Evaluation and Management of Dementia/ALz

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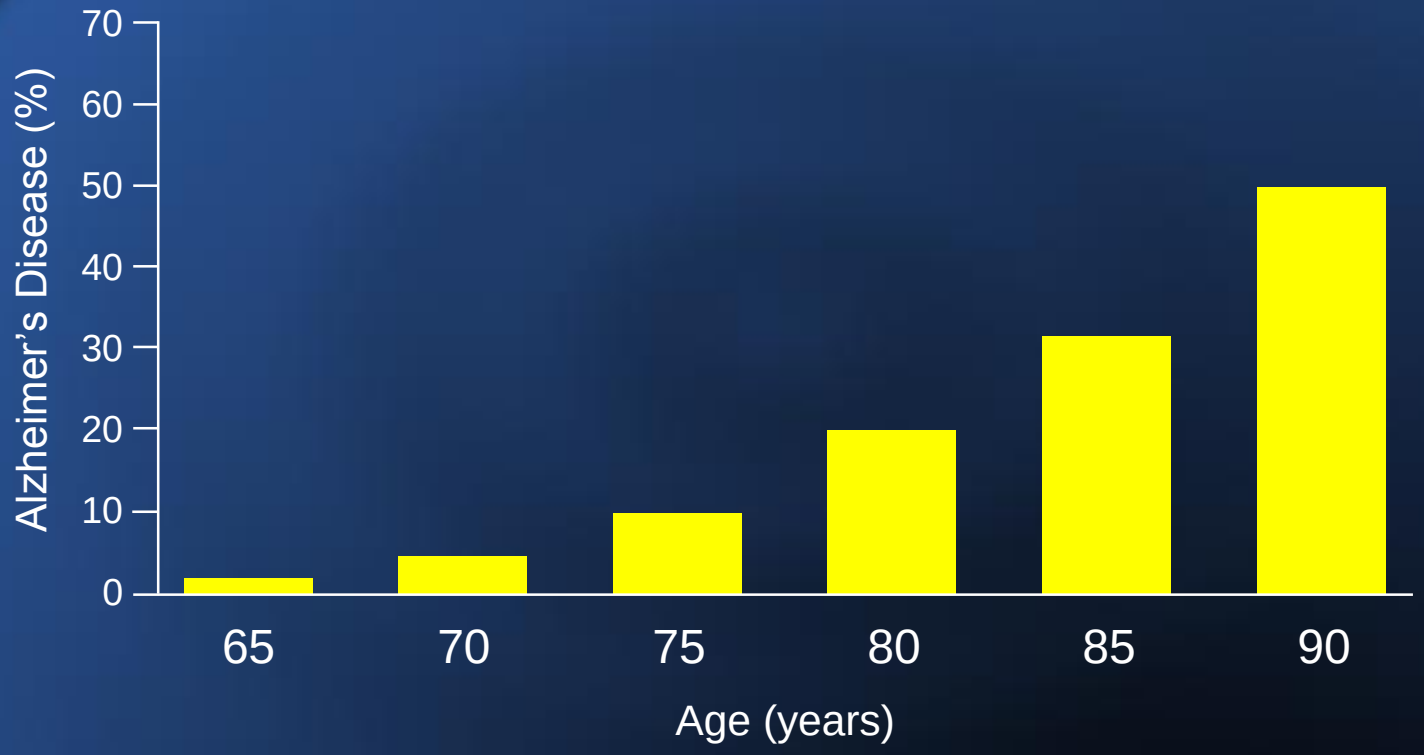
Prevalence of Alzheimer's Disease/Dementia



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)

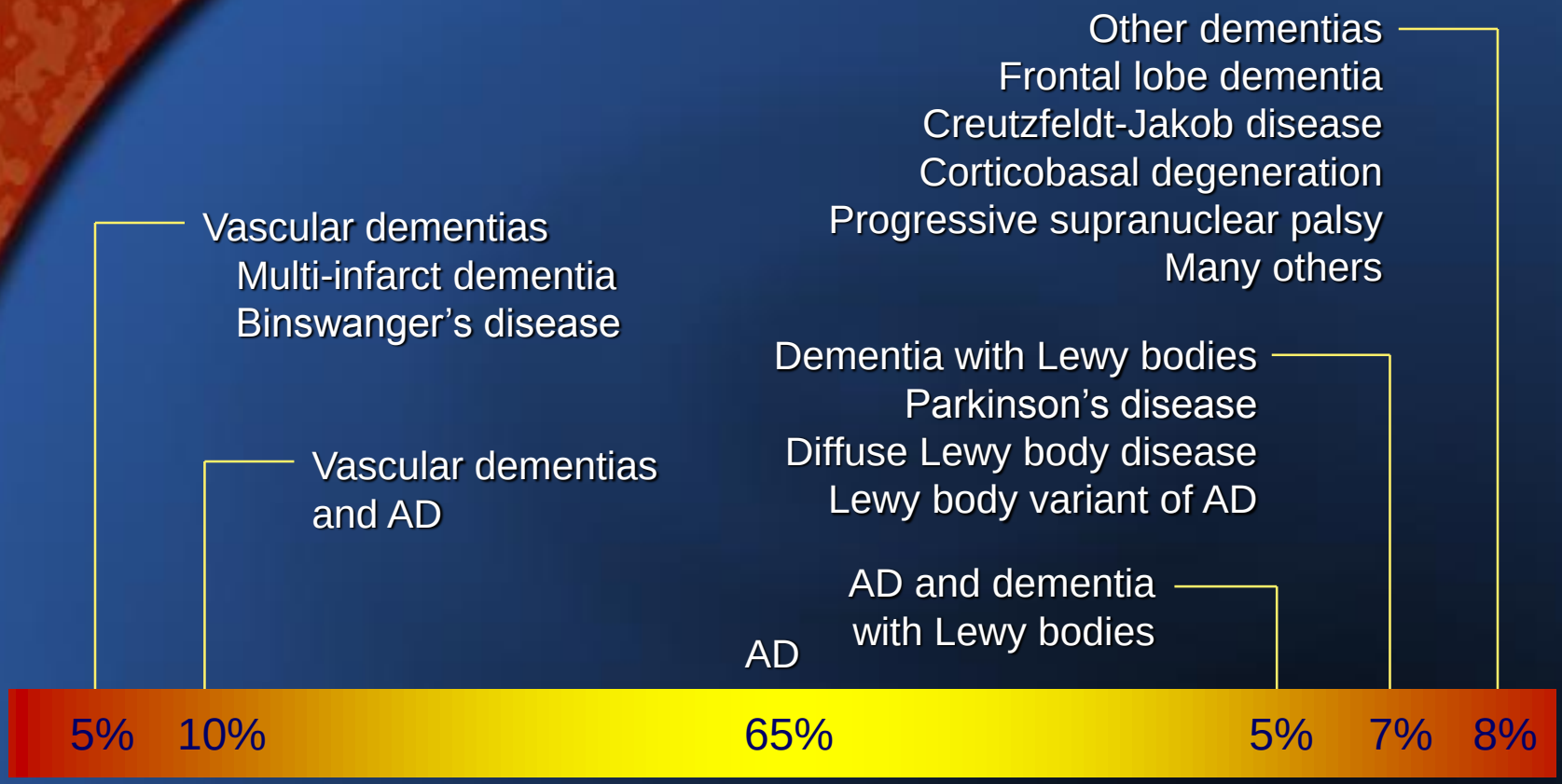
    Gutterman EM et al. J Am Ger Soc. 47:1065-1071, 1999

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)/Alzmeimer's disease

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

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
- Anti-spasmodics
- Major Phenathiazine 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

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 Deficiency
- Hypothyroidism Or Hyperparathydroidism

Workup of Dementia/Alz

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

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 FEELTHAT 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 fell 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?

MINI-MENTAL

MAX SCORE	SCORE	ORIENTATION
5	_____	What is the year (season) (date) (day) (month)?
5	_____	Where are we: (state) (country) (city) (hospital) (floor)
		REGISTRATION
3	_____	Name 3 objects (cat, flower, bat). 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		

Levels of Dementia

- MMSE > 26 normal.
- 24<MMSE <26 mild.
- 22<MMSE <24 moderate.
- MMSE < 22 severe.

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

- 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 65%
  - slow progressive linear decline over many months or years
  - ave. dur. of illness-9.2 yrs;length 3-25 years
- Multiinfarct (formally called Vascular) Dementia 5%
  - history of vascular risk factors-HBP, stroke,Dm, CAD, PVD, hyperlipidemia
  - usually slow stepwise decline over months/yrs
- Mixed AD/Vascular Dementia 10%

- The onset of AD is gradual
- VD begins abruptly and progresses in a stepwise manner
- motor abilities are unaffected in AD until advanced stages of the disease
- focal signs and symptoms are seen more in VD.
- AD : Brain CT normal vs atrophy
- VD : Brain CT stroke vs microvascular changes

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

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed. 1994:142-143.

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 (Psychiatric disorder)

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed. 1994:142-143.

Genetic Risk Of Alzheimers

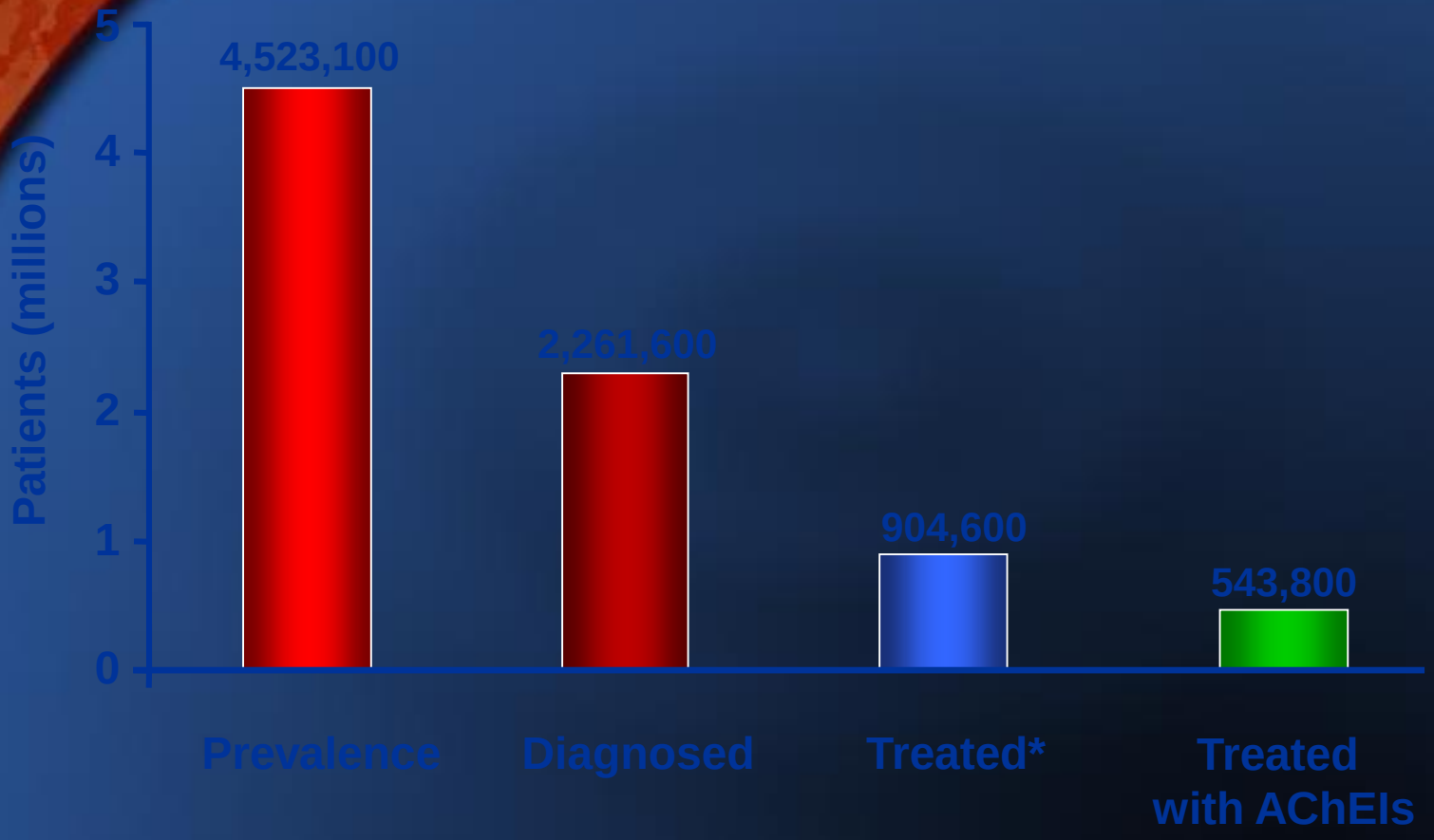
- Genes for Alzheimers found on chromosomes 21 (APP), 14 (presenilin I), and 1 (presenilin 2)-account for less than 5% of cases
- Family History or presence of 4 allele of the Apo E (chromosome 19) accounts for >30% in the general population
- History of AD in first degree relative associated with 2-3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

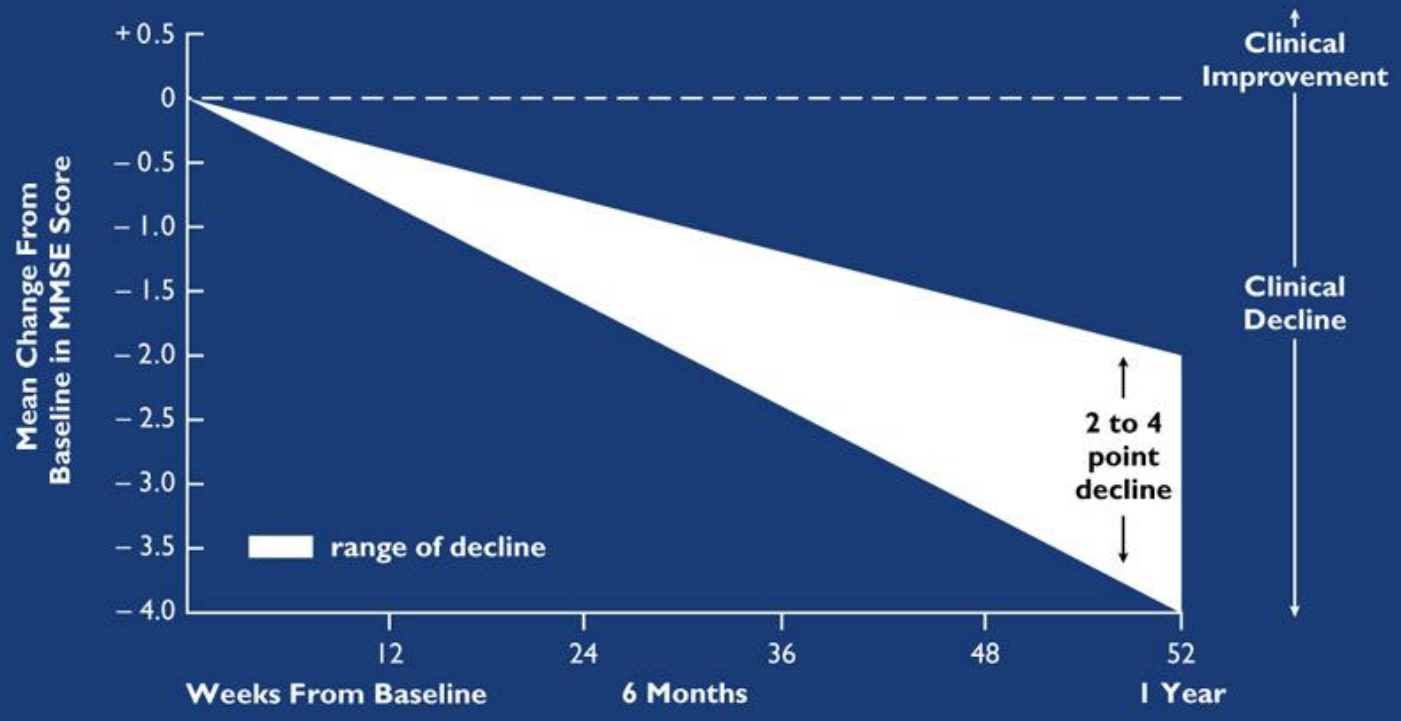
- Pharmacological Therapy
  - Donepezil (Aricept)-mild to severe
  - Rivastigmine (Exelon)-mild to moderate
  - Galantamine (Reminyl)-mild to moderate
  - Namenda-Moderate to severe

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 (anti-psychotic agents) if possible 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

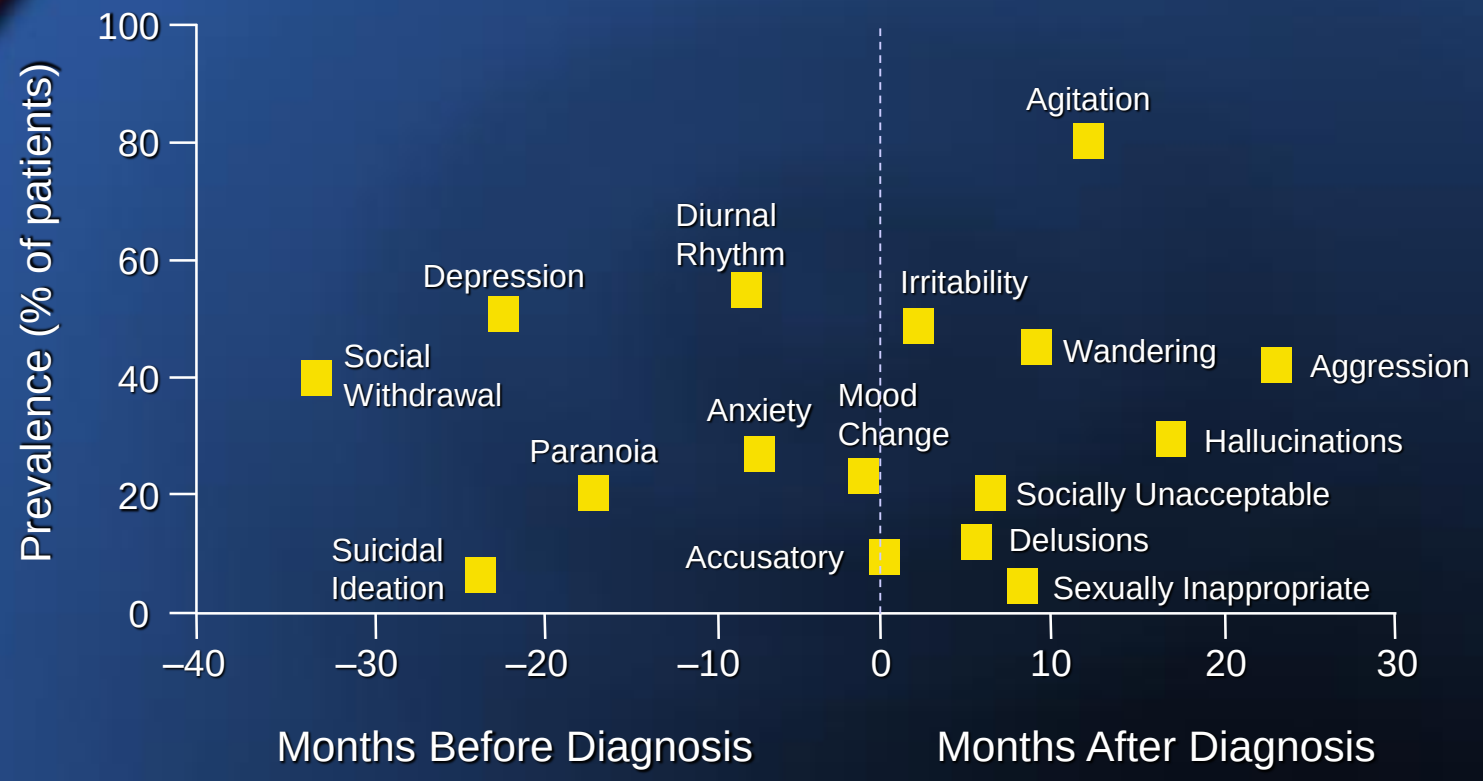
In Alzheimer's disease, cognitive decline is expected over time

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



Becker, Huff, Nebes, et al, 1998.
Mortimer, Ebbitt, Jun, et al, 1992.

Peak Frequency of Behavioral Symptoms as Alzheimer's Disease Progresses



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

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.

Hypotheses for New Therapies on the Horizon for Alzheimer's Disease

- Targeting Beta-amyloid-the chief components of plaques, considered the end result or beginning of Alz disease-development of medications that act at every point in amyloid processing
- Tau Protein-the chief component of neurofibrillary tangles-the other finding in Alzheimer's Disease. Investigating strategies to keep tau molecules from collapsing and twisting the tangles, that destroys a vital cell transport

Hypotheses for New Therapies on the Horizon for Alzheimer's Disease

- Inflammation-another brain abnormality-understanding the body's overall inflammatory response and understanding specific aspects of inflammation that might result in novel anti-inflammatory treatments to halt Alzheimer's disease
- Insulin resistance-the ways the brain cells process insulin may be linked to Alz disease

Hypotheses for New Therapies on the Horizon for Alzheimer's Disease

- Brain imaging studies and testing of the blood or spinal fluid to diagnose Alzheimer's disease in its early stages
- Testing families with a genetic disposition for Alzheimer's disease. All of these individuals have mutations that affect Beta-Amyloid.

The End