduct Informant Screen</td>
<td>9. Withdrawal from work or social activities</td>
</tr>
<tr>
<td>AD8 ≥2</td>
<td>10. Changes in mood and personality</td>
</tr>
<tr>
<td><strong>IF PASS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Reassure Patient &amp; Family</strong></td>
<td></td>
</tr>
<tr>
<td>Note: Passing cognitive screen does not preclude a mild, early or subclinical problem. Consider rescreening in 12 months, or sooner if changes become more noticeable.</td>
<td></td>
</tr>
<tr>
<td><strong>ASSESS REVERSIBLE FACTORS</strong></td>
<td></td>
</tr>
<tr>
<td>• Depression • Hearing • Delirium • Alcohol • Medications • Uncontrolled illness or infection</td>
<td></td>
</tr>
<tr>
<td><strong>RED FLAG SYMPTOMS</strong></td>
<td></td>
</tr>
<tr>
<td>Rapid Progression (w/in 6 mos) Recent Sudden Changes Young Onset (&lt;65)</td>
<td></td>
</tr>
<tr>
<td><strong>IF FAIL COGNITIVE SCREEN OR RED FLAGS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CONDUCT OR REVIEW RECENT LAB TESTS</strong></td>
<td></td>
</tr>
<tr>
<td>CBC, Comprehensive Metabolic Panel, TSH, B12</td>
<td></td>
</tr>
<tr>
<td><strong>TREAT REVERSIBLE FACTORS</strong></td>
<td></td>
</tr>
<tr>
<td>NO Improvement After Treating Reversible Factors</td>
<td></td>
</tr>
<tr>
<td><strong>NO Reversible Factors</strong></td>
<td></td>
</tr>
<tr>
<td><strong>PROCEED TO EVALUATION</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CONSIDER REFERRAL TO PSYCH IF SEVERE DEPRESSION</strong></td>
<td></td>
</tr>
</tbody>
</table>
Case Scenario (cont)

• KB is an 82-year-old female who presents to her PCP for a routine annual wellness visit (AWV). She has a history of hypertension and a family history of dementia. She presents with her husband who usually accompanies her to appointments.

• Her husband reports cognitive difficulties for KB that have worsened over the past year, but this is only noticeable to those who know KB well.

• She does not have trouble with most daily activities but has stopped driving and balancing her checkbook because she is “concerned she’ll make a mistake.”

• KB scored 21 on the MoCA, indicating possible MCI or AD.

Would you conduct a full workup for MCI and AD in the primary care setting or refer to a specialist?
### Core Clinical Criteria for Diagnosis of MCI

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concern regarding a change in cognition</td>
<td>Concern can be from patient, reliable informant, or skilled clinician</td>
</tr>
<tr>
<td>Impairment in one or more cognitive domains</td>
<td>Lower performance in memory, attention, visuospatial, executive function, and language skills</td>
</tr>
<tr>
<td>Preservation of independence in functional abilities</td>
<td>Generally maintains independent function, but may have mild problems with complex functional tasks</td>
</tr>
<tr>
<td>Not demented</td>
<td>Absence significant impairment in occupational or social functioning</td>
</tr>
</tbody>
</table>

The primary differentiator for MCI compared to dementia is the ability to function at work or in usual daily activities without significant interference, which is a clinical judgment made by a skilled physician.

## Making the Diagnosis

### Core Clinical Criteria for Diagnosis of All-Cause Dementia

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive or behavioral symptoms that interfere with functioning at work or in usual activities</td>
</tr>
<tr>
<td>Cognitive decline from previous levels of functioning and performing</td>
</tr>
<tr>
<td>Symptoms not explained by a major psychiatric disorder</td>
</tr>
<tr>
<td>Cognitive impairment detected and diagnosed through history and objective assessment</td>
</tr>
<tr>
<td>Impairment in at least 2 cognitive domains: memory, attention, visuospatial, executive function, and language skills</td>
</tr>
</tbody>
</table>

Dementia caused by AD is classified into two groups in the clinical setting: probable AD dementia and possible AD dementia.

## Making the Diagnosis

### Core Clinical Criteria for Probable AD Dementia

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria for all-cause dementia are met</td>
</tr>
<tr>
<td>Insidious onset of symptoms gradually over months to years</td>
</tr>
<tr>
<td>Clear history of worsening cognition (patient/informant report or observation)</td>
</tr>
<tr>
<td>Prominent cognitive deficits present from examination and history in cognitive domains</td>
</tr>
<tr>
<td>Absence of confounding conditions such as cerebrovascular disease, prominent progressive aphasia, other neurological diseases, and non-neurological conditions that may substantially impact cognition</td>
</tr>
</tbody>
</table>

Biomarkers such as amyloid-beta, cerebrospinal fluid (CSF) tau, $^{18}$fluorodeoxyglucose (FDG), and disproportionate atrophy on magnetic resonance imaging (MRI) may increase certainty in the clinical diagnosis of probable AD dementia (not currently recommended for routine diagnostic use).

# Making the Diagnosis

## Core Clinical Criteria for Possible AD Dementia

### Criteria

**Atypical disease course** - meets core criteria for the nature of cognitive deficits of AD dementia but has a sudden onset, insufficient historical detail, or lack of objective documentation of cognitive decline.

**Etiologically mixed presentation** - meets all core criteria for AD dementia, but there is evidence of a concomitant disease or medication that may substantially impact cognition.

Making the Diagnosis

Initial Assessment

- History to identify potential risk factors for AD

- Dementia or AD in first-degree relatives
- Older age
- Female sex
- Apolipoprotein E (ApoE) status

- Physical inactivity
- Low education
- Diabetes
- Obesity

Making the Diagnosis (cont)

Initial Assessment

- History to identify potential risk factors for AD
- Exclude possible reversible causes of cognitive impairment
  - Depression, deficiencies in vitamins, hormones, or electrolytes
Making the Diagnosis (cont)

Initial Assessment

• History to identify potential risk factors for AD

• Exclude possible reversible causes of cognitive impairment

• Open-ended, probing questions
  
  • To determine cognitive changes over time
  
  • To detect how cognitive deficits might affect daily activities

Making the Diagnosis (cont)

Physical Examination and Blood Analyses

• Mental status assessment, neurological assessment
• Medication review, diet assessment
  • To identify reversible causes of cognitive impairments
  • Anticholinergics, analgesics, sleep aids, anxiolytics
Making the Diagnosis (cont)

Physical Examination and Blood Analyses

• Mental status assessment, neurological assessment
• Medication review, diet assessment
• Blood pressure, temperature, pulse, lung auscultation
Making the Diagnosis (cont)

Physical Examination and Blood Analyses

- Mental status assessment, neurological assessment
- Medication review, diet assessment
- Blood pressure, temperature, pulse, lung auscultation
- Blood tests
  - Complete blood count
  - Blood glucose, electrolytes, liver function, and renal function
  - Thyroid-stimulating hormone
  - Vitamin B\textsubscript{12} and folate

Making the Diagnosis (cont)

Cognitive, Functional, and Behavioral Assessments

• Cognitive assessments (as mentioned previously)
  • MMSE
  • MoCA
  • Mini-Cog
  • AD8
  • IQCODE
  • QDRS (Quick Dementia Rating System)

Making the Diagnosis (cont)

Cognitive, Functional, and Behavioral Assessments

• Cognitive assessments (as mentioned previously)

• Functional assessments
  
  • FAQ (Functional Activities Questionnaire)
  
  • A-IADL-Q (Amsterdam Instrumental Activities of Daily Living Questionnaire)

  • FAST (Functional Assessment Screening Tool)
Making the Diagnosis (cont)

Cognitive, Functional, and Behavioral Assessments

• Cognitive assessments (as mentioned previously)

• Functional assessments

• Behavioral assessments
  
  • GDS (Geriatric Depression Scale)
  
  • NPI-Q (Neuropsychiatric Inventory Questionnaire)
<table>
<thead>
<tr>
<th>Step 1: Detect</th>
<th>Step 2: Assess/Differentiate</th>
<th>Step 3: Diagnose</th>
<th>Step 4: Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-specialists (e.g., PCPs)</strong></td>
<td><strong>Optimal referral window</strong></td>
<td><strong>Specialists (e.g., memory clinics)</strong></td>
<td></td>
</tr>
</tbody>
</table>

### Step 1: Detect
- Patient history, including family history
- Caregiver perspective
- Medical and disease history
- Medication count
- Lifestyle data (smoking, alcohol, exercise)

### Step 2: Assess/Differentiate
- Blood tests (full blood count, TSH, BG, serum B12, liver and renal function tests)
- Genotyping
- Neurologic examination
- Physical examination
- Cognitive: AD8, IQCODE, MMSE, MoCA, Mini-Cog, or QFRDS
- Functional: A-IADL-Q, FAST, or FAQ
- Behavioral: GDS or NPI-Q
- MRI
- FDG-PET*

### Step 3: Diagnose
- Amyloid PET
- CSF Aβ42, p-tau and t-tau
- CSF Aβ42/Aβ40

### Step 4: Treat
- Symptomatic treatments (e.g., Ach inhibitors, NMDA receptor antagonist)
- Lifestyle changes
- Social work support
- Clinical trial registries
When to Refer

- Not all patients with suspected cognitive impairment, dementia, or AD should be referred …

- Following an initial assessment in the primary care setting, specialist referral may be warranted for patients with suspected AD who:
  - Are less than 65 years old/have early disease onset\(^1,2\)
  - Present with Parkinsonian features\(^2\)
  - Present with hallucinations\(^2\)
  - Have rapid progression or fluctuations of cognitive impairment\(^2\)
  - Have unexplained visual impairment\(^2\)
  - Have severe depression\(^2\)

One approach to a comprehensive diagnostic workup applicable to primary care

SLUMS = Saint Louis University Mental Status Examination
qMCI = Quick Mild Cognitive Impairment

Case Scenario (cont)

- KB is an 82-year-old female who presents to her PCP for a routine annual wellness visit (AWV). She has a history of hypertension and a family history of dementia. She presents with her husband who usually accompanies her to appointments.
- Her husband reports cognitive difficulties for KB that have worsened over the past year, but this is only noticeable to those who know KB well.
- She does not have trouble with most daily activities but has stopped driving and balancing her checkbook because she is “concerned she’ll make a mistake.”
- KB scored 21 on the MoCA, indicating possible MCI or AD.
- Full workup guides you to a diagnosis of MCI.

**How would you approach treatment of MCI for this patient?**
Managing MCI and AD in Primary Care

Following a diagnosis of AD, PCPs should consider:

• Discussing available options for nonpharmacologic and pharmacologic treatment

• Monitoring the disease progression through regular follow-up appointments (every 6-12 months)

• Helping patients and caregivers connect with resources such as social services and reliable information sources about AD

• Encouraging patients and caregivers to schedule additional follow-up appointments if needed, especially if symptoms worsen

• Conducting routine cognitive and functional assessments to monitor disease progression
  • May prompt a need for blood tests, imaging, or biomarker analyses

Managing MCI and AD in Primary Care

Nonpharmacologic Therapies

• Dietary changes (e.g., following a healthy diet high in green, leafy vegetables, fish, nuts, and berries)
• Physical exercise
• Cognitive training (e.g., reading, games)
• Social interactions with others
• Adequate sleep
• Proper personal hygiene

## Guideline-Recommended Pharmacologic Agents for AD

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Approval</th>
<th>Mechanism of Action</th>
<th>Stages Used in AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil</td>
<td>1996</td>
<td>Acetylcholinesterase inhibitor, increases acetylcholine in the CNS</td>
<td>Mild, Moderate, Severe</td>
</tr>
<tr>
<td>Donepezil and memantine</td>
<td>2014</td>
<td>Combination of an acetylcholinesterase inhibitor and NMDA antagonist</td>
<td>Moderate, Severe</td>
</tr>
<tr>
<td>Galantamine</td>
<td>2001</td>
<td>Acetylcholinesterase inhibitor, increases acetylcholine in the CNS</td>
<td>Mild, Moderate</td>
</tr>
<tr>
<td>Memantine</td>
<td>2003</td>
<td>NMDA antagonist, reduces overstimulation of glutamate receptors</td>
<td>Moderate, Severe</td>
</tr>
<tr>
<td>Rivastigmine</td>
<td>2000</td>
<td>Acetylcholinesterase inhibitor, increases acetylcholine in the CNS</td>
<td>Mild, Moderate</td>
</tr>
</tbody>
</table>

## New FDA-approved Drug for AD

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Approval</th>
<th>Mechanism of Action</th>
<th>Stages Used in AD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donepezil</strong></td>
<td>1996</td>
<td>Acetylcholinesterase inhibitor, increases acetylcholine in the CNS</td>
<td>Early, middle, end</td>
</tr>
<tr>
<td><strong>Donepezil and Memantine</strong></td>
<td>2014</td>
<td>Combination of an acetylcholinesterase inhibitor and NMDA antagonist</td>
<td>Middle, end</td>
</tr>
<tr>
<td><strong>Galantamine</strong></td>
<td>2001</td>
<td>Acetylcholinesterase inhibitor, increases acetylcholine in the CNS</td>
<td>Early, middle</td>
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<tr>
<td><strong>Memantine</strong></td>
<td>2003</td>
<td>NMDA antagonist, reduces overstimulation of glutamate receptors</td>
<td>Middle, end</td>
</tr>
<tr>
<td><strong>Rivastigmine</strong></td>
<td>2000</td>
<td>Acetylcholinesterase inhibitor, increases acetylcholine in the CNS</td>
<td>Early, middle</td>
</tr>
<tr>
<td><strong>Aducanumab</strong></td>
<td>2021 (accelerated approval)</td>
<td>Monoclonal antibody directed against amyloid beta; reduces amyloid plaques in the brain</td>
<td>Early</td>
</tr>
</tbody>
</table>

Recommended Algorithm for Mild to Moderate AD Pharmacotherapy

Initiate therapy
- Donepezil
- Galantamine
- Rivastigmine

Adverse event
- Consider switch to a different cholinesterase inhibitor

Disease progression
- Consider higher dose or switch to a different cholinesterase inhibitor

Monitor and reevaluate every 3-4 months and titrate dose as needed

Recommended Algorithm for Moderate to Severe AD Pharmacotherapy

Initiate therapy
- Donepezil
- Rivastigmine (patch)
- Memantine
- Combination cholinesterase inhibitor + memantine

Adverse event
- Consider switch to a different cholinesterase inhibitor

Disease progression
- Consider higher dose or switch to a different cholinesterase inhibitor

Discontinue therapy when all cognitive function is lost at terminal AD stages

One of your knowledge questions for discussion:

Which of the following is the most appropriate pharmacologic therapy for symptoms from mild cognitive impairment due to Alzheimer’s disease?

A. Donepezil 5 mg once daily
B. Donepezil 5 mg once daily and memantine 10 mg twice daily
C. Memantine 5 mg once daily
D. Rivastigmine patch 4.6 mg once daily
E. No pharmacologic therapy is indicated
The correct answer is...

Which of the following is the most appropriate pharmacologic therapy for symptoms from mild cognitive impairment due to Alzheimer’s disease?

A. Donepezil 5 mg once daily
B. Donepezil 5 mg once daily and memantine 10 mg twice daily
C. Memantine 5 mg once daily
D. Rivastigmine patch 4.6 mg once daily
E. No pharmacologic therapy is indicated

Symptomatic pharmacologic therapy is not indicated for patients with MCI due to AD.
Recent Advances in MCI and AD

Advances in Imaging

• **Structural MRI**: assesses atrophy and changes in tissue characteristics in the brain\(^1\)
  - **Readily accessible, but lacks ability to detect amyloid plaques and tau proteins**

• **Functional MRI**: provides an indirect measure of neuronal activity\(^1\)
  - **Sensitive to head motion - difficult to conduct, lacks ability to detect biomarkers**

• **FDG-PET**: marker of overall brain metabolism, may help distinguish AD from diseases that occur in other areas of the brain (such as frontotemporal lobar degeneration)\(^1\)
  - **Expensive with limited availability**

---


PET = positron emission tomography
Recent Advances in MCI and AD (cont)

Advances in Imaging

• **Amyloid-PET**: identification of amyloid plaques in the brain\(^1,2\)
  - Can be helpful to confirm diagnosis of AD in inconclusive cases
  - Limited due to cost and concerns for variable protocols and cutoff values for results interpretation

• **Tau-PET**: can distinguish AD dementia from other neurodegenerative disorders, can predict cognitive change
  - May be superior to amyloid-PET for predicting cognitive change; expensive, limited availability

---


PET = positron emission tomography
Recent Advances in MCI and AD (cont)

Advances in Biomarkers

A research framework for biomarkers in AD has been suggested by the NIA in 2018, intended to separate biomarker specific for pathologic tau (and thus AD) from nonspecific neurodegeneration that can occur in non-AD conditions.

• AT(N) biomarker grouping
  
  • A: Aggregated amyloid beta
    • Measured using CSF amyloid beta (also amyloid-PET)
  
  • T: Aggregated tau; measured using CSF phosphorylated tau
    • Measured using CSF phosphorylated tau (also tau-PET)
  
  • (N): Neurodegeneration or neuronal injury
    • Measured using CSF total tau (also anatomic MRI, FDG-PET)

Recent Advances in MCI and AD (cont)

Advances in Treatment

- Aducanumab was FDA-approved in June 2021, the first new agent for AD in almost 20 years. It was approved under the accelerated pathway, so confirmatory trials are needed for continued approval. Approval was based on two studies, both terminated prior to completion.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patients</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMERGE (Phase 3)</td>
<td>Met criteria for MCI or mild AD and had a positive amyloid-PET scan, age 50-85 (total = 1643)</td>
<td>Patients randomized 1:1:1 to placebo, aducanumab low dose, and aducanumab high dose</td>
<td>In the amyloid-PET and CSF biomarker substudies (302 patients), there was a 22% reduction in clinical decline ($P = .012$)</td>
</tr>
<tr>
<td>ENGAGE (Phase 3)</td>
<td>Met criteria for MCI or mild AD and had a positive amyloid-PET scan, age 50-85 (total = 1647)</td>
<td>Patients randomized 1:1:1 to placebo, aducanumab low dose, and aducanumab high dose</td>
<td>In the amyloid-PET and CSF biomarker substudies (374 patients), there was no statistically significant difference in clinical decline</td>
</tr>
</tbody>
</table>

A significant reduction in brain amyloid plaques was observed in both studies for the aducanumab groups, compared to placebo.

Key References for MCI and AD

• National Institute on Aging (NAI) Alzheimer’s Disease Diagnostic Guidelines

• NIA-Alzheimer’s Association Research Framework: Toward a biological definition of Alzheimer’s disease.
Key References for MCI and AD (cont)

• **American Academy of Family Physicians**
  

• **Alzheimer’s Association (https://www.alz.org/)**
  
  Resources to support clinicians: https://www.alz.org/professionals/health-systems-clinicians
  
  Patient-friendly content and tools
# Links to Assessment Tools

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<tr>
<th>Tool</th>
<th>Link</th>
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<td>MoCA</td>
<td><a href="https://www.parkinsons.va.gov/resources/MOCA-Test-English.pdf">https://www.parkinsons.va.gov/resources/MOCA-Test-English.pdf</a></td>
</tr>
<tr>
<td>Mini-Cog</td>
<td><a href="https://www.alz.org/getmedia/9687d51e-641a-43a1-a96b-b29eb00e72bb/cognitive-assessment-toolkit">https://www.alz.org/getmedia/9687d51e-641a-43a1-a96b-b29eb00e72bb/cognitive-assessment-toolkit</a></td>
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<tr>
<td>AD8</td>
<td><a href="https://www.alz.org/getmedia/9687d51e-641a-43a1-a96b-b29eb00e72bb/cognitive-assessment-toolkit">https://www.alz.org/getmedia/9687d51e-641a-43a1-a96b-b29eb00e72bb/cognitive-assessment-toolkit</a></td>
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<tr>
<td>IQCODE</td>
<td><a href="https://www.alz.org/getmedia/9687d51e-641a-43a1-a96b-b29eb00e72bb/cognitive-assessment-toolkit">https://www.alz.org/getmedia/9687d51e-641a-43a1-a96b-b29eb00e72bb/cognitive-assessment-toolkit</a></td>
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<tr>
<td>QDRS</td>
<td><a href="http://med.fau.edu/research/The%20Quick%20Dementia%20Rating%20System%20Instructions%20and%20Form.pdf">http://med.fau.edu/research/The%20Quick%20Dementia%20Rating%20System%20Instructions%20and%20Form.pdf</a></td>
</tr>
<tr>
<td>GDS</td>
<td><a href="https://www.woundcare.ca/Uploads/ContentDocuments/Geriatric%20Depression%20Scale.pdf">https://www.woundcare.ca/Uploads/ContentDocuments/Geriatric%20Depression%20Scale.pdf</a></td>
</tr>
<tr>
<td>NPI-Q</td>
<td><a href="https://www.alz.org/media/documents/npiq-questionnaire.pdf">https://www.alz.org/media/documents/npiq-questionnaire.pdf</a></td>
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</tbody>
</table>
Post-presentation Survey

PLEASE USE THE QR CODE OR THE LINK BELOW TO COMPLETE THE SURVEY.

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