Approach to Memory Loss: Screening

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Douglas W. Scharre, MD - Disclosures

Research Support

1. **National Institutes of Health – NIA**
2. **Alzheimer's Disease Cooperative Study**

Objective:

1) Review definitions of Mild Cognitive Impairment and dementia

2) Review cognitive assessment and screening instruments for Mild Cognitive Impairment and early dementia

Speakers Bureau

Forest

Clinical Trials

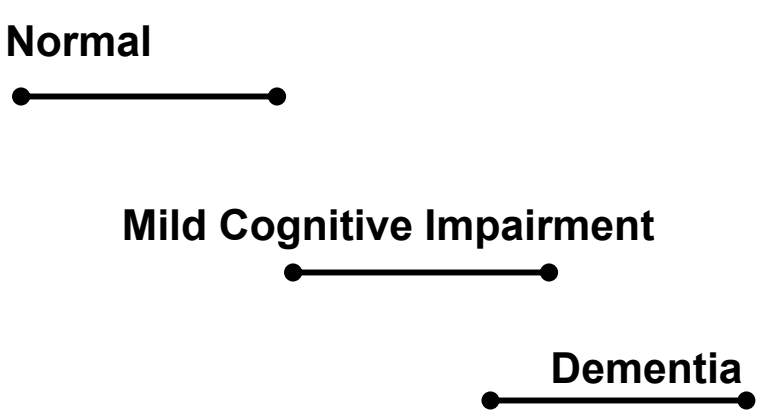
Pfizer, Janssen Alzheimer Immunotherapy, Bristol Meyers Squibb, Phylogeny

Consultant

Lilly

I own no stocks or equity in any pharmaceutical company

Definition of Dementia and Mild Cognitive Impairment (MCI)



Dementia Definition

- Syndrome of acquired persistent intellectual impairment
- Persistent deficits in at least two of the following:

  memory
  language
  visuospatial
  personality or emotional state
  cognition

- Resulting in impairment in Activities of Daily Living (ADL)

Mild Cognitive Impairment (MCI) Definition

- Memory complaint usually corroborated by an informant
- Objective memory impairment for age - that represents a change in function for the person
- Essentially preserved general cognitive function
- Largely intact functional activities
- Not demented

Petersen J Int Med 2004;256;183-194

Cognitive Assessment and Screening

Cognitive Screening

- We can use cognitive assessment and screening to help identify MCI and early dementia cases
- CSF Biomarkers and neuroimaging are too expensive or invasive for screening but could be used for high risk patients or those demonstrating cognitive impairments
- Cognitive biomarkers with good specificity and sensitivity need to be validated

Importance of Early Diagnosis of MCI and Dementia

- Amyloid plaques possibly start 15 to 20 years before clinical symptoms of AD
- Over 100 million worldwide projected to have AD by 2050
- Current AD patients progress slower if medications are started earlier
- Disease modifying agents are coming
- Preventing or delaying AD could save billions of dollars and lead to improved quality of life for patients and families

Importance of Early Diagnosis of MCI and Dementia

- May lead to earlier treatments for dementia
- May reduce potential poor judgment with finances, driving, medication use, symptom reporting of other chronic conditions
- May lead to increased supervision of individuals so they can more adequately perform their activities of daily living
- May improve treatment compliance rates of other chronic medical conditions
- May reduce medication errors

Importance of Early Diagnosis of MCI and Dementia

- May decrease hospital admissions or emergency room visits
- May improve quality of life of patient and caregiver
- May reduce burden and chronic stress effects on caregivers
- May reduce financial burden on patients, families, and the health care system

Barriers to Early Diagnosis of MCI and Dementia

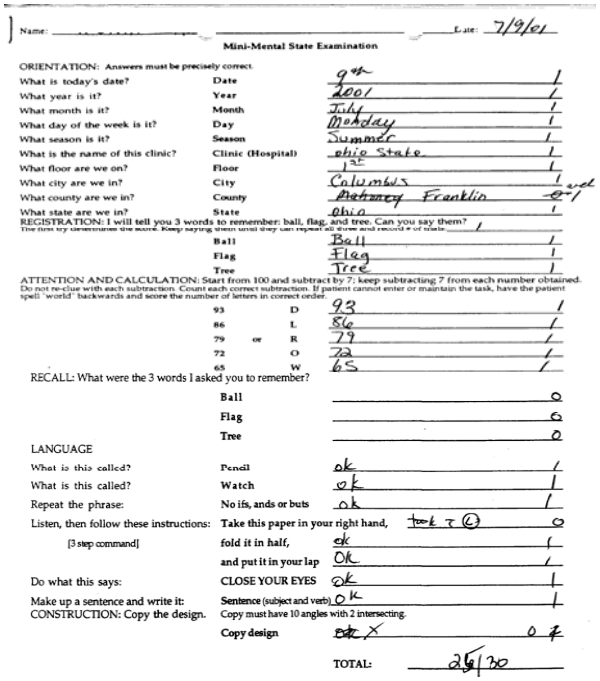
- Patients with MCI and early dementia have impaired insight
- First present to the doctor an average of 3.5 years after cognitive symptoms start
- Physicians may not notice subtle cognitive deficits in routine office visits
- Little reimbursement for cognitive screens
- Often too much time or personnel resources required to administer testing

Barker WW et al. Alzheimer Dis Assoc Disord 2005;19:1-7

Examples of Brief Cognitive Assessment/Screening Tests

- MMSE
- Mini-Cog
- AD8
- Montreal Cognitive Assessment (MOCA)
- St. Louis University Mental Status Examination (SLUMS)
- Self-Administered Gerocognitive Examination (SAGE)

MMSE



Name: _____ Date: 7/9/01

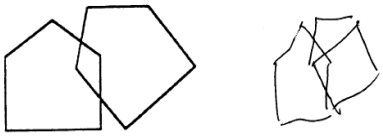
Mini-Mental State Examination

ORIENTATION: Answers must be precisely correct.			
What is today's date?	Date	9th	/1
What year is it?	Year	2001	/1
What month is it?	Month	July	/1
What day of the week is it?	Day	Monday	/1
What season is it?	Season	Summer	/1
What is the name of this clinic?	Clinic (Hospital)	ohio State	/1
What floor are we on?	Floor	1st	/1
What city are we in?	City	Columbus	/1
What county are we in?	County	~~Delaney~~ Franklin	~~0~~/1
What state are we in?	State	Ohio	/1
REGISTRATION: I will tell you 3 words to remember: ball, flag, and tree. Can you say them? The first try determines the score. Keep saying them until they can repeat all three and record # of trials.			/1
	Ball	Ball	/1
	Flag	Flag	/1
	Tree	Tree	/1
ATTENTION AND CALCULATION: Start from 100 and subtract by 7; keep subtracting 7 from each number obtained. Do not re-clue with each subtraction. Count each correct subtraction. If patient cannot enter or maintain the task, have the patient spell "world" backwards and score the number of letters in correct order.			
93	D	93	/1
86	L	86	/1
79 or	R	79	/1
72	O	72	/1
65	W	65	/1
RECALL: What were the 3 words I asked you to remember?			
	Ball		0
	Flag		0
	Tree		0
LANGUAGE			
What is this called?	Pencil	ok	/1
What is this called?	Watch	ok	/1
Repeat the phrase:	No ifs, ands or buts	ok	/1
Listen, then follow these instructions:	Take this paper in your right hand,	took it	0
[3 step command]	fold it in half,	ok	/1
	and put it in your lap	Ok	/1
Do what this says:	CLOSE YOUR EYES	ok	/1
Make up a sentence and write it:	Sentence (subject and verb)	OK	/1
CONSTRUCTION: Copy the design.	Copy must have 10 angles with 2 intersecting.		
	Copy design	~~0~~ X	0/1
	TOTAL:	25/30	

Folstein et al. J Psychiat Res 1975;12: 189-98

MMSE CLOSE YOUR EYES

I LIKE TO PLAY GOLF



Folstein et al. J Psychiat Res 1975;12: 189-98

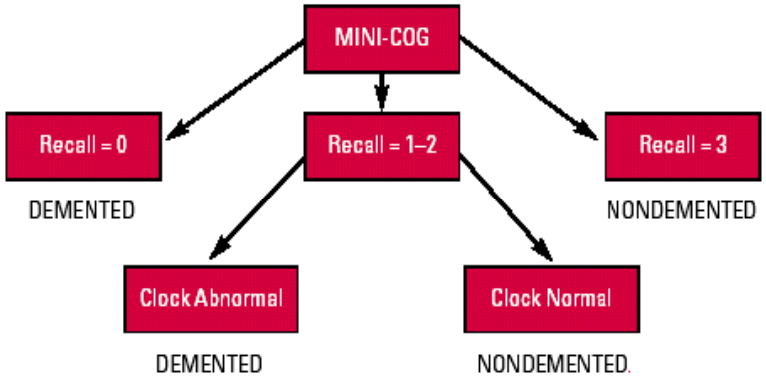
MMSE

- **Score: 0 (worst) - 30 (best)**
- **Tests orientation, attention, mental control, calculations, delayed memory (no clueing), language, and constructional praxis**
- **Easy to use, well known**
- **Not great for frontal or executive functions**
- **Sensitivity 78% and specificity 84% for dementia with a cutoff of 26/30**
- **Takes 7 to 10 minutes; needs examiner**
- **PAR bought rights – costs $1.23 per use**

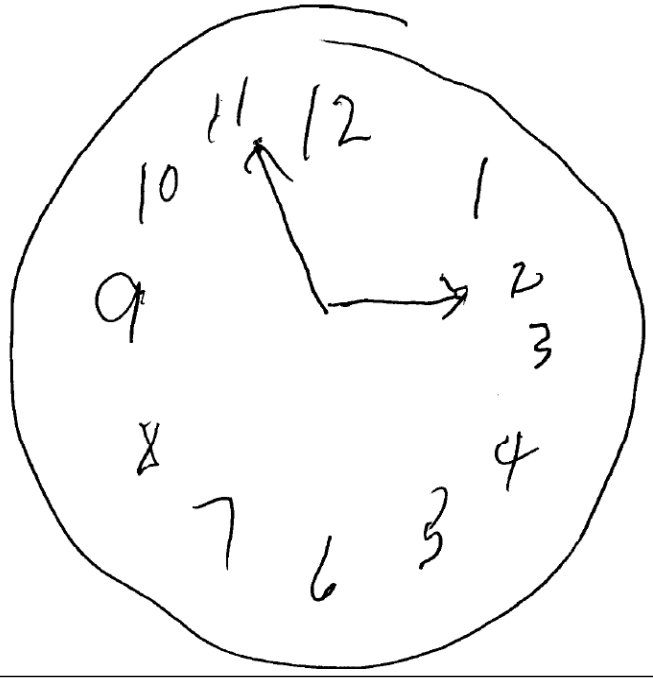
Folstein et al. J Psychiat Res 1975;12:189-98
Feher et al. Arch Neurol 1992;49:87-92

Mini-Cog

Figure 1. The Mini-Cog scoring algorithm. The Mini-Cog uses a three-item recall test for memory and the intuitive clock-drawing test. The latter serves as an "informative distractor," helping to clarify scores when the memory recall score is intermediate.



Borson S et al. Int J Geriatr Psychiatry 2000;15:1021-1027

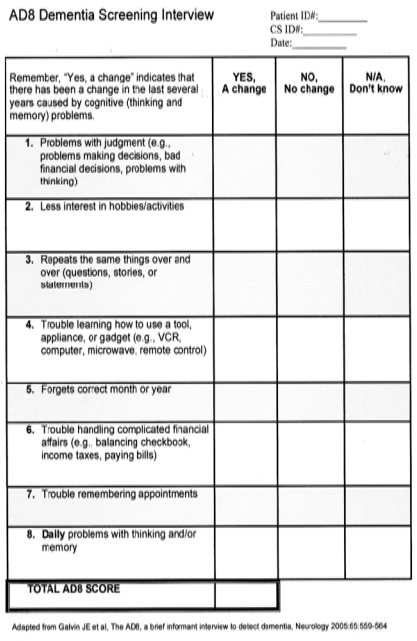


Mini-Cog

- 3-item recall and clock drawing
- Easy to use
- Limited in evaluating other cognitive domains
- Sensitivity 76% and specificity of 89% for dementia
- Score not influenced by language or education
- Takes 3 minutes; needs examiner

Borson S et al. Int J Geriatr Psychiatry 2000;15:1021-1027
Borson S et al. JAGS 2003;51:1451-1454

AD8



AD8 Dementia Screening Interview

Patient ID#:_____
CS ID#:_____
Date:_____

Remember, "Yes, a change" indicates that there has been a change in the last several years caused by cognitive (thinking and memory) problems.	YES, A change	NO, No change	N/A, Don't know
1. Problems with judgment (e.g., problems making decisions, bad financial decisions, problems with thinking)			
2. Less interest in hobbies/activities			
3. Repeats the same things over and over (questions, stories, or statements)			
4. Trouble learning how to use a tool, appliance, or gadget (e.g., VCR, computer, microwave, remote control)			
5. Forgets correct month or year			
6. Trouble handling complicated financial affairs (e.g., balancing checkbook, income taxes, paying bills)			
7. Trouble remembering appointments			
8. **Daily** problems with thinking and/or memory			
TOTAL AD8 SCORE			

Adapted from Galvin JE et al, The AD8, a brief informant interview to detect dementia, Neurology 2005;65:559-564

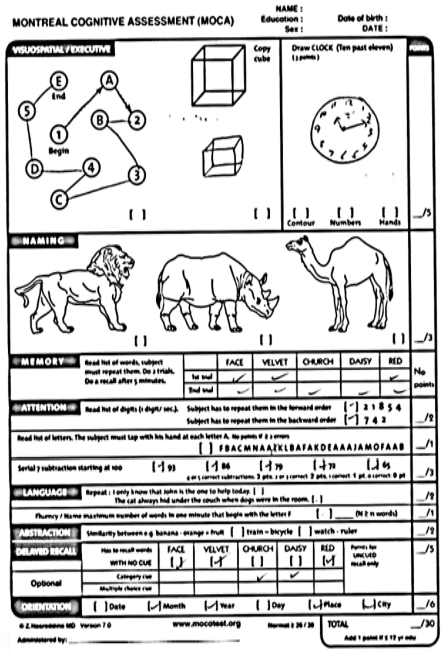
Galvin et al. Neurology 2006;67:1942-1948

AD8

- Score: 0 (best) - 8 (worst)
- Informant rates changes in the patient's judgment, interests, memory, functioning, and orientation
- Easy to use
- Does not measure patient cognition directly
- Sensitivity 84% and specificity 80% for dementia with a cutoff of 2 or greater
- Takes 3 minutes; needs examiner and informant

Galvin et al. Neurology 2006;67:1942-1948

MOCA



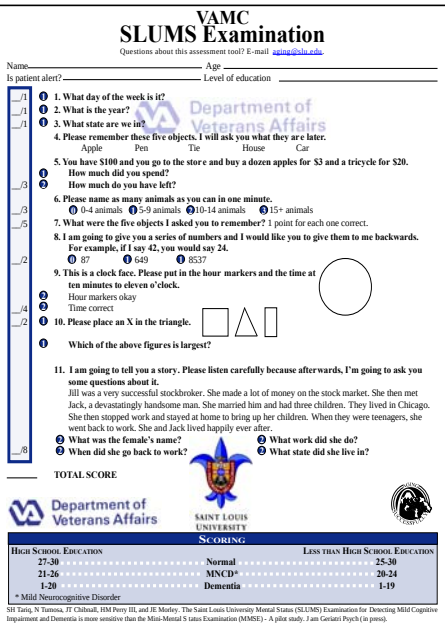
Nasreddine et al. J Am Geriatr Soc 2005;53:695-699

Montreal Cognitive Assessment (MOCA)

- Score: 0 (worst) - 30 (best)
- Tests orientation, memory, clock drawing, constructions, verbal fluency, naming, repetition, attention, abstraction, calculations, executive (trails B)
- Not easy to give in primary care office
- Sensitivity 100% and specificity 87% for dementia vs normal controls with a cutoff of 25/30
- Cannot distinguish between MCI and dementia
- Takes 10-13 minutes; needs examiner

Nasreddine et al. J Am Geriatr Soc 2005;53:695-699

St. Louis University Mental Status (SLUMS)



VAMC
SLUMS Examination

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

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

__/1 1. What day of the week is it?
__/1 2. What is the year?
__/1 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.
How much did you spend?
__/3 How much do you have left?
6. Please name as many animals as you can in one minute.
__/3 0-4 animals 1 5-9 animals 2 10-14 animals 3 15+ animals
__/5 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.
__/2 0 87 0 649 0 8537
9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.
1 Hour markers okay
__/4 1 Time correct
__/2 1 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.
__/8 1 What was the female's name? 1 What work did she do?
1 When did she go back to work? 1 What state did she live in?

_____ TOTAL SCORE

Department of Veterans Affairs
SAINT LOUIS UNIVERSITY

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 S tatus Examination (MMSE) - A pilot study. J am Geriatri Psych (in press).

St. Louis University Mental Status (SLUMS)

- Score: 0 (worst) - 30 (best)
- Tests orientation, memory, calculations, verbal fluency, mental control, clock drawing, visuospatial, and comprehension skills
- Not easy to give in primary care office
- SLUMS and MMSE had comparable sensitivities and specificities for dementia but improved receiver operator curves (ROC) for mild cognitive impairment.
- Takes 10-13 minutes; needs examiner

Tariq et al. Am J Geriatr Psychiatry 2006;143:900-910

Self-Administered Gerocognitive Exam (SAGE)

sagetest.osu.edu

- Cognitive assessment instrument
- Brief: ≈ 10-15 minutes with pen and paper
- Unique: Self-administered
- Not requiring office personnel time or special equipment
- Designed to detect cognitive impairment including MCI and early dementia

SAGE
Page 1

Self-Administered Gerocognitive Examination - SAGE© Form 1

How Well Are You Thinking?

Please complete this form in ink **without** the assistance of others.

Name_____ Date of Birth ___/___/____

How far did you get in school? I am a Man Woman

I am Asian, Black, Hispanic, White, Other_____

Have you had any problems with memory or thinking? Yes_____ Only Occasionally_____ No_____

Have you had any blood relatives that have had problems with memory or thinking? Yes_____ No_____

Do you have balance problems? Yes_____ No_____

If yes, do you know the cause? Yes (specify reason) No

Have you ever had a major stroke? Yes_____ No_____ A mirror or mini-stroke? Yes_____ No_____

Do you currently feel sad or depressed? Yes_____ Only Occasionally_____ No_____

Have you had any change in your personality? Yes (specify changes) No_____

Do you have more difficulties doing everyday activities due to thinking problems? Yes_____ No_____

1. What is today's date? (from memory - no cheating!) Month_____ Date_____ Year_____

2. Name the following pictures (don't worry about spelling):

_____ _____

SAGE© 2007 The Ohio State University, D. Scharre MD, version 4.01 www.sagetest.osu.edu

Page 1 of 4 CONTINUE NEXT PAGE

Scharre et al. Alzheimer Dis Assoc Disord 2010 at sagetest.osu.edu

SAGE
Page 2

Self-Administered Gerocognitive Examination - SAGE© Form 1

Answer these questions:

3. How are a watch and a ruler similar? Write down how they are alike. They both are ... what?

_____

4. How many nickels are in 60 cents? _____

5. You are buying $12.45 of groceries. How much change would you receive back from a $20 bill?

_____

6. Memory Test (memorize these instructions). Do later only after completing this entire test:

At the bottom of the next test page: Write "I am done" on the blank line provided.

7. Copy this picture:

8. Drawing test

Draw a large face of a clock and place in the numbers.

Position the hands for 5 minutes after 11 o'clock.

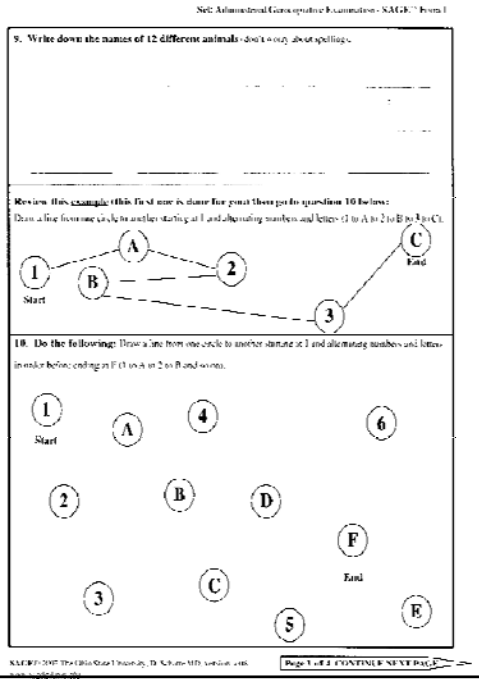
On your clock, label "L" for the long hand and "S" for the short hand.

SAGE© 2007 The Ohio State University, D. Scharre MD, version 4.01

Page 2 of 4 CONTINUE NEXT PAGE

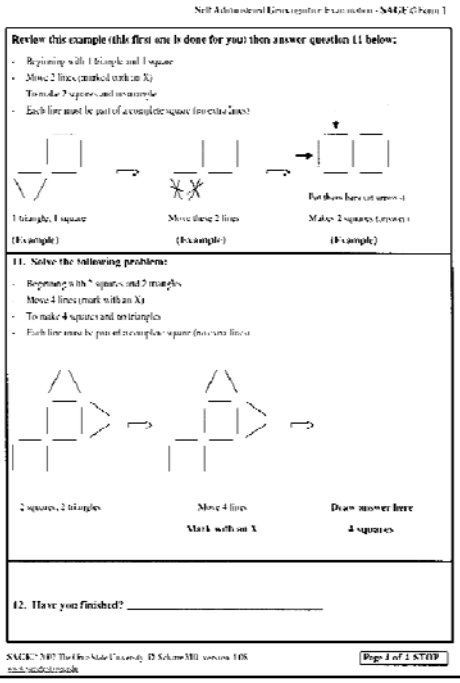
Scharre et al. Alzheimer Dis Assoc Disord 2010 at sagetest.osu.edu

SAGE
Page 3



Scharre et al. Alzheimer Dis Assoc Disord 2010 at sagetest.osu.edu

SAGE
Page 4



Scharre et al. Alzheimer Dis Assoc Disord 2010 at sagetest.osu.edu

SAGE

- **SAGE download: sagetest.osu.edu**
- **Score range: 0-22**
- **Orientation: month, date, year (4 points)**
- **Language: picture naming (2 points) and verbal fluency (2 points)**
- **Calculations: (2 points)**
- **Memory: (2 points)**
- **Abstraction: (2 points)**
- **Executive: modified Trails B (2 points) and problem solving task (2 points)**
- **Visuospatial: copying 3-dimentional constructions (2 points) and clock draw (2 points)**

SAGE and MMSE

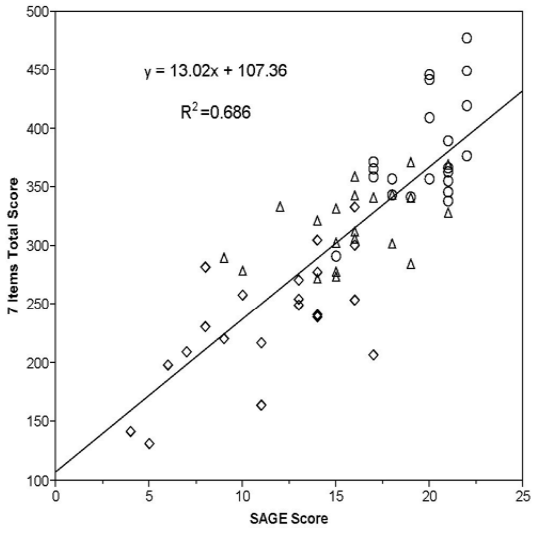
Spearman rank correlations to Specific Neuropsychological Tests

N = 63	HVLT Learning	Retention	WCSTPE	FAS	Boston	Let-Num	Blk-Des	Sum 7
SAGE	0.66	0.55	0.51	0.52	0.63	0.57	0.37	**0.84**
MMSE	0.67	0.61	0.35	0.39	0.52	0.68	0.33	**0.76**

HVLT: Hopkins Verbal Learning Test; WCSTPE: Wisconsin Card Sort Test Perseverative Errors; Let-Num: Letter-Number subtest of WAIS III; Blk-Des: Block Design subtest of the WAIS III; Sum 7: Total summed score of the 7 neuropsychological tests

Scharre et al. Alzheimer Dis Assoc Disord 2010;24:64-71 at sagetest.osu.edu

SAGE: Validity Against Neuropsychologic Tests



R=0 .84

Scharre et al. Alzheimer Dis Assoc Disord 2010;24:64-71 at sagetest.osu.edu

Sum 7, SAGE and MMSE scores: Normal, MCI, and Dementia

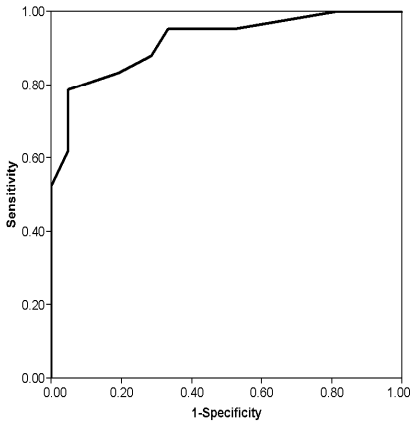
		Normal (n=21)	MCI (n=21)	Dementia (n=21)
Sum 7	Mean ± SD (Range)	**380** ± 45 (478 – 292)	**318** ± 31 (371- 272)	**238** ± 52 (333 – 132)
SAGE max = 22	Mean ± SD (Range)	**19.8** ± 2.0 (22-15)	**16.0** ± 3.2 (21-9)	**11.4** ± 3.9 (17-4)
MMSE max = 30	Mean ± SD (Range)	**28.7** ± 1.1 (30-26)	**27.7** ± 2.2 (30-23)	**22.1** ± 3.5 (28-16)

Sum 7: Total summed score of the 7 neuropsychological tests

Scharre et al. Alzheimer Dis Assoc Disord 2010 at sagetest.osu.edu

ROC for SAGE: Differentiating Normal vs Cognitive Impaired

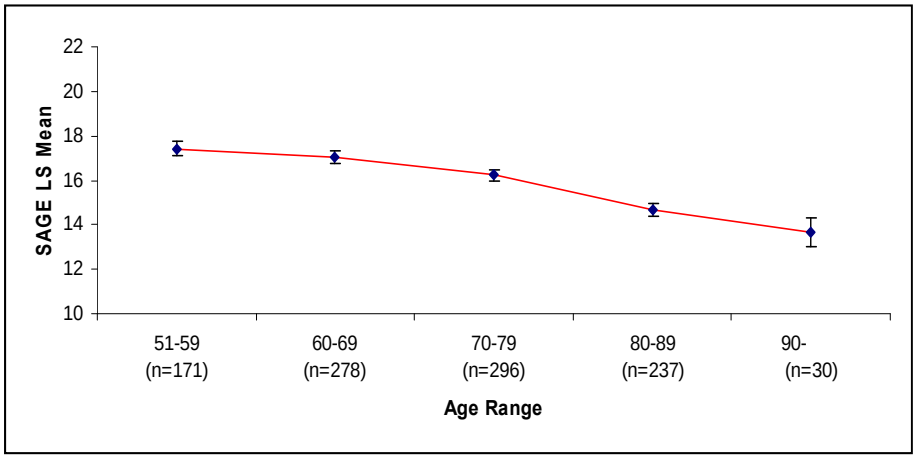
Area under curve for SAGE = 0.92 (0.80 for MMSE)



Scharre et al. Alzheimer Dis Assoc Disord 2010;24:64-71 sagetest.osu.edu

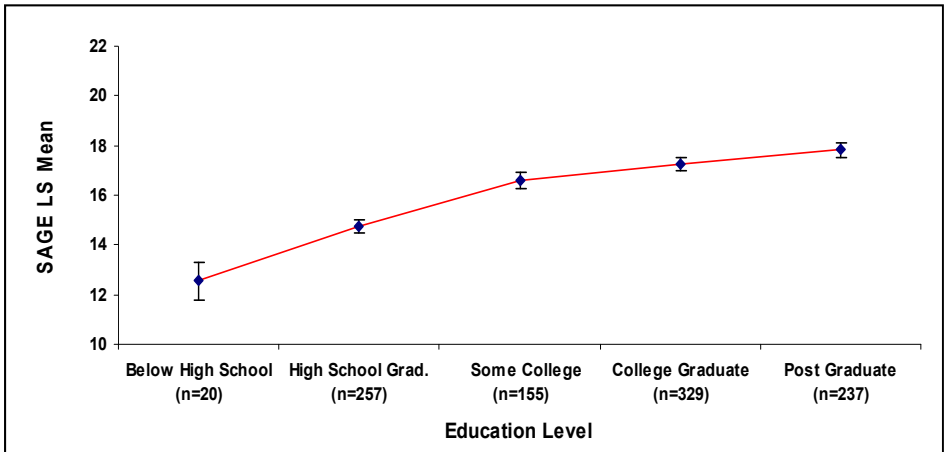
SAGE specificity is 95% (90% for MMSE) and sensitivity is 79% (71% for MMSE)

Age Effect on SAGE Score



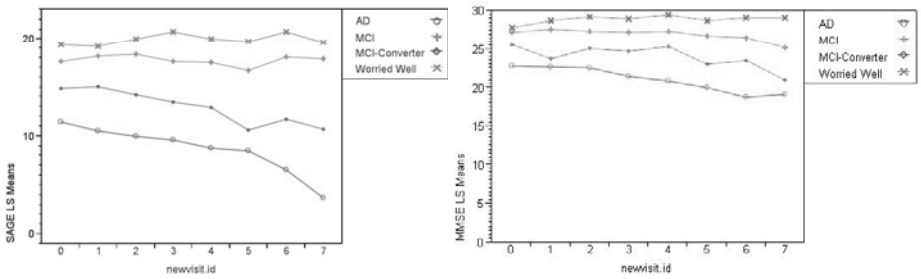
❖**One point should be added to those age ≥ 80.**

Education Effect on SAGE Score



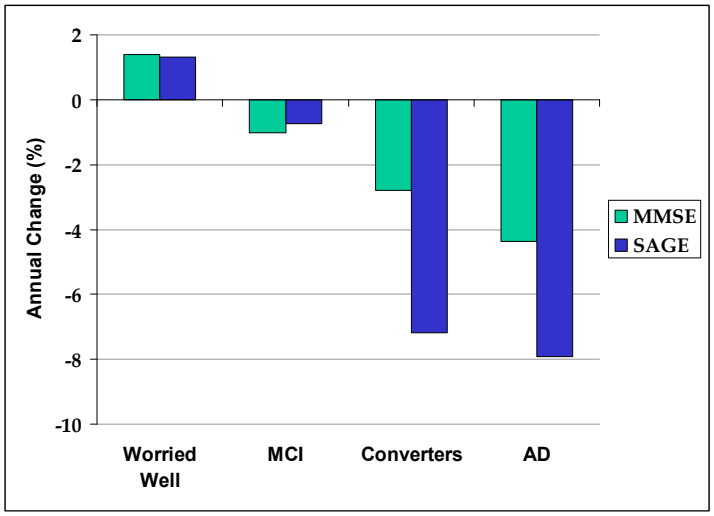
❖SAGE test may be hard to interpret in those with under 12th grade education.
❖One point should be added for those with 12 years or less of education

SAGE /MMSE Score Changes over time in Worried Well /MCI /Converter /AD



N = 186

Annual Percentage Change of SAGE (max=22) /MMSE (max=30) in Worried Well /MCI /Converter /AD



SAGE Scores

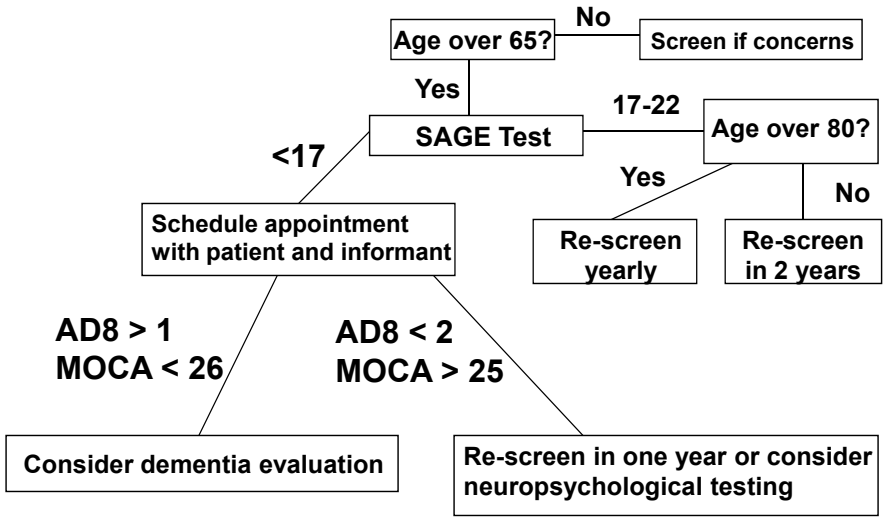
17-22: Very likely to be normal: no further evaluation

15-16: Likely to have MCI: staged screening evaluation recommended

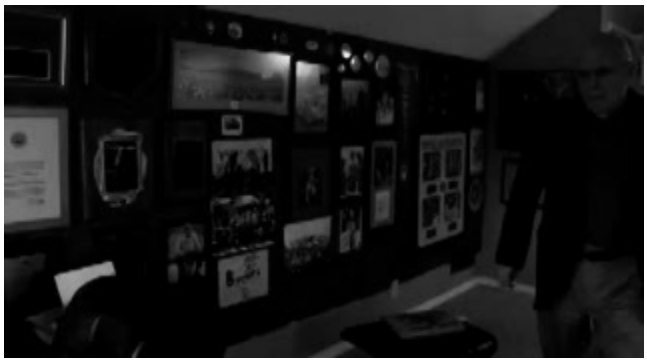
0-14: Likely to have a dementia condition: staged screening evaluation recommended

Staged Screening

Staged Screening Approach



Scharre et al. Alzheimer Dis Assoc Disord 2010;24:64-71 at sagetest.osu.edu; Galvin et al. Neurology 2006;67:1942-1948; Nasreddine et al. J Am Geriatr Soc 2005;53:695-699



Summary

- Mild Cognitive Impairment can be detected and differentiated from dementia
- Mental status examinations help to identify potential etiologies
- Cognitive assessment and screening instruments can be used to identify early cognitive problems
- Cognitive screening with a staged approach should be done

Approach to the Patient with Memory Loss: An Update

Maria Kataki, MD, PhD
Assistant Professor of Neurology
Division of Cognitive Neurology
The Ohio State University Wexner Medical Center

Overview

- Challenges in the knowledge
- Updated diagnostic criteria for preclinical stages of Alzheimer's Disease
- Updated diagnostic criteria for Mild Cognitive Impairment
- Updated diagnostic criteria for Alzheimer's Disease
- Standard of care recommendations for evaluation and treatment of Alzheimer's disease.

Historical Data…

On a Peculiar Disease of the Cerebral Cortex;
A. Alzheimer (1907)

A woman, 51 years old, showed jealousy towards her husband… Soon, rapidly increasing loss of memory could be noticed… At times she would think that someone wanted to kill her …

She was totally disoriented to time and place …

Periodically, she was totally delirious,…and seemed to have auditory hallucinations.…

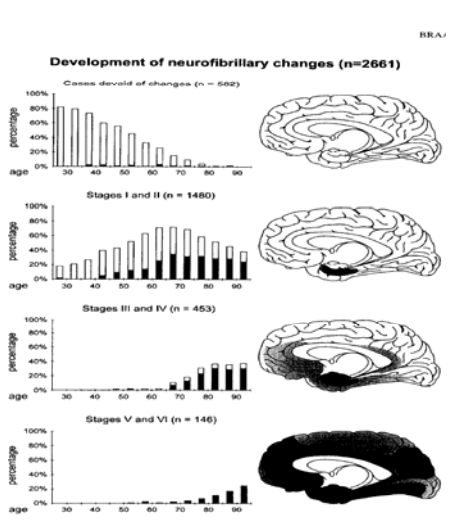
When reading, she went from one line into another, reading the letters or reading with senseless emphasis …

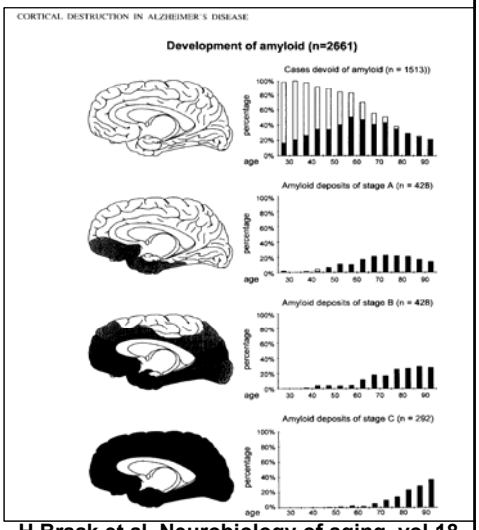
When talking she frequently used perplexing phrases and some paraphasic expressions (milk-pourer instead of cup) …

She seemed no longer to understand the use of some objects …

The generalized dementia progressed … After 4 1/2 years of the disease, death occurred.

Frequency of Stages of Alzheimer-Related Lesions in Different Age Categories





H Braak et al. Neurobiology of aging, vol 18, No 4, pp 351-357, 1997

Revision of clinical criteria

- Lack of knowledge of distinguishing features of other dementing conditions
- Dementia with Lewy Bodies
- Vascular dementia
- Behavioral variant frontotemporal dementia
- Primary progressive aphasia

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Revision of clinical criteria

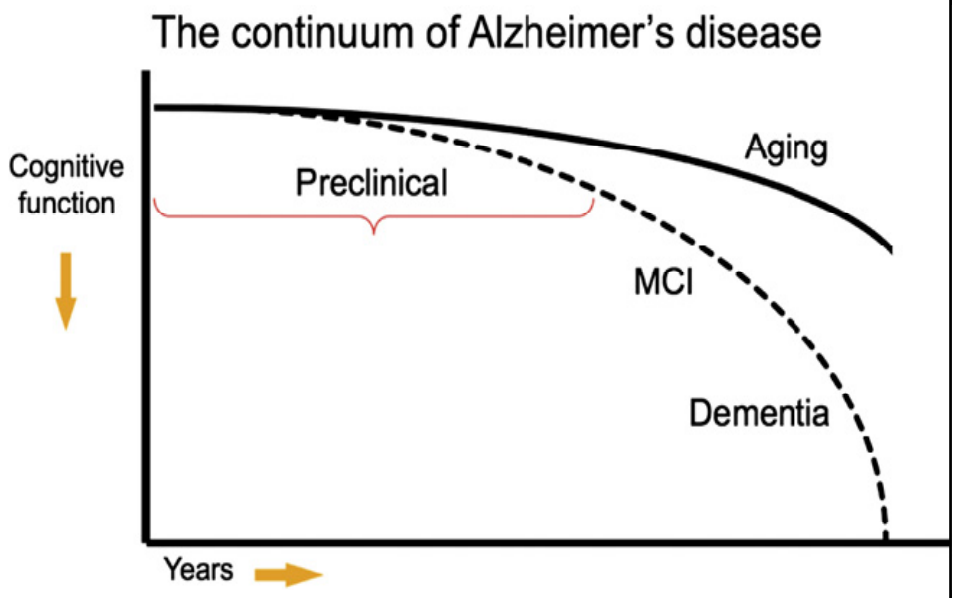
- No inclusion of results of Magnetic Resonance Imaging, Positron Emission Tomography (PET), and cerebrospinal fluid assays (CSF) (biomarkers)
- The implication that memory impairment is always the primary cognitive deficit in all patients with AD dementia
- Several non amnestic presentations of the pathopsysiological process

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Revision of clinical criteria

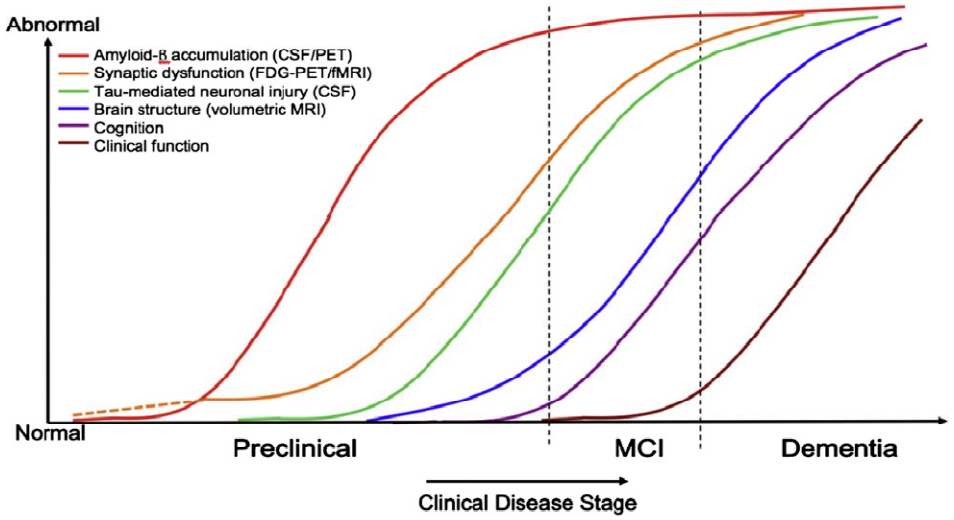
- **Proposed age cutoffs for the diagnosis of AD dementia.**
- **AD dementia in those aged <40 and >90 years is part of that same spectrum.**
- **Extreme heterogeneity of the "Possible" AD dementia category including a group of patients that would now be diagnosed as "Mild Cognitive Impairment"**

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

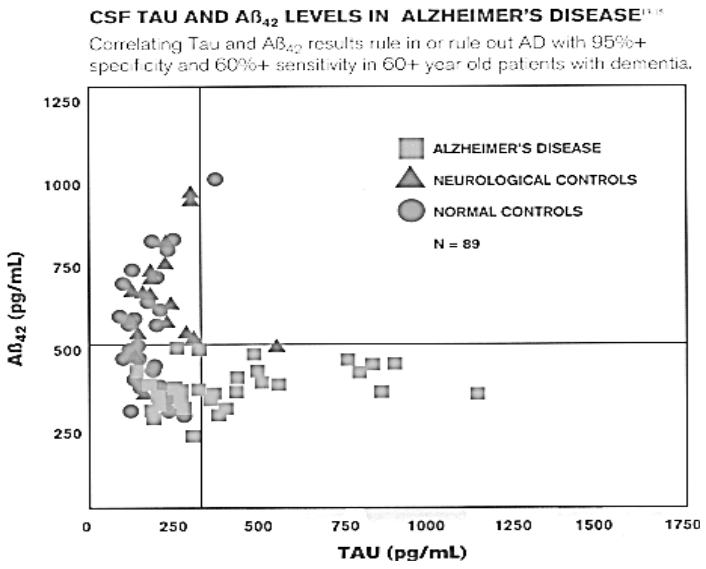


Toward defining the preclinical stages of Alzheimer's disease: Reisa A. Sperling et al. Alzheimer's & Dementia (2011) 1-13

Hypothetical model of dynamic Biomarkers of the AD

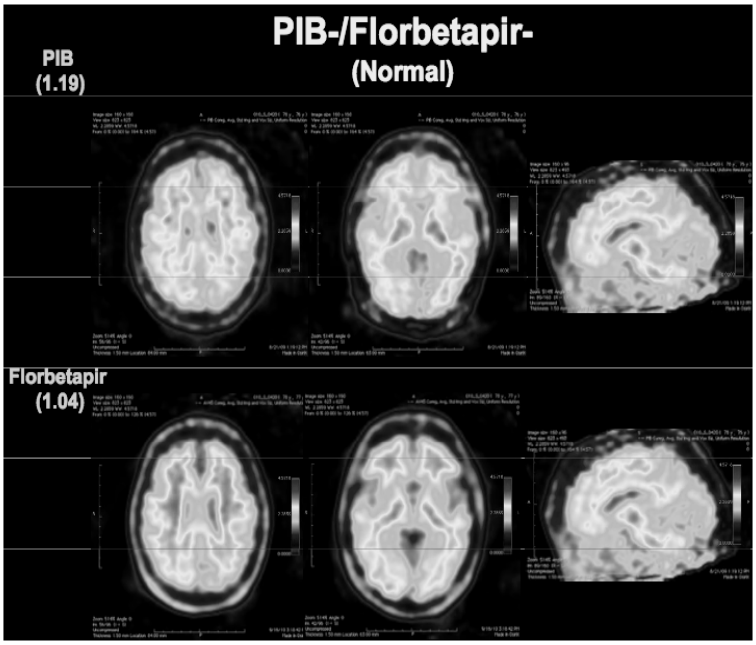


Toward defining the preclinical stages of Alzheimer's disease:Reisa A. Sperling et al. Alzheimer's & Dementia (2011) 1-13

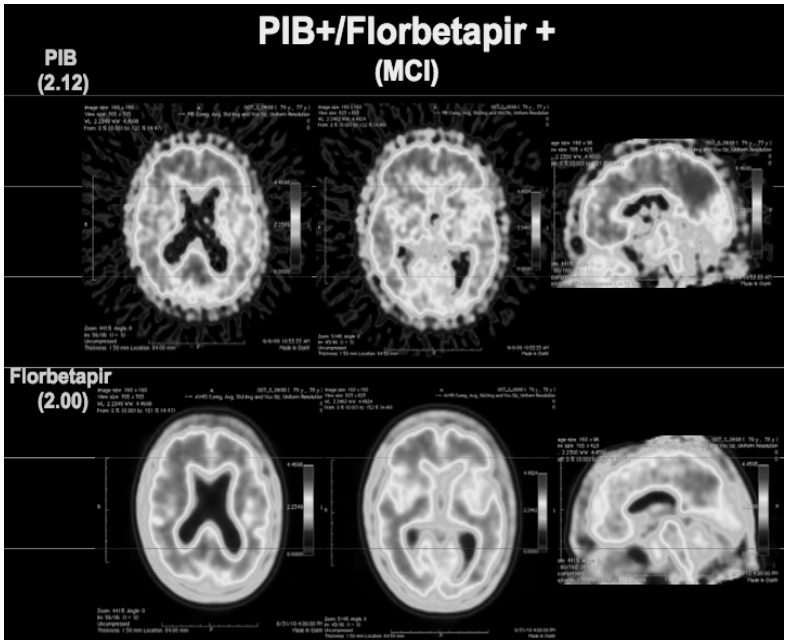


Elevated CSF tau and low Aβ42 is 95% specific and 60% sensitive for AD

Motter et al. Ann Neurol 1995;38:643-48

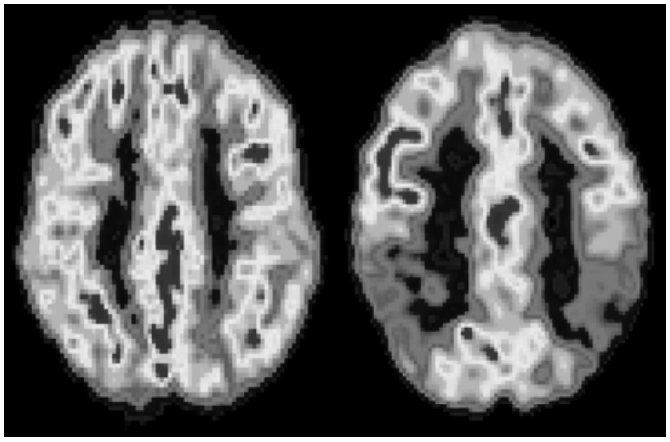


Jagust W. et al., ADNI-GO PET Core Team, 2011



Jagust W. et al., ADNI-GO PET Core Team, 2011

FDG PET Neuroimaging



Normal Brain **AD Brain**

PET shows hypometabolism in bilateral parietal, temporal, and posterior cingulate cortex in AD subjects and in those who are asymptomatic but at increased risk for AD (those with Apo E ε4)

Image provided courtesy of M. Mega, MD, PhD, Department of Neurology, UCLA School of Medicine.

Staging categories for preclinical AD research

Stage	Description	Aβ(PET or CSF)	Markers of neuronal injury (tau, FDG, sMRI)	Evidence of subtle cognitive change
Stage 1	Asymptomatic cerebral amyloidosis	Positive	Negative	Negative
Stage 2	Asymptomatic amyloidosis +"downstream" neurodegeneration	Positive	Positive	Negative
Stage 3	Amyloidosis + neuronal injury + subtle cognitive/behavioral decline	Positive	Positive	Positive

Toward defining the preclinical stages of Alzheimer's disease:Reisa A. Sperling et al. Alzheimer's & Dementia (2011) 1-13

Summary of clinical and cognitive evaluation for MCI due to AD

- Memory complaint, preferably corroborated by an informant
- Objective memory impairment
- Normal general cognitive function
- Intact activities of daily living
- Not demented
- Examine etiology of MCI consistent with AD pathophysiological process.
- Rule out vascular, traumatic, medical causes of cognitive decline, where possible
- Provide evidence of longitudinal decline in cognition, when feasible.
- Report history consistent with AD genetic factors, where relevant.

The diagnosis of mild cognitive impairment due to Alzheimer's disease:M S Albert et al. Alzheimer's & Dementia (2011) 1-10

Biomarkers under examination for AD

- Biomarkers of αβ deposition
  - CSF αβ42
  - PET amyloid imaging
- Biomarkers of neuronal injury
  - CSF tau/phosphorylated-tau
  - Hippocampal volume or medial temporal atrophy by volumetric measures or visual Rating.
  - Rate of brain atrophy
  - FDG-PET imaging
  - SPECT perfusion imaging

The diagnosis of mild cognitive impairment due to Alzheimer's disease:M S Albert et al. Alzheimer's & Dementia (2011) 1-10

MCI criteria incorporating biomarkers

Diagnostic category	Biomarkers probability of AD etiology	Aβ(PET or CSF)	Neuronal injury (tau, FDG, sMRI)
MCI-core clinical criteria	Uniformative	Conflicting/indeterminant/untested	Conflicting/indeterminant/untested
MCI due to AD-intermediate likelihood	Intermediate	Positive Untested	Untested Positive
MCI due to AD-high likelihood	Highest	Positive	Positive
MCI –unlikely due to AD	Lowest	Negative	Negative

The diagnosis of mild cognitive impairment due to Alzheimer's disease:M S Albert et al. Alzheimer's & Dementia (2011) 1-10

Core Clinical Criteria Dementia

- Cognitive impairment is detected and diagnosed through a combination of
  - (1) history-taking from the patient and a knowledgeable informant and
  - (2) an objective cognitive assessment, either a "bedside" mental status examination or neuropsychological testing.
- Neuropsychological testing should be performed when the routine history and bedside mental status examination cannot provide a confident diagnosis.

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Core Clinical Criteria Dementia

- The cognitive or behavioral impairment involves a minimum of two of the following domains:
- Impaired ability to acquire and remember new information-symptoms include: repetitive questions or conversations, misplacing personal belongings, forgetting events or appointments, getting lost on a familiar route.

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Core Clinical Criteria Dementia

- Impaired reasoning and handling of complex tasks, poor judgment-symptoms include: poor understanding of safety risks, inability to manage finances, poor decision-making ability, inability to plan complex or sequencial activities.
- Impaired visuospatial abilities-symptoms include: inability to recognize faces or common objects or to find objects in direct view despite good acuity, inability to operate simple implements or orient clothing to the body.

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Core Clinical Criteria Dementia

- Impaired language functions (speaking, reading, writing)-symptoms include: difficulty thinking of common words while speaking, hesitations; speech, spelling and writing errors.
- Changes in personality, behavior, or comportment-symptoms include: uncharacteristic mood fluctuations such as agitation, impaired motivation, initiative, apathy, loss of drive, social withdrawal, decreased interest in previous activities, loss of empathy, compulsive, or obsessive behaviors, socially unacceptable behaviors.

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Core Clinical Criteria

- Probable AD dementia
- Possible AD dementia
- Probable or possible AD dementia with evidence of the AD pathopsysiological process

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Core Clinical Criteria

- **Probable AD is diagnosed when:**
- **Dementia**
- **Insidious onset**
- **Clear –cut history of worsening of cognition by report or observation and**
- **The initial and most prominent cognitive deficits are evident by history and examination in one of the following:**
  - **Amnestic presentations**
  - **Non Amnestic presentations (Language, Visuospatial presentation, executive dysfunction)**

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

AD dementia incorporating biomarkers

Diagnostic accuracy	Biomarker probability of AD etiology	Aβ(PET or CSF)	Neuronal injury (tau, FDG, structural MRI)
Probable AD Dementia based on clinical criteria	Uniformative	Unavailable, conflicting, or indeterminate	Unavailable, conflicting, or indeterminate
With three levels of evidence of AD pathophysiological process	High	Positive	Positive
Possible Ad dementia (atypical clinical presentation) Based on clinical criteria	Uniformative	Unavailable, conflicting, or indeterminate	Unavailable, conflicting, or indeterminate
With evidence of AD pathophysiological process	High but does not rule out second etiology	Positive	Positive
Dementia-unlikely due to AD	Lowest	Negative	Negative

The diagnosis of dementia due to Alzheimer's disease. G M McKhann et al. Alzheimer's & Dementia (2011) 1-7

Criteria for all cause dementia: Core clinical criteria

- The core clinical criteria provide very good diagnostic accuracy and utility in most patients
- Biomarker evidence may increase the certainty that the basis of the clinical dementia syndrome is the AD pathophysiological process.

Practice Recommendations

- Structural neuroimaging (Guideline).
- Depression (Guideline).
- B12 deficiency (Guideline).
- Hypothyroidism (Guideline).

Knopman et al. Neurology Volume 56 • Number 9 • May 8, 2001

Pharmacologic treatment of AD

- **Practice recommendations**
  Cholinesterase inhibitors (Standard), small average degree of benefit.
- **Vitamin E (1000 I.U. PO BID) - slows progression of AD (Guideline).**
- **Selegiline (5 mg PO BID)- less favorable risk–benefit ratio (Practice Option).** ***Doody et al, Neurology 56(9) May 8, 2001***
- **Memantine Treatment in Patients with Moderate to Severe Alzheimer's disease Already receiving Donepezil: A randomized Controlled Trial.** ***Tarriot:JAMA, V 291(3) 2004.317-324***

Pharmacologic treatment of AD
Practice recommendations

- **There is insufficient evidence**
  - **Antioxidants (Practice Option)**
  - **anti-inflammatories (Practice Option).**
- **Estrogen should not be prescribed (Standard).**

Doody et al, Neurology 56(9) May 8, 2001

Conclusions

- **Early diagnosis and treatment**
- **Early recognition of patients at high risk for developing AD will be extremely important for purposes of prevention.**
- **Reducing the mean age at onset of AD by 5 years will reduce the number of patients with AD dementia by 57% and will reduce the projected Medicare costs of AD from $627 to $344 billion dollars. (Hypothetical intervention).**