

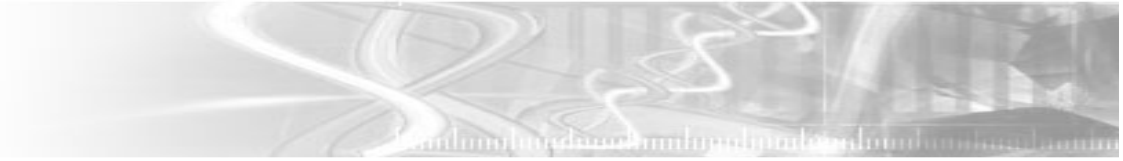


**HOTCHKISS  
BRAIN INSTITUTE**

## Dementia: Brief Overview and Latest Research

Eric E. Smith, MD  
Associate Professor of Neurology

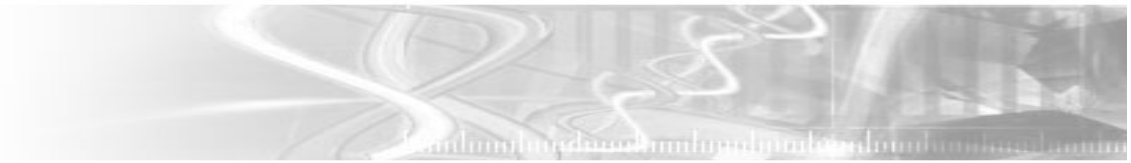
Jan 18, 2014



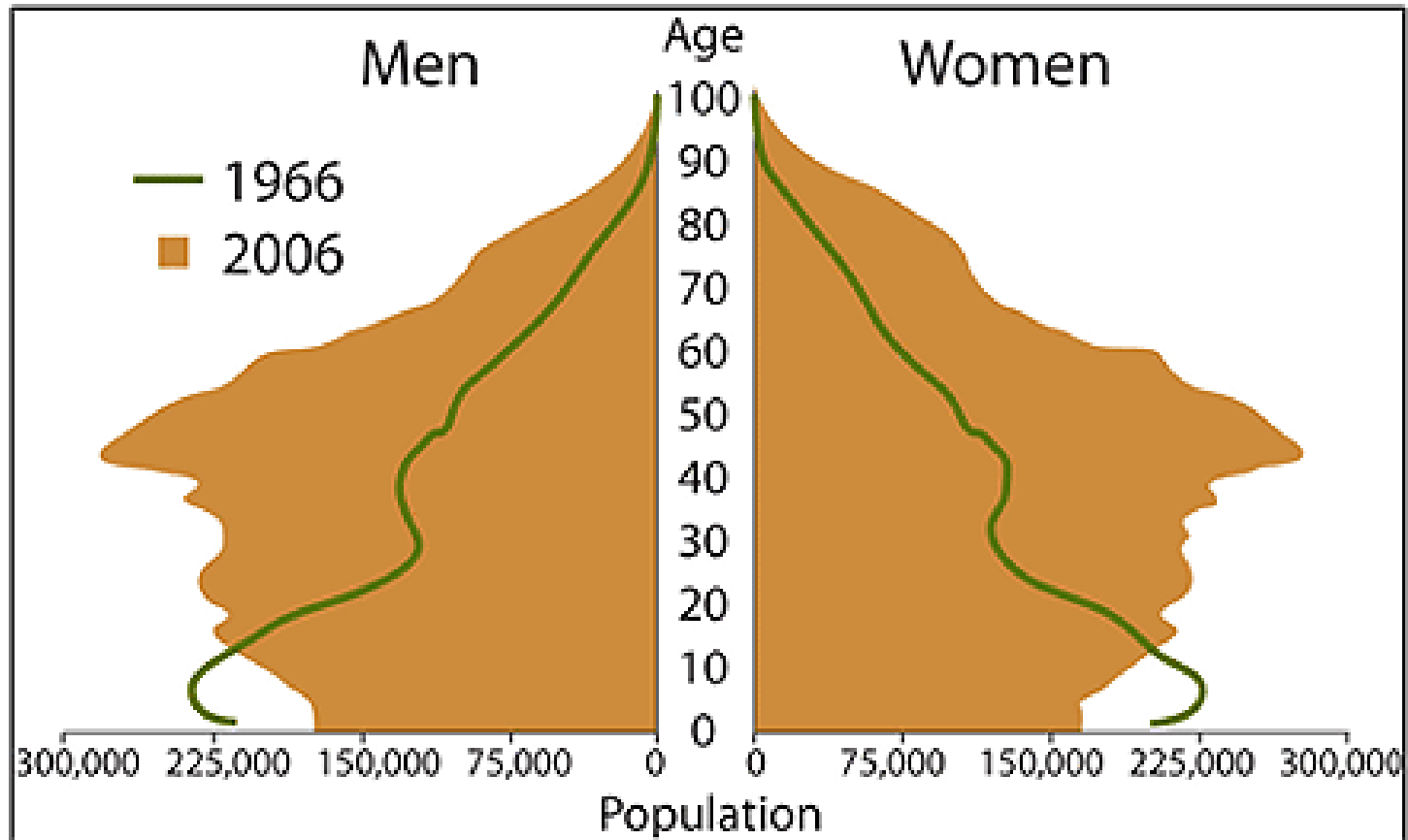
## OUTLINE

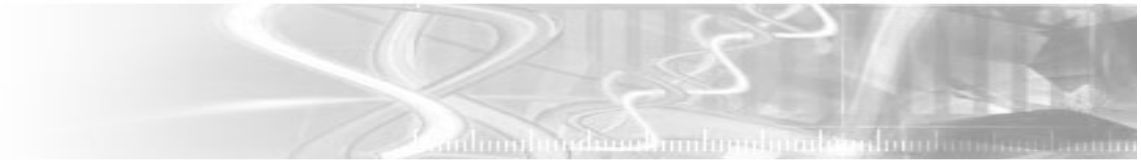
- Dementia and our aging population.
- Dementia statistics.
- Causes of dementia.
- Diagnosis and management—physician perspective.
- Trends in research.



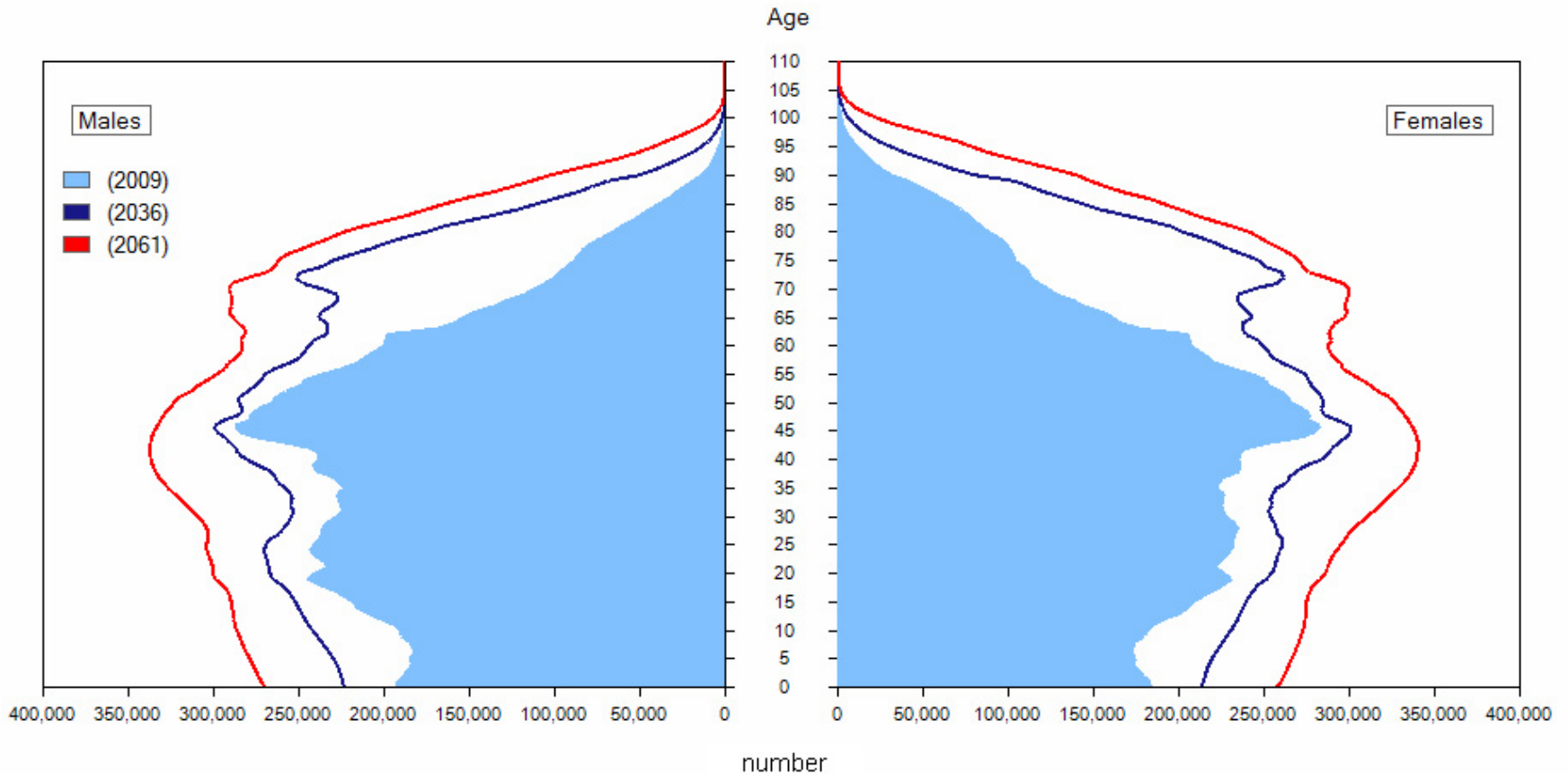


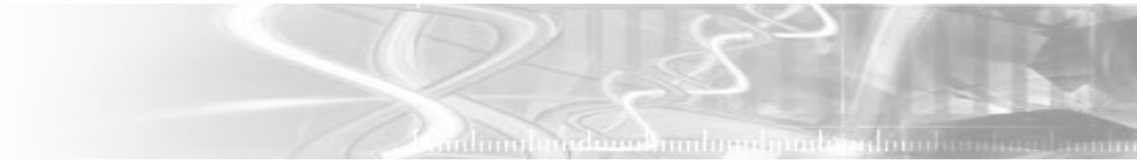
## AGE OF CANADIANS



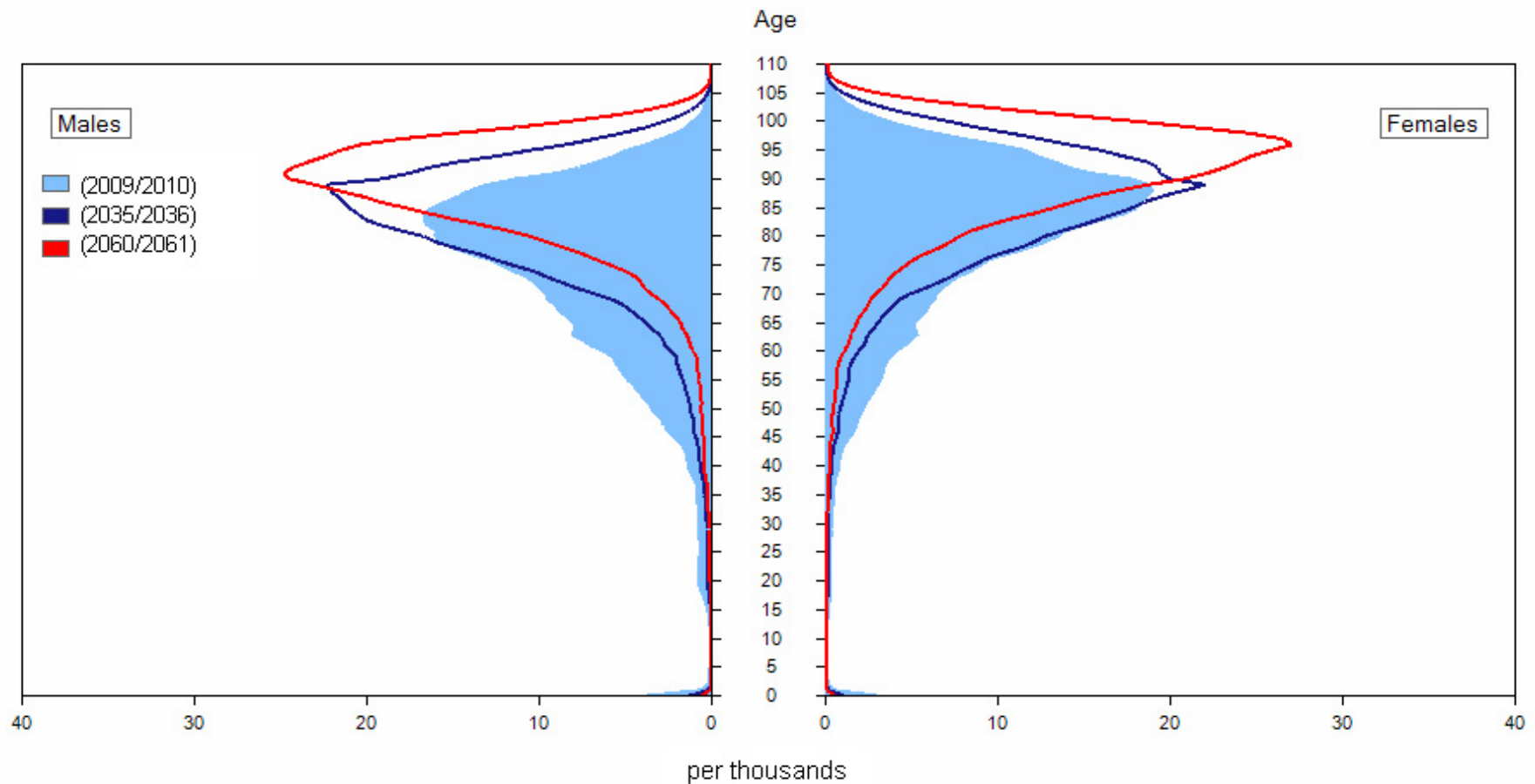


# An Aging Population Requires An Increased Emphasis on Healthy Brain Aging

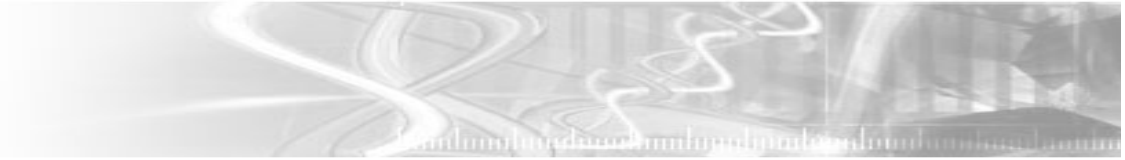




# CANADIANS ARE LIVING LONGER THAN EVER BEFORE



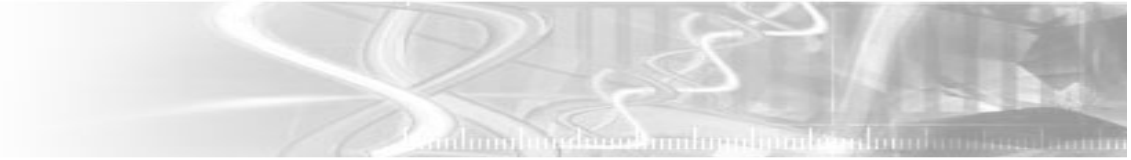
- Current modal age of death 84; 88 in 2036; 91 in 2061



## CANADIANS ARE OLDER THAN EVER BEFORE

Stats Canada

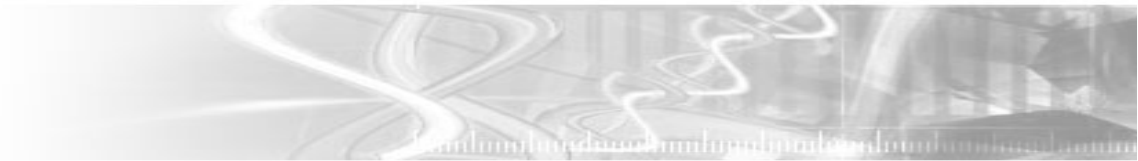
- Population is aging
- Number of seniors will more than double by 2036, about 25% of the population
- First time in history there will be more seniors than children <15 years, and almost twice as many seniors by 2061
- By 2036 there will be a 260% increase in persons over 80, 400% increase in persons >100



## AGE AND MEMORY

- Memory and reasoning abilities decline with age, and this decline is detectable by at least age 45, and possibly sooner.
- “Crystalline” intelligence changes little, however.



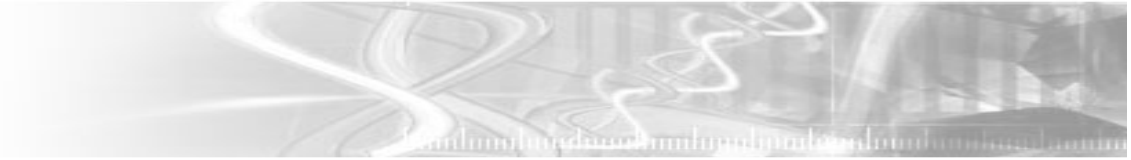


DEMENTIA: impaired activities of living because of cognitive difficulties.

MILD COGNITIVE IMPAIRMENT: cognitive concerns with objective evidence of poor cognitive performance, but without the significantly impaired activities that characterize dementia.







# LIFETIME RISK OF DEMENTIA in Women Is **1** in **4**, and in Men is **1** in **6**.

Lifetime risk of:

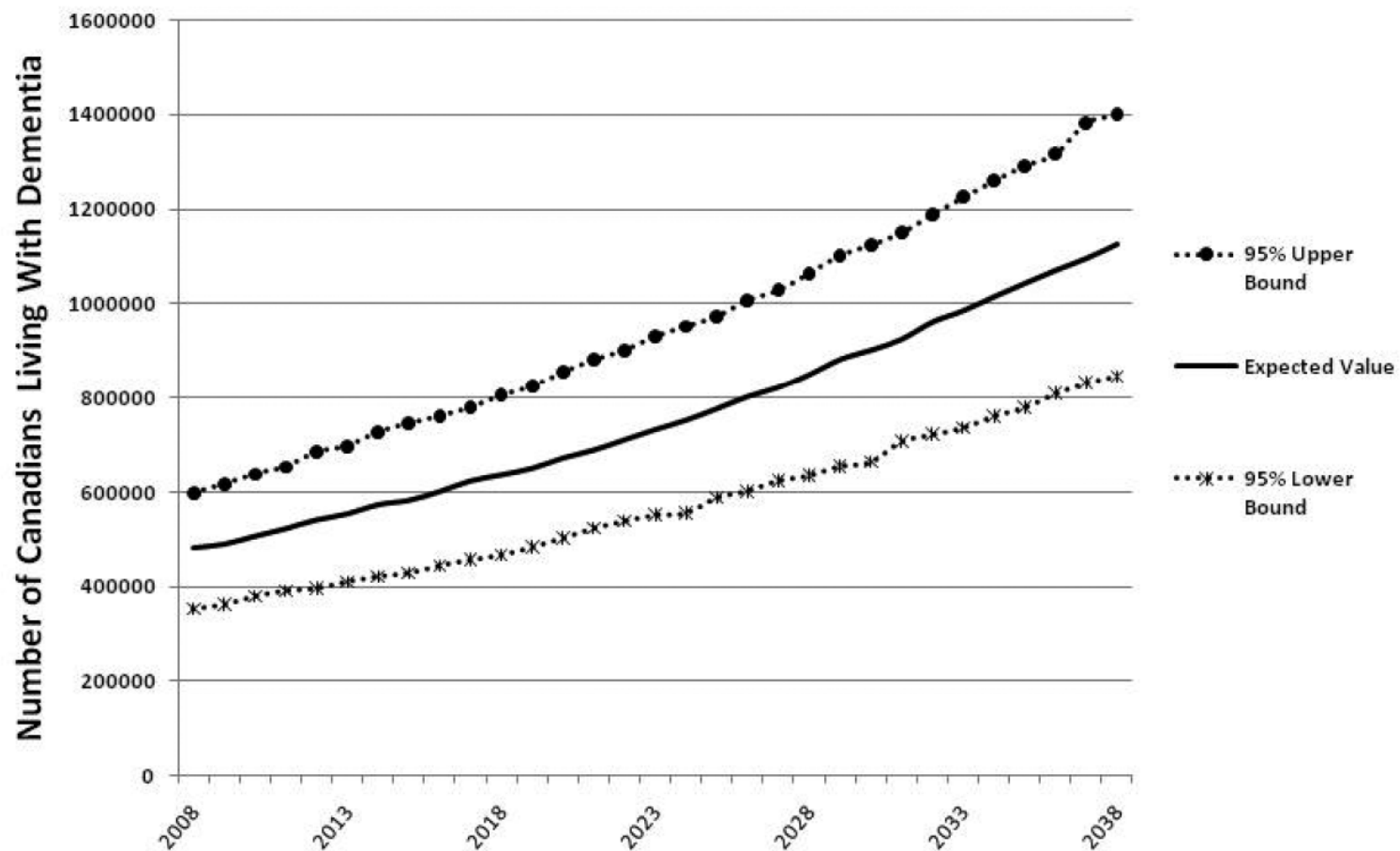
- Breast cancer in women: 1 in 8
- Prostate cancer in men: 1 in 6
- Parkinson's disease: 1 in 15
- Epilepsy: 1 in 26
- Multiple sclerosis: 1 in 500

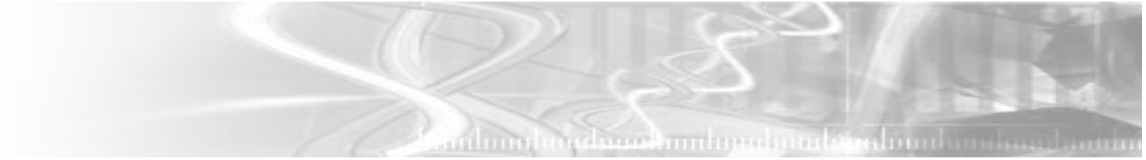




Projected prevalence: 2008 – 480,618 people, or 1.5% of the Canadian population  
2038 – 1,125,184 people, or 2.8% of the Canadian population

Prevalence of Dementia in Canada 2008 to 2038



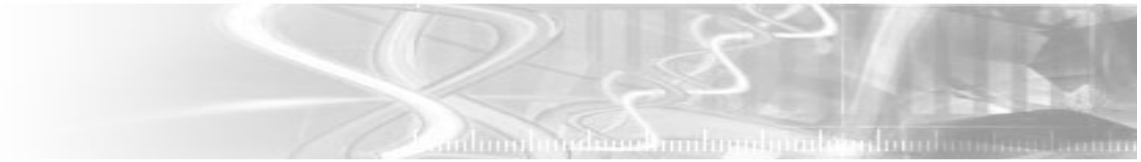


## DEMENTIA IN CALGARY

Currently living with dementia: **11,700**

Newly diagnosed cases per year: **2,800**





## DEMENTIA IN CALGARY

### Seniors ( $\geq 65$ ):

- Prevalence: 11,700.
- Incidence: 2,787 per year.

### Early onset ( $< 65$ ):

- Prevalence: 353.
- Incidence: 92 per year.

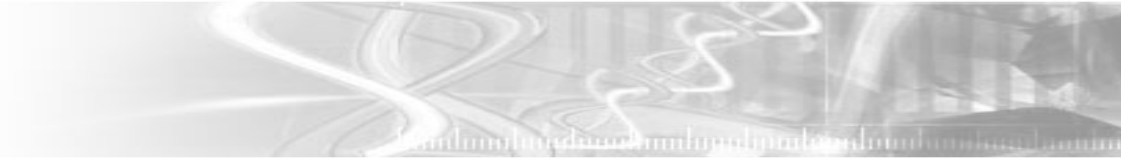
Canadian Study of Health and Aging: study methods and prevalence of dementia. CMAJ. 1994;150:899-913.

The incidence of dementia in Canada. The Canadian Study of Health and Aging Working Group. Neurology. 2000;55:66-73.

<http://www.calgaryeconomicdevelopment.com/live-work-play/live/demographics>.

Harvey RJ, et al. The prevalence and causes of dementia in people under the age of 65 years. J Neurol Neurosurg Psychiatry. 2003;74:1206-1209.

Garre-Olmo J et al. Incidence and subtypes of early-onset dementia in a geographically defined general population. Neurology. 2010;75:1249-1255.

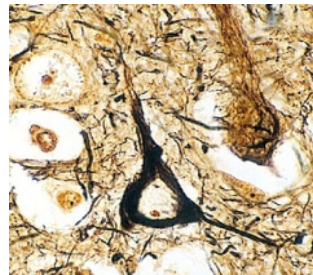
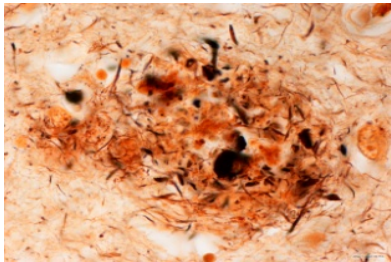


# BRAIN DISEASES THAT AFFECT MEMORY

## Alzheimer's Disease

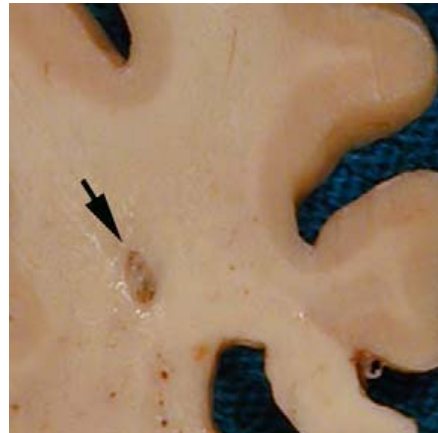
Senile Neuritic  
Plaques

Neurofibrillary  
Tangles



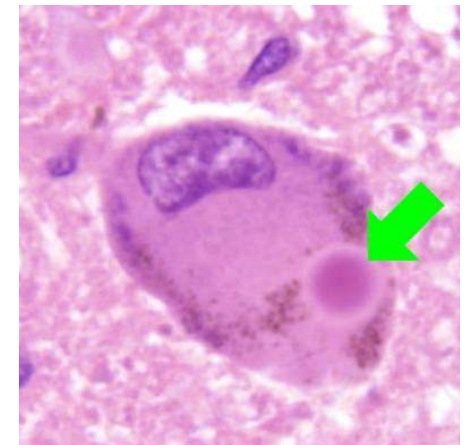
50%

## Cerebrovascular (Blood Vessel) Diseases



33%

## Lewy Body Disease





# *Alois Alzheimer, 1906*

- 52 year old woman
- Progressive neurological decline
- Memory impairment
- Paranoia
- Immobility
- Death at 56 years
- Autopsy (plaques and tangles)
- **Alzheimer disease**
- **Senile Dementia S.D.A.T**
- Dementia - Probable Alzheimer disease



Auguste Deter 1850-1906





# *The Brain and Alzheimer Disease*

**A. Cerebral Cortex:** Involved in conscious thought and language.

**B. Basal forebrain:** Has large numbers of neurons containing acetylcholine, a chemical important in memory and learning. Early in AD there is a decline in ACh.

**C. Hippocampus:** Essential to memory storage. The earliest signs of AD are found in the nearby entorhinal cortex (not shown).

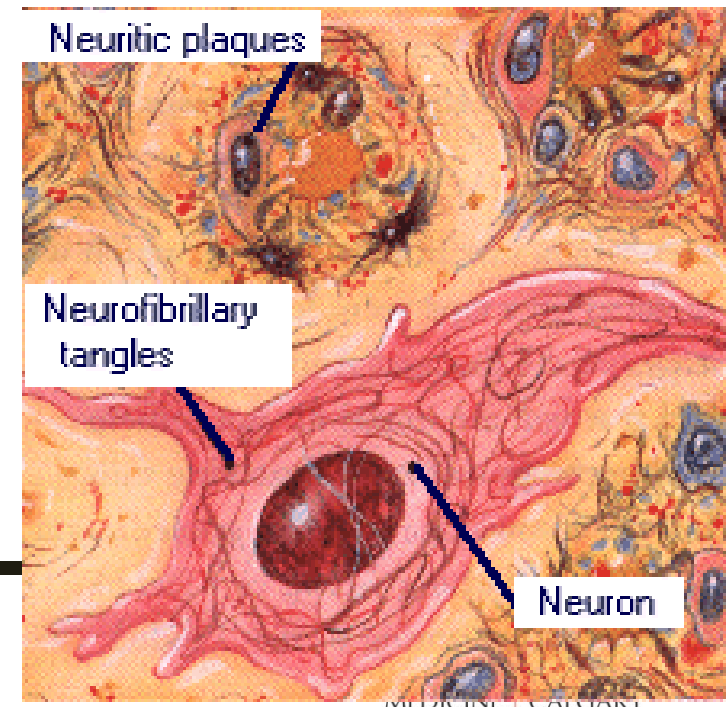
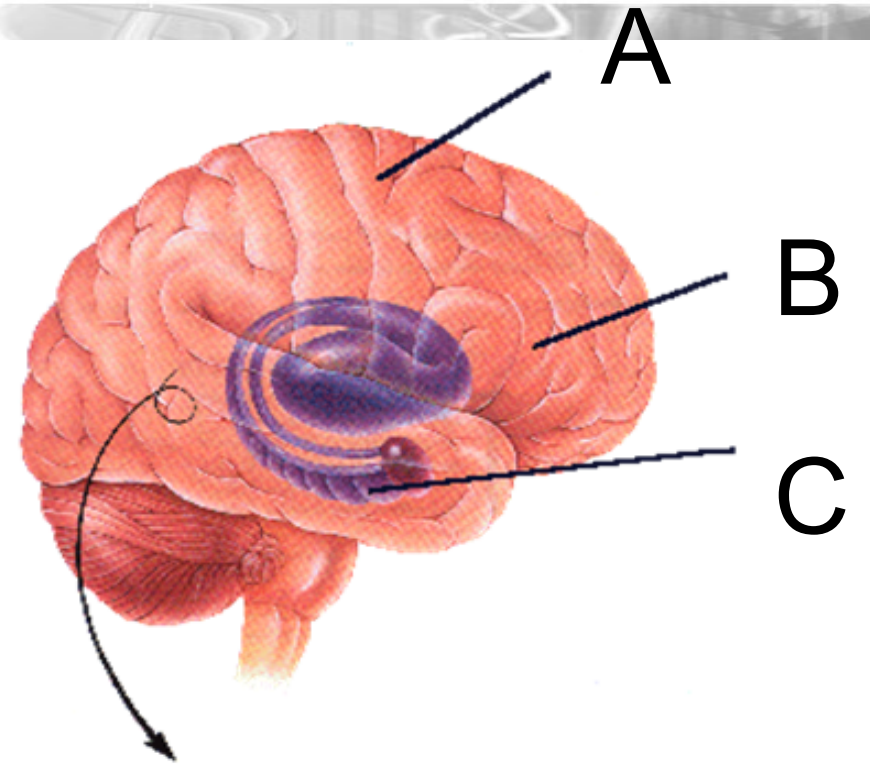
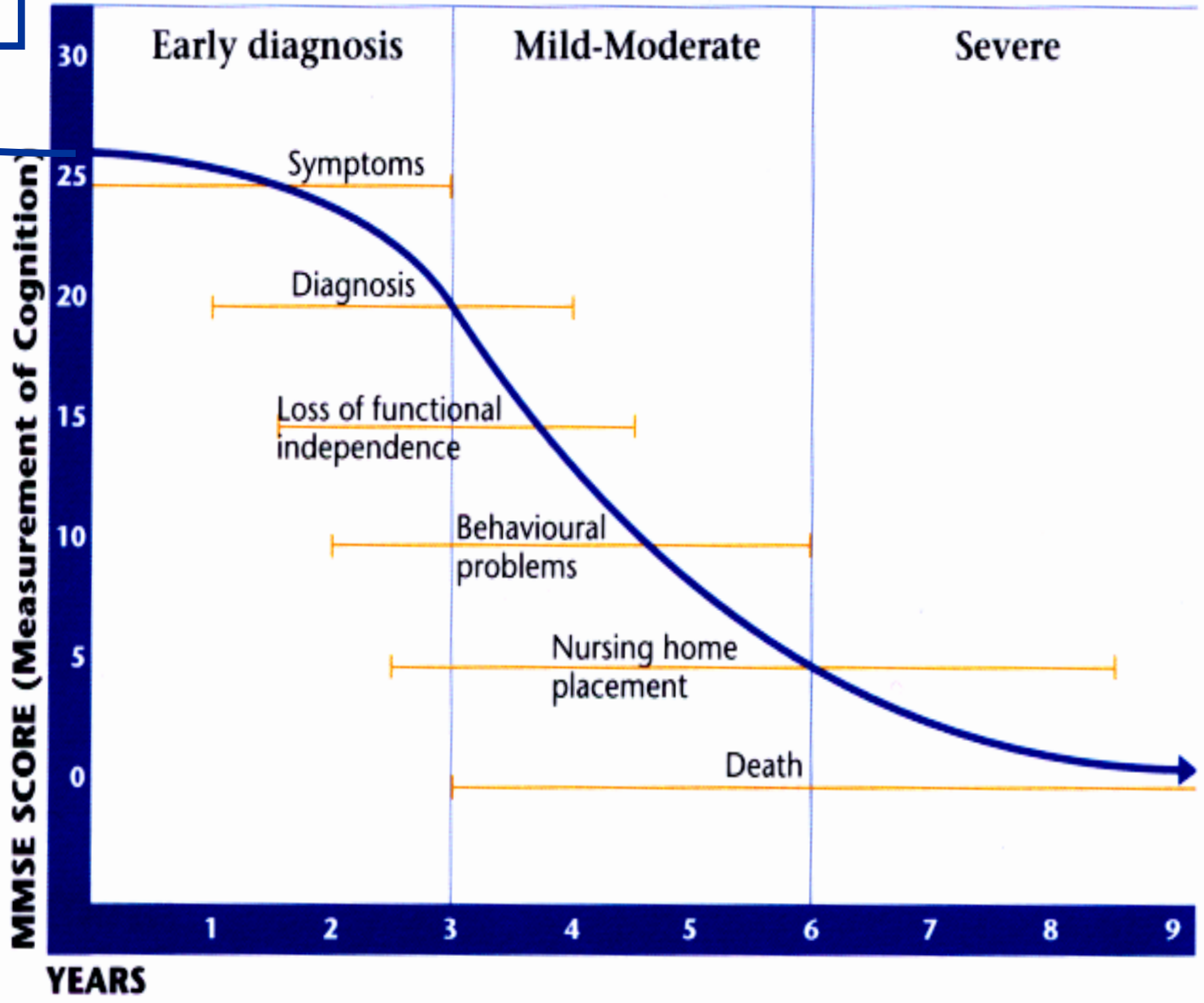


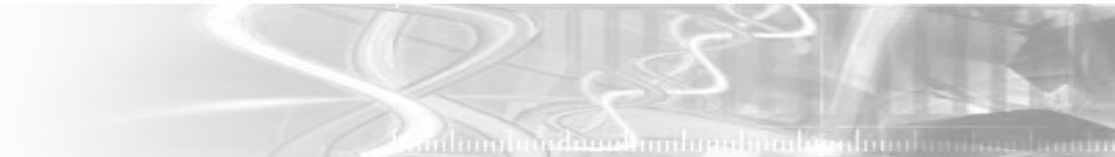
Figure 1. Progression of AD  
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# Natural history of Alzheimer's disease

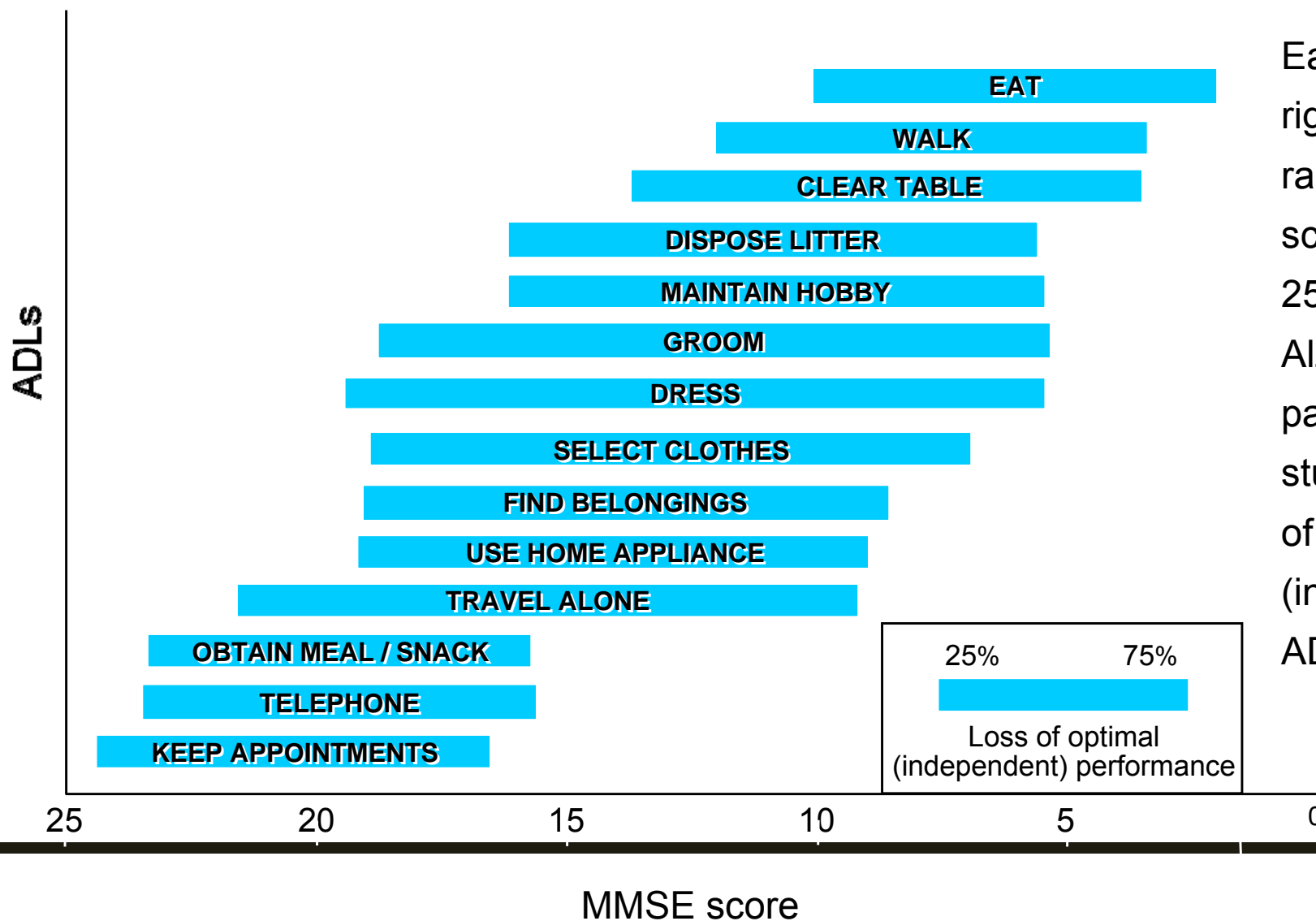
MCI







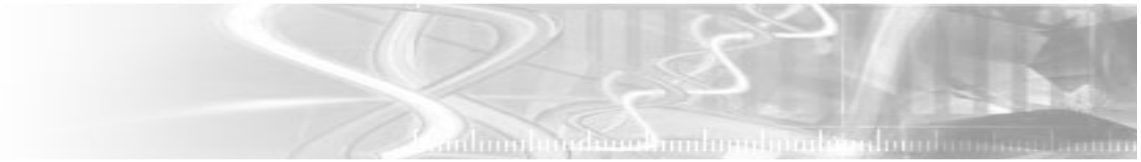
# Progressive Loss of Activities of Living



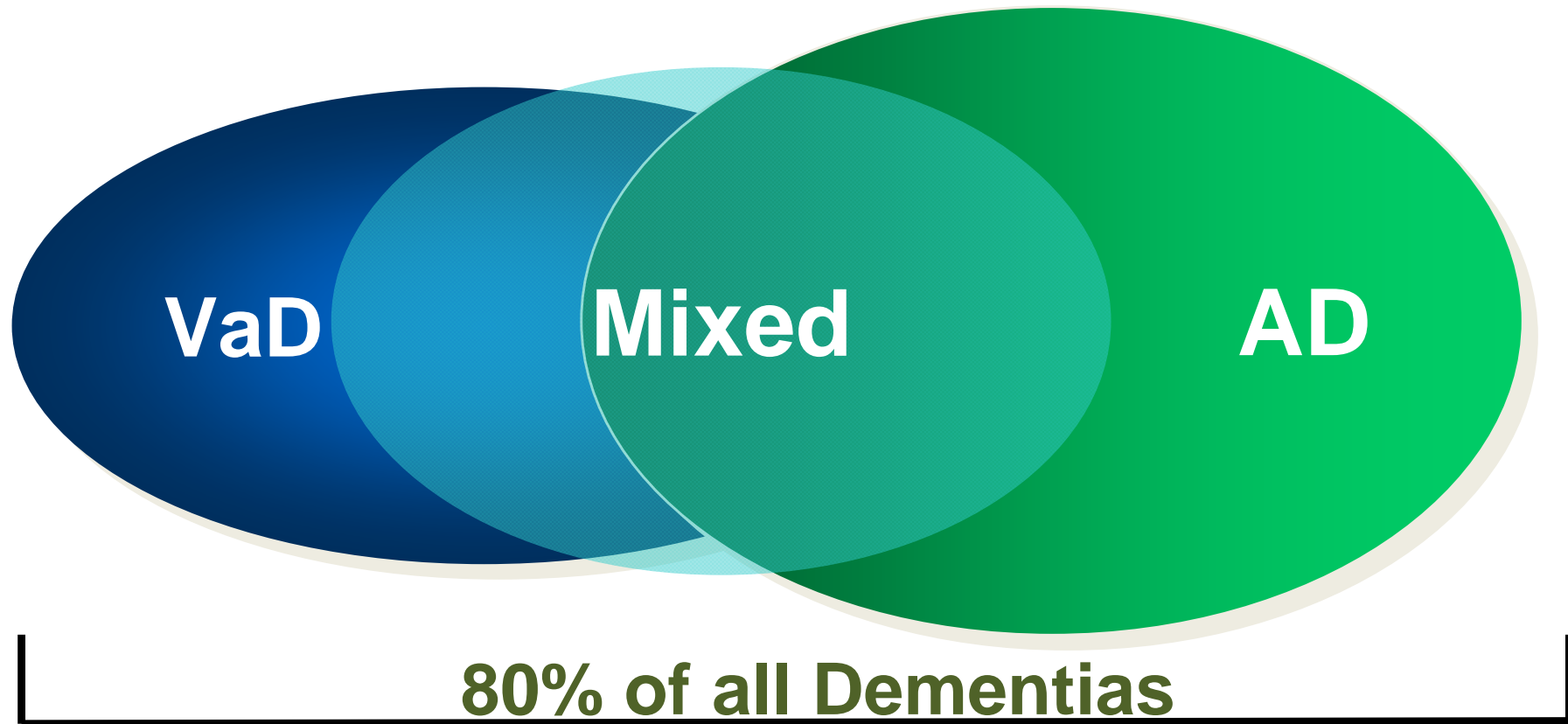
Each bar from left to right represents the range of MMSE scores over which 25–75% of Alzheimer’s patients in one study† showed loss of optimal (independent) ADL performance

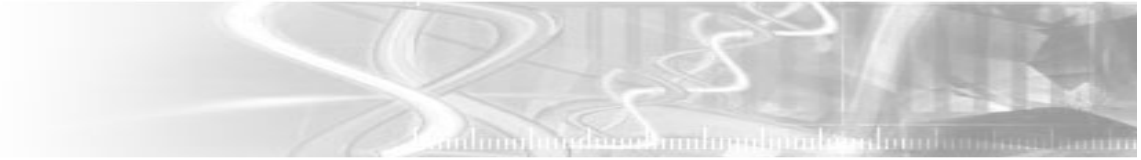
25% 75%  
Loss of optimal (independent) performance





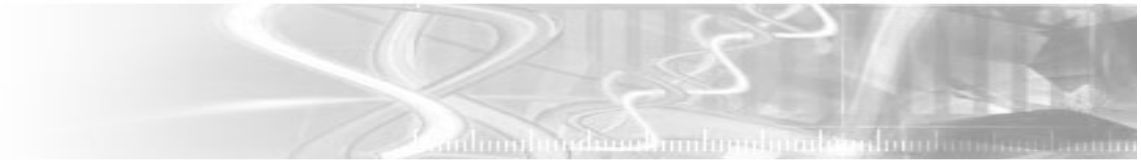
## *Figure 5. Interactions Between Vascular Dementia and Alzheimer's Disease*





# ***FTD Degeneration (Dementia)*** ***“Picks Disease”***

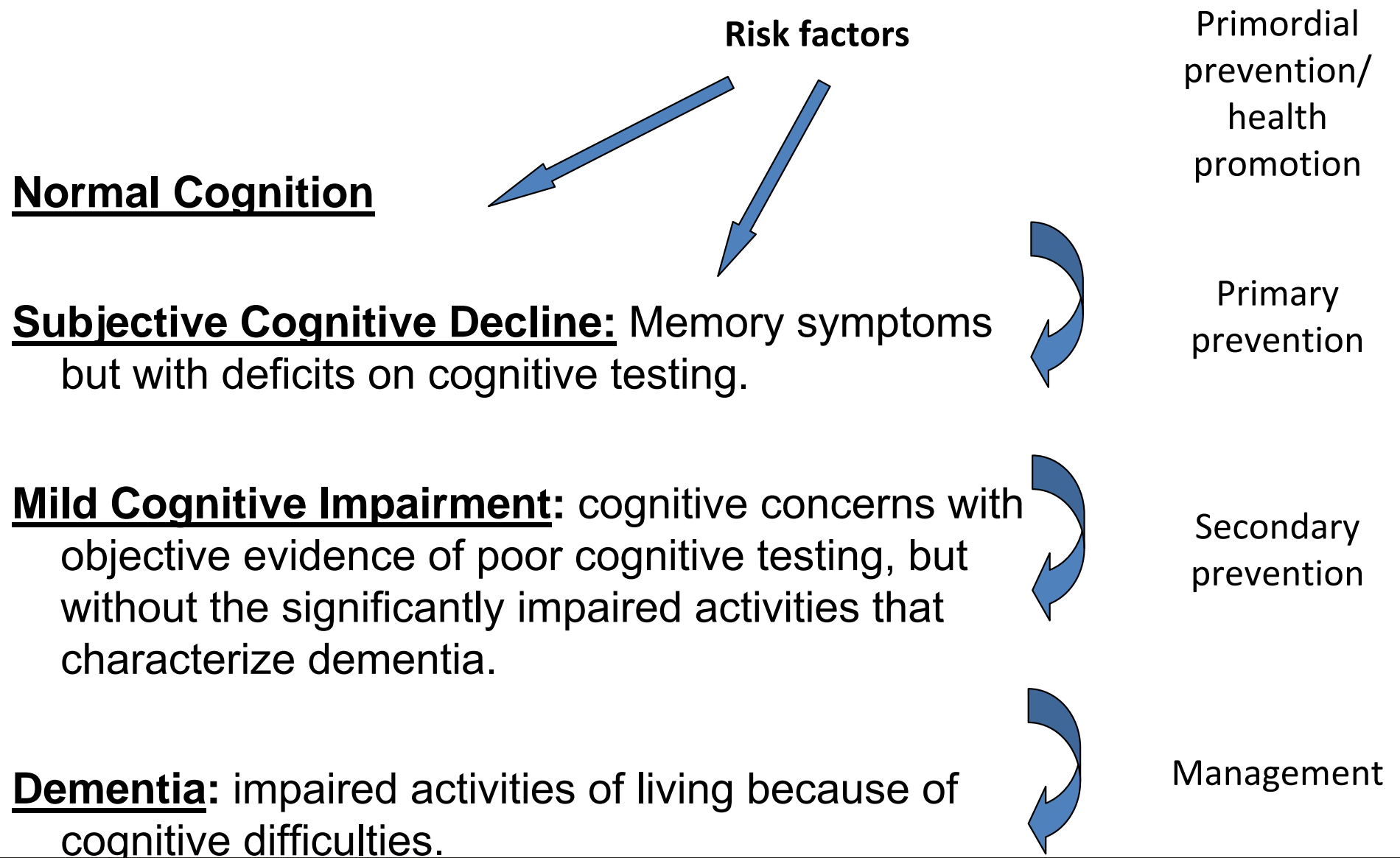
- Behavioural variant:
  - Early signs: disinhibited behaviour, change in personality, apathy (Frontal Behavioural Inventory)
- Primary Progressive Aphasias
  1. Progressive non fluent aphasia variant
    - Early signs: effortful hesitant speech, word finding difficulties
  2. Semantic variant
    - Early signs: fluent grammatically correct speech, word finding difficulties

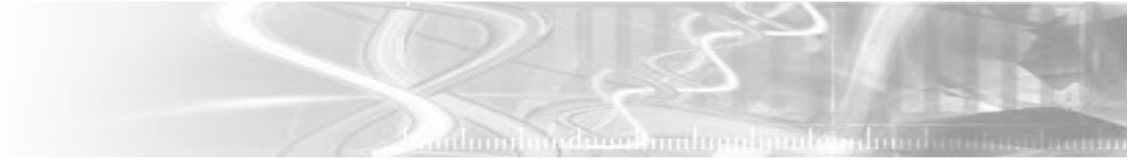


# *Lewy Body Disease (dementia)*

1. Early visual hallucinations
2. Parkinsonism
3. Fluctuation in level of consciousness
  - Sensitivity to the typical and atypical antipsychotic drugs
  - Restless legs







- **Increased Risk**
  - Age – If you plan to get old ... you are at risk!
  - High blood pressure
  - High cholesterol
  - Diabetes
  - Smoking
  - Atrial fibrillation (stroke)
  - Head injury, concussion (i.e. hockey)
  - Risk gene - APOE4 +ve (see next slide)
  - Family History
  - Low education level
  - Down Syndrome
- **Reduced Risk**
  - Regular exercise
  - Adherence to Mediterranean Diet

## ***Risk factors for Dementia***



# Mediterranean Style Diet

## THE MEDITERRANEAN DIET PYRAMID

Oldways, the umbrella organization for the Mediterranean Foods Alliance and the Whole Grains Council, developed the Mediterranean Diet Pyramid in 1993 to encourage and help consumers incorporate these healthful foods into their diets. For more information, recipes, and resources on the Mediterranean diet, visit [www.oldwayspt.org](http://www.oldwayspt.org).

**Meats and Sweets**  
*Less often*

**Poultry, Eggs, Cheese, and Yogurt**  
*Moderate portions, daily to weekly*

**Fish and Seafood**  
*Often, at least two times per week*

**Fruits, Vegetables, Grains (mostly whole), Olive oil, Beans, Nuts, Legumes and Seeds, Herbs and Spices**  
*Base every meal on these foods*

**Wine In Moderation**

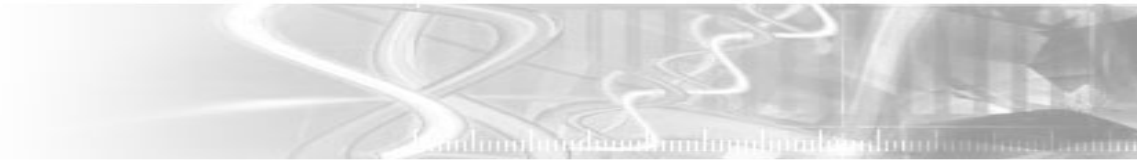
**Drink Water**

**Be Physically Active; Enjoy Meals with Others**

ILLUSTRATION BY GEORGE MIDDLETON  
© 2009 Oldways Preservation & Exchange Trust, [www.oldwayspt.org](http://www.oldwayspt.org)

SEPTEMBER 2011 21





# Genetics

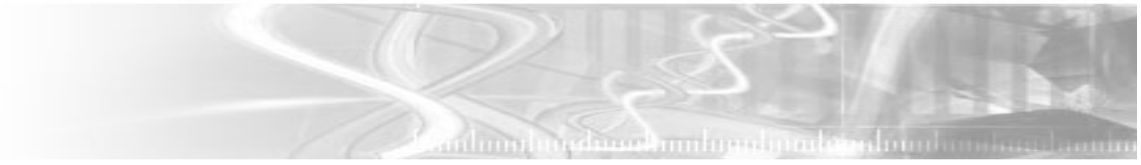
- Most AD cases are sporadic, not inherited.
- Affected immediate family member increases risk by 50%.
- Rarely, can be caused by a single bad gene (<3% of cases): presenilin or APP mutation.
- 19 other genes identified that modify risk, most prominent is APOE.
- APOE gene:
  - 3 isoforms E2, E3, E4.
  - Every person has 2 APoE genes – one from each parent.
  - APOE E4 is present in about 25% of the population, but 40% of AD cases.





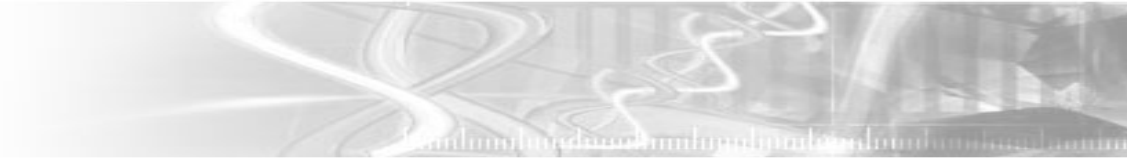


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# MEDICAL WORK UP FOR COGNITIVE IMPAIRMENT

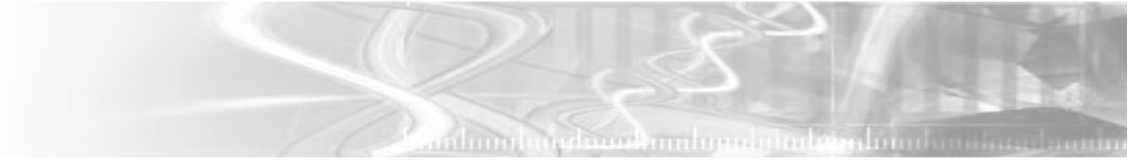




## ***Blood test all patients***

- CBC (anemia)
- TSH (thyroid ↑ or ↓)
- Electrolytes (Na<sup>+</sup> or K<sup>+</sup>)
- Kidney Function (Bun creatinine)
- Calcium (↑ or ↓)
- Glucose (diabetes)
- Vitamin B12

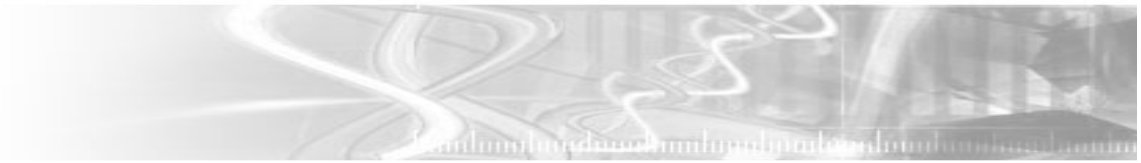




# ***MRI or CT Scan***

Recommended by guidelines for most but not all clinical scenarios:

- Short duration (less than 2 years)
- Younger age
- Suspicion of focal structural problem—e.g. based on physical exam findings, history of recent head trauma or active cancer, etc.



# ***Current Treatment Options***

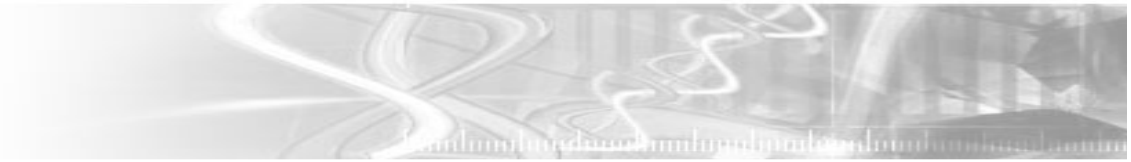
## Mild to Moderate Alzheimer Disease

- Acetylcholinesterase Inhibitors
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Reminyl)

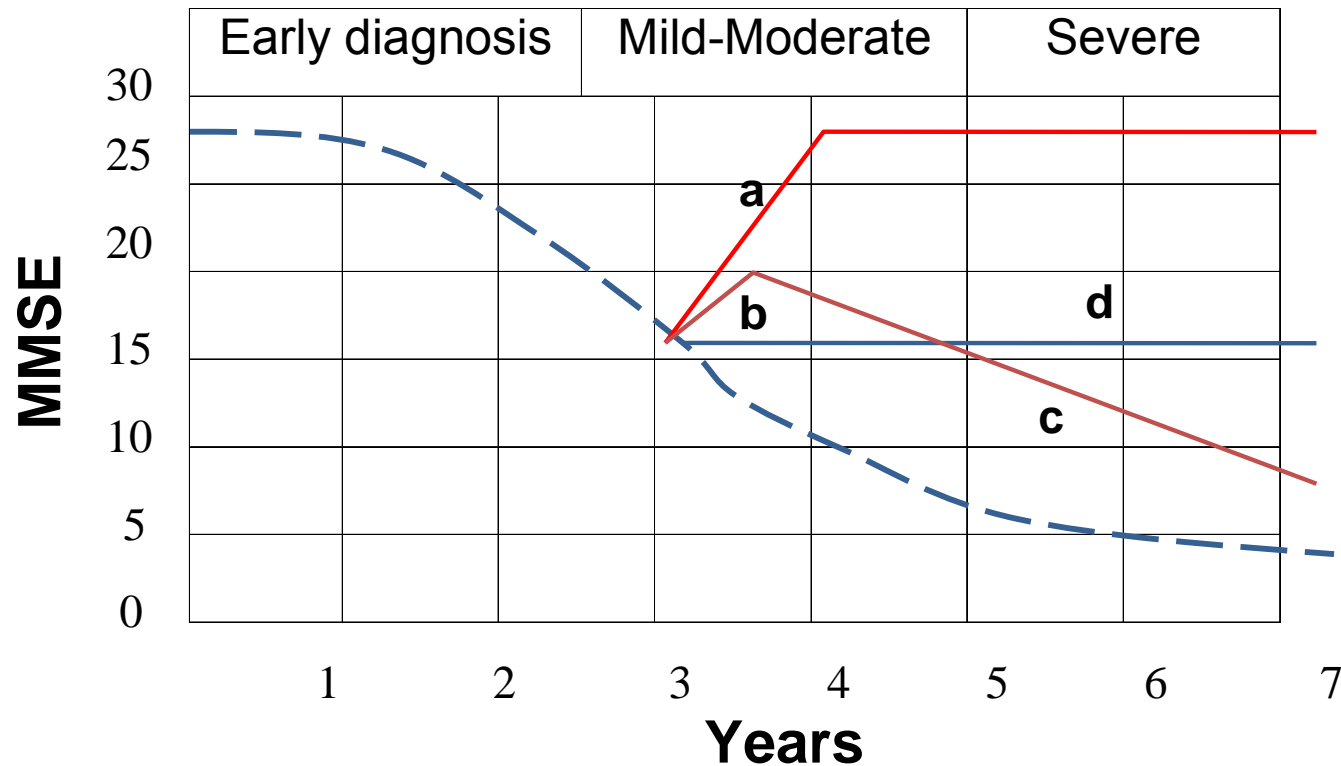
## Moderate to Severe Alzheimer Disease

- Memantine (Ebixa) – not covered by AB Blue Cross



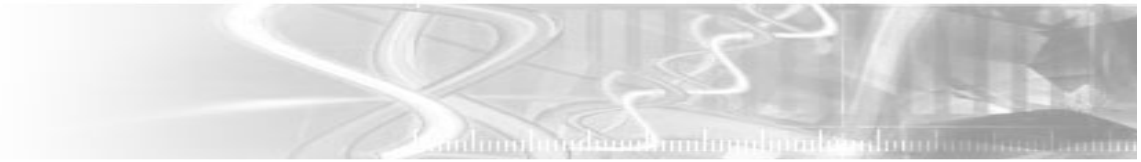


**Figure 4. Hypothetical Treatment Responses in AD**



- a) ideal response - complete normalization      b) partial improvement  
c) maintained improvement while on medication      d) stabilization



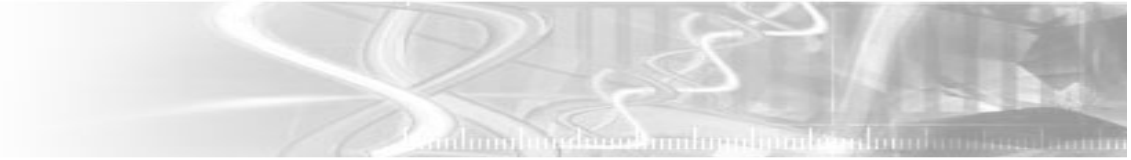


“OUR government is ignoring what is likely to become the single greatest threat to the health of Americans: Alzheimer’s disease, an illness that is 100 percent incurable and 100 percent fatal...Experience has taught us that we cannot avoid Alzheimer’s disease by having regular medical checkups, by being involved in nourishing relationships or by going to the gym or filling in crossword puzzles...[U]nless unless we get to work now, any breakthrough will come too late to benefit the baby boomers. ***Whether the aging of America turns out to be a triumph or a tragedy will depend on our ability to fight this horrific disease and beat it before it beats us.***”

SANDRA DAY O’CONNOR, STANLEY PRUSINER and KEN DYCHTWARD

New York Times Op-Ed, October 27, 2010

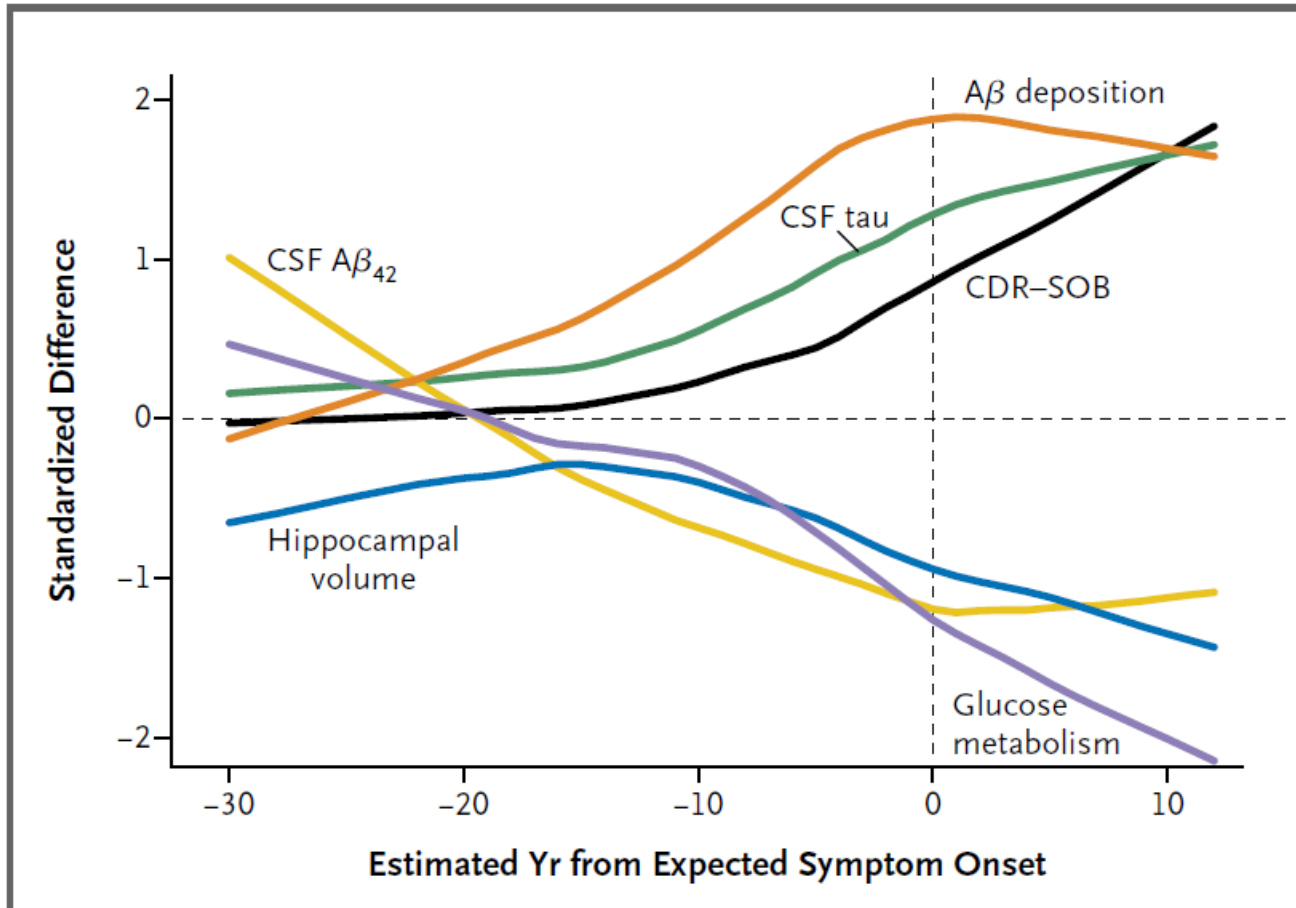
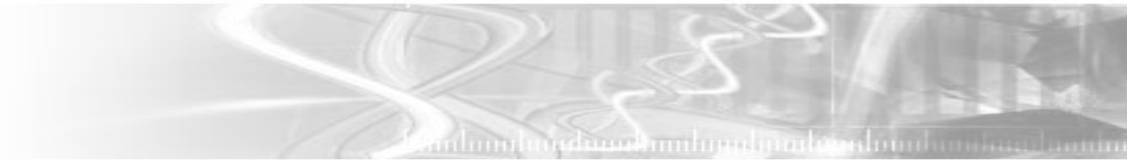




## MOST EXCITING RECENT RESEARCH IN ALZHEIMER'S AND DEMENTIA

- AD may begin 20-30 years before symptoms.
- Dementia is preventable!
- Failure, so far, of anti-amyloid drugs and vaccines.

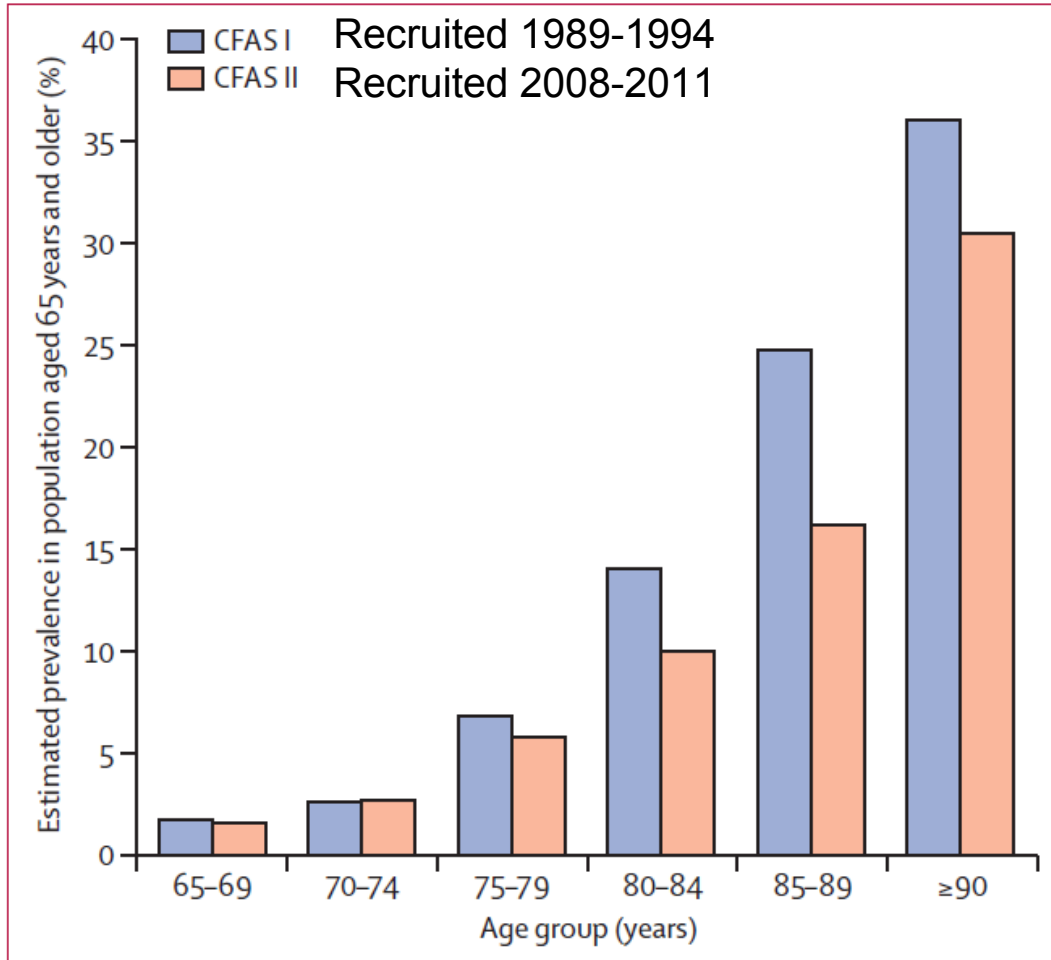
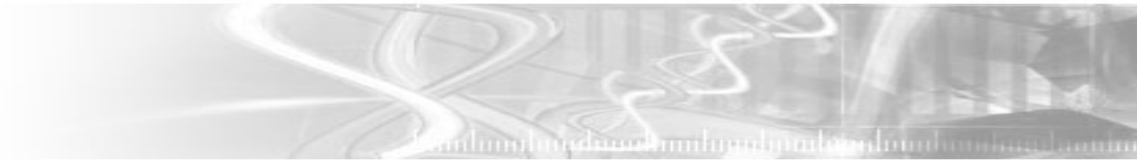




Alzheimer's  
Begins 20  
Years Before  
Symptom  
Onset in  
Mutation  
Carriers

**Figure 2.** Comparison of Clinical, Cognitive, Structural, Metabolic, and Biochemical Changes as a Function of Estimated Years from Expected Symptom Onset.

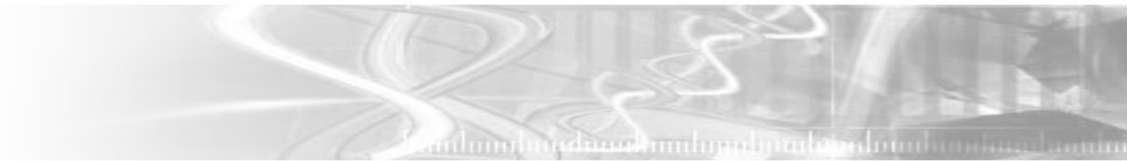




**Figure 1: CFAS I and CFAS II age-specific dementia prevalence**  
CFAS=Cognitive Function and Ageing Study.

**Overall Dementia  
Prevalence 1.5%  
Lower Among >65  
Yr Olds in 2008-  
2011 vs. 1989-1994**

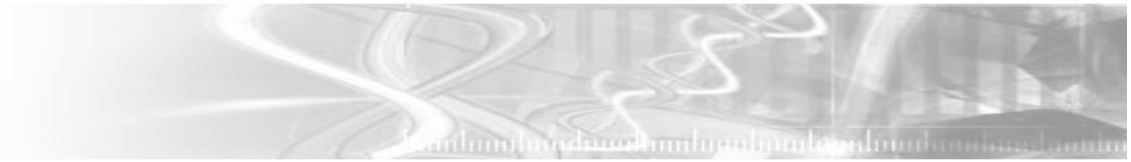




## TRIALS OF ANTI-AMYLOID VACCINES AND DRUGS

- Large clinical trials of anti-beta amyloid (anti-plaque) vaccines and drugs (gamma secretase inhibitors) reported as failures in 2012 and 2013.
- Next generation of trials:
  - Testing anti-beta amyloid vaccines in cognitively healthy people with PET scan evidence of senile plaques (A4 trial).
  - Testing anti-beta amyloid vaccines or drugs in pre-symptomatic disease mutation carriers.
  - Testing beta secretase inhibitors.

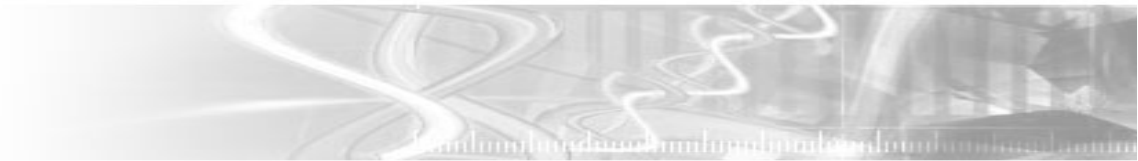




## TAKE HOME MESSAGES

- Dementia means disabling cognitive impairment; it is caused by diseases of the brain.
- Medical work up consists of blood tests and, depending on the situation, a brain scan.
- There are medical treatment options but no cure.
- There are opportunities to partly prevent or delay dementia, but no cure.

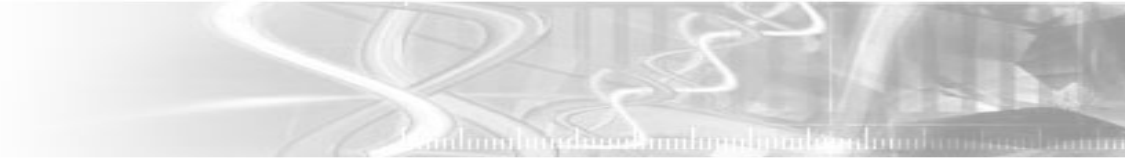




## WHAT CAN I DO TO LOWER MY RISK?

- See a family physician to have your blood pressure checked.
- Exercise!
- Healthy diet with fruits and vegetables.
- Stay mentally active.





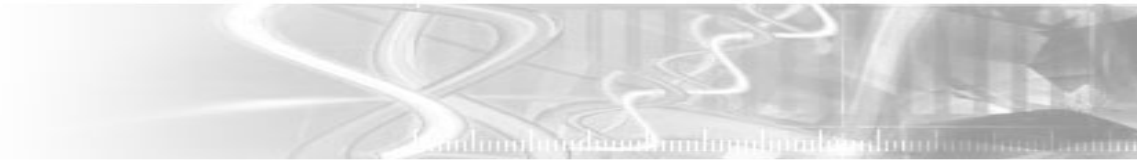
## HOW CAN I HELP?

- Get medical help for friends and family if needed.
- Fight against stigma.
- Support research.





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THANK YOU

[www.ucalgary.ca/esmithresearch](http://www.ucalgary.ca/esmithresearch)



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