

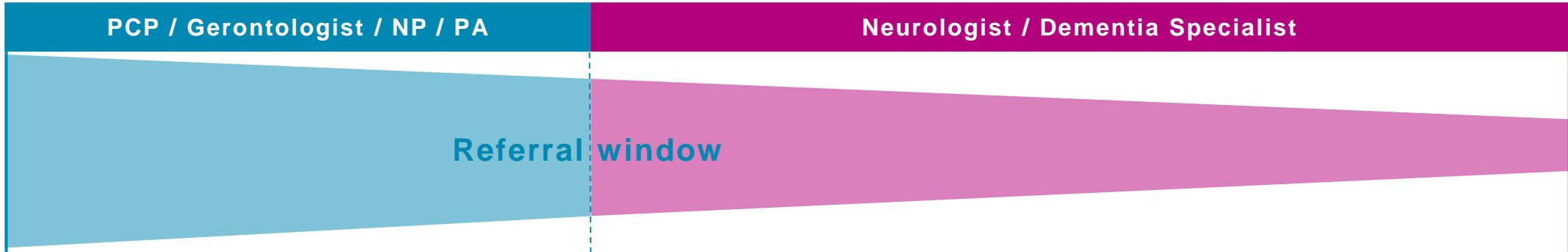
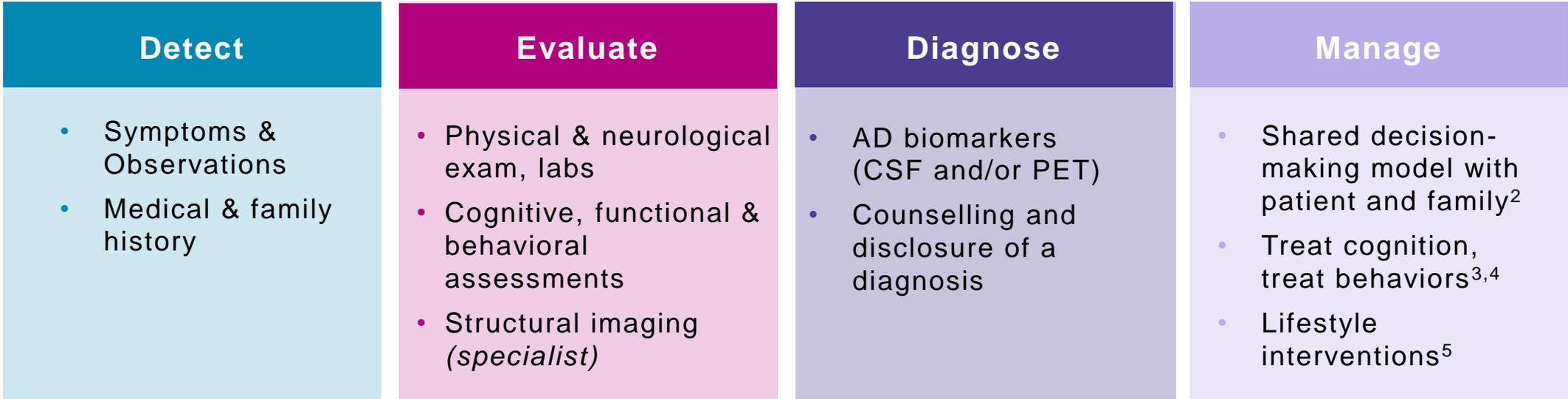
# Case study: Mild cognitive impairment (MCI) due to Alzheimer's disease (AD)

This content is intended for health care professionals only for educational and informational purposes and does not substitute for sound medical judgement or clinical decision making in the context of medical treatment

# The Early AD diagnostic pathway



*Patient presents with symptoms*



Adapted image from: Porsteinsson AP, et al. J Prev Alz Dis 2021;8:371–386; [This work](#) is licensed by Porsteinsson et al under [CC BY 4.0](#)  
 CSF, cerebrospinal fluid; PCP, primary care physician; NP, nurse practitioner; PA, physician associate; PET, positron emission tomography  
 1. Porsteinsson AP, et al. J Prev Alzheimers Dis 2021;8:371–386; 2. Mattos MK, et al. Dementia. 2023;22(4):875-909; 3. Livingston G, et al. Lancet 2020;396:413–446; 4. Livingston G, et al. Lancet 2017;390:2673–2734; 5. Chen J, et al. Clin Interv Aging 2019;14:1243–1254

# Delays in early detection of AD

PCPs, neurologists, psychiatrists, and geriatricians play a crucial role in the detection, diagnosis, and treatment of AD<sup>1-6</sup>

**Detection** of early stages of AD is challenging.<sup>1-4</sup>

- **AD-related early cognitive decline is difficult to differentiate from normal aging<sup>1,5</sup>**
- Comorbid medical conditions (e.g., stroke, depression) can impact cognitive and functional abilities<sup>1</sup>
- Patients wait years for an accurate diagnosis and appropriate intervention<sup>6</sup>

Cognitive impairment may remain unrecognized in up to 80% of affected patients in primary care<sup>7</sup>

AD, Alzheimer's disease; MCI, mild cognitive impairment; PCP, primary care provider

1. Galvin JE. *Curr Geriatr Rep* 2018;7:19-25; 2. Dubois B, et al. *J Alzheimers Dis* 2016;49:617-631; 3. Sabbagh MN, et al. *J Prev Alz Dis* 2020; 4. Porsteinsson AP, *J Prev Alzheimers Dis*. 2021;8:371-386; 5. Liss JL, et al. *J Intern Med*. 2021;290(2):310-334; 6. Galvin JE, et al. *Front Neurol* 2021;11:592302; 7. Cordell CB, et al. *Alzheimers Dement*. 2013;9(2):141-150

# 1

## Detect



African American Female, 75 yrs

### Meet Lisa

*Retired pediatrician, mother of 3, grandmother of 3  
Walks 3 times/week, active in church, avid reader and cook*

**Medical history:** Mild hypertension (controlled), mild hyperlipidemia, and type 2 diabetes well-controlled w/ medications (amlodipine, rosuvastatin, metformin)

PCP, primary care physician

**History of Present Illness (HPI):** Lisa visits her PCP for her routine yearly physical with her husband. He mentions that she is “forgetting things”. Lisa denies any difficulties, says she is just tired.....and her husband is overprotective

Over the past 6 months, he witnessed increased signs of **cognitive changes:**

- Forgetting why she walked into a room
- Misplacing keys, wallet
- Mild word-finding difficulties often w/ frustration

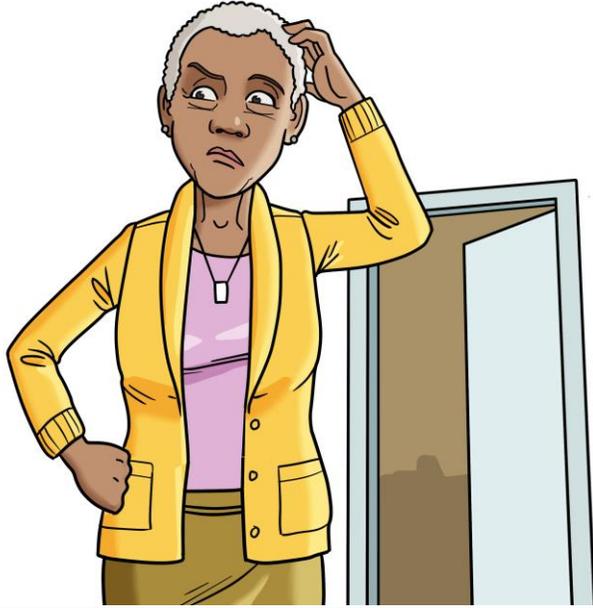
**Functional changes:** Preservation of reading ability and daily functioning, but less motivated to initiate or complete tasks or socialize with peers

**Behavior:** Mild anxiety, irritability, argumentativeness

### Family history

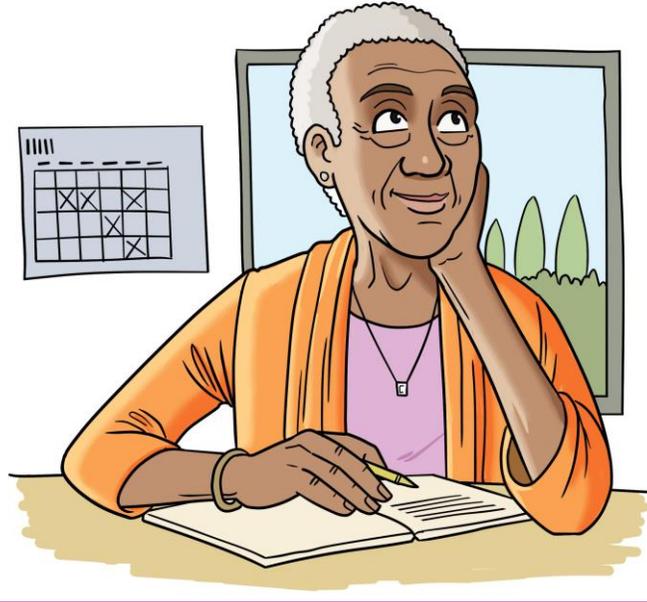
- Father (85 years) and mother (79 years) both died from cardiovascular-related complications; mother had suspected memory decline
- Two younger brothers and one younger sister with no remarkable medical history

# Identifying key symptoms in the early stages and how they differ from typical aging



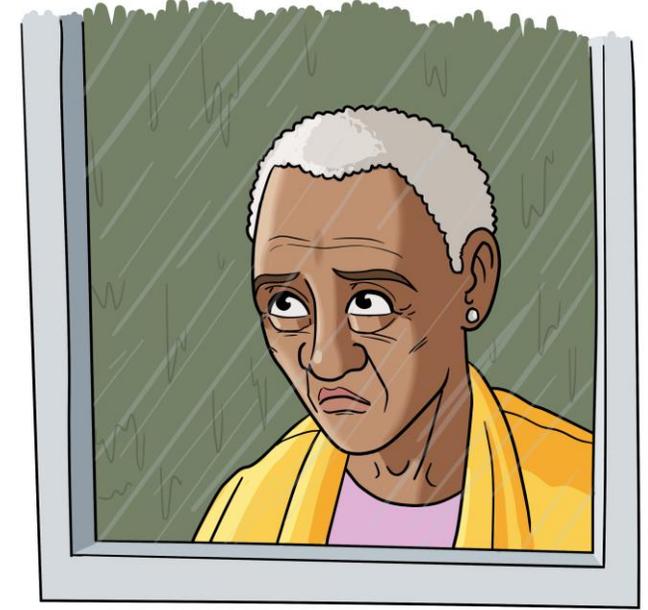
## Cognition<sup>1,2</sup>

- Experiencing short-term memory loss?
- Struggling to learn new things?
- Experiencing word-finding difficulties or communication difficulties?
- Repeating him/herself?



## Function<sup>3</sup>

- Starting to need support with complex activities related to independent living, such as managing finances?



## Behavior/psychological<sup>1</sup>

- Struggling to participate in meaningful social situations?
- Signs of impulsivity?
- Signs of apathy or depression?

Is the family member/care partner sharing/communicating concerns?<sup>4</sup>

1. Porsteinsson AP, et al. J Prev Alzheimers Dis 2021;8:371–386; 2. NIH. What Are the Signs of Alzheimer's Disease?: <https://www.nia.nih.gov/health/what-are-signs-alzheimers-disease> (Accessed April 2023); 3. NIH. Managing Money Problems in Alzheimer's Disease: <https://www.nia.nih.gov/health/managing-money-problems-alzheimers-disease> (Accessed April 2023); Centers for Disease Control and Prevention. 10 Warning Signs of Alzheimer's: <https://www.cdc.gov/aging/healthybrain/ten-warning-signs.html> (Accessed April 2023)

# The AD clinical continuum and disease staging

## Evidence of AD pathology<sup>1</sup>

Preclinical AD<sup>2</sup>

MCI due to AD<sup>2</sup>

Mild AD dementia<sup>2</sup>

Moderate AD dementia<sup>2</sup>

Severe AD dementia<sup>2</sup>



Cognition

No or only subtle cognitive symptoms<sup>3</sup>

Short-term memory loss; decline in overall attention skills, language skills; mild abnormalities in visuospatial and executive functions<sup>4,5</sup>

Anomia, aphasia, severe memory loss, severe abnormalities in executive functions, visuospatial abilities, attention<sup>4-6</sup>

Cognitive impairment



Function

No impact on ADLs<sup>2</sup>

No significant impairment in IADLs<sup>2</sup>

Functional impact in IADLs, require occasional assistance with ADLs<sup>5</sup>

Extensive impact in BADLs, require frequent assistance with ADLs<sup>5</sup>

Severe functional impact on ADLs (complete dependency) and BADLs<sup>5</sup>

Functional impairment



Behavior

No or subtle changes in behavior<sup>7</sup>

Depression; anxiety; irritability; apathy; disinhibition; agitation; aggression; psychosis; hallucinations; sleep disturbances<sup>8,9</sup>

Behavioral and Neuropsychological features

AD, Alzheimer's disease; ADL, activities of daily living; BADL, basic activities of daily living; IADL, instrumental activities of daily living;

MCI, mild cognitive impairment

1. Aisen PS, et al. *Alzheimers Res Ther* 2017;9:60; 2. Jack CR Jr, et al. *Alzheimers Dement* 2018;14:535-562; 3. Harada CN, et al. *Clin Geriatr Med* 2013;29:737-752; 4. Kazim SF, Iqbal K. *Mol Neurodegener* 2016;11:50

5. Mayo Clinic. Alzheimer's stages: How the disease progresses. <https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers-stages/art-20048448> (Accessed April 2023); 6. Kipps CM, Hodges JR. *J Neurol Neurosurg Psychiatry* 2005;76(Suppl. 1):i22-i30;

7. Ismail Z, et al. *Alzheimers Dement* 2016;12:195-202; 8. Eikelboom WS, et al. *Neurology* 2021;97:e1276-e1287; 9. Lancôt KL, et al. *Alzheimers Dement (N Y)* 2017;3:440-449; 11.

# What tools can we use to **assess** early changes in cognition, function and behavior?

Some assessments are less sensitive/specific to early stages than others and often cannot support dementia staging when administered in isolation

## Cognition<sup>1</sup>

### MMSE

Mini-Mental State Examination

### MoCA

Montreal Cognitive Assessment

### Mini-Cog

Mini cognitive assessment instrument

### AD8

Alzheimer's Disease 8 Interview

### IQCODE

Informant Questionnaire on Cognitive Decline in the Elderly

## Function<sup>1,2</sup>

### FAQ

Functional Activities Questionnaire

### Lawton IADL scale

Lawton Instrumental Activities of Daily Living

### Amsterdam IADL

Amsterdam Instrumental Activities of Daily Living

### FAST

Functional Assessment Screening Tool

## Behavior<sup>1,3</sup>

### NPI-Q

Neuropsychiatric Inventory Questionnaire

### BEHAVE-AD

Behavioral Pathology in Alzheimer's Disease Rating Scale

### GDS

Geriatric Depression Scale

Consider factors that may affect test performance and interpretation: education, skills, pre-morbid functioning/attainment, language, sensory impairment, psychiatric illness, physical or neurologic problems<sup>1,4</sup>

AD8, Alzheimer's Disease 8 Interview; A-IADL-Q, Amsterdam Instrumental Activities of Daily Living Questionnaire; ADSC-ADL, AD Cooperative Study – Activities of Daily Living ;BEHAVE-AD, Behavioral Pathology in Alzheimer's Disease Rating Scale; FAQ, Functional Activities Questionnaire; FAST, Functional Assessment Screening Tool; GDS, Geriatric Depression Scale; IQ-CODE, Informant Questionnaire on Cognitive Decline in the Elderly; Mini-Cog, mini cognitive assessment instrument; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NPI-Q, Neuropsychiatric Inventory Questionnaire; QDRS, Quick Dementia Rating System

1. Porsteinsson AP, et al. J Prev Alzheimers Dis 2021;8:371–386; 2. Alzheimer's Association. Lawton Instrumental Activities of Daily Living (IADL) Scale <https://www.alz.org/careplanning/downloads/lawton-iadl.pdf> (Accessed April 2023); 3. Reisberg B, et al. Dement Geriatr Cogn Disord 2014;38:89–146; 4. Kipps CM, Hodges JR. J Neurol Neurosurg Psychiatry 2005;76(Suppl. 1):i22–i30

# 2

## Evaluate: initial test

### Findings from the initial office exam

- **Cognition:** MMSE: 27/30
  - Orientation → 1 point lost
  - Memory → 2 points lost
- **Blood work** (CMP, CBC, TSH, Vitamin B12, lipid profile, HbA1c) and findings:
  - Elevated lipid profile
  - HbA1c (<6.5%) and all other assessments were within normal limits

### Referral to neurologist...



Lisa's **MMSE** is low for her education level. Most points are lost on the memory portion of the test

### MMSE test interpretation

Time to use (minutes)	Scoring system	Validity to detect dementia
5–10 minutes	Cutoff: 23–24 for dementia	Sensitivity: 89% Specificity: 89% <sup>1</sup>

CBC, complete blood count; CMP, comprehensive metabolic panel; HbA1c, hemoglobin 1AC; MMSE, mini-state mental exam; TSH, thyroid stimulating hormone.  
1. Patnode CD, et al. Screening for Cognitive Impairment in Older Adults: An Evidence Update for the U.S. Preventive Services Task Force. In: Rockville (MD): Agency for Healthcare Research and Quality (US); Report No: 19-05257-EF-1. US Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews

# 2

## Evaluate: cognition



- Neurologic examination within normal limits
- Neurologist decides to perform further testing
- **Cognition:** Montreal Cognitive Assessment (MoCA): 23/30 (impairment)

MoCA		Subject's File Number : testtest	
ELECTRONIC VERSION 8.1 ENGLISH		MOCA FILE NUMBER : CA-46178-46178-12002	
		AGE RANGE :	
		EDUCATION :	
		SEX : DATE : 2023/04/13	
<b>VIOSPATIAL/EXECUTIVE</b>	copy cube	DRAW CLOCK (Ten past eleven) (3 points)	TIME POINTS
			01:35 3/5
<b>NAMING</b>			00:38 3/3
<b>MEMORY</b>	RECALL LIST OF WORDS SUBJECT MUST REPEAT THE WORDS AFTER 5 MINUTES	FACE [✓] VELVET [✓] CHURCH [✓] DAISY [X] RED [X]	00:17 NO POINTS
<b>ATTENTION</b>	READ LIST OF DIGITS (1 DIGIT/SEC) SUBJECT HAS TO REPEAT THEM IN THE FORWARD ORDER	[✓] 2 1 8 5 4	00:07 2/2
	READ LIST OF LETTERS. THE SUBJECT MUST TAP WITH HIS HAND AT EACH LETTER A. NO POINTS IF > 2 ERROR	[✓] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B	00:15 3/4
	SERIAL 7 SUBTRACTION STARTING AT 100	[✓] 193 [✓] 186 [✓] 179 [✓] 172 [✓] 165	00:10 3/3
<b>LANGUAGE</b>	REPEAT: I ONLY KNOW THAT JOHN IS THE ONE OF TO HELP TODAY. [✓] THE CAT ALWAYS HIDE UNDER THE COUCH WHEN DOGS WERE IN THE ROOM. [✓]		00:08 2/2
	FLUENCY / NAME MAXIMUM NUMBER OF WORDS IN ONE MINUTE THAT BEGIN WITH THE LETTER F	[✓] 13 (N ≥ 11 WORDS)	01:03 1/1
<b>ABSTRACTION</b>	SIMILARITY BETWEEN E.G. BANANA - ORANGE = FRUIT	[✓] TRAIN - BICYCLE [✓] WATCH - RULER	00:48 2/2
<b>DELAYED RECALL</b>	HAS TO RECALL WORDS WITH NO QUE	FACE [X] VELVET [X] CHURCH [X] DAISY [X] RED [X]	01:03 0/5
<b>MEMORY INDEX SCORE (MIS)</b>	CATEGORY CLUE	[X] [X] [✓] [X] [X]	POINTS FOR ENIGMERS RECALL ONLY MIS = 4/15
	MULTIPLE CHOICE CLUE	[X] [X] [✓] [✓]	
<b>ORIENTATION</b>	[X] DATE [✓] MONTH [✓] YEAR [✓] DAY [✓] PLACE [✓] CITY		00:09 0/5
© Z. Nasreddine MD WWW.MOCATESTORG MIS: 4/15 (NORMAL ≥ 26/30)		TOTAL TIME	06:04
ADMINISTERED BY Rima Nasreddine		TOTAL	23/30



Lisa's ability to recall words in the memory portion (delayed recall) of the MoCA test is the most impacted, suggesting an amnesic syndrome

### MoCA test interpretation

Time to use (minutes)	Scoring system	Validity
10–12	Less than 26 detects MCI or dementia	Sensitivity for MCI: 90% Sensitivity for dementia: 100%

MCI, mild cognitive impairment; MoCA, Montreal Cognitive Assessment  
Galvin JE. Curr Geriatr Rep 2018;7:19–25

# What do the differences in MMSE and MoCA scores mean?

**Shared measures**  
Orientation; Memory; Language; Attention<sup>1</sup>

**Assessed only by MoCA<sup>1</sup>**  
Executive function

**MMSE**

**MoCA**

Easy to administer<sup>1</sup>

Requires training<sup>1</sup>

Moderate psychometric properties<sup>2</sup>

Psychometrically robust (high test-retest reliability and content validity)<sup>2</sup>

Floor (not able to discern progression) and ceiling effects (in highly educated)<sup>3</sup>

Low education, primary language, culture can impact interpretation<sup>5\*</sup>

Not ideal at detecting mild impairment<sup>4</sup>

Superior to MMSE in identification of MCI<sup>6</sup>

\*addition of one point for individuals with less than a 12th grade education

**MINI MENTAL STATE EXAMINATION (MMSE)**

Name: \_\_\_\_\_  
DOB: \_\_\_\_\_  
Hospital Number: \_\_\_\_\_

DATE: \_\_\_\_\_

One point for each answer

<b>ORIENTATION</b> Year Season Month Date Time	...../5	...../5	...../5
Country Town District Hospital Ward/Floor	...../5	...../5	...../5
<b>REGISTRATION</b> Examiner names three objects (e.g. apple, table, penny) and asks the patient to repeat (1 point for each correct. THEN the patient learns the 3 names repeating until correct).	...../3	...../3	...../3
<b>ATTENTION AND CALCULATION</b> Subtract 7 from 100, then repeat from result. Continue five times: 100, 93, 86, 79, 72, 65 (Alternative: spell "WORLD" backwards: D U R O W).	...../5	...../5	...../5
<b>RECALL</b> Ask for the names of the three objects learned earlier.	...../3	...../3	...../3
<b>LANGUAGE</b> Name two objects (e.g. pen, watch). Repeat "No ifs, ands, or buts". Give a three-stage command. Score 1 for each stage. (e.g. "Place index finger of right hand on your nose and then on your left ear"). Ask the patient to read and obey a written command on a piece of paper. The written instruction is: "Close your eyes". Ask the patient to write a sentence. Score 1 if it is sensible and has a subject and a verb.	...../2	...../2	...../2
<b>COPYING:</b> Ask the patient to copy a pair of intersecting pentagons	...../1	...../1	...../1
<b>TOTAL:</b>	...../30	...../30	...../30

**MMSE scoring**  
24-30: no cognitive impairment  
18-23: mild cognitive impairment  
0-17: severe cognitive impairment

**MONTREAL COGNITIVE ASSESSMENT (MOCA<sup>®</sup>)**  
Version 8.1 English

Name: \_\_\_\_\_ Education: \_\_\_\_\_ Sex: \_\_\_\_\_ Date of birth: \_\_\_\_\_  
DOB: \_\_\_\_\_ Date: \_\_\_\_\_

**VISUOSPATIAL/EXECUTIVE**  
Draw CLOCK (Ten past eleven) (3 points) \_\_\_\_\_/5

**NAMING**  
FACE VELVET CHURCH DAISY RED \_\_\_\_\_/3

**MEMORY**  
1<sup>st</sup> TRIAL \_\_\_\_\_/2  
2<sup>nd</sup> TRIAL \_\_\_\_\_/2

**ATTENTION**  
Serial 7 subtraction starting at 100: [ ] 99 [ ] 86 [ ] 79 [ ] 72 [ ] 65 \_\_\_\_\_/3

**LANGUAGE**  
Repeat: I only know that John is the one to help today. [ ] \_\_\_\_\_/2

**ABSTRACTION**  
Similarity between e.g. orange - banana = fruit [ ] train - bicycle [ ] watch - ruler \_\_\_\_\_/2

**DELAYED RECALL**  
Memory Index Score (MIS) \_\_\_\_\_/15

**ORIENTATION**  
Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City \_\_\_\_\_/6

**TOTAL:** \_\_\_\_\_/30

MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; image on the right: Montreal Cognitive Assessment (MoCA) Version 8.1. Available from: <https://www.mocatest.org/the-moca-test/>  
Image on the left from Oxford Medical Education. MMSE. Available from: <https://oxfordmedicaleducation.com/geriatrics/mini-mental-state-examination-mmse/>;

1. Sheehan B. Ther Adv Neurol Disord 2012;5:349–358; 2. Dementia Action Collaborative – Washington State. Available from: <https://www.dshs.wa.gov/sites/default/files/AL TSA/stakeholders/documents/AD/DAC%20Screening%20Position%20Paper.pdf>;  
3. Franco-Marina F, et al. *International Psychogeriatrics*, 22(1), 72-81. 4. Arevalo-Rodriguez I, et al. *Cochrane Database Syst Rev* 2021;7:CD010783; 5. Galvin JE. *Curr Geriatr Rep* 2018;7:19–25; 6. Pinto TC, et al. *Int Psychogeriatr* 2019;31:491–504

# 2

## Evaluate: function

### Informant (function): Functional assessment questionnaire (FAQ): 4/30

- **Writing checks, paying bills, keeping financial records → 1**
- **Assembling tax or business records → 1**
- Shopping alone → 0
- Playing a game of skill 0
- Making coffee or tea → 0
- Preparing a balanced meal → 0
- Keeping track of current events → 0
- Attending to and understanding a television program, book, or magazine → 0
- **Remembering appointments, family occasions, medications → 1**
- **Traveling out of the neighborhood → 1**

**SCORE: 0 = normal; 1 = has difficulty but does without assistance; 2 = requires assistance; 3 = dependent<sup>1</sup>**



Lisa has difficulty in some of the more complex tasks but is still able to complete them by herself

### Test performance:

- ❑ The FAQ is a **consistently accurate** instrument with **good sensitivity** (85%) to identify an individual's functional impairment<sup>1</sup>
- ❑ The FAQ demonstrates **high reliability** (exceeding 0.90)<sup>1</sup>

FAQ, functional assessment questionnaire

1. Alzheimer's Association. Available from: <https://www.alz.org/careplanning/downloads/functional-activities-questionnaire.pdf> (Accessed April 2023)

# 2

## Evaluate: behavior

**Behavior:** Neuropsychiatric Inventory Questionnaire (NPI-Q): **total severity = 2; total caregiver distress = 2**

- Symptoms endorsed in three domains:
  - Anxiety
  - Depression
- 1 point (**mild**) for each of the domains for severity
- 1 point (**minimal distress**) for each of the domains for caregiver distress



Lisa is experiencing mild anxiety and depression based on her NPI-Q score; this is creating some distress for her husband

### 12 Domains:

- Agitation
- Delusions
- Hallucinations
- Depression
- Euphoria
- Aberrant motor behavior
- Apathy
- Irritability
- Disinhibition
- Anxiety
- Sleep
- Eating



- NPI-Q has **three scores** reported for each domain:<sup>1</sup>
  - Presence of symptoms
  - Severity on a 0–3 scale (0 = none, 1 = mild, 2 = moderate, 3 = severe)
  - Caregiver distress on a 0–5 scale (0 = no distress, 5 = extreme distress)
- NPI-Q takes approximately **5 minutes** to complete<sup>1</sup>

1. Alzheimer's Association. The Neuropsychiatric Inventory Questionnaire. Available from: <https://www.alz.org/careplanning/downloads/npiq-questionnaire.pdf> (Accessed April 2023)

## 2

### Evaluate: structural imaging

- Neurologist orders brain magnetic resonance imaging (MRI) to assess brain structure and rule out other causes<sup>1</sup>
  - Mild hippocampal atrophy (right) observed on MRI (image)

💡 Lisa has some hippocampal atrophy (albeit mild). Hippocampal atrophy (or MTA) is the most established structural imaging biomarker of AD but it is also seen in LATE (with hippocampal sclerosis) and FTD<sup>2,3</sup>

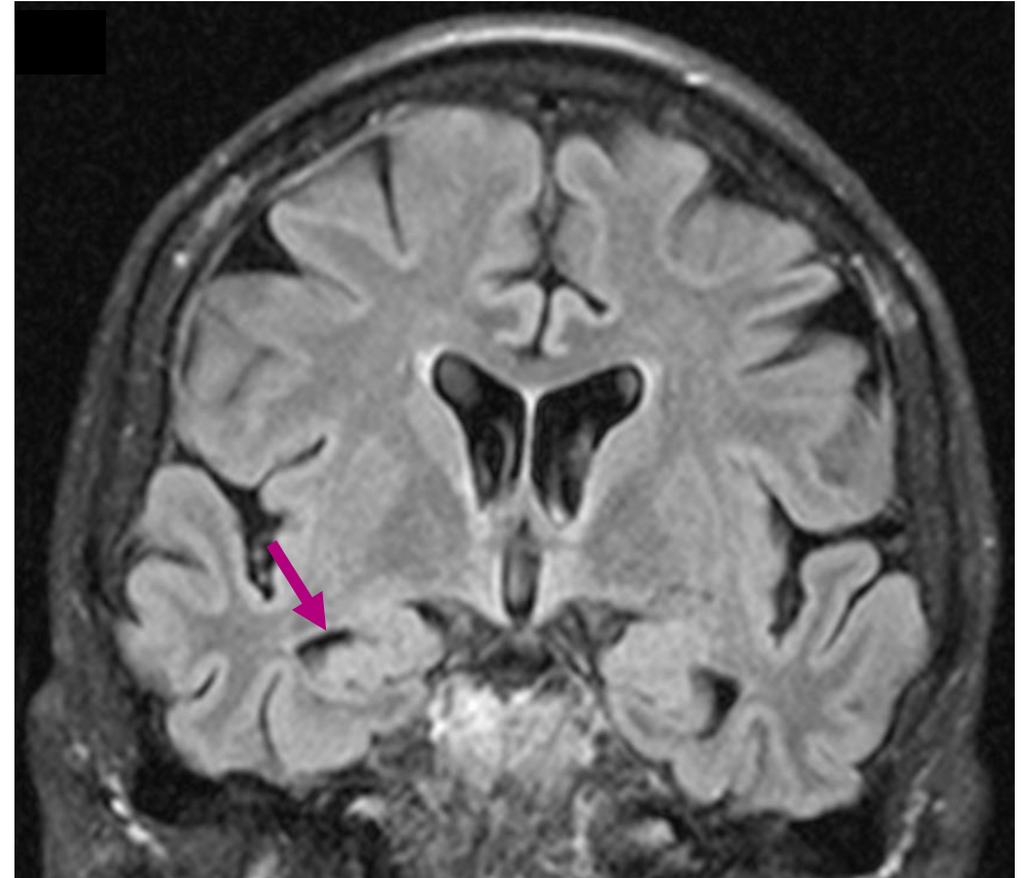


Image from Marinescu, I et al. Rom J Morphol Embryol. 2017;58(4):1165-1173.

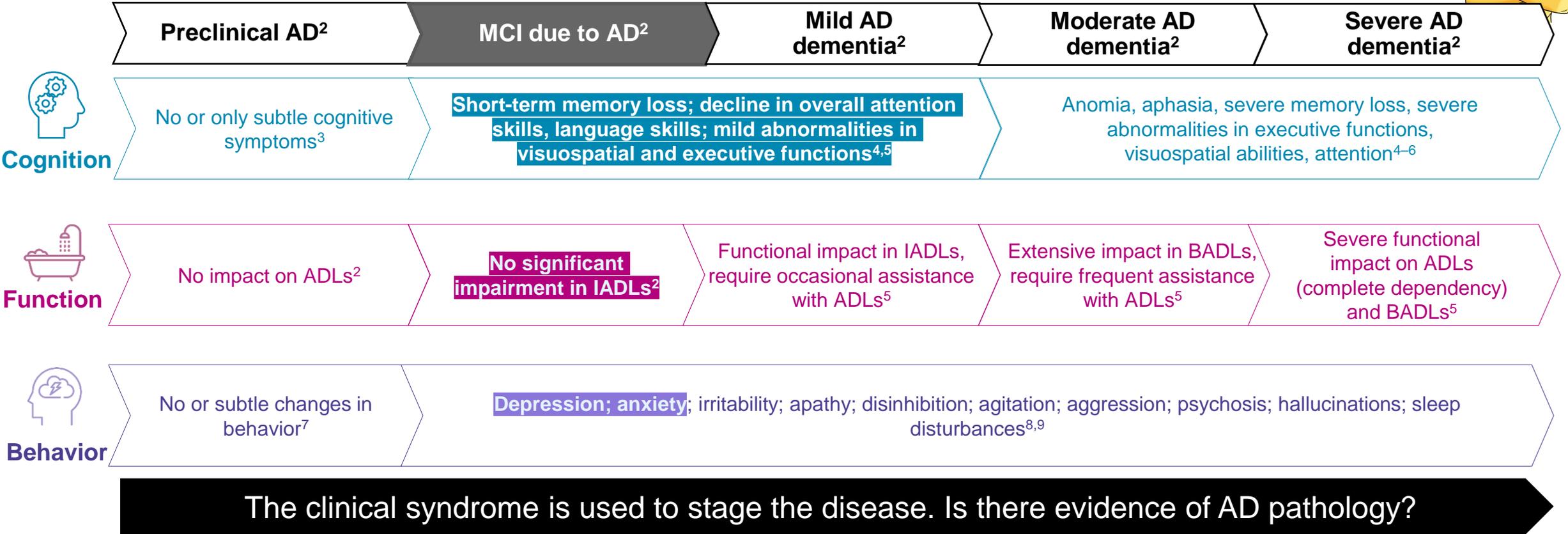
AD, Alzheimer's disease; FTD, frontotemporal dementia; LATE, Limbic-predominant age-related TDP-43 encephalopathy; MRI, magnetic resonance imaging; MTA, medial temporal atrophy

MTA, medial temporal lobe atrophy; TDP-43, TAR DNA-binding protein 43

1. Zhou Y, et al. ACS Chem Neurosci 2021;12:4209 – 4223; 2. Raskin R, et al. Curr Alzheimer Res 2015;12:712–722;

3. Harper L, et al. J Neurol Neurosurg Psychiatry 2014;85:692–698

# Where does Lisa potentially sit on the continuum?



AD, Alzheimer's disease; ADL, activities of daily living; BADL, basic activities of daily living; IADL, instrumental activities of daily living;

MCI, mild cognitive impairment

1. Aisen PS, et al. *Alzheimers Res Ther* 2017;9:60; 2. Jack CR Jr, et al. *Alzheimers Dement* 2018;14:535-562; 3. Harada CN, et al. *Clin Geriatr Med* 2013;29:737-752; 4. Kazim SF, Iqbal K. *Mol Neurodegener* 2016;11:50

5. Mayo Clinic. Alzheimer's stages: How the disease progresses. <https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers-stages/art-20048448> (Accessed April 2023); 6. Kipps CM, Hodges JR. *J Neurol Neurosurg Psychiatry* 2005;76(Suppl. 1):i22-i30;

7. Ismail Z, et al. *Alzheimers Dement* 2016;12:195-202; 8. Eikelboom WS, et al. *Neurology* 2021;97:e1276-e1287; 9. Lancôt KL, et al. *Alzheimers Dement (N Y)* 2017;3:440-449; 11.

# 2

## Evaluate: syndromal diagnosis

**Syndromal diagnosis: amnestic MCI due to probable AD** based on cognitive, behavioral, and functional assessments



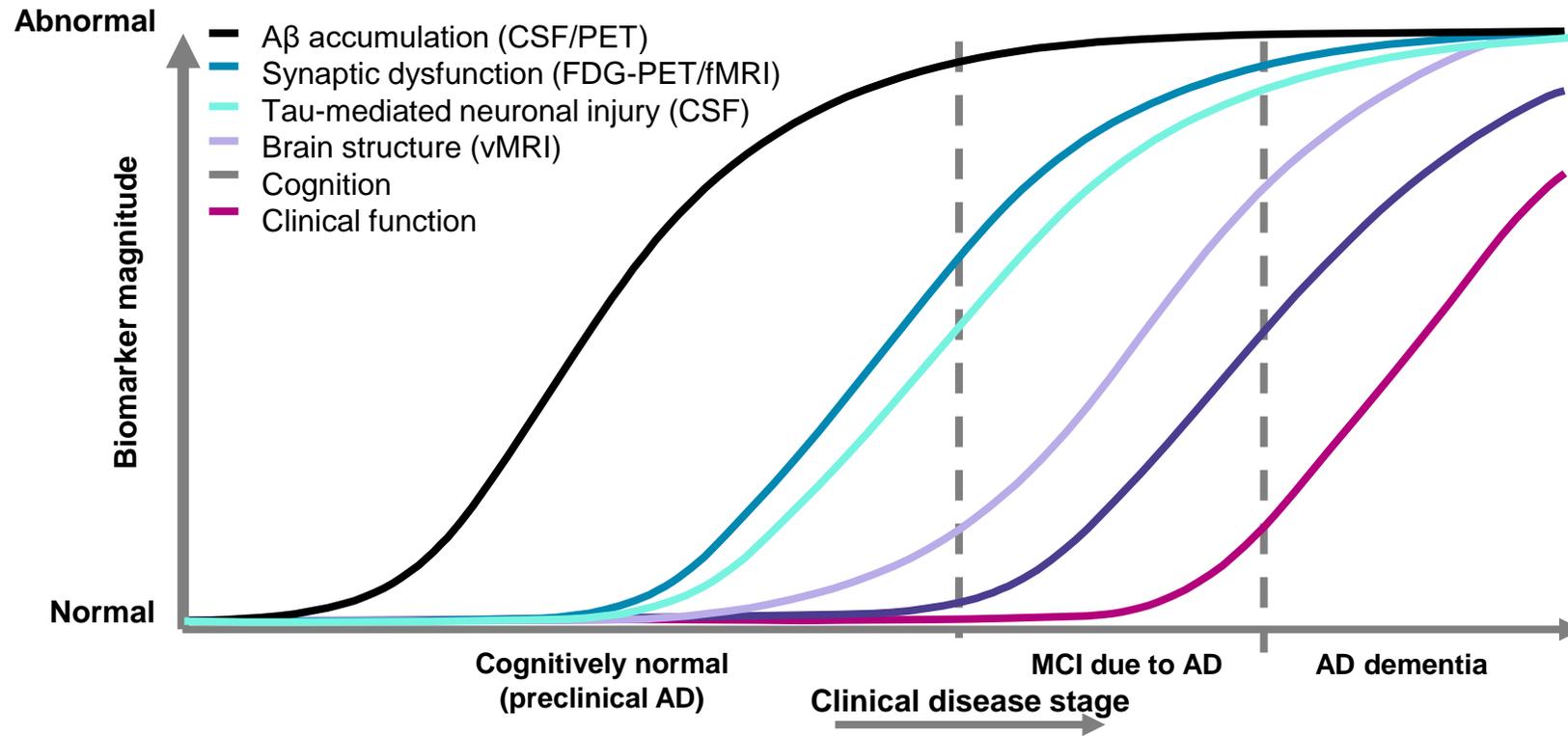
Lisa's assessments have been consistent with probable AD etiology (amnestic syndrome and structural MRI changes in an area crucial for episodic memory).

**Neurologist refers the patient for a lumbar puncture to assess AD biomarkers in the cerebrospinal fluid (CSF) to confirm a diagnosis**



AD, Alzheimer's disease; CSF, cerebrospinal fluid; MCI, mild cognitive impairment; MRI, magnetic resonance imaging; RPR, rapid plasma reagin

# Biomarker changes indicative of AD may be detected before clinical symptoms arise



AD pathophysiological changes can occur up to 20 years prior to symptom onset<sup>2</sup>

A $\beta$ , amyloid beta; CDR, Clinical Dementia Rating; CSF, cerebrospinal fluid; FDG-PET, fluorodeoxyglucose positron emission tomography; MCI, mild cognitive impairment; fMRI, functional magnetic resonance imaging; PET, positron emission tomography; vMRI, volumetric magnetic resonance imaging  
Figure adapted from Jack CR Jr, et al. Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *Lancet Neurol* 2010;9:119–128 with permission from Elsevier, Jessen F, et al. *Alzheimer's Dement* 2014;10:844–852, and Sperling et al. *Alzheimers Dement* 2011;7:280–292  
1. Sperling et al. *Alzheimers Dement* 2011;7:280–292; 2. Jack CR Jr, et al. *Alzheimers Dement* 2018;14:535–562

# 3

## Confirm diagnosis: biomarkers (CSF)

- Biomarker profile of the patient (applying the research ATN criteria)<sup>1</sup>
  - Abnormal amyloid and p-tau levels (measured by CSF) [A,T]
  - Abnormal t-tau and structural atrophy according to MRI [N]
- **Diagnosis: MCI due to AD** owing to the combination of clinical presentation and biomarker results

Biomarker	Patient result (concentration – pg/mL)	Cutoff (concentration – pg/mL)	Result compared with cutoff
Aβ42	650	<1098	Lower
t-tau	285	>242	Higher
p-tau	36	>19.2	Higher

Cutoff concentrations are appropriate for Elecsys Aβ42, t-tau, and p-tau automated assays<sup>2</sup>



Lisa's Aβ42 levels are lower than the cut-off (sign of amyloid deposition), while p-tau and t-tau (presence of tangles and neurodegeneration, respectively) are higher, consistent with AD pathology

Aβ, amyloid beta; AD, Alzheimer's disease; CSF, cerebrospinal fluid; p-tau, phosphorylated-tau; t-tau, total-tau  
 1. Jack CR Jr, et al. *Alzheimers Dement* 2018;14:535–562; 2. Schindler SE, et al. *Alzheimers Dement* 2018;14:1460–1469

# Putting ourselves in the shoes of a person in the early stages of Alzheimer's disease

# 3

## Disclosing the diagnosis

- ❑ Discuss how the biomarker test results help confirm a diagnosis
- ❑ Provide information about MCI and AD and what to expect
- ❑ Ensure they understand the information and provide further guidance around local support, resources, and options (research, registry, treatment)
- ❑ Discuss the social and safety implications, such as managing finances, medications, and appointments
- ❑ Agree on a plan for follow-up or referral



AD, Alzheimer's disease; MCI, mild cognitive impairment

1. McDade EM, et al. Continuum (Mineap Minn) 2022;28:648–675; 2. Gauthier S et al. Progress in Neurobiol 2013;110:102–113; 3. Frank CC, et al. Can Fam Physician 2018;64:518;

# 4

## Manage

- Following diagnosis, Lisa wanted to optimize the management of her comorbidities; her husband was eager for any additional interventions available to them
- Treatment options for MCI were discussed
- Lisa was encouraged to return for additional follow-up visits
- Her neurologist made her aware of clinical trials available where she may be eligible and local registries
- Provided details for a local social worker and directed toward further disease-specific information from the Alzheimer's Association related to her disease



# Benefits



Activation of family and/or support network/community<sup>1</sup>



Better management of cognitive, functional, and psychological disabilities<sup>1</sup>



Better management of comorbid conditions<sup>1</sup>



Proactive patient safety measures (falls, driving, fire, medication errors)<sup>1</sup>



Shared-decision making and future planning<sup>1</sup>



Maximize independence and prolonged community living<sup>1</sup>

# Barriers<sup>2,3</sup>

Capacity constraints, healthcare disparities

Stigma / awareness and cultural differences

Disease awareness and understanding

Fear of losing driving and other privileges

Access to care and support services

EMR, electronic medical record; MCI, mild cognitive impairment

1. Liss JL, et al. J Intern Med. 2021;290(2):310–334; 2. Alzheimer's Association. Alzheimers Dement 2021;17:327–406;

3. Laura M & Rainville C. AARP Research 2021. <https://doi.org/10.26419/res.00471.001>.

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