

Evaluation and Management of Dementia/ALz

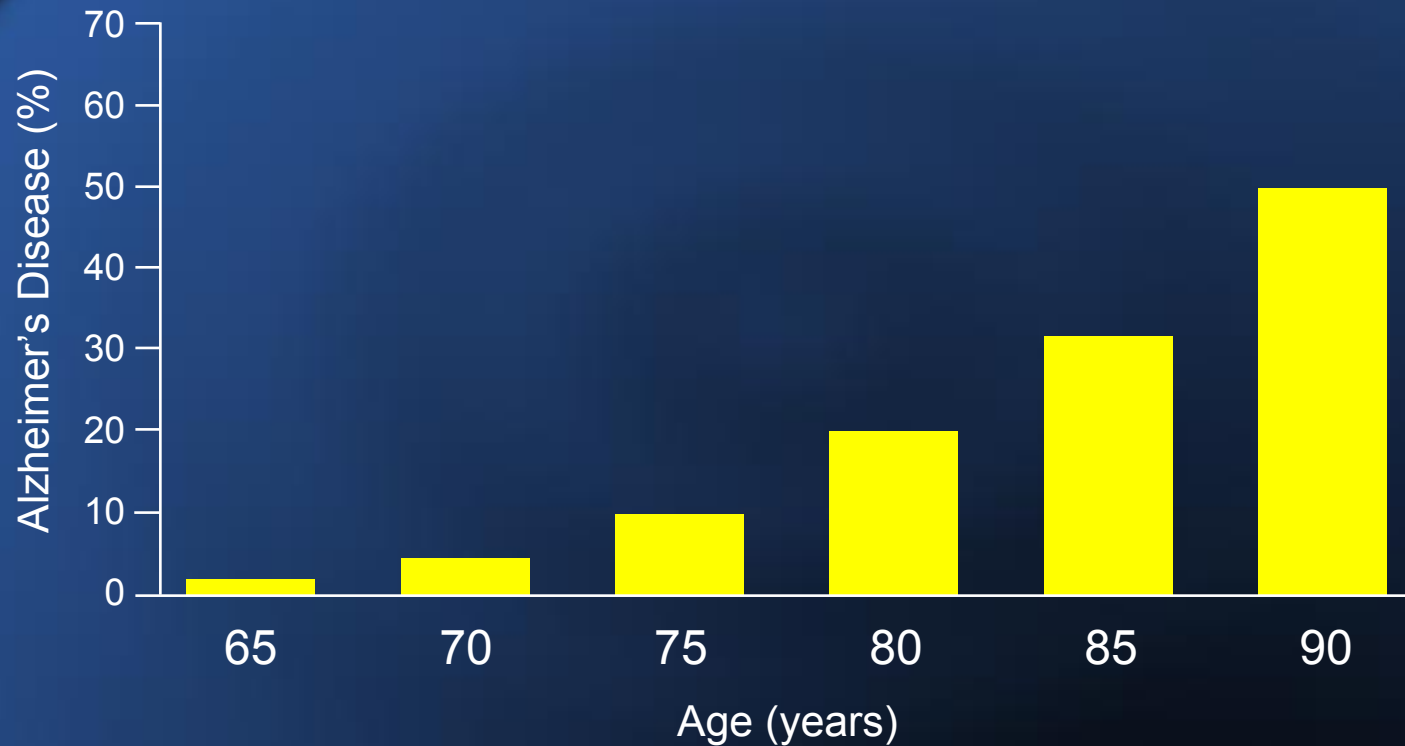
Charles A. Cefalu MD, MS

Professor and Chief, Section of Geriatric Medicine

Department of Fam. Med

LSU Health Science Center, NO, La.

Prevalence of Alzheimer's Disease/Dementia



Adapted from Hebert LE, et al. *JAMA*. 1995;273:1354-1359.

Cost of Dementia to Medicare HMOs

- Retrospective study of medical and prescription claims for an HMO with 80,000 Medicare enrollees diagnosed with dementia from January 1, 1996-March 31, 1998.
 - Mean total costs for dementia patients was 1.5 times higher than for non-dementia patients: (\$13,487 versus \$9,276)

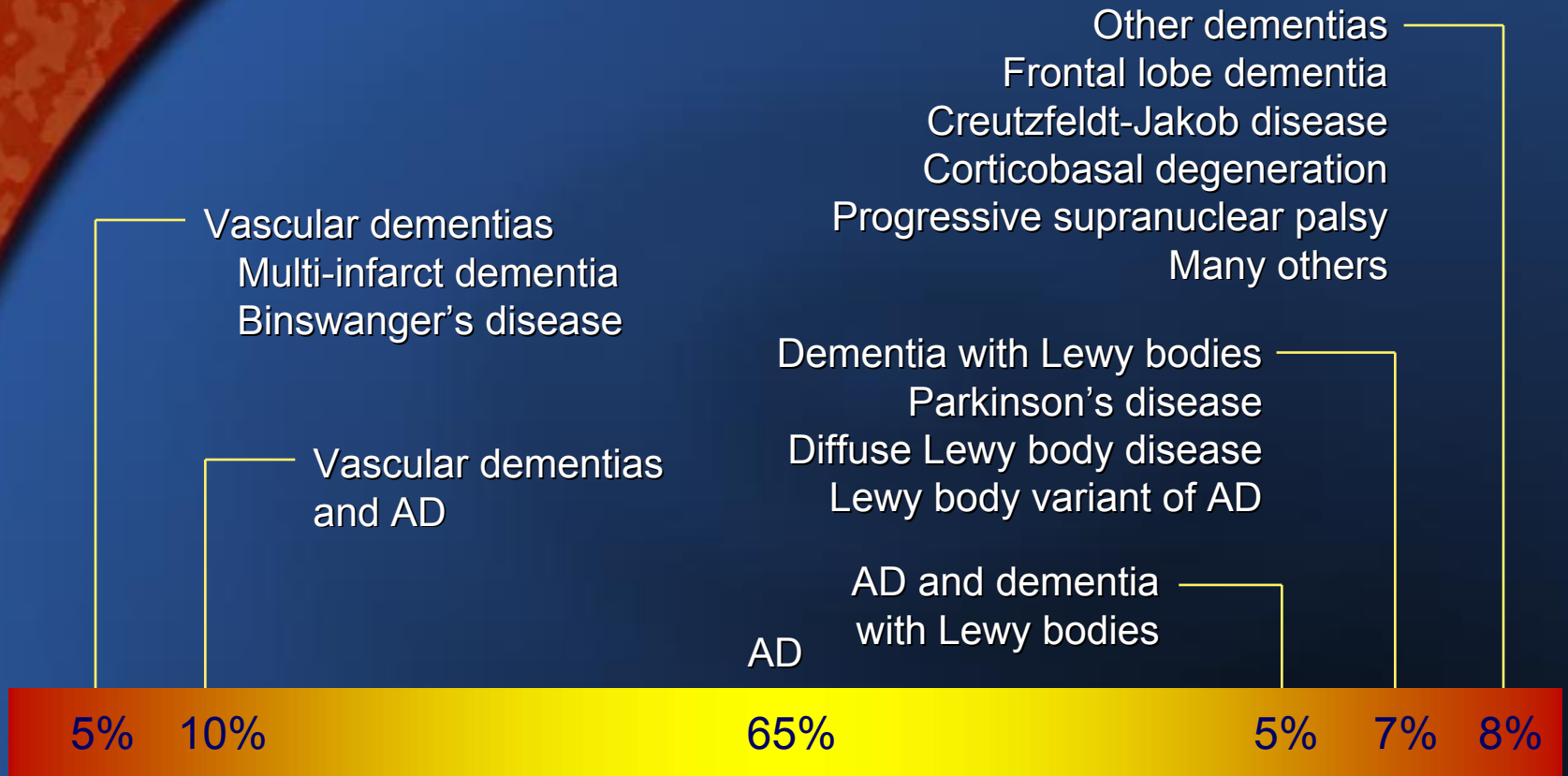
Gutterman EM et al. J Am Ger Soc. 47:1065-1071, 1999

Pneumonic for D-E-M-E-N-T-I-A

Remember: D E M E N T I A

- D---drugs
- E---emotional (depression)
- M-metabolic (CHF, COPD, CRF)
- E-endocrine (Hypothyroid, Hyperparathyroid)
- N-nutrition (B12, malnutrition)
- T-trauma
- I-infection (fungus, TB)
- A-arterial (vascular)

Differential Diagnosis of Dementia



Small GW, et al. *JAMA*. 1997;278:1363-1371; American Psychiatric Association. *Am J Psychiatry*. 1997;154(suppl):1-39; Morris JC. *Clin Geriatr Med*. 1994;10:257-276.

Other Metabolic Causes

- CHF
- COPD
- Liver Failure
- Renal Failure
- Stroke
- Parkinson's Disease
- Endocrine-Thyroid, Parathyroid
- Nutritional

Cognitive Dysfunction-A Key Phrase That Needs To Be Fully Understood:

- Implies Intellectual Dysfunction With Memory Loss-Usually Recent First
- Implies Reversibility Until Proven Otherwise
- Once The “Reversible Causes” Ruled Out, Then Call It Dementia

Consider “Reversible” Causes of Cognitive Dysfunction If:

- Time Frame Consistent With Onset Over Several Months
- Other Associated Signs And Symptoms That Make You Think Of A Reversible Type Such As:
 - cough
 - fever
 - ataxia
 - positive lab work-up - Increased TSH Or Ca, +RPR And FTA, Low B12, +PPD
- Be Highly Suspicious Of Depression Complicating The Cognitive Dysfunction Or Depression Causing It And Always Evaluate For Depression

Drug-induced Causes of Cognitive Dysfunction-Notice the Word Used!

- Propranolol
- Clonidine
- Alpha Methyl Dopa
- Tricyclic antidepressants
- Major Phenothiazine Tranquilizers
- Antihistamines-cold meds
- Anti-cholinergics-narcotics

Drugs and Cognitive Dysfunction

- Principle pathological factor in ALz/Dementia is anti-cholinergic disruption of nerve fibers
- Avoid use of any anti-cholinergic drug!
- REMOVE SUSPECTED OFFENDING DRUGS PRIOR TO CALLING IT DEMENTIA/ALZ

Workup of Dementia/Alz

- Hx and PE
- Labs-CBC, Chem Profile-liver, renal, etc.
- CT/MRI? Rule of Thumb
- GDS
- MMSE

Other “Reversible” Causes-Not Completely Reversible:

- Normal Pressure Hydrocephalus
- Metastatic Lesions To Brain
- Fungal and Parasitic Infections Of The Meninges
- Tuberculous Meningitis
- Tertiary Lues
- Cobalamin and Folate Deficiency - More Associated With A Normocytic Rather Than A Macrocytic Anemia And Usually As A Result Of Nutritional Deficiency From The Dementia Rather Than As A True Cause Of Dementia
- Hypothyroidism Or Hyperparathyroidism

GERIATRIC DEPRESSION SCALE

1. ARE YOU BASICALLY SATISFIED WITH YOUR LIFE?
2. HAVE YOU DROPPED MANY OF YOUR ACTIVITIES AND INTEREST?
3. DO YOU FEEL THAT YOUR LIFE IS EMPTY?
4. DO YOU OFTEN GET BORED?
5. ARE YOU IN GOOD SPIRITS MOST OF THE TIME?
6. ARE YOU AFRAID THAT SOMETHING BAD IS GOING TO HAPPEN TO YOU?
7. DO YOU FEEL HAPPY MOST OF THE TIME?
8. DO YOU OFTEN FEEL HELPLESS?
9. DO YOU PREFER TO STAY HOME AT NIGHT RATHER THAN GO OUT AND DO NEW THINGS?
10. DO YOU FEEL THAT YOU HAVE MORE MEMORY PROBLEMS THAN MOST?
11. DO YOU THINK IT IS WONDERFUL TO BE ALIVE?
12. DO YOU FEEL PRETTY WORTHLESS THE WAY YOU ARE NOW?
13. DO YOU FEEL FULL OF ENERGY?

14. DO YOU FEEL THAT YOUR SITUATION IS HOPELESS?
15. DO YOU THINK THAT MOST PEOPLE ARE BETTER OFF THAN YOU ARE?
16. Are you hopeful about the future?
17. Are you bothered by thoughts that you can't get out of your head?
18. Do you often get restless and fidgety?
19. Do you frequently worry about the future?
20. Do you often feel downhearted and blue?
21. Do you worry a lot about the past?
22. Do you find life very exciting?
23. Is it hard for you to get started on new projects?
24. Do you frequently get upset over little things?
25. Do you frequently feel like crying?
26. Do you have trouble concentrating?
27. Do you enjoy getting up in the morning?
28. Do you prefer to avoid social gatherings?
29. Is it easy for you to make decisions?
30. Is your mind as clear as it used to be?

FOLSTEIN MINI-MENTAL

MAX

SCORE

5

SCORE

ORIENTATION

What is the year (season) (date) (day) (month)?

5

Where are we: (state) (country) (city) (hospital) (floor)

REGISTRATION

3

Name 3 objects (ball, flag, tree). 1 second to say each. Then ask patient all three objects after you have said them. Give 1 point for each correct answer. Then repeat objects until patient learns all three, Count trials and record:

ATTENTION AND CALCULATION

5

Serial 7's. One point for each correct. Stop after 5 answers. If education level precludes math, spell "world" backwards. (93-86-79-72-

65)

Max
Score

Score

RECALL

3

Ask for three objects repeated above. Give one point for each correct answer.

2

Name a pencil and a watch.

1

Repeat the following: "No ifs, ands, or buts".

3

Follow this stage 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor".

1

Read and obey the following:

CLOSE YOUR EYES

1

Write a sentence:

1

Copy this design:

30

Is it Dementia or Depression (Pseudodementia) or Both

- Time frame of onset
- Risk factors for Depression
- Family History of Depression
- When is confusion worse
- Ability to answer questions
- Presence of vegetative symptoms
- Type of memory loss

Distinguishing Depression versus Dementia

- Rapid onset of weeks or months versus slow onset with dementia
- Early morning confusion versus late night confusion with Dementia/Alz
- Somatization versus Anomia-Alz/Dementia
- Spotty versus recent memory loss-Alz/Dementia
- Hx of Depression versus no Hx

Depression versus Dementia/Alz

- Depression with Dementia early in process of dementia-common
- Treat Depression and dementia may improve
- Depression (Pseudodementia)-rare-rewarding to discover and treat

Role of Neuropsychological Testing

- When confused about diagnosis, laboratory and radiological workup and Hx and PE are not sufficient to make diagnosis
- When competency issues is a major issue- Caregiver, Potential Abuse issues, financial competency

Clinical Diagnosis of AD/Vascular Dementia

- Alzheimer's Disease-50%
 - slow progressive linear decline over many months or years
 - ave. dur. of illness-9.2 yrs;length 3-25 years
- Vascular Dementia-17%
 - history of vascular risk factors-HBP, stroke,Dm, CAD, PVD, hyperlipidemia
 - usually slow stepwise decline over months/yr
- Mixed AD/Vascular Dementia-25%

Alzheimer's

Risk Factors

- Caucasian or Oriental Race
- Down's Syndrome
- Lower Educational Level
- Lack of Socialization
- Genetic Predisposition

Protective Factors

- Estrogen???
- Smoking???
- Alcohol?
- Higher Education
- Socialization
- NSAIDs?

Diagnostic Criteria for Alzheimer's Disease

- Development of multiple cognitive deficits manifested by both
 - Memory impairment
 - One (or more) of the following cognitive disturbances: aphasia; apraxia; agnosia; disturbance in executive functioning
- Significant impairment in social or occupational functioning representing a significant decline from a previous level of functioning
- Gradual onset and progressive cognitive decline

Diagnostic Criteria for Alzheimer's Disease (cont.)

- Cognitive deficits are NOT due to any of the following
 - Other central nervous system conditions that cause progressive deficits in memory and cognition
 - Systemic conditions known to cause dementia
 - Substance-induced conditions
- Deficits do not occur exclusively during delirium
- Disturbance is not better accounted for by another Axis I disorder

Cost of Alzheimer's

- 1994-analysis of claims history (starting with time after diagnosis and using a 12 year retrospective period to identify patients with Alzheimer's Disease-medical care practices, hospitals, and other providers of service to identify prevalent cases of Alzheimer's Disease
 - Average cost of care for Alzheimer's-\$6021
 - Average cost of care for Non-Alzheimer's-\$2310

Taylor DH & Sloan FA. J Am Ger Soc. 48:639-646,
2000

Genetic Risk Of Alzheimers

- Genes for Alzheimers found on chromosomes 21 (APP), 14 (presenilin I), and 1 (presenilin 2)-account for less than 5% of cases
- Family History or presence of 4 allele of the Apo E (chromosome 19) accounts for >30% in the general population
- History of AD in first degree relative associated with 2-3 times risk

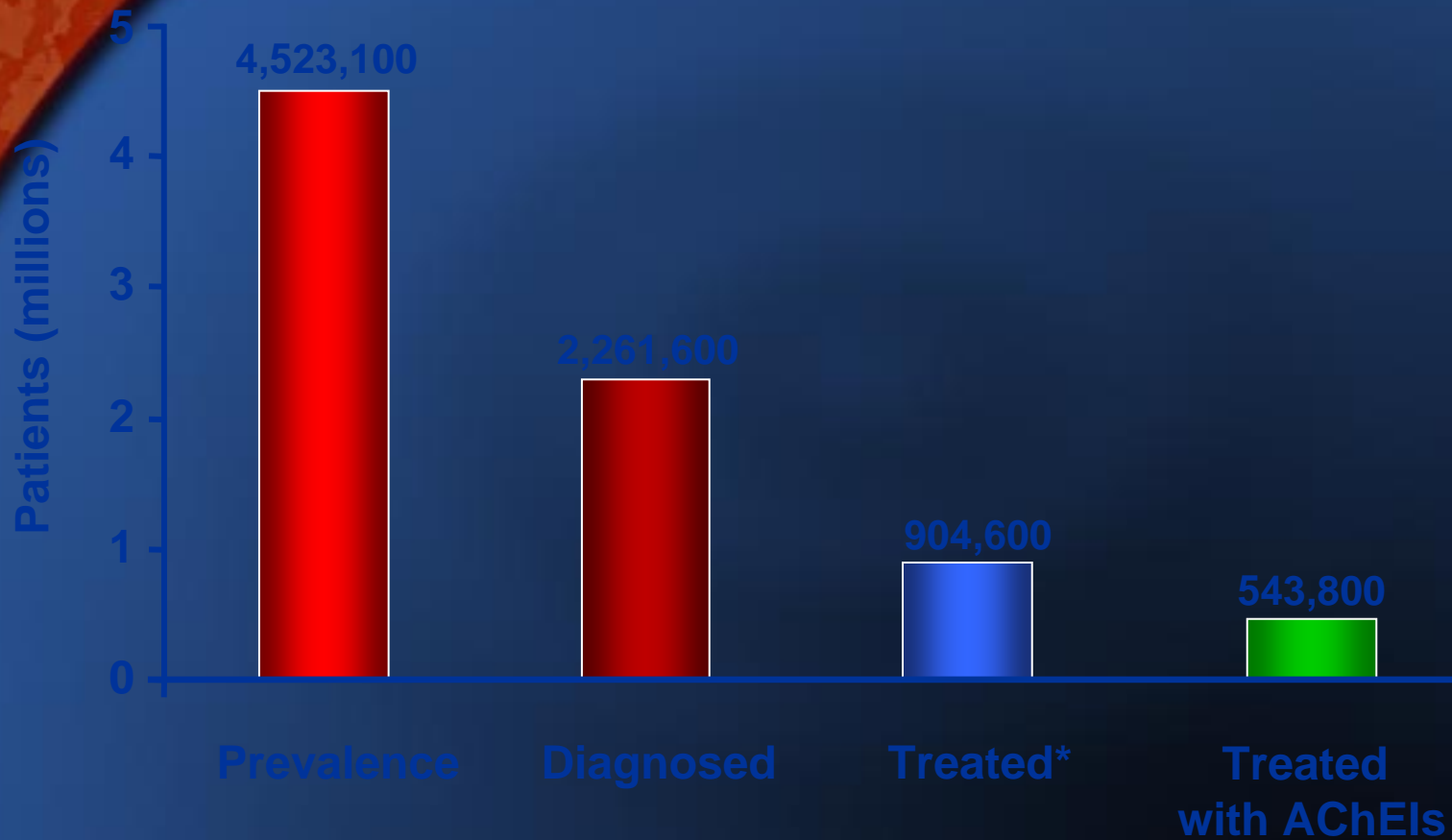
Genetic Risk of AD

- ApoE gene on Chromosome 19 increases risk of AD and reduces the age of onset.
- <25% of late onset AD patients have the gene.
- 50% of people with a least one Apo E4 allele never develop AD
- Lifetime risk of AD=1%
- Child, sibling or parent of AD pt. Unlikely to develop AD

ABC: The Key Symptom Domains of Alzheimer's Disease



Treatment of Alzheimer's Disease



* Any drug treatment, not limited to acetylcholinesterase inhibitors.

Source: Decision Resources, March 2000.

Treatment of Dementia/Cognitive Dysfunction

- REMOVE SUSPECTED OFFENDING DRUG AND OBSERVE RESPONSE
- DOES NOT MAKE SENCE TO USE DRUG THAT WOULD CAUSE COGNITIVE DYSFUNCTION AND START PHARMACOLOGICAL THERAPY

Treatment Of Dementia

- Socialization And Mental Stimulation - Slows The Progress Of Disease
- Adult Day Care
- Avoid Institutionalization Or Movement To New Environment
 - Fabrigoule C et al. J Am Ger Soc. 43:485-490, 1995

Therapeutic Options

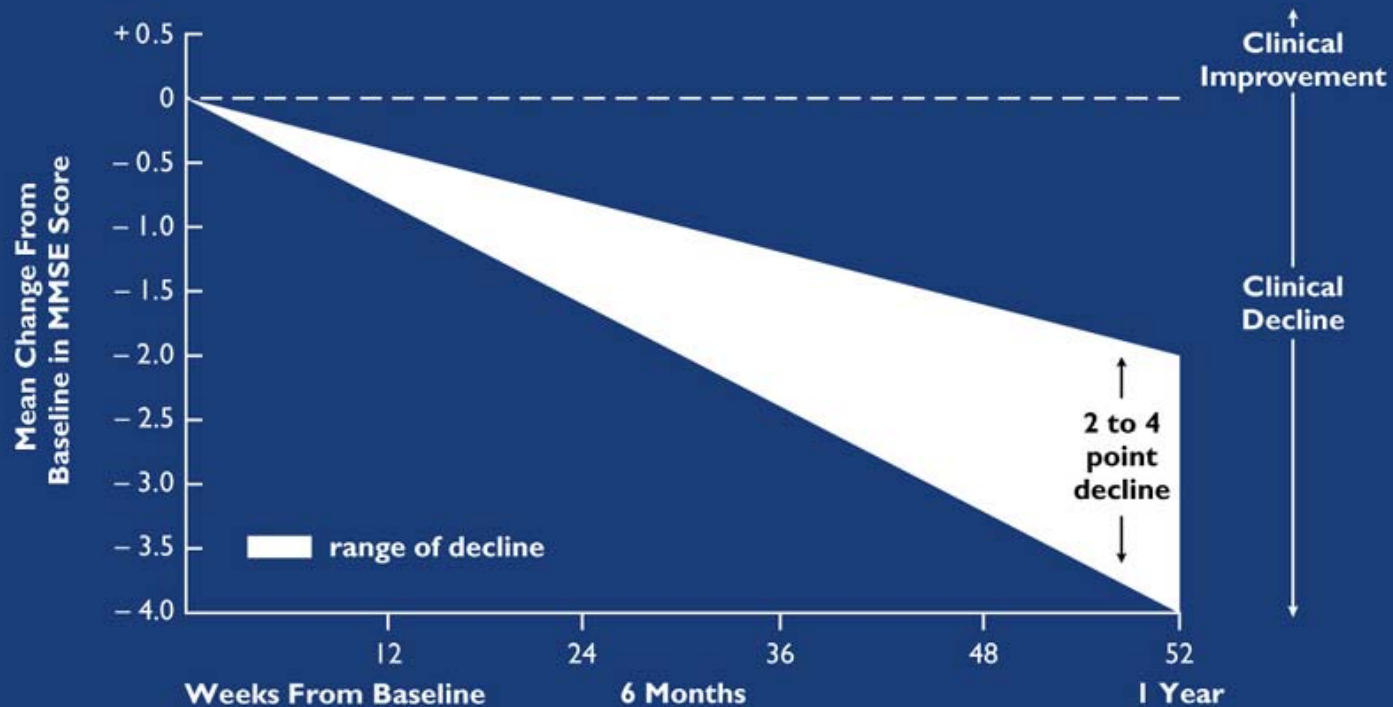
- Pharmacological Therapy
 - Donepezil (Aricept)-mild to moderate
 - Rivastigmine (Exelon)-mild to moderate
 - Galantamine (Reminyl)-mild to moderate
 - Nemanda-Moderate to severe

Basic Principles of Treatment

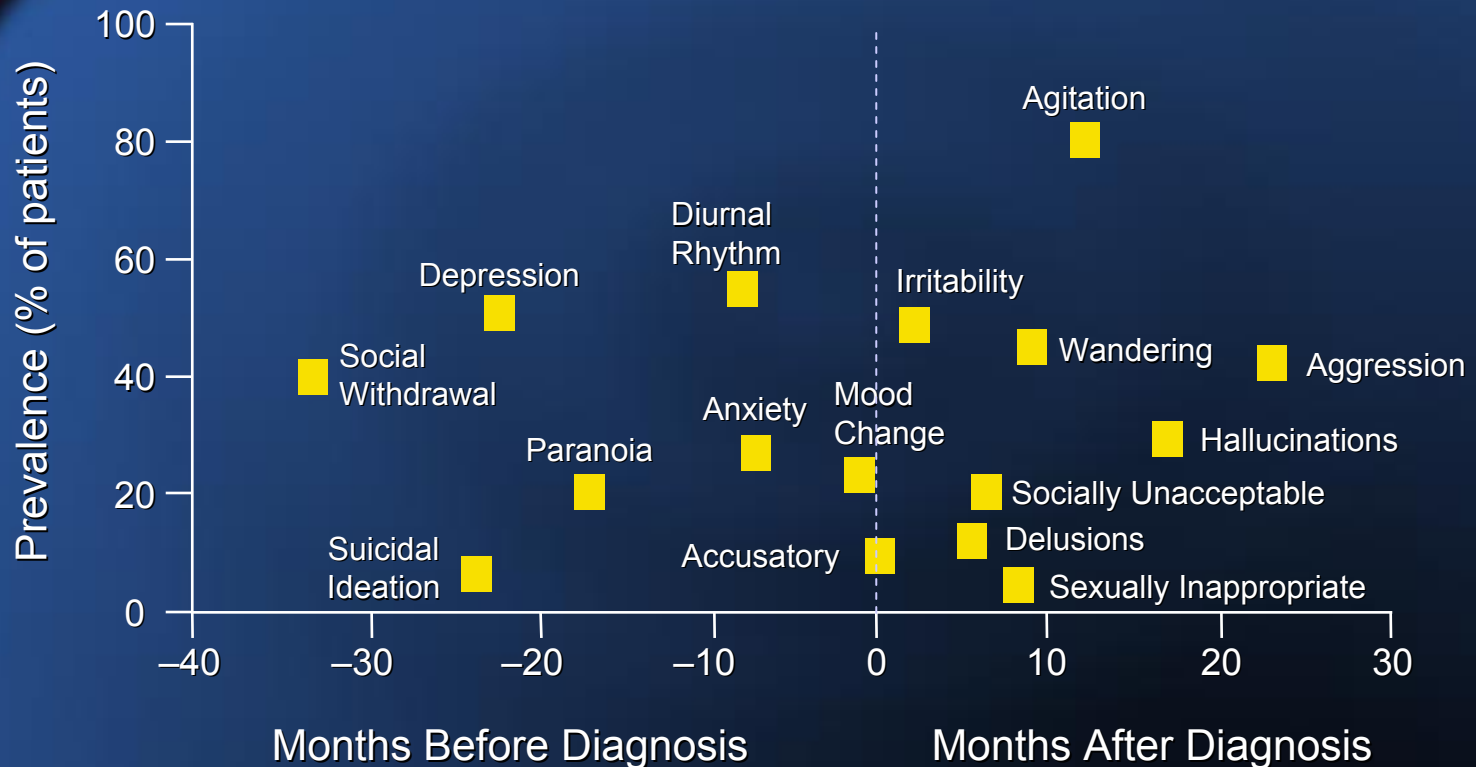
- Drug therapy is indicated for :
 - for hallucinations or delusions that are disabling to the patient or surroundings
 - aggressive, combative, hostile behavior
 - avoid anti-cholinergic drugs that worsen the anti-cholinergic disruption of Alzheimers Disease that accounts for 51% of dementias in the pure form and 76% in the mixed form (Alzheimers and Vascular)
 - use of short acting SSRIs preferred for treatment of the Alzheimers patient with Depressive symptoms.
 - Start early with cholinergic therapy and titrate up slowly

In Alzheimer's disease, cognitive decline is expected over time

If untreated, the expected decline in MMSE scores of mild to moderate AD patients ranges from 2 to 4 points annually

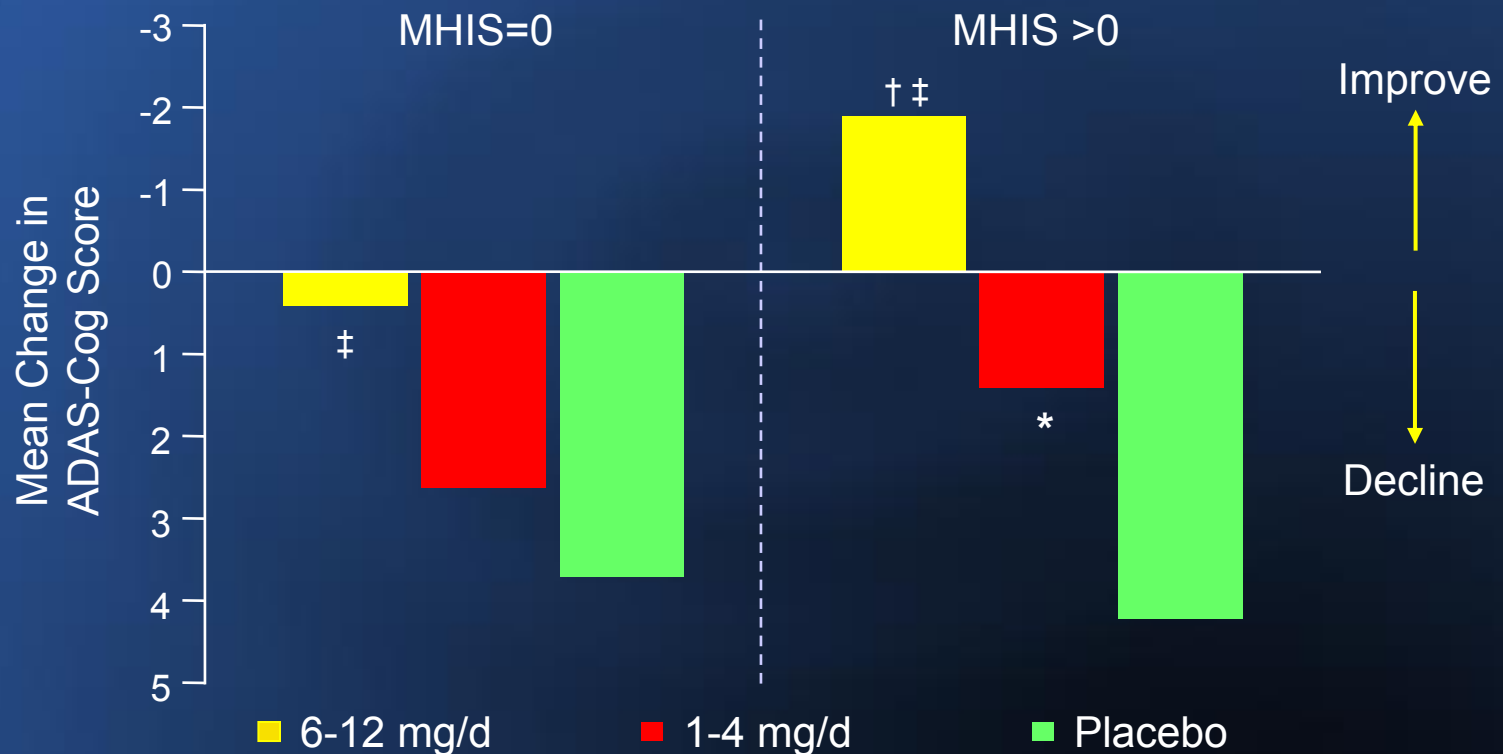


Peak Frequency of Behavioral Symptoms as Alzheimer's Disease Progresses



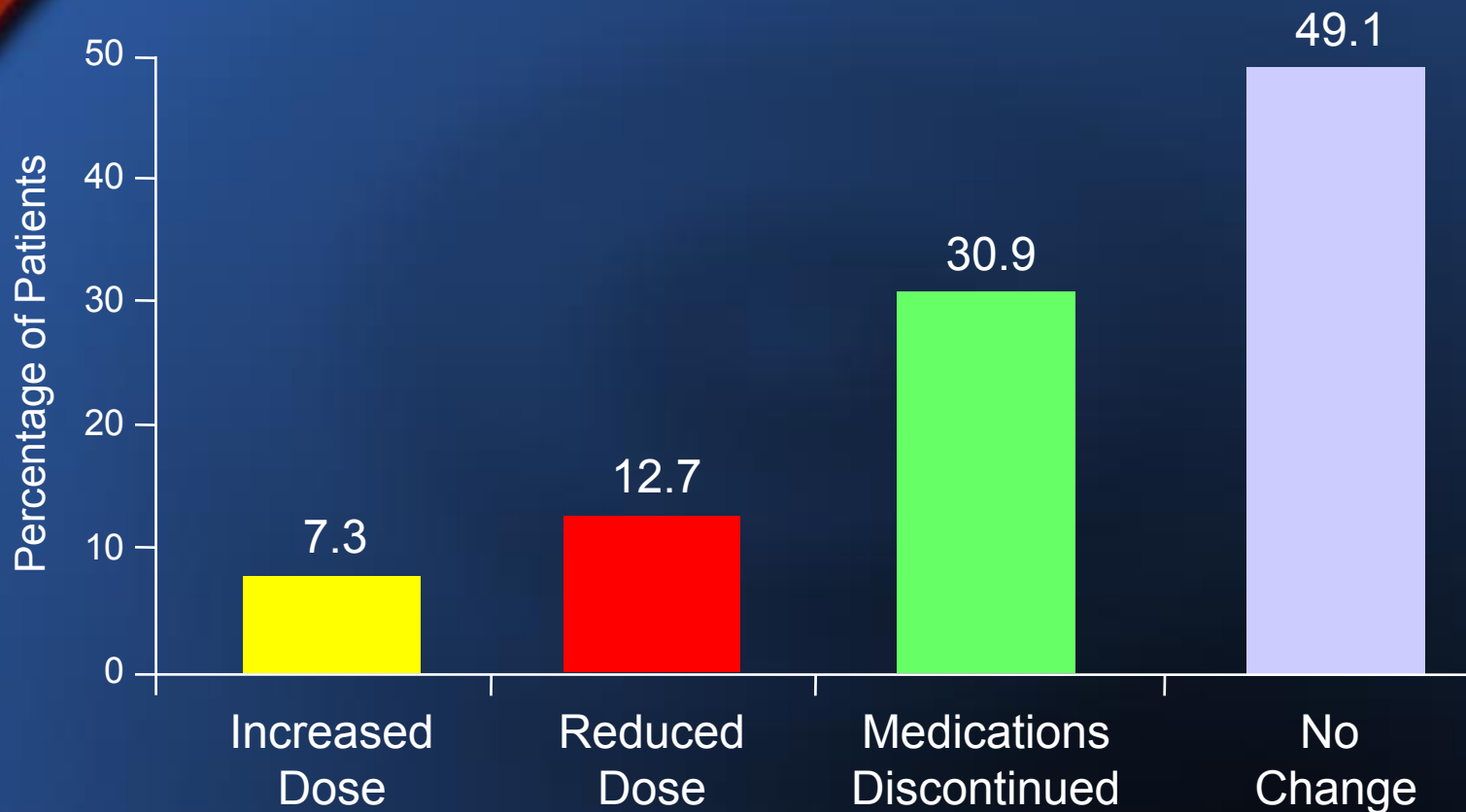
Jost BC, Grossberg GT. *J Am Geriatr Soc.* 1996;44:1078-1081.

Effect of Rivastigmine on Cognition in Patients With AD and Vascular Risk Factors



* $P < 0.002$ vs placebo; † $P = 0.02$ vs 6-12 mg/d (MHIS=0); ‡ $P < 0.001$ vs placebo.
Adapted from Kumar V, et al. *European J Neurology*. 2000;7:159-169.
MHIS = Modified Hachinski Ischemic Scale.

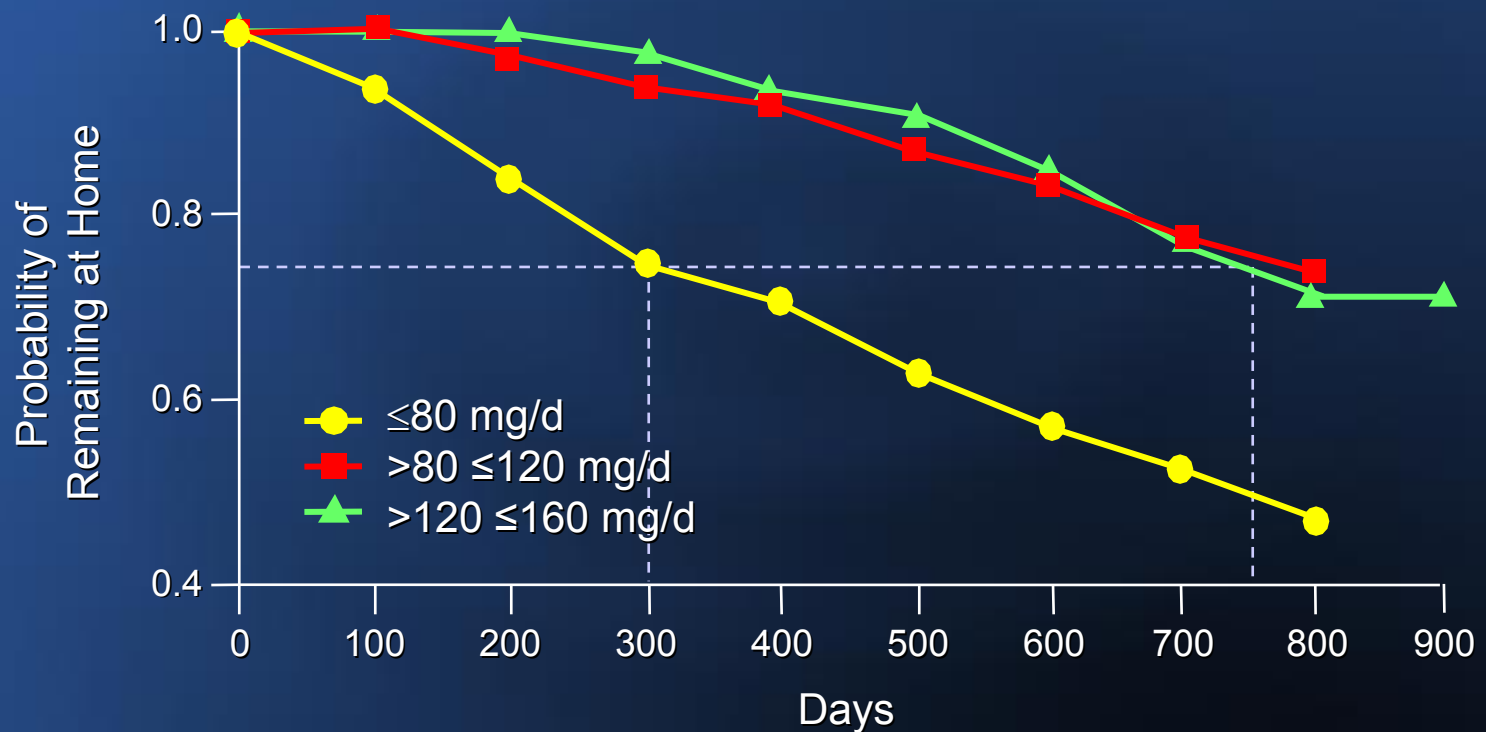
Effect of Rivastigmine on Antipsychotic Use in Nursing Home AD Patients at Week 52



n = 55

Adapted from Messina J, et al. The 3rd Annual International Meeting of the College of Psychiatric and Neurologic Pharmacists. April 6-9, 2000. Washington, DC.
Novartis Pharmaceuticals Corporation, data on file.

Long-term Effects of Tacrine on Nursing Home Placement



Knopman D, et al. *Neurology*. 1996;47:166-177.

Treatment for Dementia and Depression

- When in doubt-
 - Treat suspected Depression!
 - Treat suspected Depression!
 - Treat suspected Depression!
 - Treat suspected Depression!
 - Treat suspected Depression!
 - Treat suspected Depression!
 - Treat suspected Depression!
 - ACTUALLY IMPROVES COGNITION!!!!!!!!!!

Cognition and Exercise

- Cohort of 5925 women, mean age, 70.5 yrs, mostly Caucasian followed for 6-8 years
- Women with baseline cognitive deficits or physical mobility problems excluded
- Cognition measured by MMSE
- Exercise associated with a decreased risk of dementia, dose response noted
 - Gabb MG & Yaffe K. *Advanced Studies in Med* 2001; 1(8):324-326.

Rehab for the Dementia Pt.

- Any patient with dementia who is incapable of following the command of folding an 8 x 11" piece of paper in half and placing it on the floor will generally not be a good candidate for formal physical therapy.