

# Dementia

(major neurocognitive disorder):  
what you need to know

detection

diagnosis

drug therapy

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# Disclosures

- Inventor on patent / patent application with MassGeneral Brigham on the Alzheimer's and COVID smell tests and therapeutic targets for Alzheimer's and ALS
- Scientific Co-founder and Shareholder, Aromha, Inc.
- Will discuss some off-label uses of drugs for Alzheimer's disease

**By 2050, the number of people age 65 and older with Alzheimer's dementia is projected to reach 12.7 million.**

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**Family members and friends provided more than \$271 billion in unpaid care to people living with Alzheimer's and other dementias in 2021.**

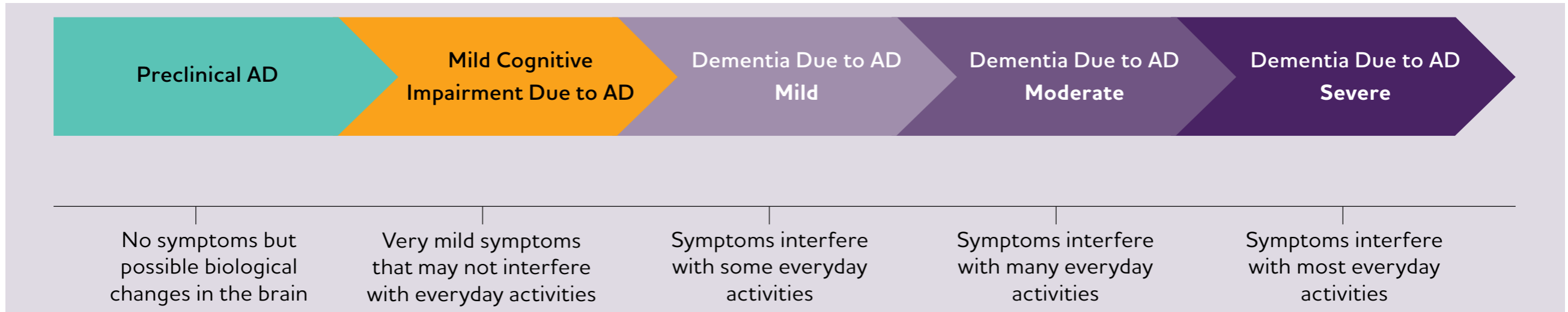
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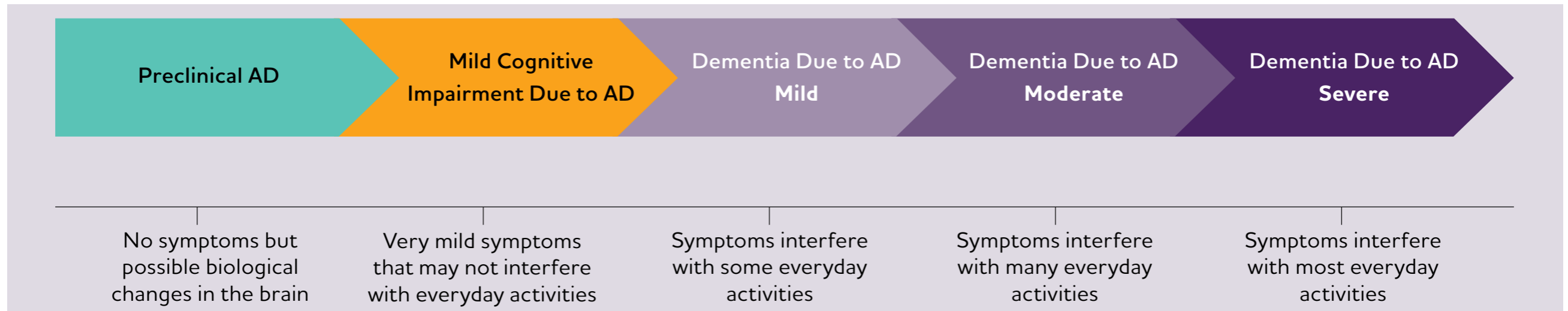
**1 in 3 seniors dies**

**with Alzheimer's or other dementias.**

**55% of primary care physicians caring for people living with Alzheimer's report there are not enough dementia care specialists in their communities to meet patient demands.**

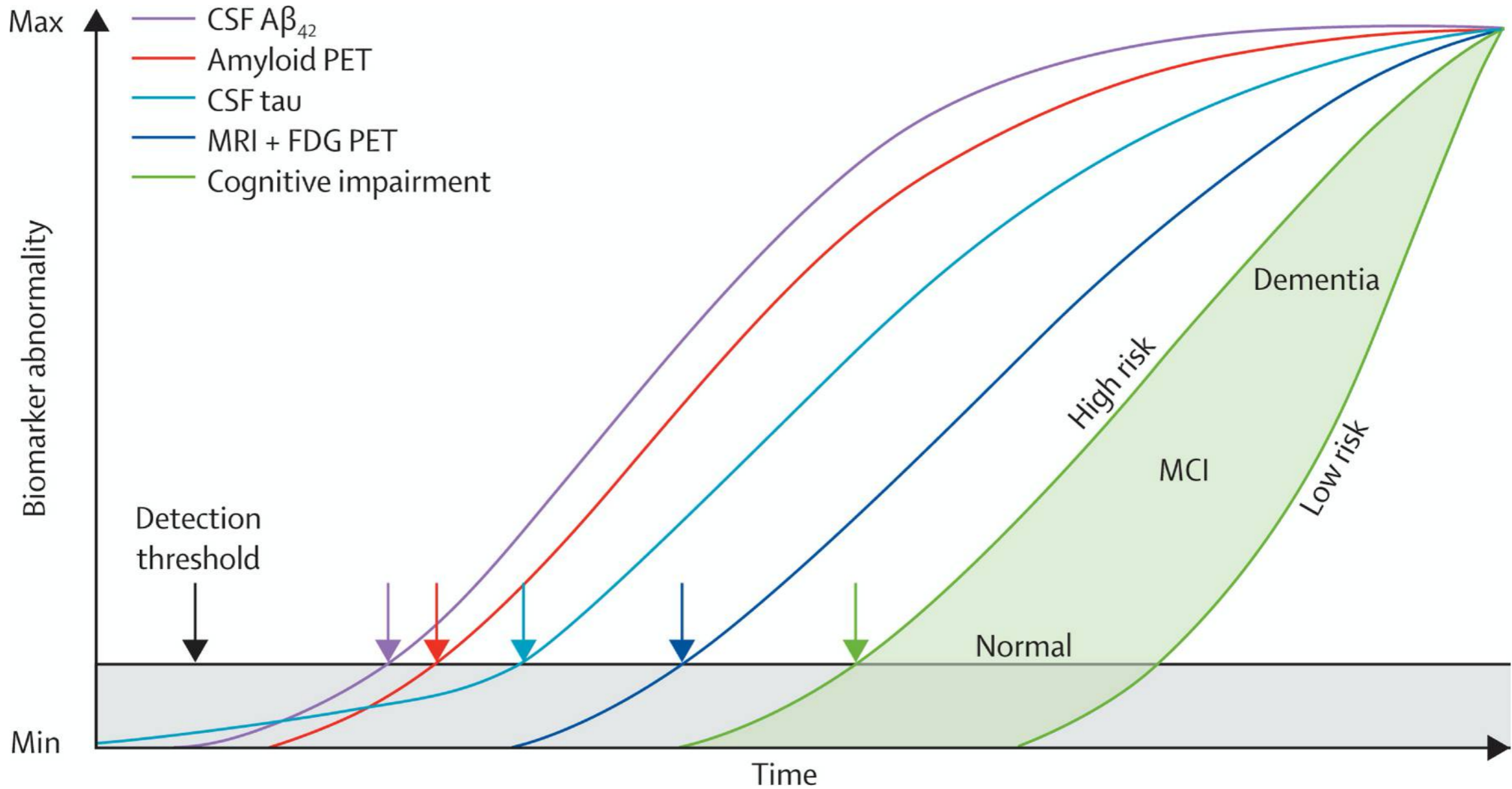
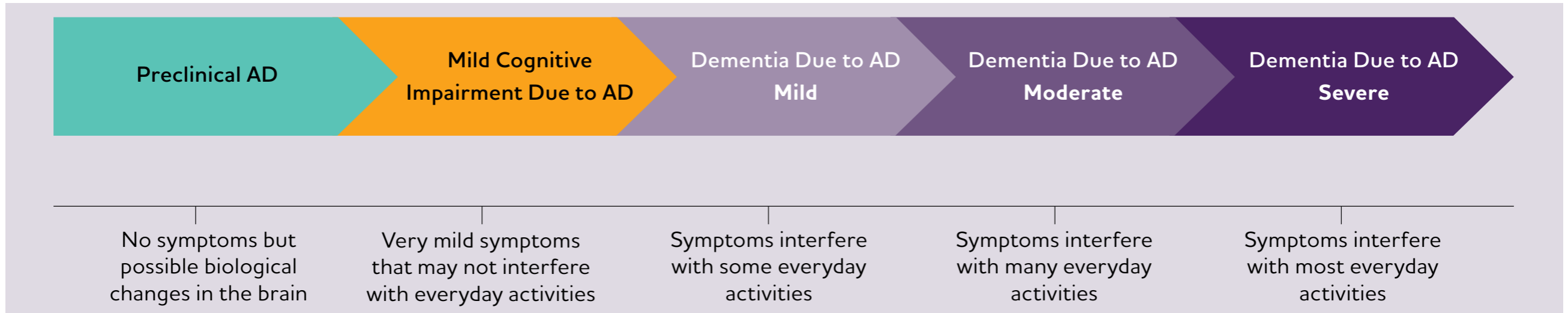
**with Alzheimer's and other dementias in 2021.**





**Fewer than 1 in 5 Americans (18%) are familiar with mild cognitive impairment (MCI).**





# 2 cases - trajectories of cognitive decline

## Patient 1

- 74 year old housewife with minimal worries about memory, but family has noted some changes
- Family history of AD
- MRI shows atrophy
- PET scan positive for amyloid
- Rx: Aricept (and support)

# 2 cases - trajectories of cognitive decline

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- Family history of AD
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## Patient 2

- 68 year old lawyer
- Family history of AD
- 23 and me says high risk
- Losing details in highly demanding situations
- MRI shows atrophy in hippocampus and parietal lobe
- CSF positive for AD biomarkers
- Rx: Aricept (and support)

# 2 cases - trajectories of cognitive decline

## Patient 1

- 74 year old housewife with minimal worries about memory, but family has noted some changes
  - Family history of AD
  - MRI shows atrophy
  - PET scan positive for amyloid
  - Rx: Aricept (and support)
- 
- 10 years later still living at home, conversant about current events, somewhat inaccurate

## Patient 2

- 68 year old lawyer
  - Family history of AD
  - 23 and me says high risk
  - Losing details in highly demanding situations
  - MRI shows atrophy in hippocampus and parietal lobe
  - CSF positive for AD biomarkers
  - Rx: Aricept (and support)
- 
- 2 years later wandering, needs nursing home placement

# Differential Diagnosis of Dementia

- Alzheimer's disease
- Lewy Body Dementia
- Vascular Dementia
- Fronto-temporal dementia - (behavioral, semantic, logopenic)
- Tauopathies: progressive supranuclear palsy (falls, impaired upgaze); corticobasal ganglion degeneration (generally unilateral)
- Normal Pressure Hydrocephalus (magnetic gain, urinary incontinence)
- CJD and other rapidly progressive dementias
- Autoimmune encephalitis

# Differential Diagnosis of Dementia

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# DSM-IV and DSM-5 criteria for dementia

DSM-IV criteria for dementia	DSM-5 criteria for major neurocognitive disorder (previously dementia)
<b>A1.</b> Memory impairment	<b>A.</b> Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains*: - Learning and memory - Language - Executive function - Complex attention - Perceptual-motor - Social cognition
<b>A2.</b> At least one of the following: - Aphasia - Apraxia - Agnosia - Disturbance in executive functioning	
<b>B.</b> The cognitive deficits in A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.	<b>B.</b> The cognitive deficits interfere with independence in everyday activities. At a minimum, assistance should be required with complex instrumental activities of daily living, such as paying bills or managing medications.
<b>C.</b> The cognitive deficits do not occur exclusively during the course of delirium.	<b>C.</b> The cognitive deficits do not occur exclusively in the context of a delirium.
	<b>D.</b> The cognitive deficits are not better explained by another mental disorder (eg, major depressive disorder, schizophrenia).

For diagnostic criteria of dementia subtypes such as Alzheimer disease or frontotemporal dementia, please refer to UpToDate topics on the clinical manifestations and diagnosis of individual dementia subtypes.

DSM: Diagnostic and Statistical Manual of Mental Disorders.

\* Evidence of decline is based on concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function and a substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.

*References:*

1. American Psychiatric Association *Diagnostic and Statistical Manual, 4th ed*, APA Press, Washington, DC 1994.
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, American Psychiatric Association, Arlington, VA 2013.

# Evaluation

- Forgetting proper names
- short term memory (repeating questions, new compensatory techniques under equal load)
- Word finding difficulty
- Visual perceptual deficits
- Changes in emotion
- Gait instability
- Urinary incontinence
- Rule out on depression, although new onset depression can be AD or FTD



# Evaluation

routine

- review medications: beta blockers, anti-cholinergics for prostatism, recent change in statin prescription
- MOCA (18 - 25 Mild Cognitive Impairment; 10-17 moderate cognitive impairment) / Depression screen
- Blood Tests for Reversible Causes: vitamin B12, TSH
- neuroimaging (MRI / CT)

specialized

- 
- if rapidly progressive, consider anti-TPO, autoimmune panel (Mayo Clinic), CJD testing
  - LP (to rule out NPH and rule in amyloid)  
*-large volume LP (30 cc) with timed gait test before and after tap. Would only pursue if the patient is a surgical candidate.*
  - FDG-PET imaging (very rarely used; covered by Medicare if AD vs. FTD)
  - Apolipoprotein E genotyping (not clinically useful if considering aducanumab)

# MOCA - Training required 9/1/2020

<b>MONTREAL COGNITIVE ASSESSMENT (MOCA-B) BASIC</b>		Name _____ Sex _____ Age _____ Education _____ Date of exam _____ Administered by _____					
<b>EXECUTIVE FUNCTION</b>			<b>SCORE</b>				
			START TIME				
			( /1)				
<b>IMMEDIATE RECALL</b>		ROSE	CHAIR	HAND	BLUE	SPOON	No point
	Perform 2 trials even if 1st trial is successful	1st trial					
		2nd trial					
<b>FLUENCY</b>	Name maximum numbers of <b>FRUITS</b> in 1 minute				N items		( /2)
	1.....	2.....	3.....	4.....	5.....	6.....	2 points if N=13 or more 1 point if N=8-12 0 point if N= 7 or less
	7.....	8.....	9.....	10.....	11.....	12.....	
	13.....	14.....	15.....	16.....	17.....	18.....	
<b>ORIENTATION</b>	<input type="checkbox"/> time (± 2 hr) <input type="checkbox"/> day <input type="checkbox"/> month <input type="checkbox"/> year <input type="checkbox"/> place <input type="checkbox"/> city						( /6)
<b>CALCULATION</b>	Provide 3 ways to pay using 1 dollar coins, 5 dollar and 10 dollar bills for an object that costs exactly "13 Dollars" (3 points if 3 ways, 2 points if 2 ways, 1 point if 1 way, 0 point if no correct way)						( /3)
	<input type="checkbox"/> 1..... <input type="checkbox"/> 2..... <input type="checkbox"/> 3.....						
<b>ABSTRACTION</b>	To what category these objects belong to ? (e.g. orange - banana = fruit)						( /3)
	<input type="checkbox"/> train - boat <input type="checkbox"/> north - south <input type="checkbox"/> drum - flute						
<b>DELAYED RECALL</b>		ROSE	CHAIR	HAND	BLUE	SPOON	( /5)
	Recall with No cue	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Recall with category cue	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Recall with multiple choice cue	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<b>VISUOPERCEPTION</b>		scissors	T-shirt	banana	lamp	candle	( /3)
	Identify drawings. No more than 60 seconds. See complementary sheet.	watch	cup	leaf	key	spoon	
		3 points if N=9-10 2 points if N=6-8 1 point if N=4-5 0 point if N=0-3    N —					
<b>NAMING</b>	Identify animals. See complementary sheet. <input type="checkbox"/> zebra <input type="checkbox"/> peacock <input type="checkbox"/> tiger <input type="checkbox"/> butterfly						( /4)
<b>ATTENTION</b>	Name the numbers in circles. See complementary sheet.    1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5		ERROR ___ N				( /1)
			No point if 2 errors or more				
	Name the numbers in circles & squares: 3 8 5 1 3 0 2 9 2 0 4 9 7 8 6 1 5 7 6 4		ERROR ___ N				( /2)
	See complementary sheet.    1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5		2 points if 2 errors or less 1 point if 3 errors 0 point if 4 errors or more				
					END TIME		
Adapted by : Parunyou Julayanont MD Copyright : Z. Nasreddine MD		Final Version June 04, 2014		<b>TOTAL SCORE ( /30)</b> Add 1 point if education < 4 year AND add 1 point if illiterate			
				<b>TOTAL TIME</b> min    sec			

# MOCA - Training required 9/1/2020

**MONTREAL COGNITIVE ASSESSMENT (MOCA-B) BASIC**

Name \_\_\_\_\_  
 Sex \_\_\_\_\_ Age \_\_\_\_\_  
 Education \_\_\_\_\_ Date of exam \_\_\_\_\_  
 Administered by \_\_\_\_\_

EXECUTIVE FUNCTION						SCORE
						START TIME ( / )
IMMEDIATE RECALL						No point
ROSE CHAIR HAND BLUE SPOON						
Perform 2 trials even if 1st trial is successful						
FLUENCY						( / 2)
Name maximum numbers of FRUITS in 1 minute						
1..... 2..... 3..... 4..... 5..... 6..... 2 points if N=13 or more 7..... 8..... 9..... 10..... 11..... 12..... 1 point if N=8-12 13..... 14..... 15..... 16..... 17..... 18..... 0 point if N= 7 or less						
ORIENTATION						( / 6)
[ ] time (± 2 hr) [ ] day [ ] month [ ] year [ ] place [ ] city						
CALCULATION						( / 3)
Provide 3 ways to pay using 1 dollar coins, 5 dollar and 10 dollar bills for an object that costs exactly "13 Dollars" (3 points if 3 ways, 2 points if 2 ways, 1 point if 1 way, 0 point if no correct way)						
[ ] 1..... [ ] 2..... [ ] 3.....						
ABSTRACTION						( / 3)
To what category these objects belong to? (e.g. orange - banana = fruit) [ ] train - boat [ ] north - south [ ] drum - flute						
DELAYED RECALL						( / 5)
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Recall with No cue [ ] [ ] [ ] [ ] [ ] Recall with category cue [ ] [ ] [ ] [ ] [ ] Recall with multiple choice cue [ ] [ ] [ ] [ ] [ ]						
VISUOPERCEPTION						( / 3)
Identify drawings. No more than 60 seconds. See complementary sheet.						
scissors T-shirt banana lamp candle watch cup leaf key spoon						
NAMING						( / 4)
Identify animals. See complementary sheet. [ ] zebra [ ] peacock [ ] tiger [ ] butterfly						
ATTENTION						( / 1)
Name the numbers in circles. See complementary sheet. 1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5 ERROR ___ N No point if 2 errors or more						
Name the numbers in circles & squares: 3 8 5 1 3 0 2 9 2 0 4 9 7 8 6 1 5 7 6 4 ERROR ___ N See complementary sheet. 1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5 1 point if 3 errors 0 point if 4 errors or more						
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<b>TOTAL SCORE ( / 30)</b> Add 1 point if education < 4 year AND add 1 point if illiterate <b>TOTAL TIME min sec</b>						

**MONTREAL COGNITIVE ASSESSMENT (MOCA-B) BASIC** COMPLEMENTARY WORKSHEET

**VISUOPERCEPTION**

**NAMING**

**ATTENTION**

1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5

3 8 5 1 3 0 2 9 2 0 4 9 7 8 6 1 5 7 6 4

1 5 8 3 9 2 0 3 9 4 0 2 1 6 8 7 4 6 7 5

Adapted by: Parunyou Julayanont MD  
 Copyright: Z. Nasreddine MD  
 Final Version June 04, 2014

# Depression Screen

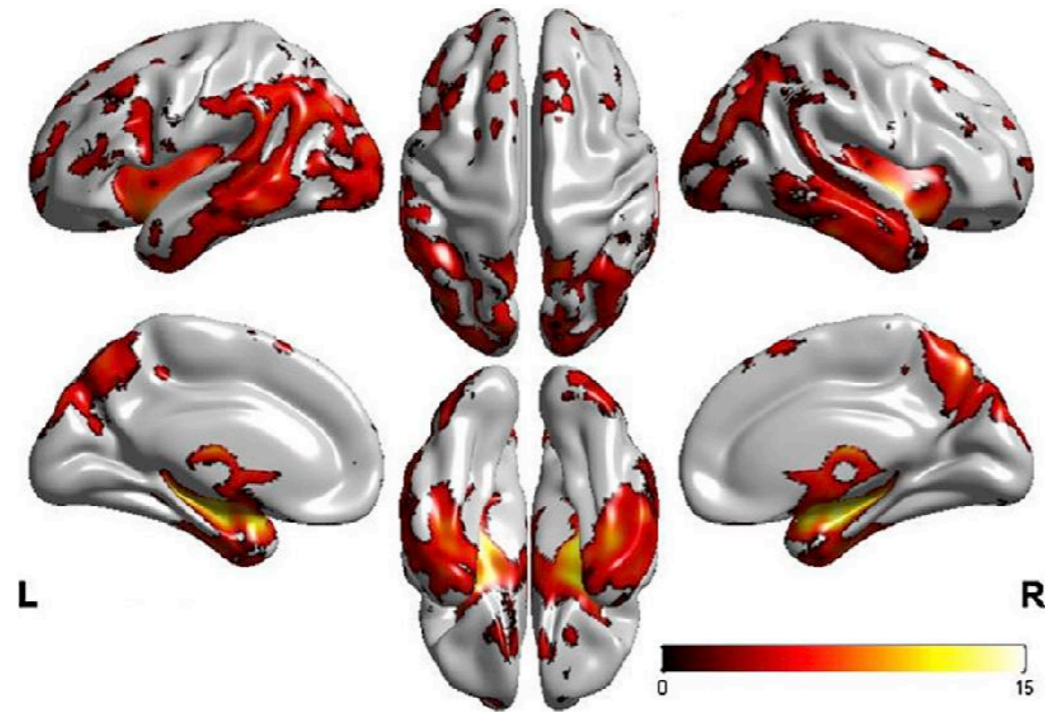
## Short Patient Health Questionnaire (PHQ-2)

Name:		Date:			
Over the past 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day	
	0	1	2	3	
Little interest or pleasure in doing things?	0	1	2	3	
Feeling down, depressed, or hopeless?	0	1	2	3	
<b>Total point score:</b>	_____	_____	+ _____	+ _____	+ _____
<b>Score interpretation [1]:</b>					
<b>PHQ-2 score</b>	<b>Probability of major depressive disorder (%)</b>		<b>Probability of any depressive disorder (%)</b>		
1	15.4		36.9		
2	21.1		48.3		
3	38.4		75.0		
4	45.5		81.2		
5	56.4		84.6		
6	78.6		92.9		

*Reference:*

1. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003; 41:1284.

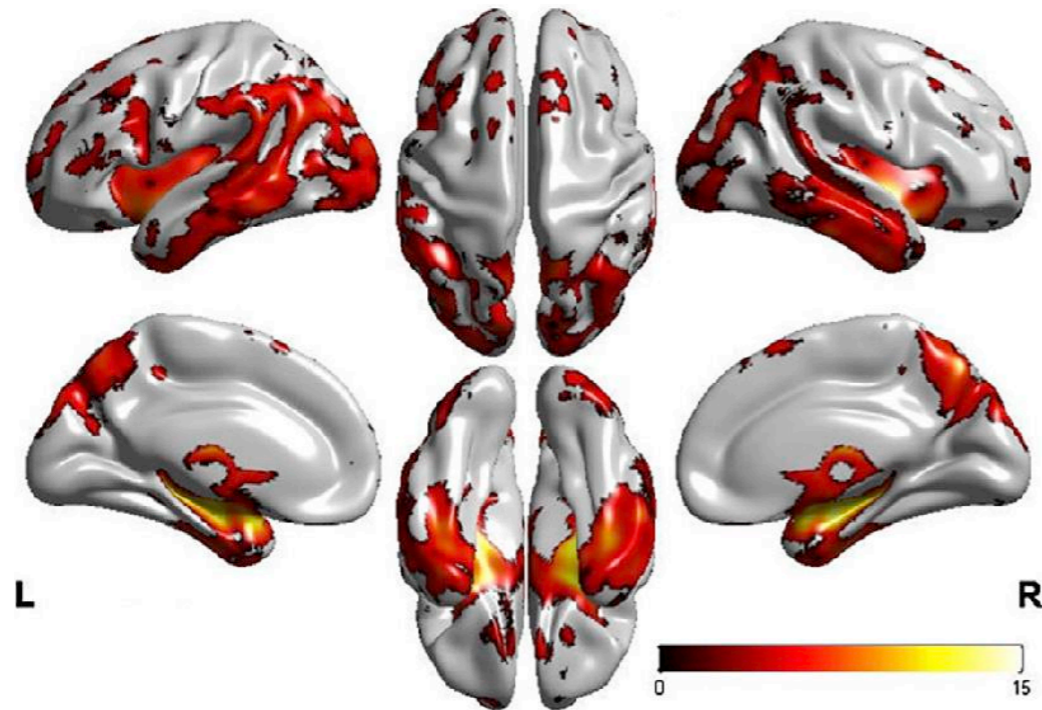
# Imaging Neurodegeneration in Living Seniors



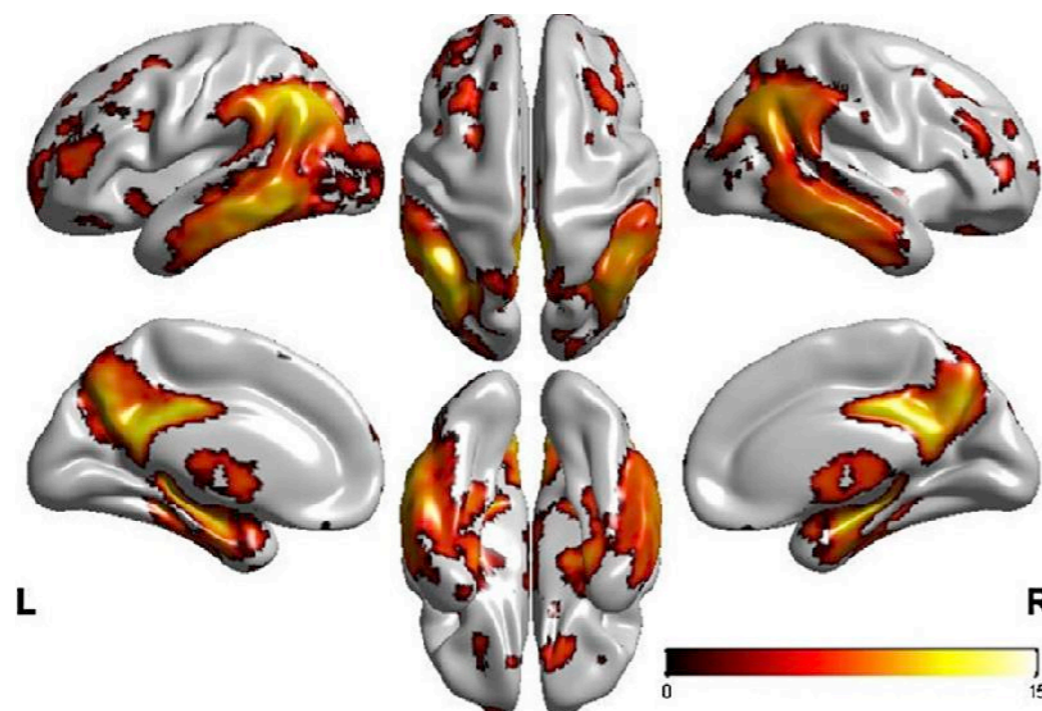
Atrophy of brain tissue  
(Structural MRI)



# Imaging Neurodegeneration in Living Seniors



Atrophy of brain tissue  
(Structural MRI)



Glucose uptake  
(FDG PET)

# Treatment - cognitive phase

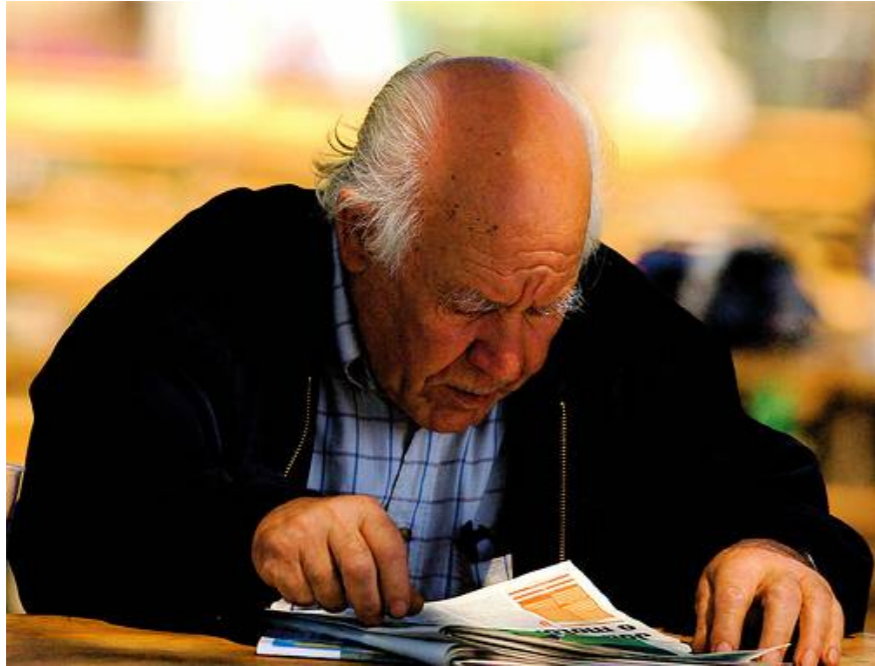
- Acetylcholinesterase inhibitors (titrate after 1 month)
  - donepezil: 5 mg or 10 mg PO qd
  - galantamine ER 8 mg, 16 mg, then 24 mg PO qd
  - rivastigimine 4.6 mg / 9.5 mg / 13.3 mg patches
    - *also FDA approved for parkinson's disease dementia*
- adverse effect (10%): nausea / vomiting, diarrhea usually in first few days. Taking on full stomach will alleviate.
- adverse effect: vivid dreams - taking after breakfast will alleviate
- adverse effect: urinary urgency - timed urination

# Treatment - behavioral phase

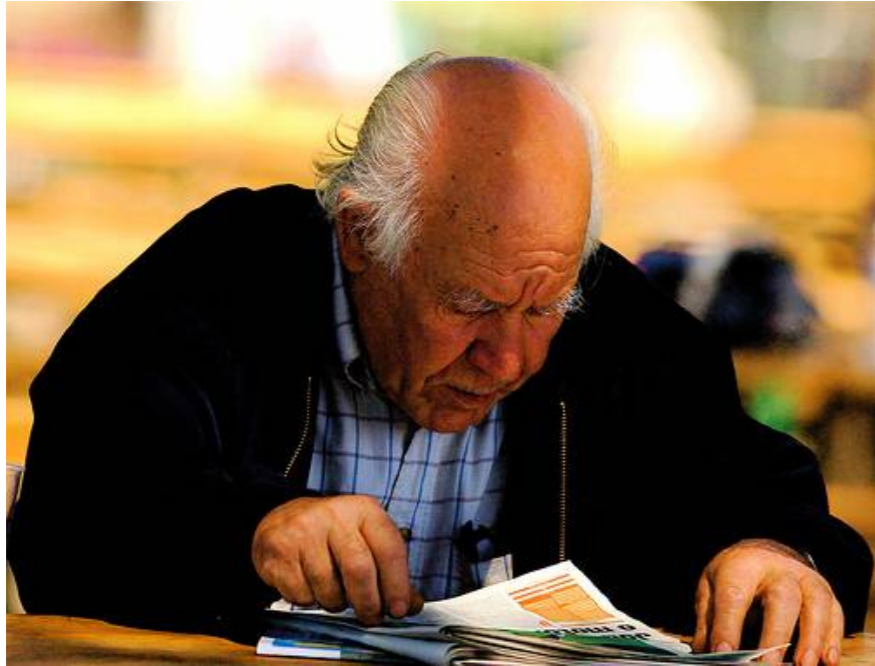
- memantine (behavioral changes) - starter pack for 1st month, then 10 mg bid
- optimize sleep - sleep hygiene, melatonin 1 h before bedtime
- Caregiver counseling - behavioral techniques to de-escalate irritability, agitation including distraction and anchoring with music, pictures, and other senses
- anti-psychotics (off-label with black box warning)
  - check EKG and refer to geriatric psychiatrist or neurologist



# Evidence-based lifestyle recommendations

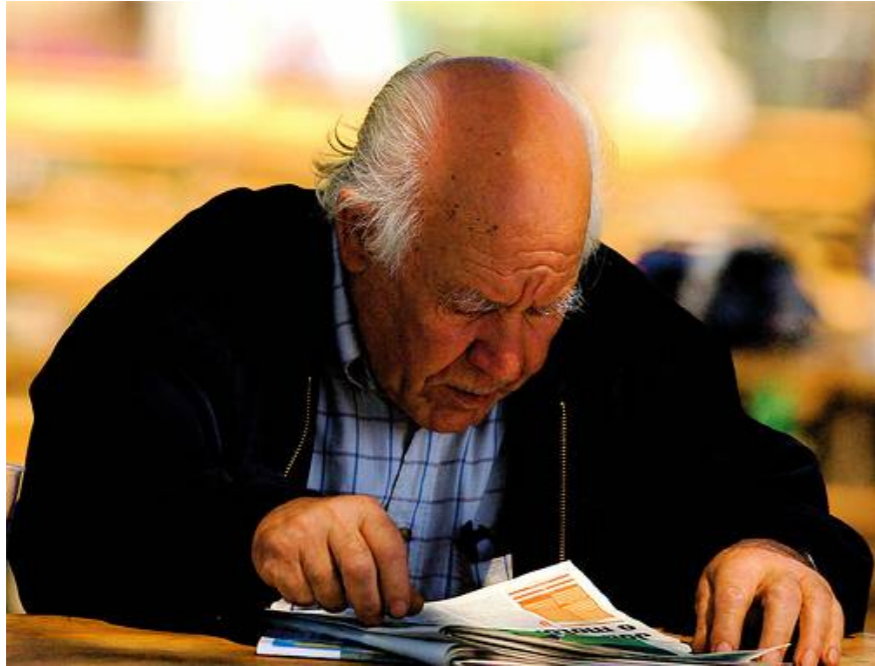


# Evidence-based lifestyle recommendations





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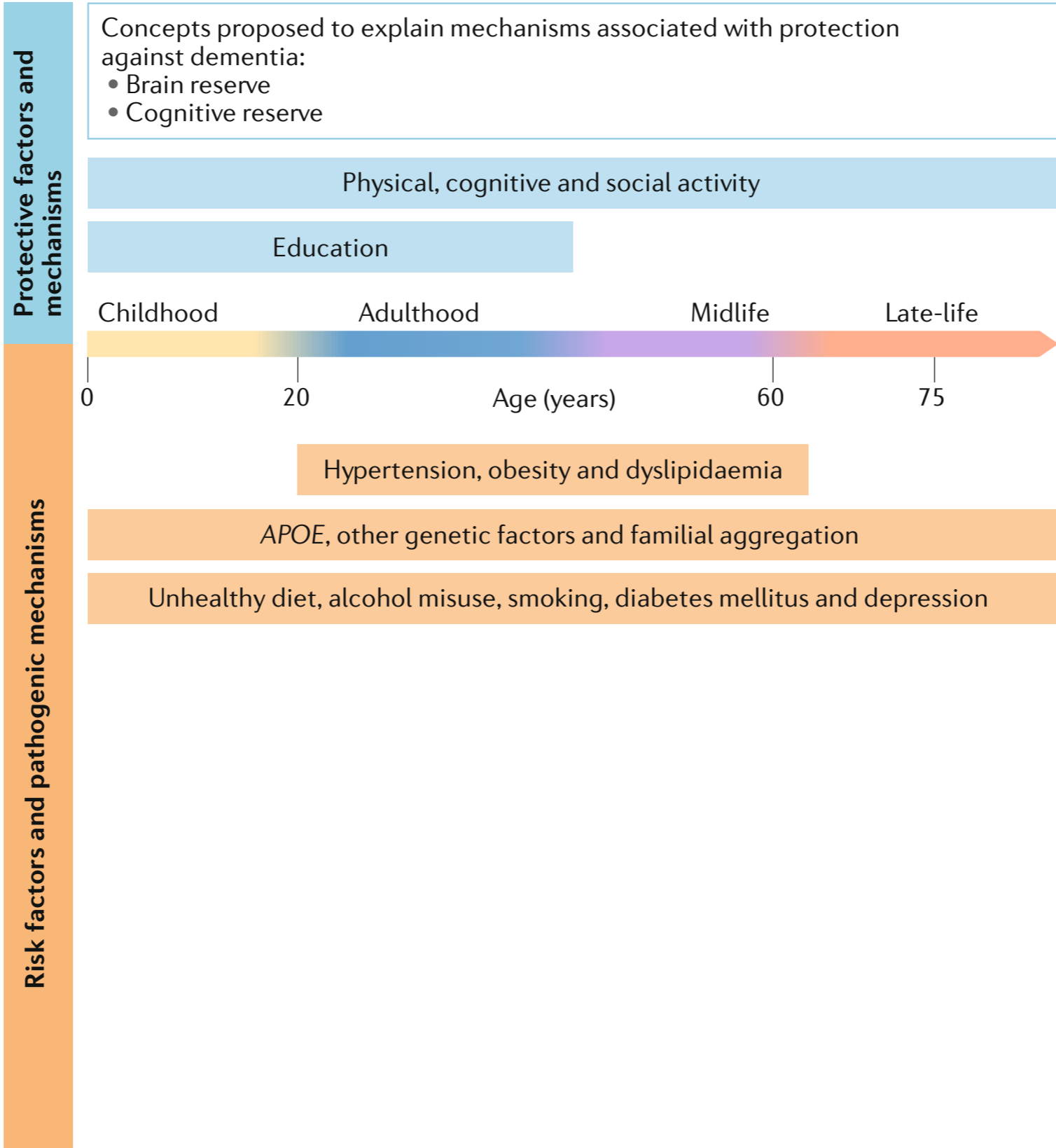




# Evidence-based lifestyle recommendations



# Prevention of Dementia: Lifestyle Modifications



# Prevention of Dementia: Lifestyle Modifications

### The CAIDE dementia risk score

Risk factor		Points
Age	<47 years	0
	47–53 years	3
	>53 years	4
Education	≥10 years	0
	7–9 years	2
	<7 years	3
Sex	Female	0
	Male	1
Blood pressure	≤140 mmHg	0
	>140 mmHg	2
BMI	≤30 kg/m <sup>2</sup>	0
	>30 kg/m <sup>2</sup>	2
Total cholesterol	≤6.5 mmol/l	0
	>6.5 mmol/l	2
Physical activity	Yes	0
	No	1

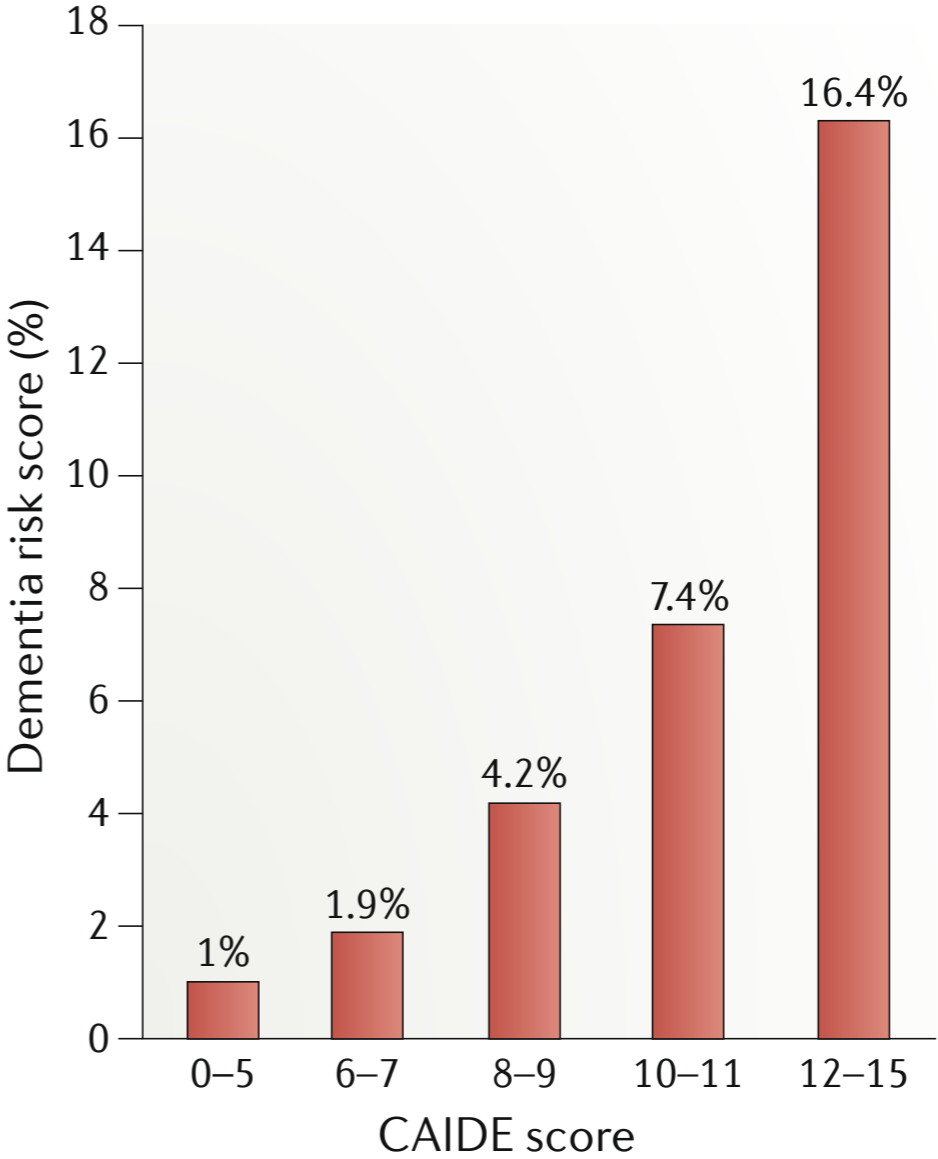


Fig. 2 | **CAIDE risk score.** The Cardiovascular Risk Factors, Aging and Dementia (CAIDE) risk score enables the prediction of the later risk of dementia on the basis of the risk factor profile present in midlife (age 40–65 years).



# Aduhelm aducanumab

