

# Alzheimer's Disease

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# Introduction

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- Goals of the discussion
  - Have a better understanding of dementing diseases.
  - Feel more comfortable understanding this illness and the diagnosis.
  - Have basic understanding of the medications available for this illness.



# Alzheimer's Disease

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- What is Alzheimer's?
- Who is at risk?
- What are the stages?
- How is a patient diagnosed?
- What can we do for treatment?



# Alzheimer's Facts

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- Degenerative brain disorder.
- The MOST Common type of demyelinating illness of the elderly.
- Prevalence increases with age, uncommon before age 65.
- Majority of patients are female.
- Characterized by insidious, irreversible cognitive decline.



# Dementia

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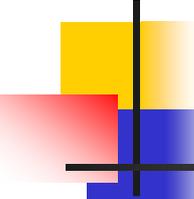
- Latin – ‘out of mind’
- Syndrome that is progressive and affects at least 1 cognitive function with decline in memory
- Assoc. w/ an Alert person
- Insidious onset
- Relentless progression



# Dementia con't

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- **Cortical symptoms (AD)** – difficulty forming new memories, aphasia, apraxia, agnosia, visual-spatial impairment
- **Subcortical (vascular dementia)** – cognitive slowing, impaired memory retrieval and attention, apathy, depression, mood liability and disinhibition, EPS



# Dementia types

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- 60% all demented patients have AD type.
- 20% have Parkinson's or Vascular type.
- 15% have Mixed dementia.
- 5% have 'other'
  - Picks
  - Lewy body
  - Multiple Sclerosis
  - Cancer
  - Alcoholic



# Alzheimer's Prevalence

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- 8% > age 65
- 20% > age 75
- 50% > age 85
  
- 2/3 of Demented patients on Autopsy have Alzheimer's.



# Alzheimer's Costs

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- | ■ Setting of care | Mild   | Moderate | Severe | Total  |
|-------------------|--------|----------|--------|--------|
| ■ All             | \$1543 | \$2508   | \$3011 | \$2306 |
| ■ Community       | \$1158 | \$1874   | \$2266 | \$1549 |
| ■ Institutional   | \$2840 | \$3069   | \$3288 | \$3130 |
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- Based on 1996 costs and nursing home admissions that a 1 month delay in nursing home placement could yield a savings of \$1.12 billion annually. (Estimated cost per patient of nursing home care is estimated at \$42,000/yr)



# Co-morbidity

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- Other diseases of the elderly:
  - 50% with arthritis
  - 35% with hypertension
  - 30% with heart disease
  - 10 % with diabetes



# Gross Anatomical changes

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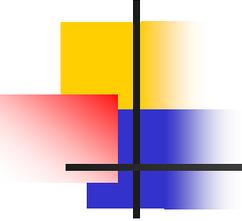
- Atrophy of frontal, temporal, and parietal cortex.
- Widening of sulci between gyri.
- Enlargement of ventricular system.



# Microscopic changes

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- **Senile plaques** – Amyloid (extracellular) structure in neocortex and hippocampus. Dense and insoluble.
- **Neurofibrillary tangles** – intracellular inclusion bodies made of paired helical filaments, composed of tau protein.
- Neurons surround a central core of an abnormal protein (Amyloid), preventing normal function



# AD Characteristics

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- Marked by personality changes and impaired judgment.
- Progressive decline in intellectual function that interferes with:
  - ADL
  - Behavior (social skills)
  - Cognitive ability



# Who is at risk for AD?

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- Risk increases with age.
- Down's syndrome
- Illiteracy or low education
- Parkinson's disease
- Family history of:
  - AD
    - first degree relative = 3x (35%)
    - APOE4 = 3x (35%)
    - Autosomal Dominant = 100%
  - Parkinson's disease



# More AD risk

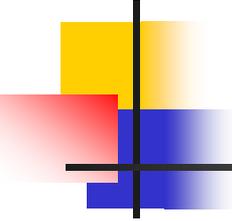
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- ? Increased with:

- Advanced parental age
- Hx depression
- Hx heavy alcohol use
- Hx head trauma

- ? Decrease with:

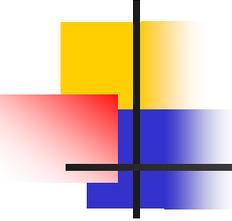
- Arthritis or heavy NSAID use
- Oral estrogen use
- Ginko Biloba
- Anti-oxidant use



# AD stages

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- Early
- Mid-stage
- Severe
- Terminal



# AD progression

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- Typically progression occurs over 8 – 10 years (extremes of 2 – 20 years).
- Patients noted to have more rapid cognitive decline if:
  - Psychotic symptoms
  - Early age of onset
  - Seizures occur
  - Extra pyramidal features



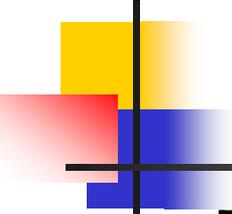
# What to look for:

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Aphasia, Apraxia, Agnosia, Dysnomia, and disturbance in executive function.

ADL impairment

Cognition changes and decreased ability to perform common tasks with ease and completeness.



# Definitions:

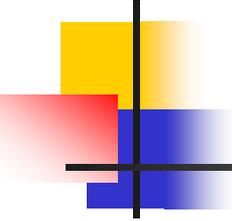
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Aphasia – language disturbance

Apraxia – reduced ability to carry out motor function despite intact mental function

Agnosia – failure to recognize common objects

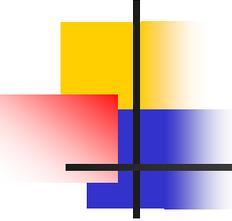
Executive function – Plan, organize, sequence, and abstract thinking



# Activities of Daily Living

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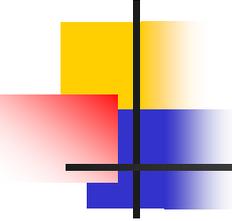
- Toileting
- Feeding
- Dressing
- Grooming
- Ambulation
- Bathing



# Personality changes

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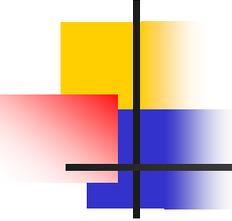
- Depressive - passivity, disinterest, withdrawal
- Agitation – Anger, suspicion
- Social relationship confusion



# Early AD stage

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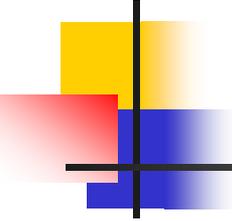
- ADL decline
- Misplacement of items w/o self retrieval
- Impaired acquisition of new information
- Inability to recall recent conversation or event
- Personality changes



# More Early symptoms

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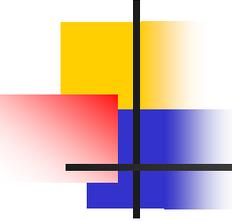
- Dressing inappropriately
- Poor: judgment, attention, problem solving
- Day/date/time disorientation and confusion
- Speech hesitancy and decreased verbal output
- Dysnomia – word finding difficulty



# Delirium

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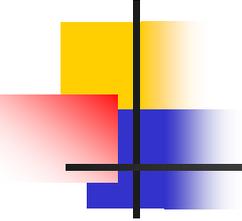
- Confusion with over activity of autonomic nervous system – treat and evaluate for cause
  - ? intoxication (amphetamine)
  - ? withdrawal (alcohol, benzodiazepines, barbiturates)
  - ? systemic toxic state (fever, sepsis)



# Acute Confusion

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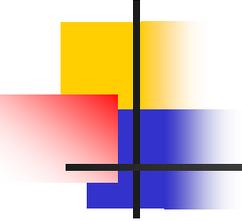
- Inability to maintain a coherent thought stream.
- Need to treat, but need to determine cause.
  - Toxic
  - Infection or infarct
  - Epilepsy
  - Mass



# Mid-stage

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- Progressive decline
- Suspicious
- Written and verbal language impairment
- Agitation, restlessness, wandering
- Day/night disorientation
- Aggression
- Delusions
- Hallucinations

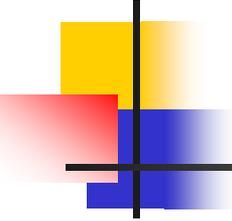


# Agitation

a symptom, not a diagnosis

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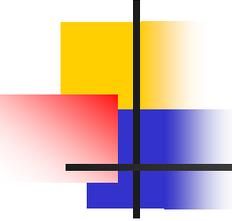
- Verbal – yelling, moaning, preservation, crying, belligerent
- Motor – pacing, fidgeting, restless, sleep disturb., aggression
- Psychotic – delusions, suspicious, hallucinations



# Anxiety symptoms

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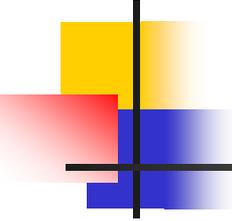
- Facial expressions
- Guarding
- Tension
- Shaking
- Hyper vigilance
- Attention inability
- Physical complaints
- Resists care



# Depressive symptoms

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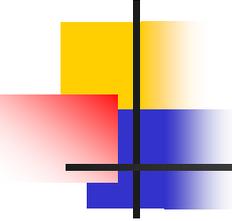
- Irritable
- Dysphoric
- Tearful
- Sleep disturbance
- Anorexia
- Apathy
- Numerous somatic complaints



# Risky Behaviors

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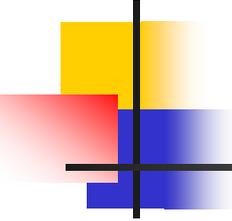
- Wandering
- Elopement
- Sexually inappropriate behavior
- Rummaging
- Hoarding
- Stealing



# Severe or End Stage

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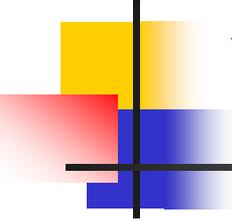
- Total dependence for ADL
- Hallucinations
- Minimal remnant of memory
- Restricted verbal output
- Urinary and fecal incontinence
- Tonic-clonic seizures



# Terminal

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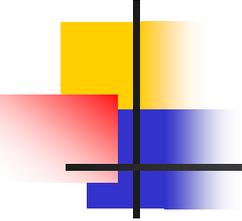
- Bedridden
- Uncomprehending
- Vegetative state
- Weight loss
- Dysphasia



# “Extra Care Required”

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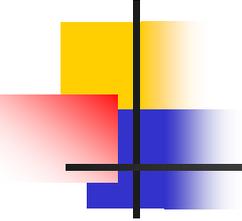
- Pressure sores
  - Poor nutrition
  - Decreased activity
- Dehydration
  - Non-verbal
  - Trying not to be incontinent
  - Swallowing problems
- Infection



# Prognosis

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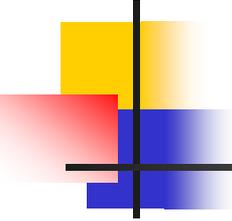
- Death, if not due to some other cause, is usually due to:
  - Aspiration
  - Inanition
  - Pulmonary embolism
  - Infection



# Diagnosis

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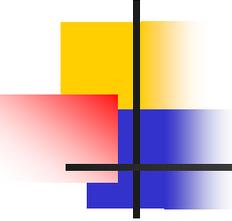
- History
  - Past medical
  - Past surgical
  - Past social
  - Family
- Exam
- Testing



# Alzheimer's Differential

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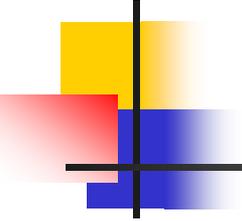
- Depression – may have both, especially if >65
- Drug effect
- Thyroid abnormality
- B12 deficiency
- Normal Pressure Hydrocephalus
- Subdural hemotoma
- Tumor



# Barriers to diagnosis

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- Futility – thought either by the physician, care giver, or the patient.
- Denial
- Fear that diagnosis will result in negative effects

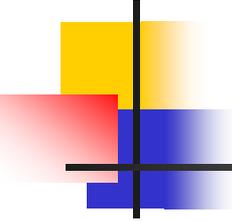


# Objective Evaluation

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- Lab: CBC, CMP, Thyroid, RPR, B12, ?HIV
- Cognitive Tests – MMSE, Clock drawing, Short Blessed Test, Information/Memory/Concentration – and need longitudinal testing
- Imaging – CT, MRI, PET, ?CXR

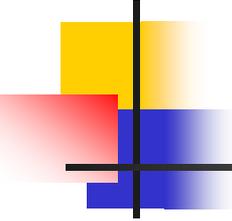




# Mini-Mental Status Exam

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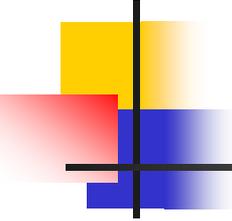
- Evaluates: (retest 2 times annually)
  - Orientation
  - Registration
  - Language
  - Attention and Calculation
  - Recall
  
- Scoring (24 is the cutoff)
  - 30 – 20 Mild
  - 19 – 10 Moderate
  - < 9 Severe



# Alzheimer's Treatment Goals

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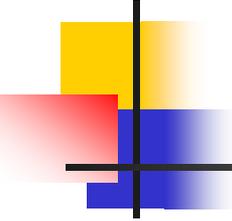
- Instrumental ADL
  - Phone, appliance use, shopping, hobbies, money management, food preparation, mail, comprehension
- Basic ADL
  - Dressing, Eating, Toileting, Bathing, Ambulating



# Treatment needs

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- Prevent further progression at earliest point.
- Toileting problems
- Sleep disturbances
- Weight loss
- Depression and Anxiety
- Inappropriate behavior

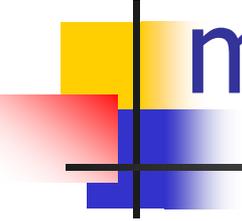


# Dementia Medications

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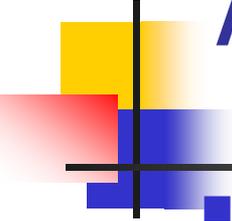
- Atypical antipsychotics
- Antidepressants
- Cholinesterase inhibitors
- Dopamine Agonists
- Stimulants

# Prevent or slow further memory loss



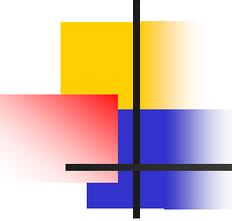
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- Goal is to keep these individuals as independent as long as possible.
- Different meds available for this:
  - Tacrine
  - Donepezil
  - Galantamine
  - Rivastigmine



# Anticholinesterase Inhibitors

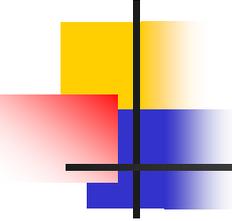
- Precise mechanism of action is unknown.
- The 2 newer agents also affect the Nicotinic receptors. The clinical significance of this is unknown.
- All 3 of the newer agents affect, improve or slow deterioration of:
  - General function
  - Cognition (memory and thinking)
  - ADL
  - Behavior



# Chemically in the AD pt.

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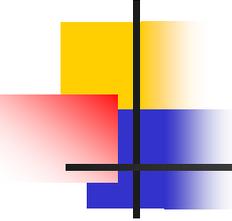
- Decrease acetylcholinesterase
- Decreased choline acetyltransferase
- Loss of cholinergic neurons
- Loss of acetylcholine availability
- Loss of muscarinic receptors



# Cholinergic Hypothesis

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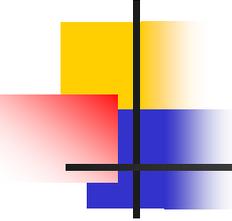
- Meds developed to enhance central cholinergic function.
- Proposed link between: cognitive decline and loss of cholinergic neurotransmission (hippocampus and cortex) .
- Improve cognitive and global function by increasing cholinergic function.



# Tacrine

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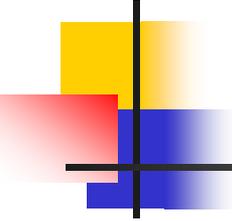
- First drug developed for treatment.
- Not used any longer due to side effects, and better meds available.



# Donepezil

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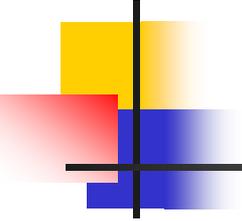
- Side effect profile of this medication is very similar to newer generation meds.
- Shown positive results.
- Simple dosing schedule
- Simple titration schedule



# Galantamine

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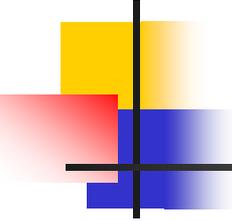
- A competitive and reversible agent that enhances cholinergic function.
- Start with 4 mg bid with food for 4 weeks.
- Maintenance is 8 mg bid with food.
- Treatment goals are to sustain cognition and preserve global function/performance.



# Rivastigmine

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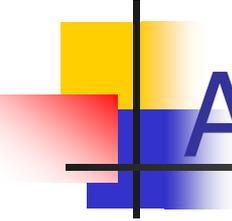
- 3 to 12mg daily (divided bid)
- Requires monthly titration
- Side effects similar to others in class



# Treatment success

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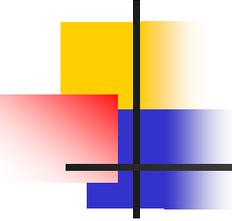
- Maximize function
- Maintain independence
- Continue in own home environment
  
- ALL depends on early medication initiation and continuation.



# Anticholinesterase Inhibitors

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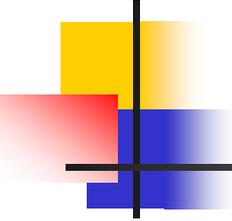
- Needs:
  - To show positive results
  - Tolerability
    - Side effect
    - Financial
    - Dosing schedule
    - Drug interaction



# Caution with anticholinergics

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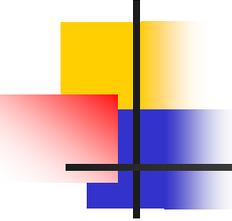
- Antispasmodics
- TCA
- Conventional antipsychotics



# Making things worse

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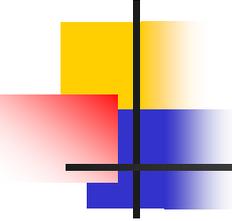
- Levodopa/carbidopa
- Cimetidine
- NSAID
- Antihistamine
- TSA
- Antiarrhythmics
- Anticonvulsants
  
- But some of these may be needed in certain circumstances.



# Other disturbances

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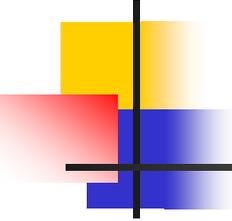
- Motor restlessness
- Verbal or physical aggression
- Irritability
- Dysphoria
- Delusions
- Hallucinations
- Sleep disturbances
- Wandering



# Behavior not likely to respond to meds.

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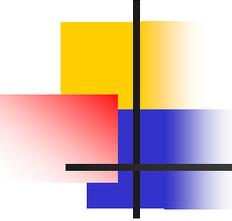
- Wandering
- Inappropriate verbalizing
- Inappropriate sexual behavior
- Willfulness
- Hoarding/appropriating
- Inappropriate voiding



# Toileting problems

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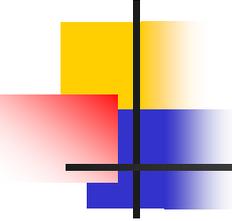
- Meds
- Behavior
  - Timing of use
  - More Velcro and less buttons/zippers
  - Watch for non-verbal clues



# Sleep disturbance

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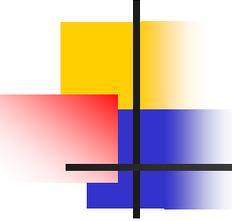
- Meds
  - Try to line up side effects with patient needs
- Environmental
  - Alter 'naps', feeding, and activity times



# Inappropriate behavior

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- Not completely understood.
- Can be multifactorial.
- The toughest problem to treat.
- Can be delayed if Anticholinesterase meds are used early in disease course.

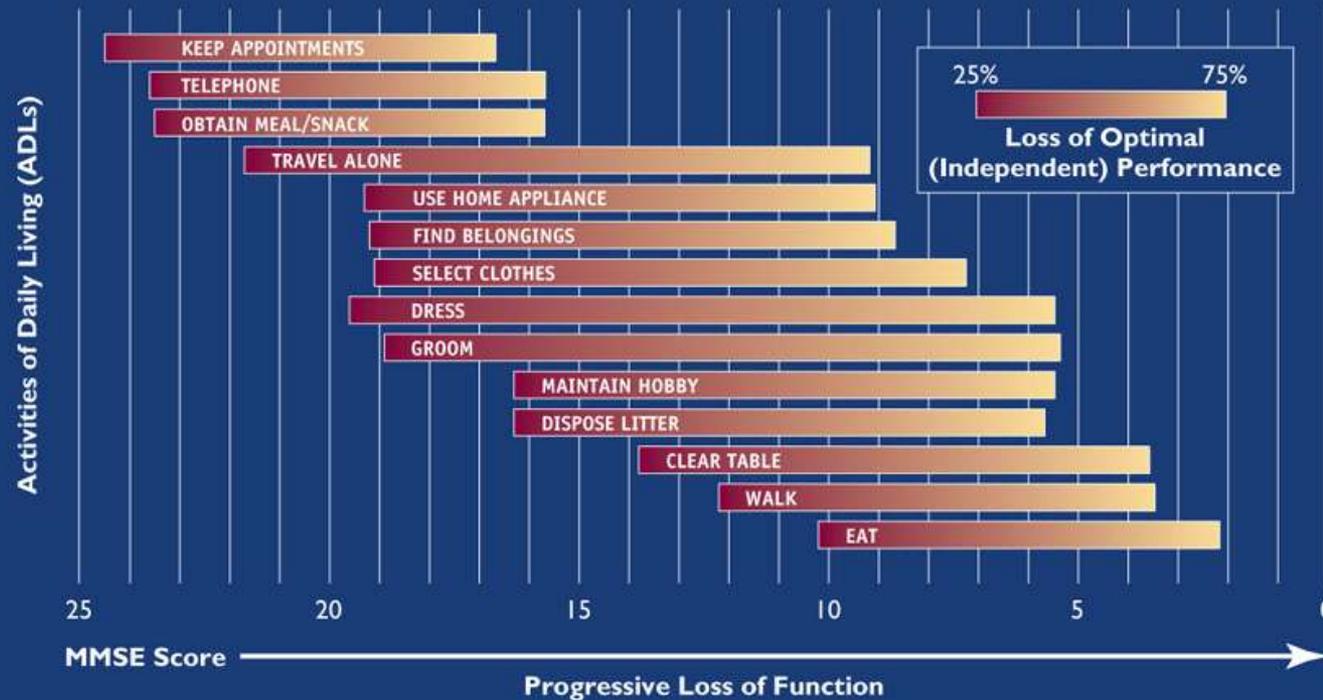


# Real Life

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- About 4 million Americans have this disease.
- This number will more than double in the next 50 years.

# Higher MMSE scores correlate with increased ability to perform activities of daily living (ADLs)



Galasko, Bennett, Sano, et al, 1997.  
Galasko D, 1996.

# Treatment expectations

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In Alzheimer's disease, clinical success is defined as:

- Improvement
- No change
- Less-than-expected decline