

Evaluation and Management of Dementia

Courtney Wellman, MD

Marshall University Department of Family and Community Health

Family Medicine and Geriatrics

Objectives

- Evaluate memory impairment
- Discuss tools for use in the diagnosis of dementia
- Understand the diagnostic criteria for dementia
- Examine methods to prevent dementia and mild cognitive impairment
- Learn how to treat dementia
- Discuss the new medications soon to be available for the treatment of dementia

Objectives

- **Evaluate memory impairment**
- Discuss tools for use in the diagnosis of dementia
- Understand the diagnostic criteria for dementia
- Examine methods to prevent dementia and mild cognitive impairment
- Learn how to treat dementia
- Discuss the new medications soon to be available for the treatment of dementia

Memory Impairment

- Subjective memory complaint
- PMHx
- Medications
- Social history
- Functional assessment: ADLs IADLs

Dressing

Eating

Ambulating

Toileting

Hygiene

Shopping

Housekeeping

Accounting

Food prep



Memory Impairment

- Incontinence
- Falls
- Hx CVA/TIA
- Hallucinations
- Behaviors
- Head trauma
- Substance use (alcohol)

Physical Exam

- Full neurologic examination
- Key findings:
 - EOM
 - Muscle tone
 - Tremor
 - Gait
 - Coordination

Objectives

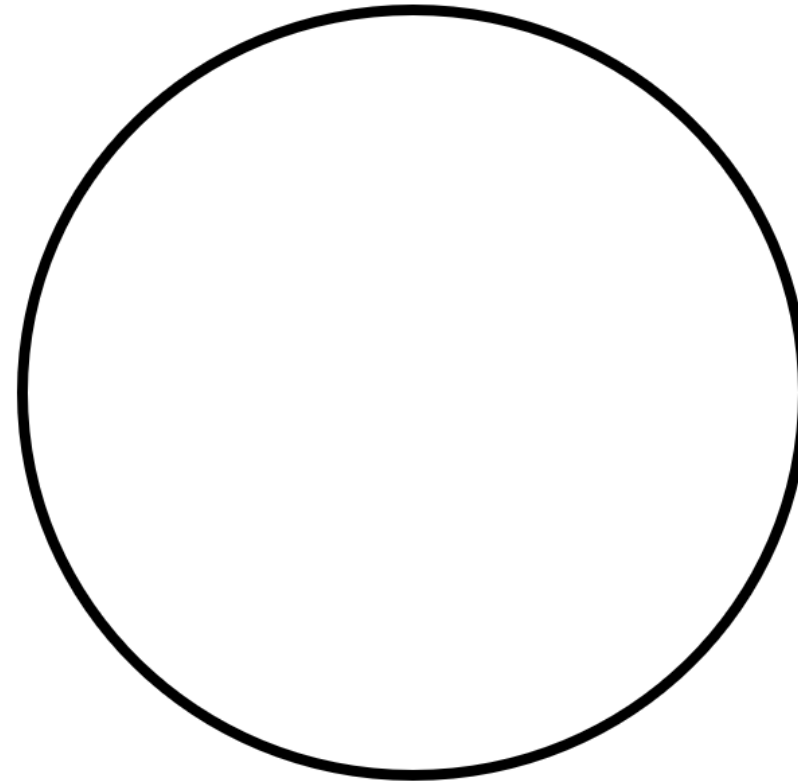
- Evaluate memory impairment
- **Discuss tools for use in the diagnosis of dementia**
- Understand the diagnostic criteria for dementia
- Examine methods to prevent dementia and mild cognitive impairment
- Learn how to treat dementia
- Discuss the new medications soon to be available for the treatment of dementia

Diagnostic tools

- Memory Evaluation:
 - Mini-Cog
 - Mini Mental Status Exam (MMSE)
 - Montreal Cognitive Assessment (MoCA)
 - St. Louis University Mental Status Examination (SLUMS)
- Mood evaluation
 - Geriatric depression scale (GDS)
 - Patient Health Questionnaire 9 (PHQ9)
 - Generalized Anxiety Disorder 7 (GAD7)

Patient Name: _____ DOB: _____

Mini-Cog
SN: 76-100%
SP: 27-85%



Mini-Cog © S. Borson. All rights reserved. Reprinted with permission of the author solely for clinical and educational purposes. May not be modified or used for commercial, marketing, or research purposes without permission of the author (soob@uw.edu).


v. 01.19.16

MMSE

Mini-Mental State Examination (MMSE)

Patient's Name: _____ Date: _____

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

Rovner BW, Folstein MF. Mini-mental state exam in clinical practice. *Hosp Pract* (Off Ed) 1987;22:99,103,106,110.

MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME : _____
 Education : _____ Date of birth : _____
 Sex : _____ DATE : _____

VISUOSPATIAL / EXECUTIVE		Copy cube		Draw CLOCK (Ten past eleven) (3 points)		POINTS			
		<div style="display: flex; justify-content: space-around;"> [] [] </div>		<div style="display: flex; justify-content: space-around;"> [] [] [] </div>		<div style="text-align: right;">___/5</div>			
NAMING									
			<div style="display: flex; justify-content: space-around;"> [] [] [] </div> <div style="text-align: right;">___/3</div>						
MEMORY									
Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.	1st trial	2nd trial	FACE	VELVET	CHURCH	DAISY	RED	No points	
Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [] 2 1 8 5 4 Subject has to repeat them in the backward order [] 7 4 2			Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [] 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					___/2	
Serial 7 subtraction starting at 100 [] 93			[] 86	[] 79	[] 72	[] 65	4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt		___/3
LANGUAGE							___/2		
Repeat : I only know that John is the one to help today. [] The cat always hid under the couch when dogs were in the room. []							___/1		
Fluency / Name maximum number of words in one minute that begin with the letter F [] ____ (N ≥ 11 words)							___/2		
ABSTRACTION							___/2		
Similarity between e.g. banana - orange = fruit [] train - bicycle [] watch - ruler							___/5		
DELAYED RECALL		Has to recall words WITH NO CUE	FACE []	VELVET []	CHURCH []	DAISY []	RED []	Points for UNCUE recall only	___/6
Optional		Category cue							___/30
		Multiple choice cue							___/30
ORIENTATION							___/6		
[] Date [] Month [] Year [] Day [] Place [] City							___/30		

© Z.Nasreddine MD Version November 7, 2004
 www.mocatest.org

Normal ≥ 26 / 30




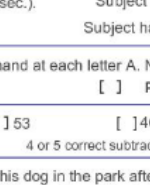
TOTAL

Add 1 point if ≤ 12 yr edu

MONTREAL COGNITIVE ASSESSMENT (MoCA®)

Version 8.3 English

Name: _____
Education: _____ Date of birth : _____
Sex: _____ DATE : _____

VISUOSPATIAL / EXECUTIVE							POINTS																												
<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>Copy bed</p> </div> <div style="text-align: center;"> <p>Draw CLOCK (Five past ten)</p> <p>(3 points)</p> </div> </div>				<div style="display: flex; justify-content: space-between;"> <div> <p>[] Contour</p> </div> <div> <p>[] Numbers</p> </div> <div> <p>[] Hands</p> </div> </div>			<p>___/5</p>																												
NAMING																																			
 <p>[]</p>		 <p>[]</p>		 <p>[]</p>		<p>___/3</p>																													
MEMORY		<p>Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th></th> <th>LEG</th> <th>COTTON</th> <th>SCHOOL</th> <th>TOMATO</th> <th>WHITE</th> </tr> </thead> <tbody> <tr> <td>1st TRIAL</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>2nd TRIAL</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table>							LEG	COTTON	SCHOOL	TOMATO	WHITE	1st TRIAL						2nd TRIAL															
	LEG	COTTON	SCHOOL	TOMATO	WHITE																														
1st TRIAL																																			
2nd TRIAL																																			
ATTENTION		<p>Read list of digits (1 digit/sec.).</p> <p style="text-align: right;">Subject has to repeat them in the forward order. [] 2 4 8 1 5</p> <p style="text-align: right;">Subject has to repeat them in the backward order. [] 4 2 7</p>																																	
<p>Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors.</p> <p style="text-align: right;">[] 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</p>		<p>Serial 7 subtraction starting at 60. [] 53 [] 46 [] 39 [] 32 [] 25</p> <p style="text-align: right;">4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt</p>																																	
LANGUAGE		<p>Repeat: The child walked his dog in the park after midnight. []</p> <p style="text-align: right;">The artist finished his painting at the right moment for the exhibition. []</p>																																	
<p>Language Fluency. Name maximum number of words in one minute that begin with the letter B. [] _____ (N ≥ 11 words)</p>		<p>Similarity between e.g. banana - orange = fruit [] hammer - screwdriver [] matches - lamp</p>																																	
ABSTRACTION		<p>Repeat: The child walked his dog in the park after midnight. []</p> <p style="text-align: right;">The artist finished his painting at the right moment for the exhibition. []</p>																																	
DELAYED RECALL		<p>Language Fluency. Name maximum number of words in one minute that begin with the letter B. [] _____ (N ≥ 11 words)</p>																																	
ORIENTATION		<p>Similarity between e.g. banana - orange = fruit [] hammer - screwdriver [] matches - lamp</p>																																	
<p>Memory Index Score (MIS)</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th></th> <th>Has to recall words WITH NO CUE</th> <th>LEG</th> <th>COTTON</th> <th>SCHOOL</th> <th>TOMATO</th> <th>WHITE</th> </tr> </thead> <tbody> <tr> <td>X3</td> <td></td> <td>[]</td> <td>[]</td> <td>[]</td> <td>[]</td> <td>[]</td> </tr> <tr> <td>X2</td> <td>Category cue</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>X1</td> <td>Multiple choice cue</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p style="text-align: right;">MIS = ___/15</p>			Has to recall words WITH NO CUE	LEG	COTTON	SCHOOL	TOMATO	WHITE	X3		[]	[]	[]	[]	[]	X2	Category cue						X1	Multiple choice cue						<p>Points for UNCUE recall only</p>					
	Has to recall words WITH NO CUE	LEG	COTTON	SCHOOL	TOMATO	WHITE																													
X3		[]	[]	[]	[]	[]																													
X2	Category cue																																		
X1	Multiple choice cue																																		
ORIENTATION		<p>[] Date [] Month [] Year [] Day [] Place [] City</p>																																	
<p>© Z. Nasreddine MD</p> <p>Administered by: _____</p>		<p>www.mocatest.org</p>		<p>MIS: /15</p> <p>(Normal ≥ 26/30)</p>		<p>TOTAL</p>																													
<p>Training and Certification are required to ensure accuracy.</p>		<p>Add 1 point if ≤ 12 yr education</p>		<p>___/30</p>		<p>___/30</p>																													

Diagnostic Tools

Received: 15 June 2022 | Revised: 20 September 2022 | Accepted: 14 October 2022
DOI: 10.1111/jgs.18124

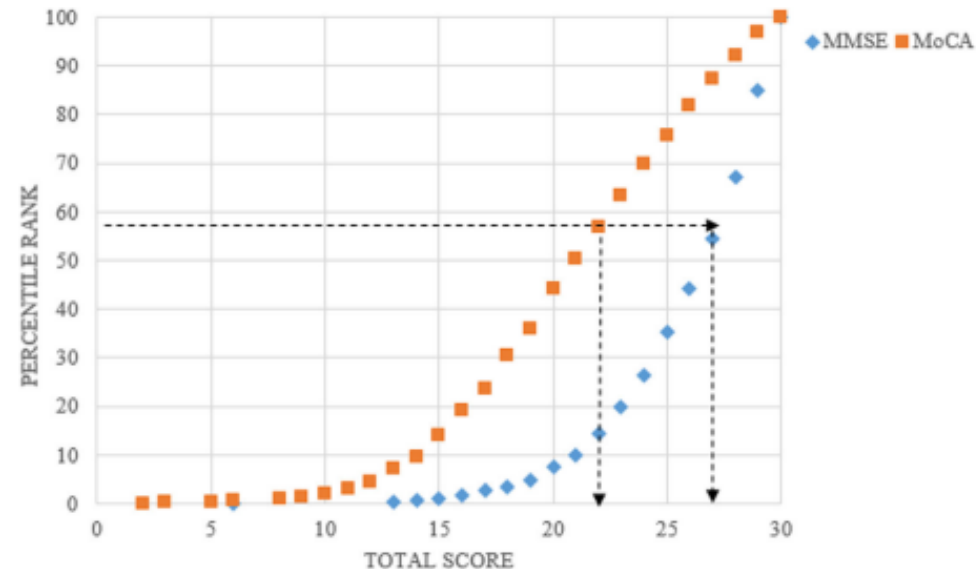
Conversion between MoCA and the Mini-Mental State Examination

Jael S. Fasnacht MSc¹
Alessandra E. Thoman MSc²
Klemens Gutbrod PhD³
Andreas U. Monsch PhD⁴

A COMPREHENSIVE TABLE OF EQUIVALENT SCORES

JAGS | 873

FIGURE 2 Equipercile equating in MoCA and MMSE values in 803 patients from the Memory Clinic FELIX PLATTER, Switzerland. MMSE values are given in raw values. MoCA values correspond to education-adjusted values. The dotted lines indicate that MoCA and MMSE values are set equal when their corresponding percentile ranks are equal. MMSE, mini mental status examination; MoCA, montreal cognitive assessment.



MARSHALL UNIVERSITY
Joan C. Edwards School of Medicine

SLUMS

VAMC SLUMS Examination

Questions about this assessment tool? E-mail aging@slu.edu.

Name _____ Age _____
Is patient alert? _____ Level of education _____

____/1

____/1

____/1

____/3

____/3

____/5

____/2

____/4

____/2

____/8

1. What day of the week is it?
2. What is the year?
3. What state are we in?
4. Please remember these five objects. I will ask you what they are later.
Apple Pen Tie House Car
5. You have \$100 and you go to the store and buy a dozen apples for \$3 and a tricycle for \$20.
1 How much did you spend?
2 How much do you have left?
6. Please name as many animals as you can in one minute.
1 0-4 animals 2 5-9 animals 3 10-14 animals 4 15+ animals
7. What were the five objects I asked you to remember? 1 point for each one correct.
8. I am going to give you a series of numbers and I would like you to give them to me backwards.
For example, if I say 42, you would say 24.
1 87 2 649 3 8537
9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.
2 Hour markers okay
2 Time correct
10. Please place an X in the triangle.
1 Which of the above figures is largest?
11. I am going to tell you a story. Please listen carefully because afterwards, I'm going to ask you some questions about it.
Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They lived in Chicago. She then stopped work and stayed at home to bring up her children. When they were teenagers, she went back to work. She and Jack lived happily ever after.
2 What was the female's name?
2 When did she go back to work?
2 What work did she do?
2 What state did she live in?

TOTAL SCORE



SCORING		
HIGH SCHOOL EDUCATION		LESS THAN HIGH SCHOOL EDUCATION
27-30	Normal	25-30
21-26	MNCD*	20-24
1-20	Dementia	1-19

* Mild Neurocognitive Disorder

SH Tariq, N Tumosa, JT Chibnall, HM Perry III, and JE Morley. The Saint Louis University Mental Status (SLUMS) Examination for Detecting Mild Cognitive Impairment and Dementia is more sensitive than the Mini-Mental Status Examination (MMSE) - A pilot study. Am J Geriatr Psychiatry 14:900-910, 2006.

Geriatric Depression Scale (short form)

Instructions: Circle the answer that best describes how you felt over the past week.

- | | | |
|---|-----|----|
| 1. Are you basically satisfied with your life? | yes | no |
| 2. Have you dropped many of your activities and interests? | yes | no |
| 3. Do you feel that your life is empty? | yes | no |
| 4. Do you often get bored? | yes | no |
| 5. Are you in good spirits most of the time? | yes | no |
| 6. Are you afraid that something bad is going to happen to you? | yes | no |
| 7. Do you feel happy most of the time? | yes | no |
| 8. Do you often feel helpless? | yes | no |
| 9. Do you prefer to stay at home, rather than going out and doing things? | yes | no |
| 10. Do you feel that you have more problems with memory than most? | yes | no |
| 11. Do you think it is wonderful to be alive now? | yes | no |
| 12. Do you feel worthless the way you are now? | yes | no |
| 13. Do you feel full of energy? | yes | no |
| 14. Do you feel that your situation is hopeless? | yes | no |
| 15. Do you think that most people are better off than you are? | yes | no |

Total Score _____

Geriatric Depression Scale



MARSHALL UNIVERSITY
Joan C. Edwards School of Medicine

Diagnostic Tools

SEVERITY

- Dementia severity rating scale (DSRS)
- Global Deterioration Scale (GDS)
- Clinical Dementia Rating Scale (CDR)
- Functional Assessment Staging Test (FAST)

NEUROPSYCHIATRIC SYMPTOMS

- Neuropsychiatric inventory (NPI)
- Dementia Signs and Symptoms Scale (DSS)

Diagnostic Tools

FAST Test

- Hospice assessment at 7A

Functional Assessment Scale (FAST)

1	No difficulty either subjectively or objectively.
2	Complains of forgetting location of objects. Subjective work difficulties.
3	Decreased job functioning evident to co-workers. Difficulty in traveling to new locations. Decreased organizational capacity. *
4	Decreased ability to perform complex task, (e.g., planning dinner for guests, handling personal finances, such as forgetting to pay bills, etc.)
5	Requires assistance in choosing proper clothing to wear for the day, season or occasion, (e.g. pt may wear the same clothing repeatedly, unless supervised.*
6	Occasionally or more frequently over the past weeks. * for the following A) Improperly putting on clothes without assistance or cueing . B) Unable to bathe properly (not able to choose proper water temp) C) Inability to handle mechanics of toileting (e.g., forget to flush the toilet, does not wipe properly or properly dispose of toilet tissue) D) Urinary incontinence E) Fecal incontinence
7	A)Ability to speak limited to approximately ≤ 6 intelligible different words in the course of an average day or in the course of an intensive interview. B) Speech ability is limited to the use of a single intelligible word in an average day or in the course of an intensive interview C) Ambulatory ability is lost (cannot walk without personal assistance.) D) Cannot sit up without assistance (e.g., the individual will fall over if there are not lateral rests [arms] on the chair.) E) Loss of ability to smile. F) Loss of ability to hold up head independently.
*Scored primarily on information obtained from a knowledgeable informant. Psychopharmacology Bulletin, 1988 24:653-659.	



Objectives

- Evaluate memory impairment
- Discuss tools for use in the diagnosis of dementia
- **Understand the diagnostic criteria for dementia**
- Examine methods to prevent dementia and mild cognitive impairment
- Learn how to treat dementia
- Discuss the new medications soon to be available for the treatment of dementia

Diagnosis

Normal Aging

- Subjective memory complaints
- Normal cognitive assessment

Mild Cognitive Impairment

- Abnormal cognitive assessment
- No functional impairment

Dementia

- Abnormal cognitive assessment
- Functional impairment



Diagnosis

DSM V Criteria

- 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)
- The cognitive deficits interfere with independence in everyday activities.
- The cognitive deficits do not occur exclusively in the context of a delirium.
- The cognitive deficits are not better explained by another mental disorder

Diagnosis

- Labs:
 - TSH
 - B12
 - CBC
 - CCP
- Imaging:
 - MRI brain w/o contrast vs CT head
 - Amyloid PET scan
 - DAT scan
- Other:
 - LP
 - Infectious workup (syphilis, etc)

Diagnosis

- MRI: white matter hyperintensities
- 7,547 people age 35-69 w/o cardiovascular disease
 - Statistically significant cognitive decline with high white matter hyperintensities

Diagnosis

- Amyloid PET scan
 - + can indicate increased risk of developing dementia, but not always
 - Rule out AD if negative
 - Not useful to predict dementia in MCI
 - \$\$\$\$
- LP for A β 1-42/1-40 ratio
 - May be helpful in predicting MCI progression to AD in 3 yr
 - Rule out AD if negative

Objectives

- Evaluate memory impairment
- Discuss tools for use in the diagnosis of dementia
- Understand the diagnostic criteria for dementia
- **Examine methods to prevent dementia and mild cognitive impairment**
- Learn how to treat dementia
- Discuss the new medications soon to be available for the treatment of dementia

Prevention

Dementia prevention, in the *Lancet* Commission

Gill Livingston, Jonathan Huntley, Andrew Sommerlad, Davi Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, A Eric B Larson, Adesola Ogunniyi, Vasiliki Orgeta, Karen Ritchie Geir Selbæk, Linda Teri, Naaheed Mukadam

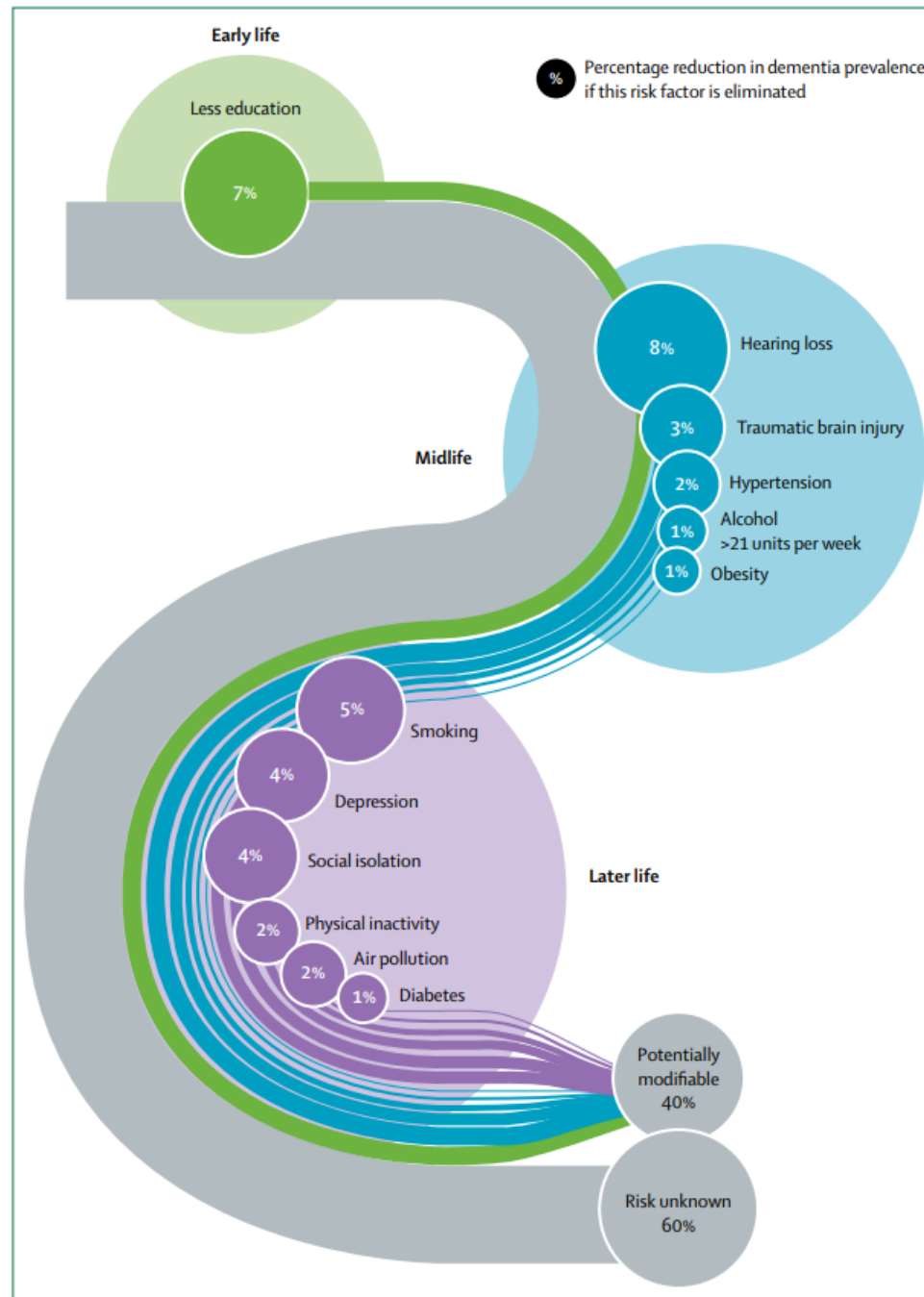


Figure 7: Population attributable fraction of potentially modifiable risk factors for dementia



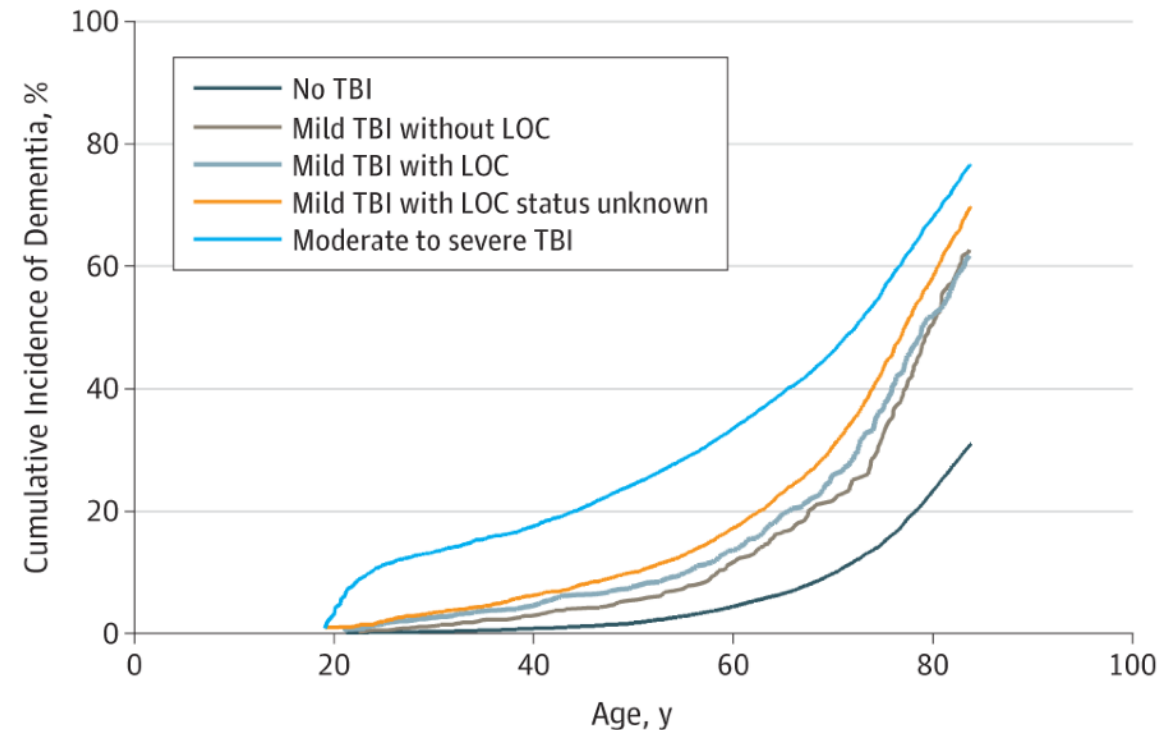
MARSHALL UNIVERSITY®
Joan C. Edwards School of Medicine

Prevention – Hearing Loss

- Subclinical hearing loss is associated with decreased cognition.
- Self-reported hearing problems indicated a statistically significant correlation between disability in ADLs ($p=0.0046$) and dementia ($p=0.0238$)
- Wearing hearing aids improved their risk to that of individuals reporting no hearing impairment. No increased risk of either dementia or disability in ADLs.

Prevention – Traumatic Brain Injury

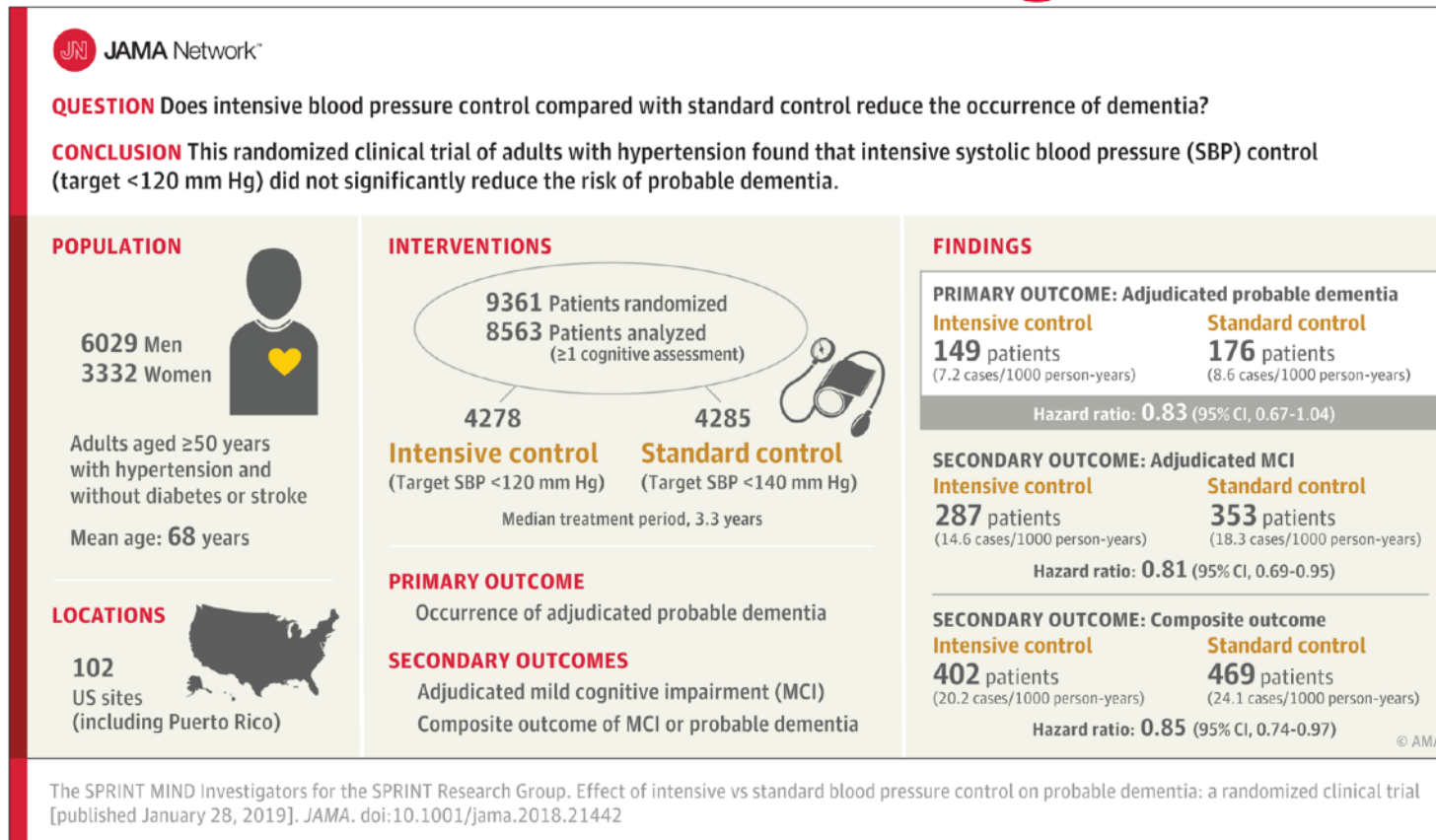
- 178,779 veterans with TBI compared to those without.
- Dementia is associated with TBI severity
- HR 2.36 for mild TBI
- HR 2.51 for mild TBI w/ LOC
- HR 3.19 for mod-severe TBI



JAMA Neurol. 2018;75(9):1055-1061. doi:10.1001/jamaneurol.2018.0815

Prevention - Hypertension

SPRINT-MIND Trial



Prevention - Exercise

- HUNT study 2017
 - 28,916 participants 30-60 yo followed 25 yr
 - Moderate-vigorous physical activity (breaking into sweat) was associated with decreased dementia risk (HR 0.8)
- Swedish 44 year study 2018
 - High peak fitness associated with decreased dementia risk vs low and medium.
- Meta-Analysis 2019 404,840 participants; self reported physical activity**
 - Inactivity 10 years prior to diagnosis associated
 - Inactivity 10-15 years prior to diagnosis not associated

Prevention - Socialization

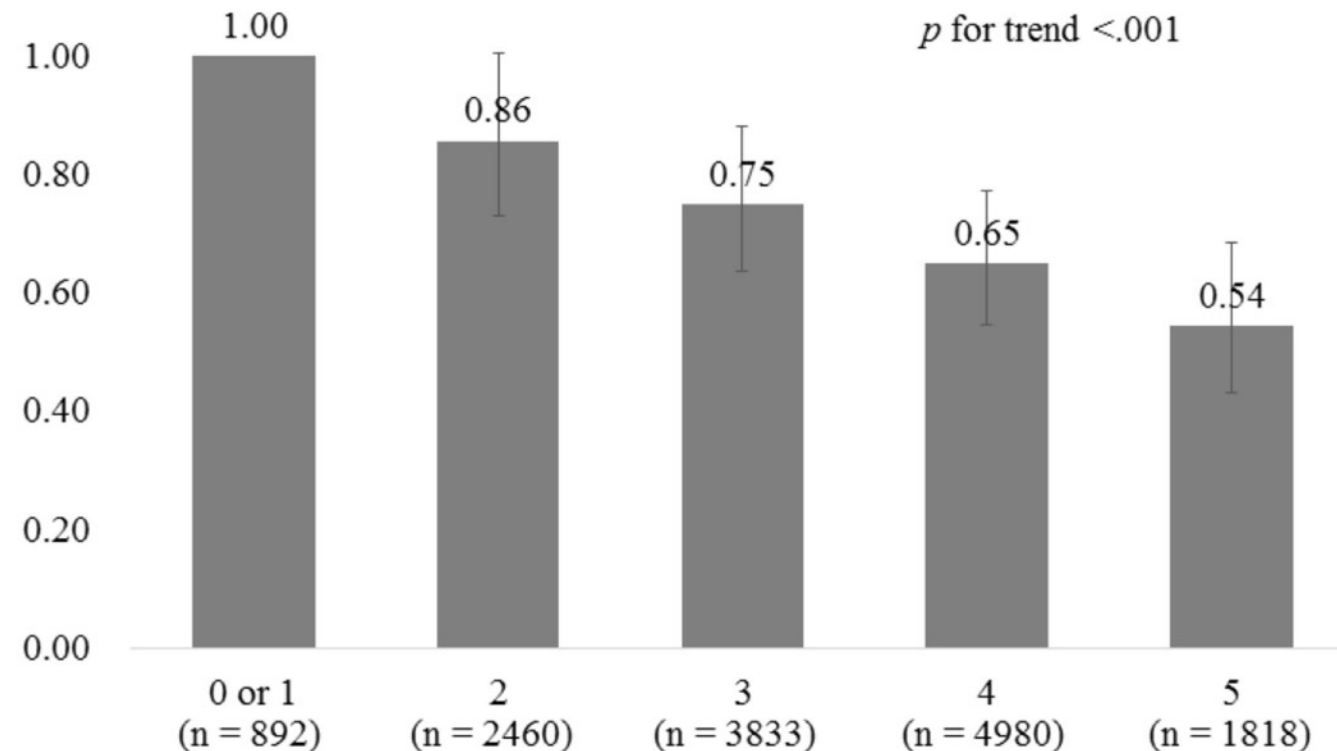
- 2019 Systematic review and meta-analysis

- 102,035 participants
- High social contact (social activity and social network) was associated with better late-life cognitive function

- 2018 prospective cohort study Japan

- 13,984 community-dwelling 65yo+
- married, contact with friends, group participation, work engagement and social support exchanges with family

Hazard ratio
1.20
1.00
0.80
0.60
0.40
0.20
0.00



Tami Saito et al. J Epidemiol Community Health 2018;72:7-12

©2018 by BMJ Publishing Group Ltd

Prevention - Diet

- Mediterranean diet
 - May improve global cognition, but did not seem to reduce incident of cognitive impairment or dementia
 - WHO recommends this
- Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND Diet)
 - May slow cognitive decline
 - May reduce incidence of Alzheimer's Dementia

Prevention

- No evidence supporting:
 - Statins
 - ASA
 - Supplements
 - Vitamins A, B, C, D, and E
 - Calcium, zinc, copper, MV, n-3 fatty acids, antioxidant vitamins and herbs
- Prevagen:
 - 10 mg apoaequorin (synthetic protein originally from jellyfish), 50 mcg Vitamin D.
 - \$\$\$\$
 - Sponsored study showing benefit in people with normal memory or mild subjective impairment.

Treatment - MCI

10-15% yearly risk of progression to dementia

Prevention of progression

- Donepezil – No
- Rivastigmine - No
- Ginkgo Biloba – No
- Vitamin E – No
- Omega 3 – No
- B vitamins - No

Objectives

- Evaluate memory impairment
- Discuss tools for use in the diagnosis of dementia
- Understand the diagnostic criteria for dementia
- Examine methods to prevent dementia and mild cognitive impairment
- **Learn how to treat dementia**
- Discuss the new medications soon to be available for the treatment of dementia

Treatment

- Discuss goals of care and adjust expectations
- Discuss Quality vs Quantity of life
- Discuss safety
- Stabilize the disease
- Assess care-partner and/or care-giver needs
- Advanced care planning
- Symptom Management

Treatment

- Hobbies
- Physical Activity
- Mental Stimulation

Treatment

- Acetylcholinesterase inhibitors: Donepezil, Galantamine, Rivastigmine.
 - Small, but measurable benefits
 - Mild-moderate disease benefits more than severe disease
- SE
 - First degree AV block
 - Prolonged QT
 - N, V, D, weight loss
 - Transdermal - rash, swelling, site irritation

Treatment

- N-methyl-D-aspartate (NMDA) receptor antagonist (Memantine)
 - Moderate to severe disease stability without measurable clinical benefit
- SE
 - Confusion, dizziness, headache
 - Agitation, delusions, hallucinations

Objectives

- Evaluate memory impairment
- Discuss tools for use in the diagnosis of dementia
- Understand the diagnostic criteria for dementia
- Examine methods to prevent dementia and mild cognitive impairment
- Learn how to treat dementia
- **Discuss the new medications soon to be available for the treatment of dementia**

Aducanumab

- Recombinant monoclonal antibody directed against amyloid beta
- Accelerated approval by the FDA June 2021
- Approved for:
 - Mild Cognitive Impairment or Mild Dementia
 - Documented amyloid pathology
 - No increased hemorrhage risk (anticoagulants, prior hemorrhage, microhemorrhages on MRI, etc.)
- IV q4 weeks w/ gradually increasing dose (7 increases)
- Monitoring:
 - MRI before initiation, dose 5, 7 and 12
- SE: 40% of patients experience ARIA; greater risk in APOE ϵ 4 carriers

Aducanumab

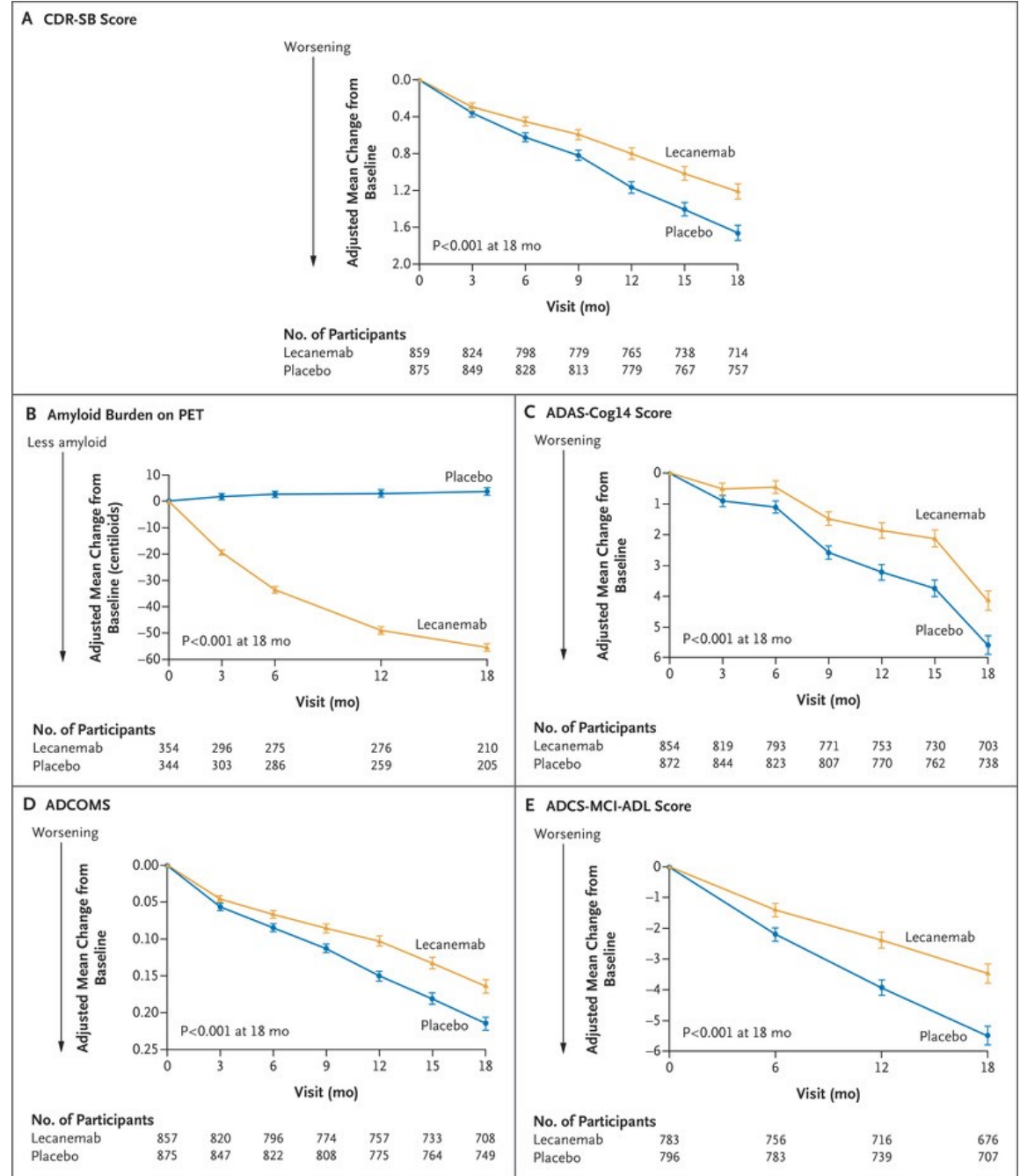
- EMERGE
 - 22% relative reduction in decline in high dose aducanumab (measured by CDR-SB)
 - Absolute reduction was 0.39
- ENGAGE
 - No difference in placebo vs high dose aducanumab (measured by CDR-SB)
- Both studies reduced plaque burden on amyloid PET (48% and 31%)

Lecanumab

- Anti-amyloid monoclonal antibody
- Accelerated approval in Jan 2023, Traditional approval in June 2023
- Approved for:
 - Mild Cognitive Impairment or Mild Dementia
 - Documented amyloid pathology (PET or LP)
 - No increased hemorrhage risk
- IV q2 weeks
- Monitoring
 - APOE ϵ 4 status testing prior to treatment
 - MRI brain prior to treatment (within 1 year), prior to 5th, 7th, and 14th infusions
- SE: 12.6% of ARIA-E, 17.3% ARIA-H

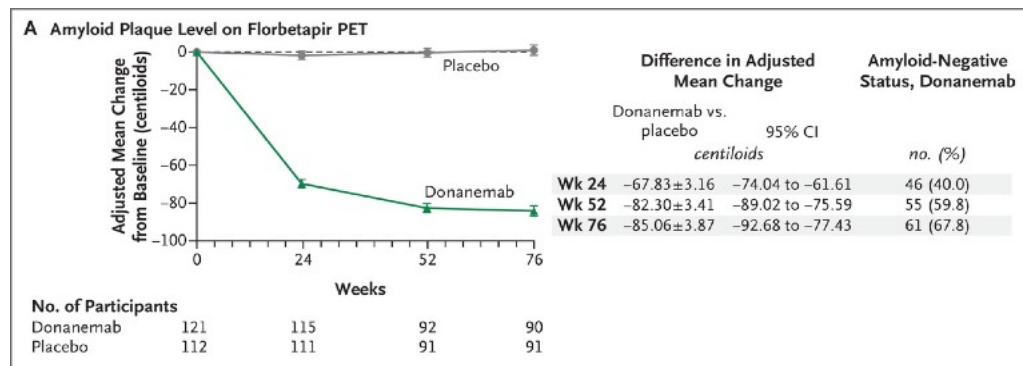
Lecanumab

- Absolute reduction of 0.45 point decline on CDR-SB over 18 months
- Reduction in amyloid plaque burden seen on PET

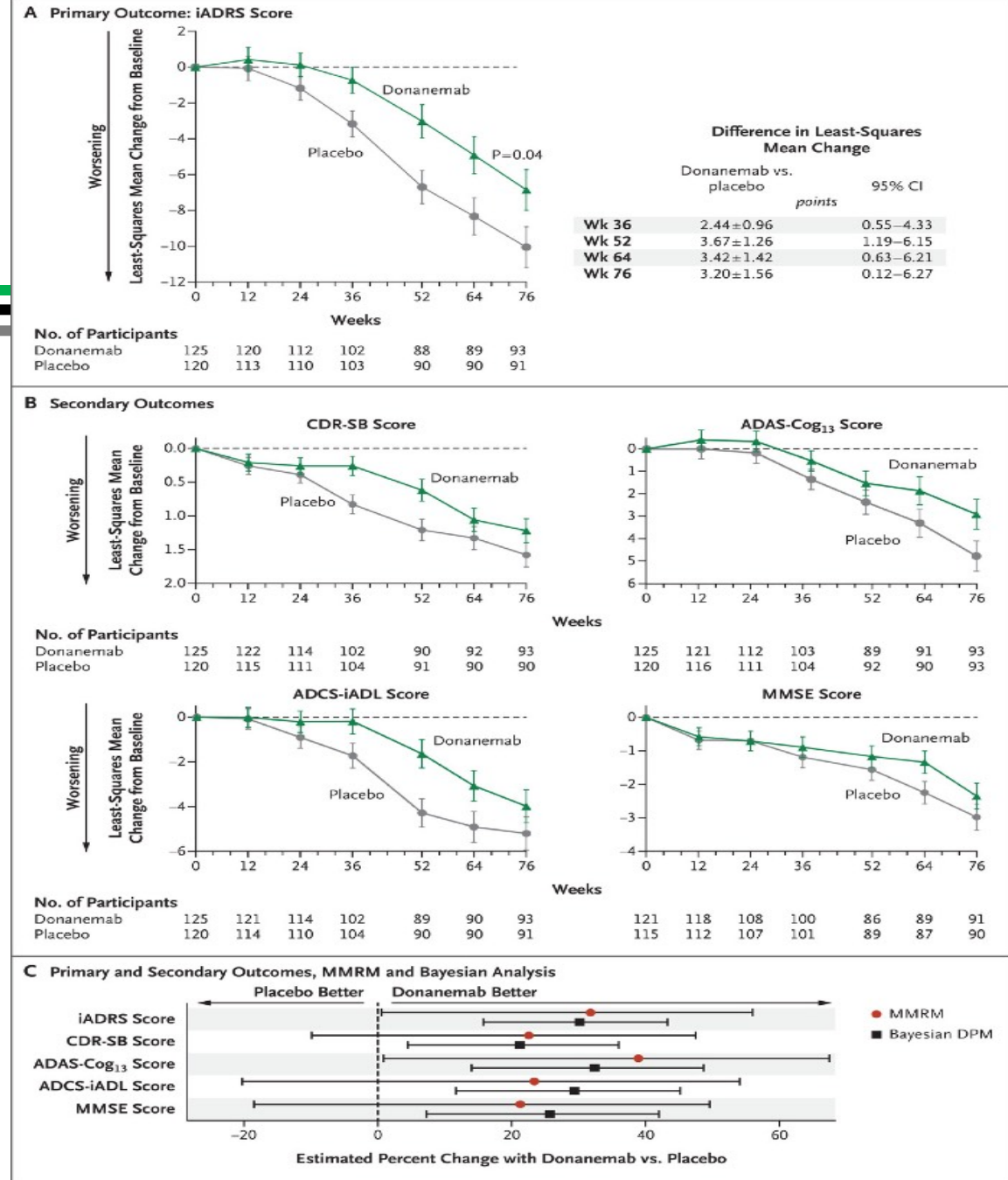


Donanemab

- Not FDA approved (yet?)
- IV q4week
- SE: 38.9% ARIA
- Did not meet aim to reduce progression of AD by half.
- CDR-SB absolute reduction of 0.36 (95% CI -0.83 to 0.12)



MA Mintun et al. N Engl J Med 2021;384:1691-1704.



MA Mintun et al. N Engl J Med 2021;384:1691-1704



The NEW ENGLAND
JOURNAL of MEDICINE

Take Home Points

- Dementia = Functional impairment + Cognitive Impairment
- Rule out other causes: delirium, mood, medications, etc.
- Severity assessment is helpful in deciding treatment
- Fancy testing is not necessary
- Dementia prevention is better than treating (no cure)
- Support is often better than medications
- The risks of the new medications are significant and often > benefits

Resources

- 1) USPSTF. Cognitive Impairment in Older Adults: Screening. U.S. Preventive Services Task Force. Published February 25, 2020. Accessed October 23, 2023 <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/cognitive-impairment-in-older-adults-screening>.
- 2) Borson S, Scanlan JM, Watanabe J, Tu SP, and Lessig M. Improving identification of cognitive impairment in primary care. *Int J Geriatr Psychiatry*. 2006;21(4):349-355.
- 3) Stewart C. Mini-Cog, IQCODE, MoCA and MMSE for the Prediction of Dementia in Primary Care. *Am Fam Physician*. 2022;105(6):590-592.
- 4) Rovner BW, Folstein MF. Mini-mental state exam in clinical practice. *Hosp Pract (Off Ed)* 1987;22:99,103,106,110.
- 5) Ma'u E and Cheung G. Ability of the Maze Navigation Test, Montreal Cognitive Assessment, and Trail Making Tests A & B to predict on-road driving performance in current drivers diagnosed with dementia. *N. Z. Med J*. 2020;133(1513).
- 6) Fasnacht J, et al. Conversion between the Montreal Cognitive Assessment and the Mini-Mental Status Examination. *J Am Geriatr Soc*. 2022;72(1):869-879.
- 7) DCRC. DOMS: Staging Measures & Tools. Dementia Centre for Research Collaboration. Accessed October 23, 2023. <https://dementiaresearch.org.au/doms/staging/#:~:text=Staging%20measures%20are%20used%20to%20assess%20the%20severity%20and%20progression%20of%20dementia.&text=The%20GDS%20is%20a%20brief,and%20its%20progression%20over%20time>.
- 8) Bryant SE, et al. Staging Dementia Using Clinical Dementia Rating Scale Sum of Boxes Scores. *Arch Neurol*. 2008;65(8):1091-1095.
- 9) American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington, VA 2013.
- 10) Anand SS, et al. Reduced Cognitive Assessment Scores Among Individual with Magnetic Resonance Imaging-Detected Vascular Brain Injury. *Stroke*. 2020;51:1158-1165.
- 11) Xu X, et al. Association of Magnetic Resonance Imaging Markers of Cerebrovascular Disease Burden and Cognition. *Stroke*. 2015 Sept; 46:2808-2814.
- 12) Livingston G, et al. Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission. *Lancet*. 2020 Aug; 396(10248): 413-446.
- 13) Herukka SK, et al. Recommendations for cerebrospinal fluid Alzheimer's disease biomarkers in the diagnostic evaluation of mild cognitive impairment. *Alzheimers Dement*. 2016 October; 13(3):285-295.
- 14) Golub JS, Brickman AM and Ciarleglio AJ. Association of Subclinical Hearing Loss with Cognitive Performance. *JAMA Otolaryngol Head Neck Surg*. 2020;145(1):57-67. doi:10.1001/jamaoto.2019.3375.
- 15) Amieva H, Ouvrard C, Meillon C, Rullier L, and Dartigues JF. Death, Depression, Disability and Dementia Association With Self-reported Hearing Problems: A 25-Year Study. *J Gerontol A Biol Sci Med Sci*. 2018 Sep 11;73(10):1383-1389. doi: 10/1093/Gerona/glx250.
- 16) Barnes DE, Byers AL, and Gardner RC. Association of Mild Traumatic Brain Injury with and without Loss of Consciousness with Dementia in US Military Veterans. *JAMA Neurol*. 2018;75(9):1055-1061. Doi:10.1001/jamaneurol.2018.0815.

Resources

- 17) The SPRINT MIND Investigators for the SPRINT Research Group. Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia: A Randomized Clinical Trial. *JAMA*. 2019;321(6):553-561. doi:10.1001/jama.2018.21442
- 18) Peters R, et al. Investigation of antihypertensive class, dementia, and cognitive decline: A meta-analysis. *Neurol*. 2020 Jan 21;94(3):e267-e281. Doi: 10.1212/WNL.0000000000008732.
- 19) Horder H, et al. Midlife cardiovascular fitness and dementia. *Neurol*. 2018;90:e1298-e1305. Doi:10.1212/WNL.0000000000005290.
- 20) Kivimaki M, et al. Physical inactivity, cardiometabolic disease, and risk of dementia: an individual-participant meta-analysis. *BMJ*. 2019;365:l1495.
- 21) Evans IEM, Martyr A, Collins R, Brayne C, and Clare L. Social Isolation and Cognitive Function in Later Life: A Systematic Review and Meta-Analysis. *J Alzheimers Dis*. 2019;70(S1):S119-S144.
- 22) Saito T, Murata C, Saito M, Takeda T and Kondo K. Influence of social relationship domains and their combinations on incident dementia: a prospective cohort study. *J Epidemiol Community Health*. 2018;72:7-12.
- 23) Morris MC, Tangney CC, et al. MIND Diet Associated with Reduced Incidence of Alzheimer's Disease. *Alzheimers Dement*. 2015 Sep;11(9):1007-1014. doi:10.1016/j.jalz.2014.11.009.
- 24) Morris MC, Tangney CC, et al. MIND diet slows cognitive decline with aging. *Alzheimers Dement*. 2015 Sep;11(9):1015-1022. doi:10.1016/j.jalz.2015.04.011.
- 25) Barnes LL, Dhana K, et al. Trial of the MID Diet for Prevention of Cognitive Decline in Older Persons. *N Engl J Med*. 2023;389:602-611. doi:10.1056/NEJMoa2302368.
- 26) Lerner KC. Madison Memory Study: A Randomized, Double-Blinded, Placebo-controlled Trial of Apoaequorin in Community-Dwelling, Older Adults. *Quincy Bioscience*. 2016 Aug 1.
- 27) Campbell NL, Unverzagt F, Lamantia MA, Khan BA and Boustani MA. Risk Factors for the Progression of Mild Cognitive Impairment to Dementia. *Clin Geriatr Med*. 2013 Nov;29(4):873-893. doi:10.1016/j.cger.2013.07.009.
- 28) Plassman B, et al. Prevalence of Cognitive Impairment without Dementia in the United States. *Ann Intern Med*. 2008 Mar 18;148(6):427-434. doi:10.7326/0003-4819-148-6-200803180-00005.
- 29) Doody RS, Ferris SH, et al. Donepezil treatment of patients with MCI: a 48-week randomized, placebo-controlled trial. *Neurol*. 2009 May 5;72(18):1555-61.
- 30) Feldman HH, et al. Effect of rivastigmine on delay to diagnosis of Alzheimer's disease from mild cognitive impairment: the InDDEX study. *Lancet Neurol*. 2001 Jun;6(6):501-12
- 31) DeKosky ST, et al. Ginkgo Biloba for prevention of dementia: a randomized controlled trial. *JAMA*. 2008 Nov 19;300(19):2253-62.
- 32) Vellas B, et al. Long-term use of standardised Ginkgo biloba extract for the prevention of Alzheimer's disease (GuigAge): a randomised placebo-controlled trial. *Lancet Neurol*. 2012 Oct;11(10):851-9.
- 33) Bohlken J, Peters O, and Kostev K. Association Between Ginkgo Biloba Extract Prescriptions and Dementia Incidence in Outpatients with Mild Cognitive Impairment in Germany: A Retrospective Cohort Study. *J Alzheimers Dis*. 2022;86(2):703-709. doi:10.3233/JAD-215348.
- 34) Petersen RC, et al. Vitamin E and donepezil for the treatment of mild cognitive impairment. *N Engl J Med*. 2005 Jun 9;352(23):2379-88.
- 35) Farina N, Llewellyn D, Isaac MGEKN, and Tabet N. Vitamin E for Alzheimer's dementia and mild cognitive impairment. *Cochrane Database Syst Rev*. 2017 Apr 18;4(4):CD002854.
- 36) Andrieu S, Guyonnet S, et al. Effect of long-term omega 3 polyunsaturated fatty acid supplementation with or without multidomain intervention on cognitive function in elderly adults with memory complaints (MAPT): a randomised, placebo-controlled trial. *Lancet Neurol*. 2017 May;16(5):377-389. doi: 10.1016/S1474-4422(17)30040-6. Epub 201

Resources

- 36) McCleery J, Abraham RP, et al. Vitamin and mineral supplementation for preventing dementia or delaying cognitive decline in people with mild cognitive impairment. *Cochrane Database Syst Rev*. 2018 Nov 1;11(11):CD011905. doi: 10.1002/14651858.CD011905.pub2. PMID: 30383288; PMCID: PMC6378925.
- 37) Epperly T, Dunay MA, Boice JL. Alzheimer Disease: Pharmacologic and Nonpharmacologic Therapies for Cognitive and Functional Symptoms. *Am Fam Physician*. 2017 Jun 15;95(12):771-778. PMID: 28671413.
- 38) Birks J, Harvey RJ. Donepezil for dementia due to Alzheimer's disease. *Cochrane Database Syst Rev*. 2006 Jan 25;(1):CD001190. doi: 10.1002/14651858.CD001190.pub2. Update in: *Cochrane Database Syst Rev*. 2018 Jun 18;6:CD001190. PMID: 16437430.
- 39) Press D and Buss SS. Treatment of Alzheimer disease. In: Wilterdink J ed. *UpToDate*. UpToDate; 2021. Accessed October 23, 2023. <https://www.uptodate.com/contents/treatment-of-alzheimer-disease>
- 40) Lexicomp. Donepezil: Drug information. *UpToDate*. UpToDate; Accessed October 23, 2023. <https://www.uptodate.com/contents/donepezil-drug-information>.
- 41) Lexicomp. Galantamine: Drug information. *UpToDate*. UpToDate; Accessed October 23, 2023. <https://www.uptodate.com/contents/galantamine-drug-information>
- 42) Lexicomp. Aducanumab: Drug information. *UpToDate*. UpToDate; Accessed October 23, 2023. <https://www.uptodate.com/contents/aducanumab-drug-information>.
- 43) van Dyck CH, Swanson CJ, et al. Lecanemab in Early Alzheimer's Disease. *N Engl J Med*. 2023 Jan 5;388(1):9-21. doi: 10.1056/NEJMoa2212948. Epub 2022 Nov 29. PMID: 36449413.