

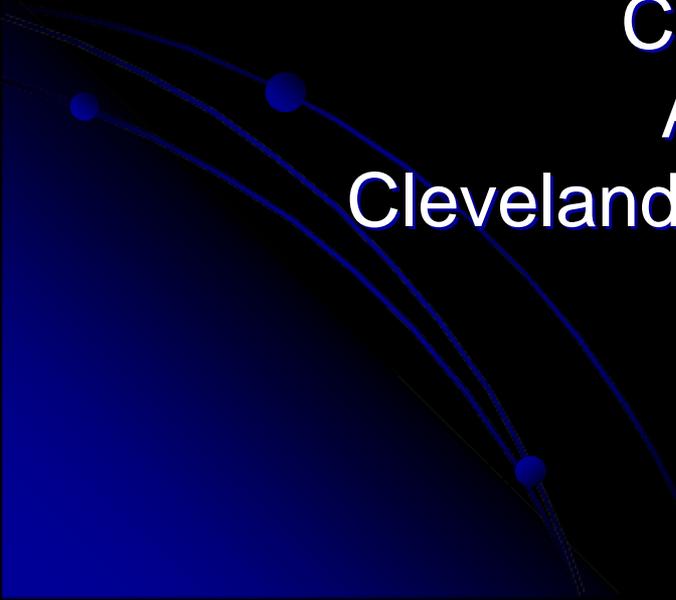


*Stay tuned...our webinar will begin shortly!
(Please note that your line has been muted.)*

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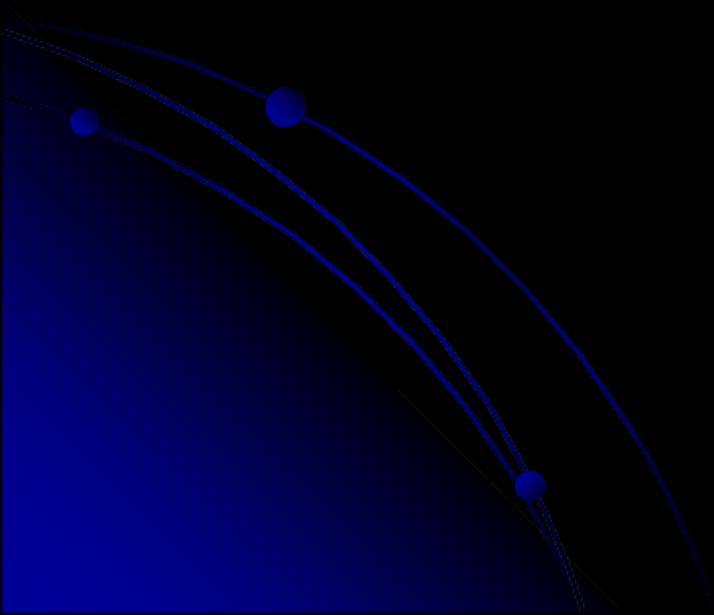
Early Detection of Alzheimer's Disease: It Pays!

Charles Bernick, MD
Associate Director
Cleveland Clinic Lou Ruvo Center for
Brain Health



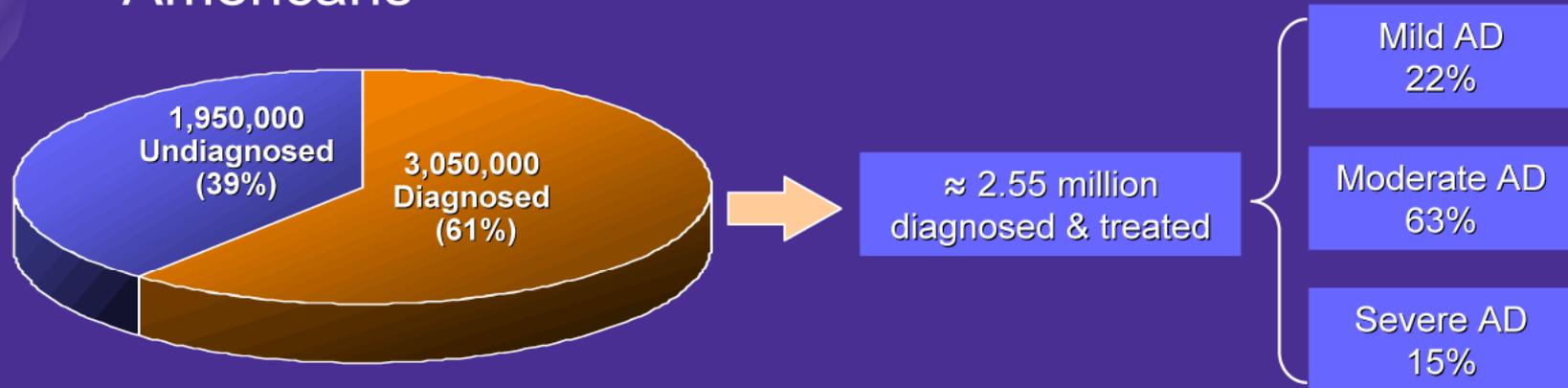
Roadmap

- AD numbers
- Pathophysiology/Risk factors
- Recognition
- Treatments



Alzheimer's Dementia

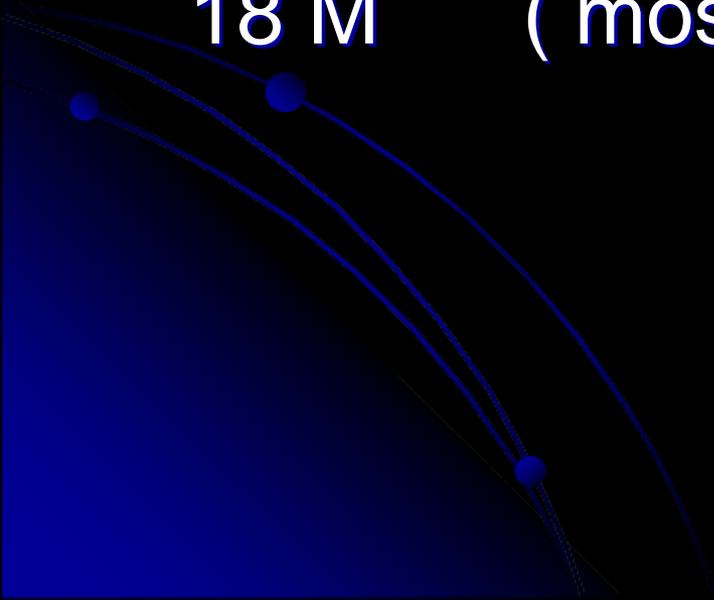
- Alzheimer's dementia (AD) affects about 5 million Americans¹



- Most are 65 years of age and older, with prevalence reaching nearly 50% at age 85 and older¹
- AD patients typically live about 7 to 10 years after diagnosis²⁻⁴

Epidemiology of AD

- 26 M worldwide now; 100 M by 2050
- Onset delay by 1 year reduces cases by 12 M
- Onset delay by 2 years reduces cases by 18 M (most in late stages)



AD Costs

\$1 Billion / year

Treatment saves \$1,100- \$2500/yr

Reduces: hospital stays

delays institutionalization

Indirect effects through reducing caregiver burden (missed work, etc.)



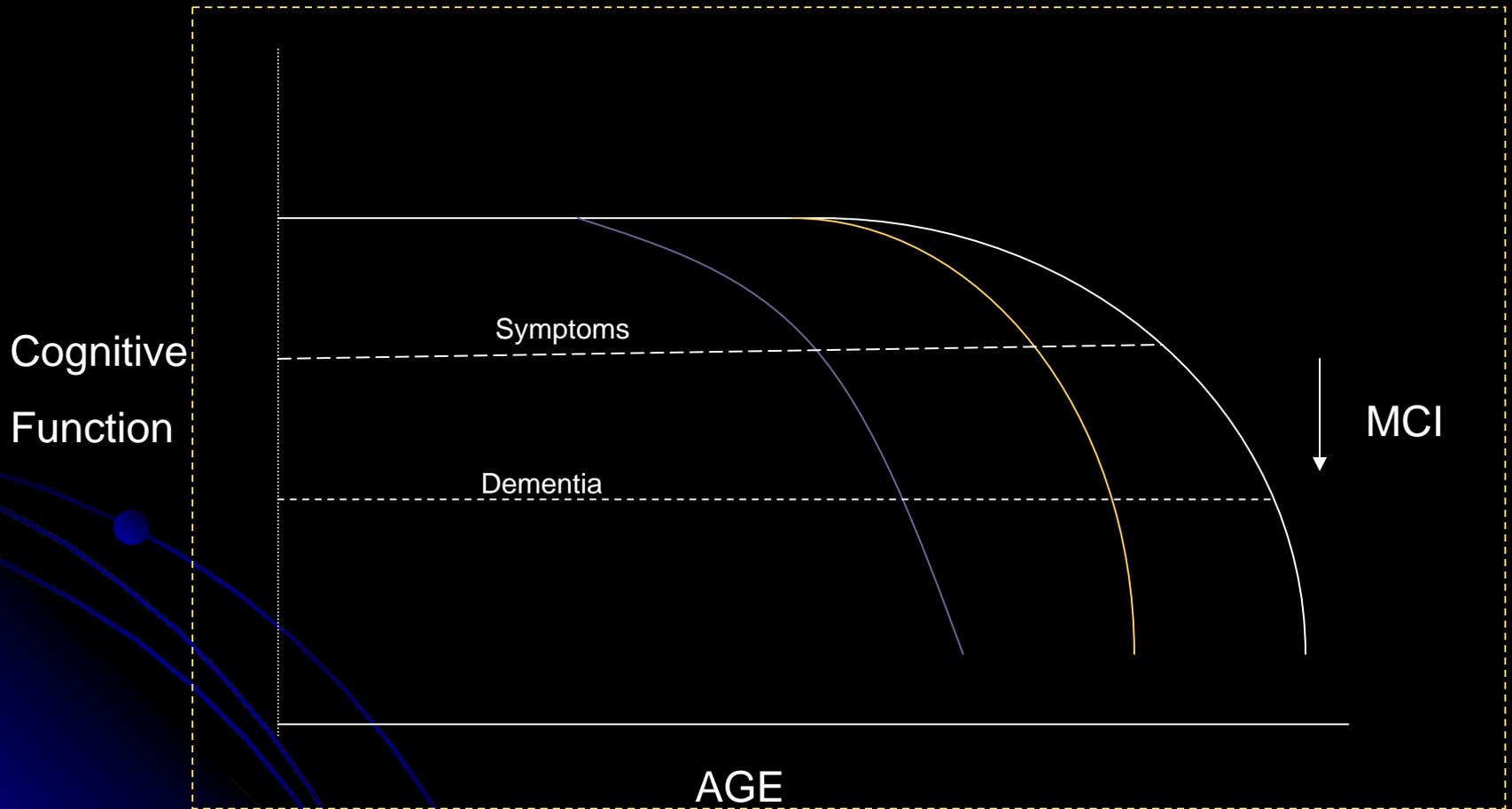
Potential Benefits of Early Recognition and Treatment

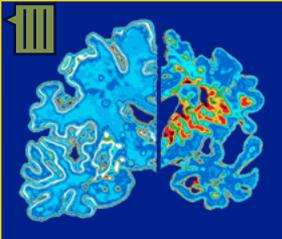
- Allows patients to participate in care plan at a time when they may still be able to express their needs and wishes
 - Facilitates family caregiver participation and planning
 - Allows family caregivers more time to avail themselves of sources of support
- Treatment may slow worsening of symptoms
- Offers potential to maintain functioning

Reasons Why AD Is Underdiagnosed

- Early AD is subtle – easy to overlook initial signs
 - Often misidentified as “normal aging”
- Social skills are often maintained in early disease
- Lack of definitive screening and diagnostic tests
- Concerns regarding time and reimbursement issues
- Patients and caregivers are often reluctant to acknowledge the signs and symptoms
 - Social stigma associated with diagnosis

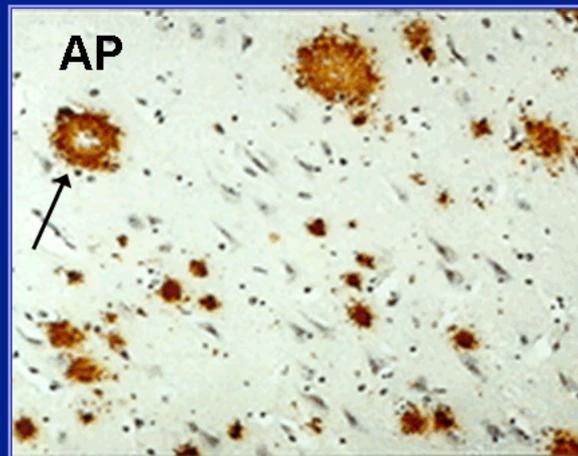
Cognitive Trajectories



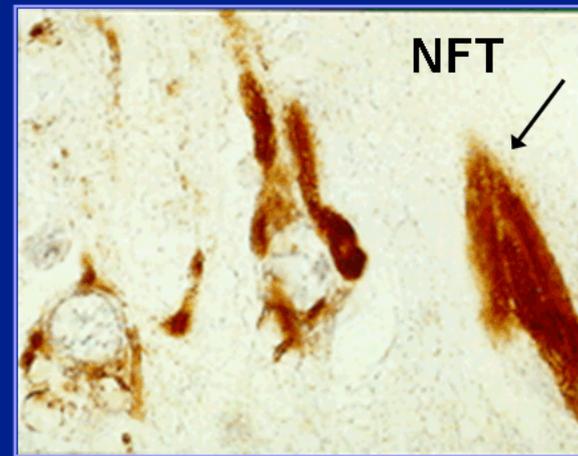


Histopathologic Hallmarks of Alzheimer's Disease (AD)

- Major histopathologic hallmarks include¹⁻³
 - Amyloid- β peptide (AP) deposition in senile plaques and blood vessels
 - Neurofibrillary tangles (NFT)
 - Neuronal and synaptic loss

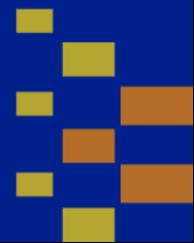


AP = amyloid plaques.



NFT = neurofibrillary tangles.

1. Green RC. Professional Communications Inc. Caddo, Okla; 2001:79-107.
2. Geula C. *Early Diagnosis of Alzheimer's Disease*. 2000:65-82.
3. Corey-Bloom J. *Continuum*. 2004;10(1):29-57.



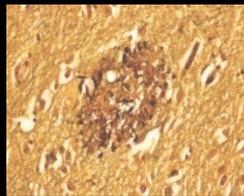
The Original Amyloid Cascade Hypothesis

Alzheimer's is the cumulative product of a series of pathological events that may begin with the deposition of beta-amyloid in the brain

AGE

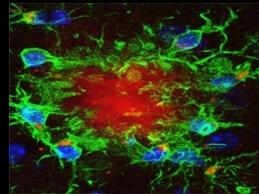
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**Amyloid
deposition**



40

**Microglial
activation**



50

**Neurofibrillary
tangles**



60

**Neuronal loss/
neurochemical
changes**



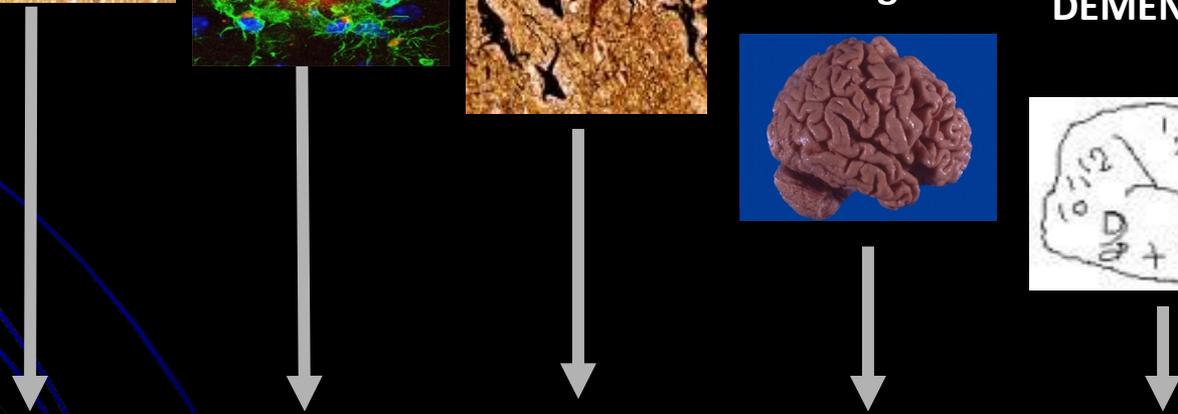
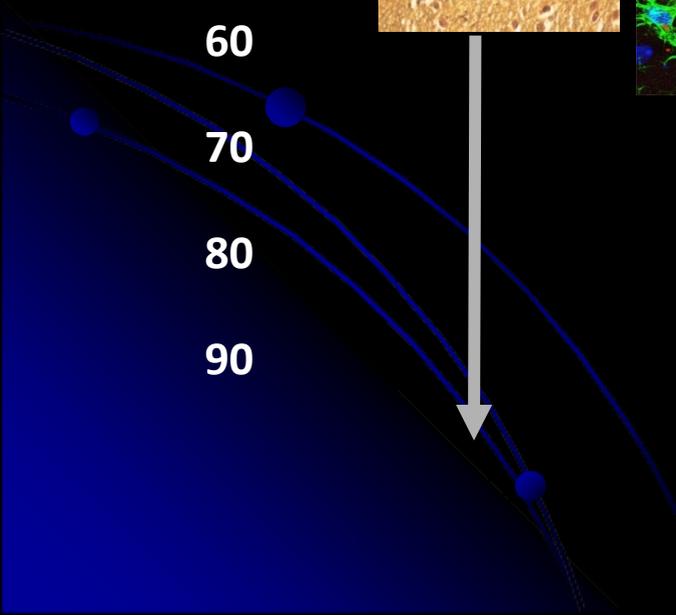
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DEMENTIA



80

90



Risk/Protective Factors for AD

RISK

- Aging
- Genetics
- Gender

- Cholesterol
- Hypertension
- Diabetes
- Head trauma

PROTECTIVE

- Education
- Anti-inflammatories
- Statins
- Omega 3 oils
- Activity

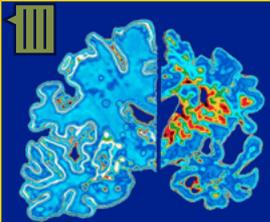
Diagnostic Evaluation

- Cognitive Screen/Informant questionnaire
 - Laboratory testing
 - Brain Imaging
 - Early detection requires a high index of suspicion
- 

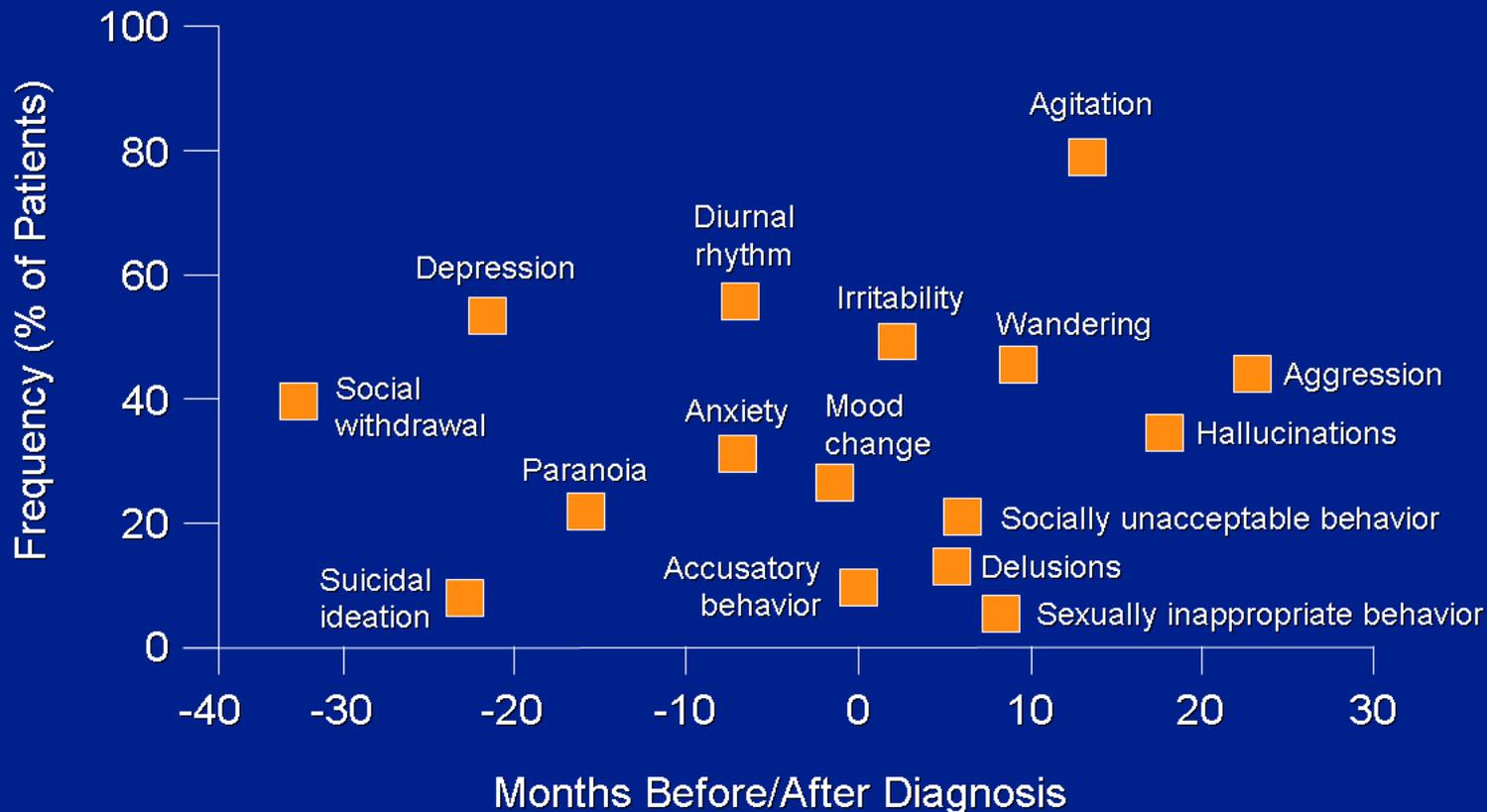


Which Older Adults Should Be Evaluated for AD?

- People with identified risk factors (eg, age, hypertension, hypercholesterolemia, head injury)
- People with memory or cognitive impairment, with or without functional impairment
- People brought to physician's attention through informant complaint, with or without patient concurrence
- Depressed or anxious patients, with or without cognitive complaints



Alzheimer's Disease (AD): Behavioral Symptoms Present Pre-Diagnosis



N = 81

Mini-Mental State Examination

- Tests cognitive function¹
- Brief, structured mental status examination¹
- 10 minutes to administer¹
- Typical deterioration of 3–4 points per year^{2,3}
- Sensitivity and specificity vary in different patient populations^{2,4}
- Adjustments for age, education, and race may be necessary^{2,5}

Scores Range from 0–30 ^{1,6}		
≥28	≈	Unimpaired
20 – 27	≈	Mild AD
10 – 19	≈	Moderate AD
<10	≈	Severe AD

Informant Interview: The AD8

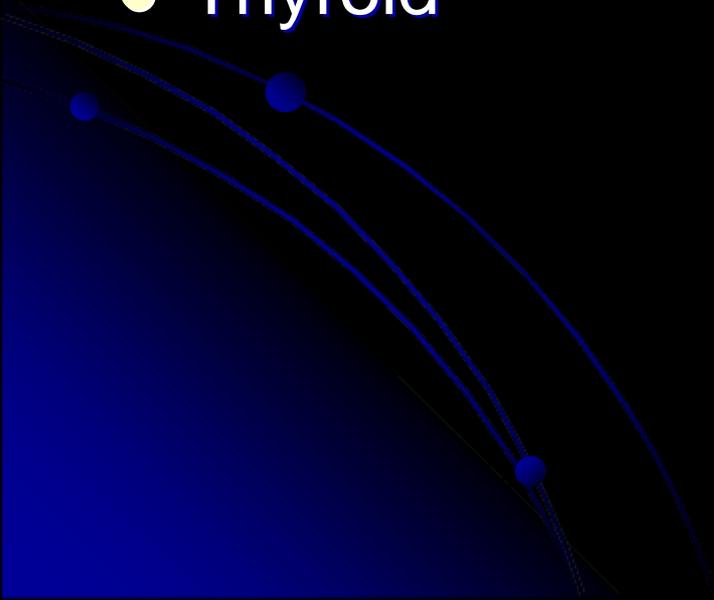
- Informant-based questionnaire
 - Can be administered at home
- Detects change in individuals compared with previous level of function
 - No need for baseline assessment
 - Patients serve as their own control
 - Minimally affected by education, race, gender
- Brief (<3 minutes), yes/no format
 - 2 or more “yes” answers highly correlated with presence of dementia
 - Sensitivity 85%, Specificity 86%

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			

Other Things Cause Memory Problems

- Depression
- Drugs
- Stroke
- Vitamin deficiencies
- Thyroid
- Parkinson's
- Tumors
- Subdurals
- Infection
- Prion Disorders



Recommended Laboratory Testing

- Complete blood count
- Serum electrolytes
- Glucose
- Blood urea nitrogen/creatinine
- Folate
- Vitamin B₁₂
- Thyroid function
- Structural neuroimaging with noncontrast CT or MR scan
- Syphilis serology*

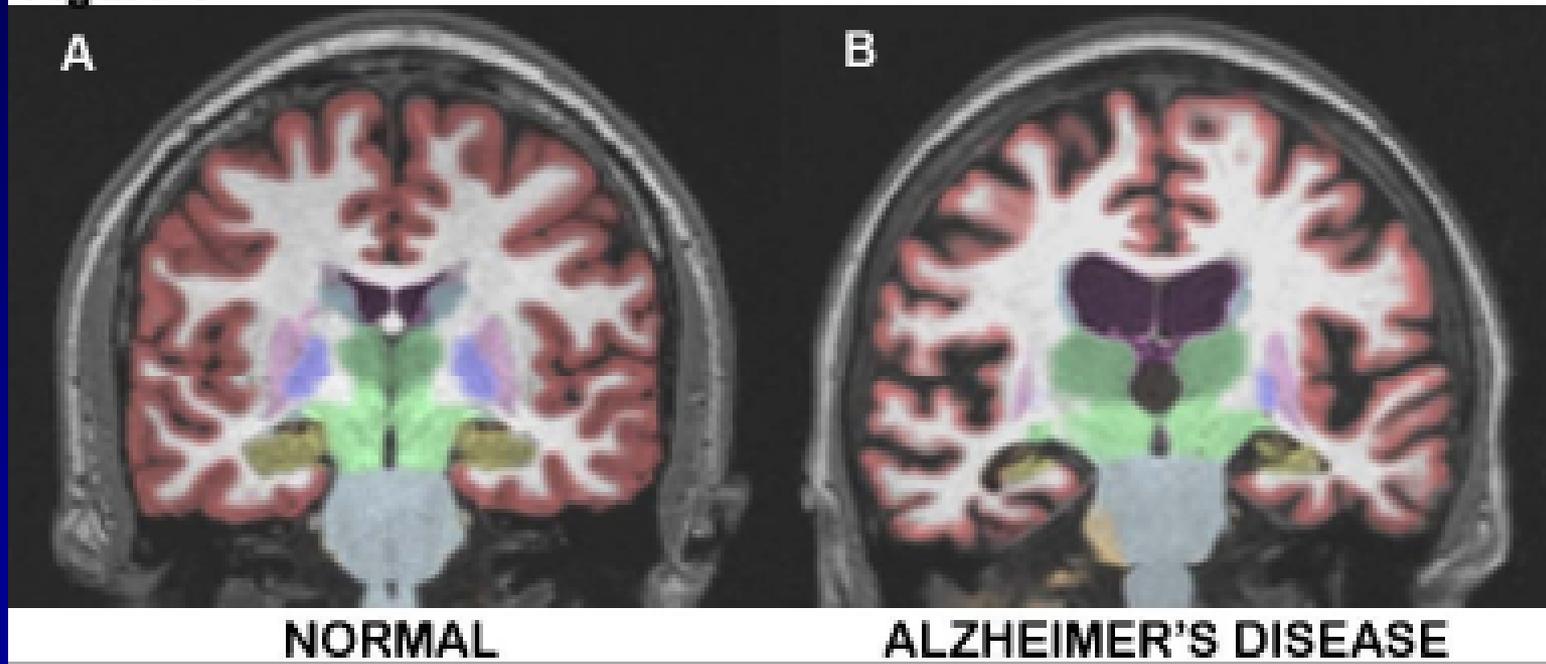
*Screening for syphilis is appropriate only if patients have a specific risk factor, prior syphilitic infection, or reside in geographic areas with high numbers of syphilis cases.

CT = computed tomography; MR = magnetic resonance.

Knopman DS, et al. *Neurology*. 2001;56:1143-1153.

Fully-Automated Volumetric MRI

Figure 1

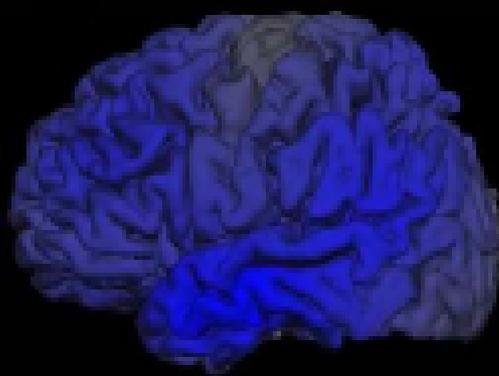


Quantification of Longitudinal Change

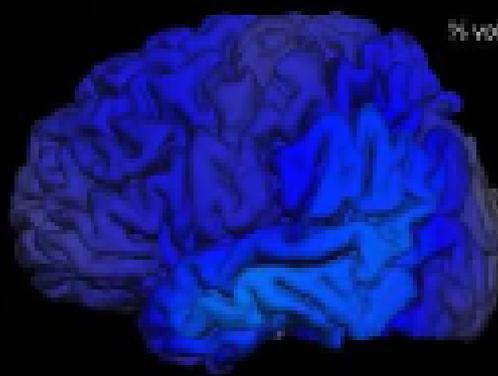
Individual ADNI Subject (70 y.o. Female, Diagnosed with MCI)



Anatomical Segmentation

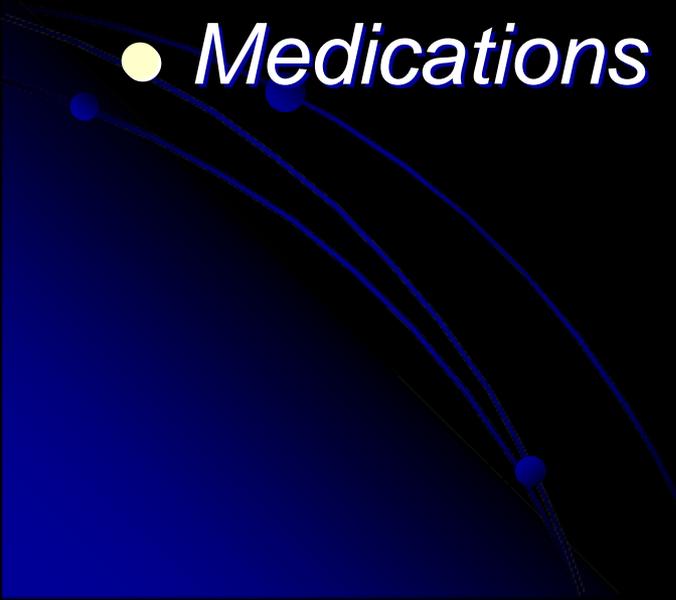


Change over 6 Months

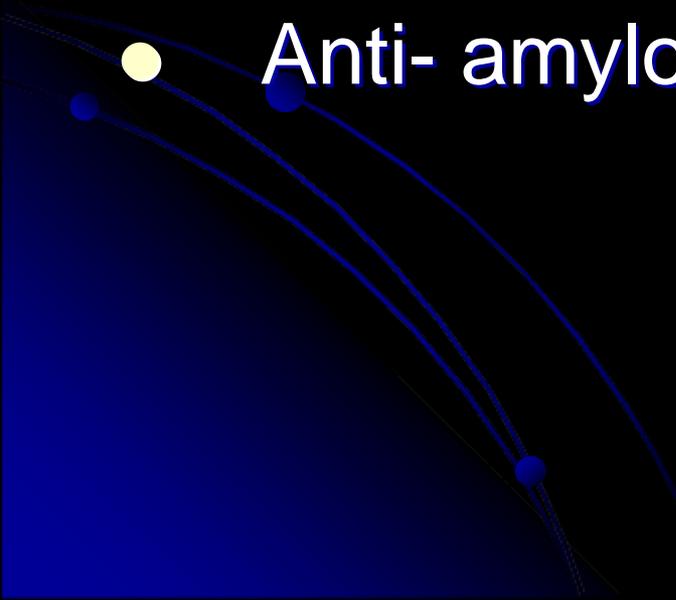


Change over 12 Months

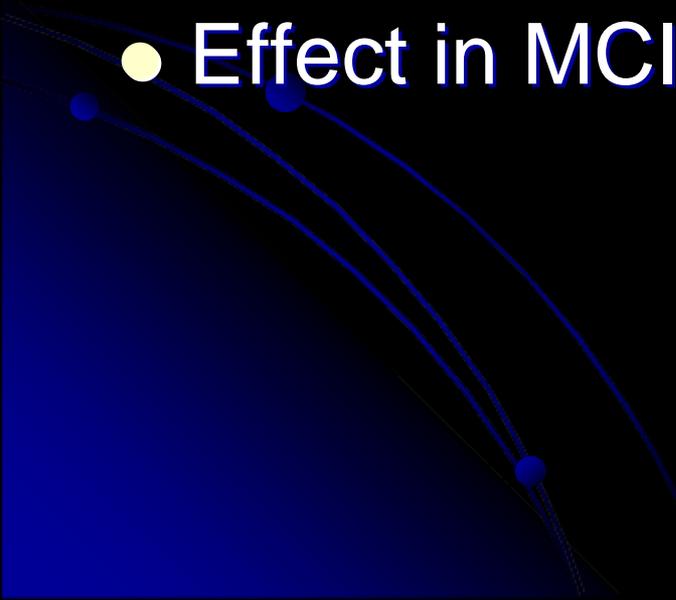
Factors Affecting Trajectory

- Genetics
 - Education/Cognitive reserve
 - *Lifestyle*
 - *Co-morbidities*
 - *Medications*
- 

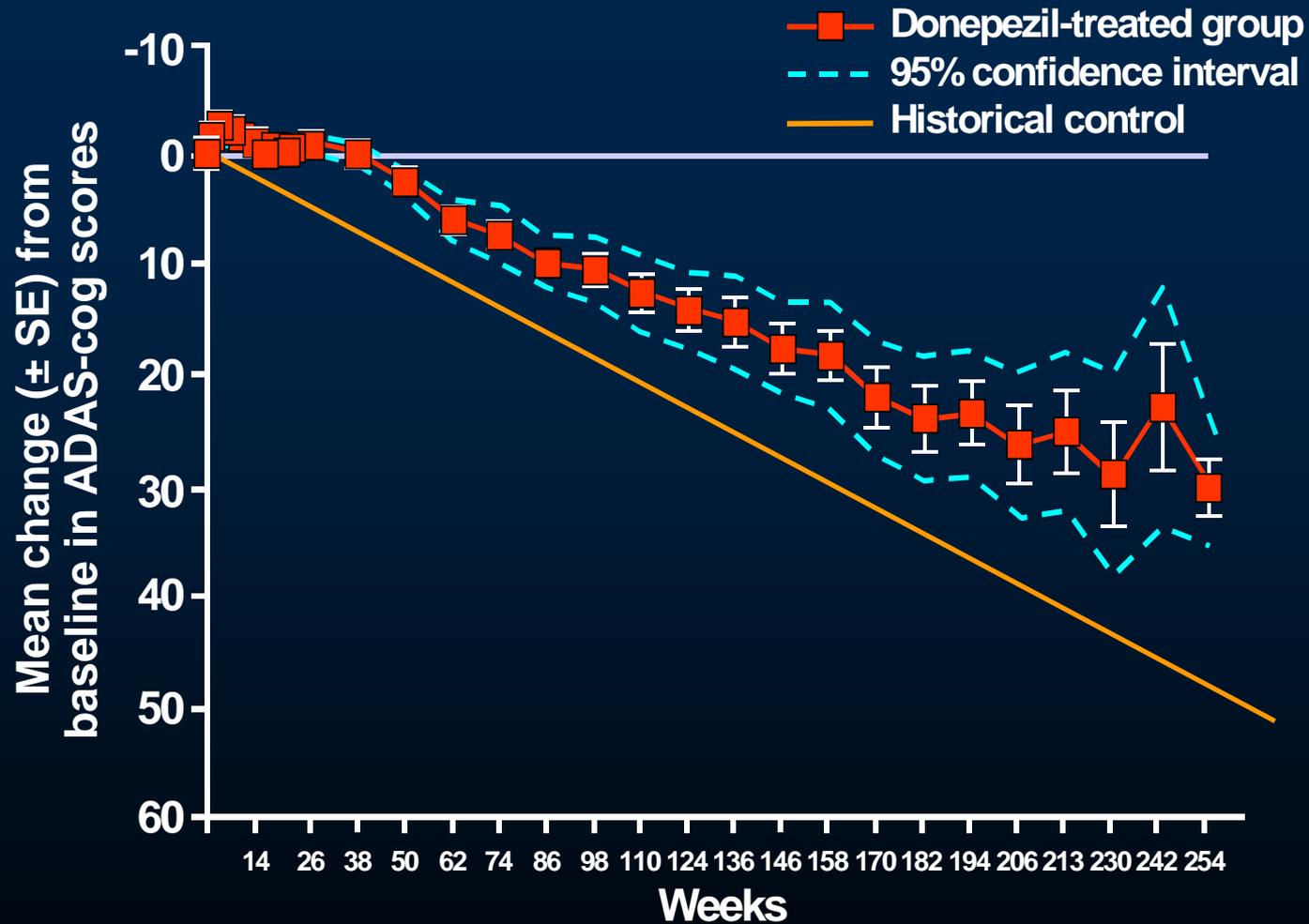
Therapeutics

- Symptomatic treatments
 - Cholinesterase inhibitors
 - NMDA receptor antagonist
 - Disease Modifying
 - Anti- amyloid?
- 

CEI Class Effect

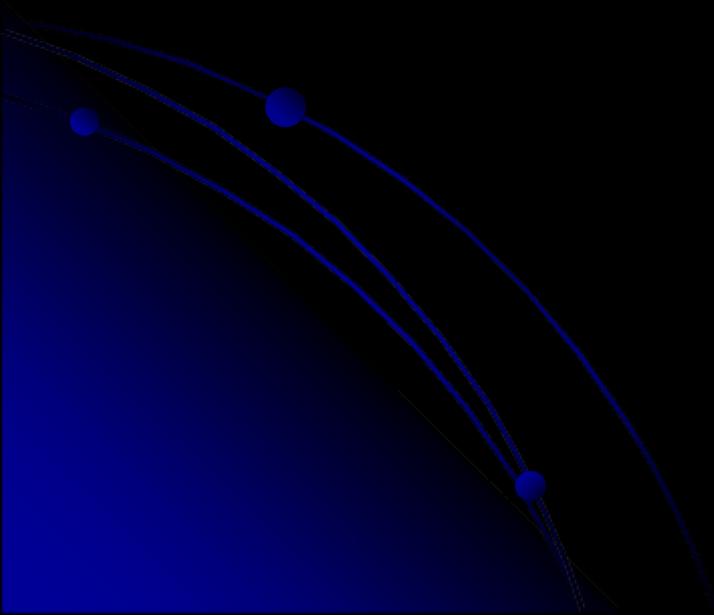
- Modest cognitive improvement
 - Slows symptomatic decline
 - Improves behavior
 - Tolerable
 - Effect in MCI not well defined
- 

Long-term Efficacy of Donepezil (Rogers)



Mementine

- NMDA receptor antagonist
- Indicated in moderate to severe AD
- Combination rx with CEI
- Positive pharmacoeconomic impact







Lifestyle Interventions

- Social Networking
- Mental Activity
- Physical Activity
- Diet

Omega 3 fish oils

Anti-oxidants

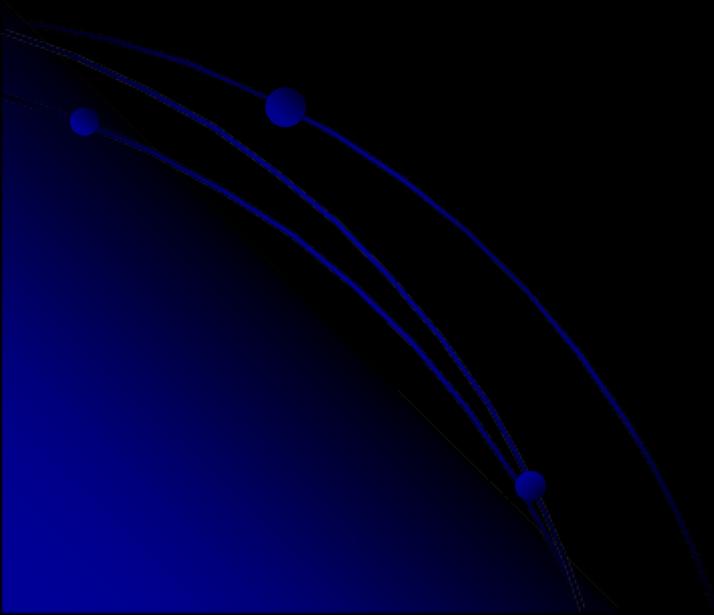
- Others

Manage Comorbidities

- Cardiovascular risk factors associated with increased risk of AD
 - Mid-life hypertension
 - Diabetes
 - Peripheral Vascular Disease (?)
- Depression may be risk factor for AD

Caregiving as a risk factor

- As potent a risk factor as smoking
- 25-50% are clinically depressed
- More hospitalizations
- More medications



Dementia Caregiving

- More Challenging because patient...

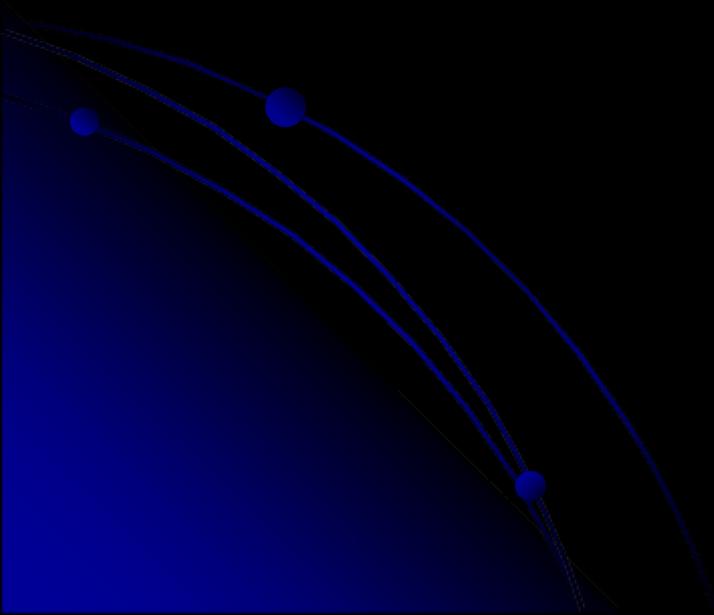
- Requires more supervision
- Less likely to express gratitude
- More likely to be depressed/ behavioral problems

- Effects influenced by:

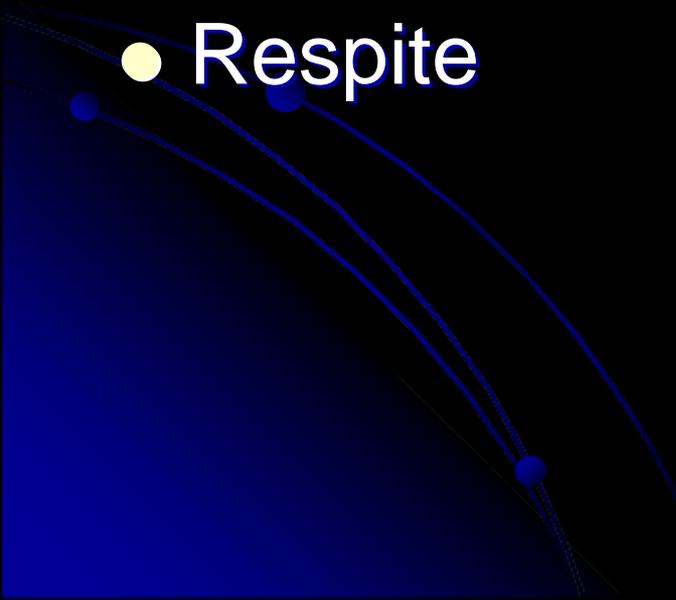
- Age
- SES
- Availability of informal support

Dementia Caregiving: + Effects

- Self worth
- Meaning to life
- New skills
- + effects may wane as disease progresses

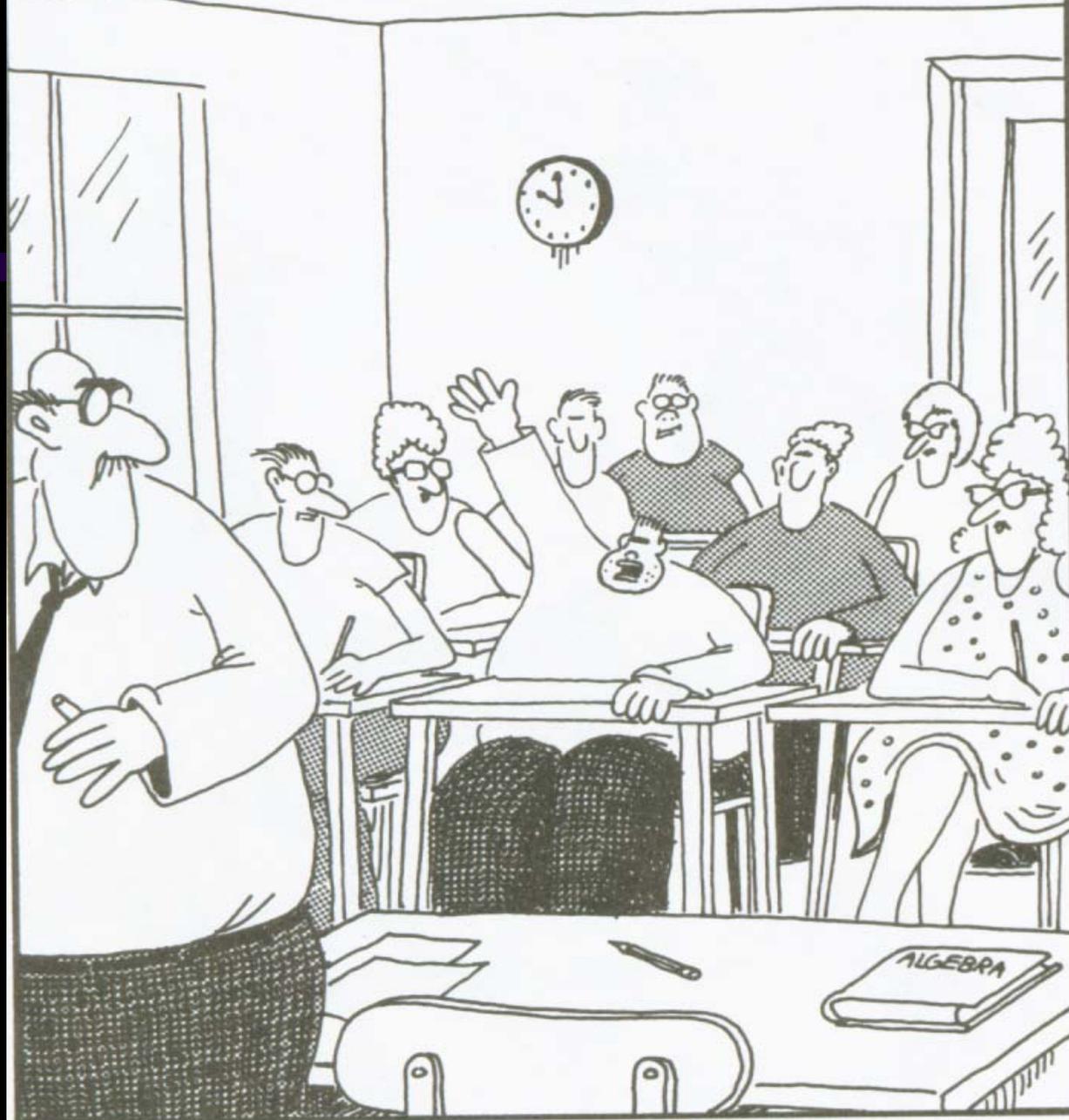


Caregiver Issues

- Safety
 - Legalities
 - Placement
 - Medical Management
 - Respite
- 

Summary

- AD is common and costly (but often not addressed early)
- Detection is possible with available techniques
- Therapies are available that can slow functional decline and reduce caregiver burden



“Mr. Osborne, may I be excused? My brain is full.”



Thank you for participating in our webinar today!

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