

# Dementia: Overview and Latest Research

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## About Me

- Associate Professor of Neurology at the University of Calgary.
- Medical Director of the Cognitive Neurosciences Clinic at Foothills Hospital.
- Grant funding for research from the Alzheimer Society, Heart and Stroke Foundation of Canada and government agencies.





## GOALS

- What is dementia? What is Alzheimer's disease? How are they different?
- How common is dementia? What are the risk factors?
- What are the causes of dementia?
- How does a doctor evaluate someone with dementia?
- Research on causes and prevention.





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.





## SUBJECTIVE COGNITIVE DECLINE

- 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.





## CANADIANS ARE OLDER THAN EVER BEFORE

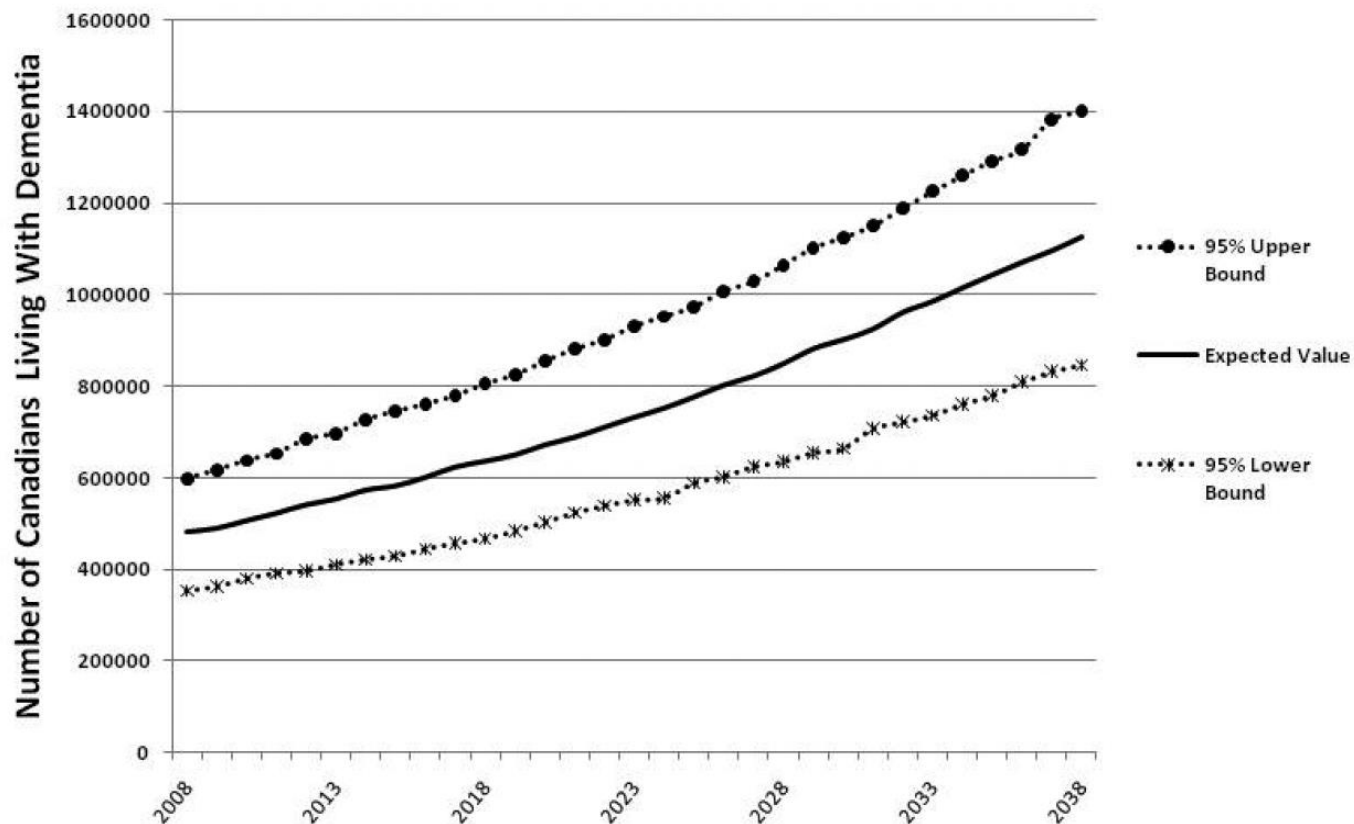
Stats Canada

- 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.



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





# LIFETIME RISK OF DEMENTIA

in Women Is **1 in 5**, and in Men is **1 in 10**.

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







## 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.

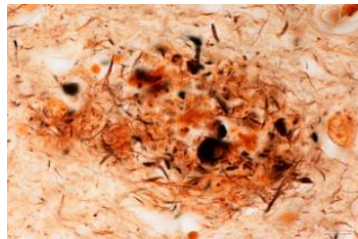




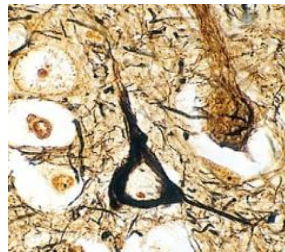
## BRAIN DISEASES THAT AFFECT MEMORY

### Alzheimer's Disease

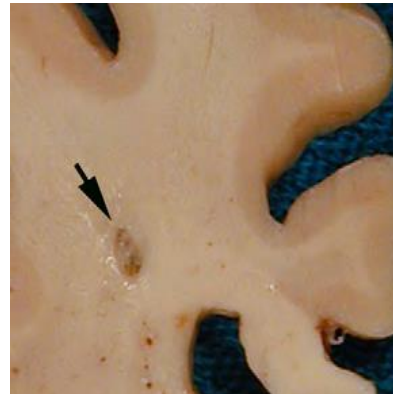
Senile Neuritic  
Plaques



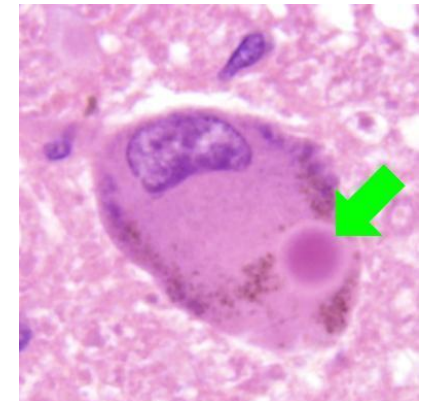
Neurofibrillary  
Tangles



### Cerebrovascular (Blood Vessel) Diseases



### Lewy Body Disease



Risk

50%

33%

7%





# ***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).

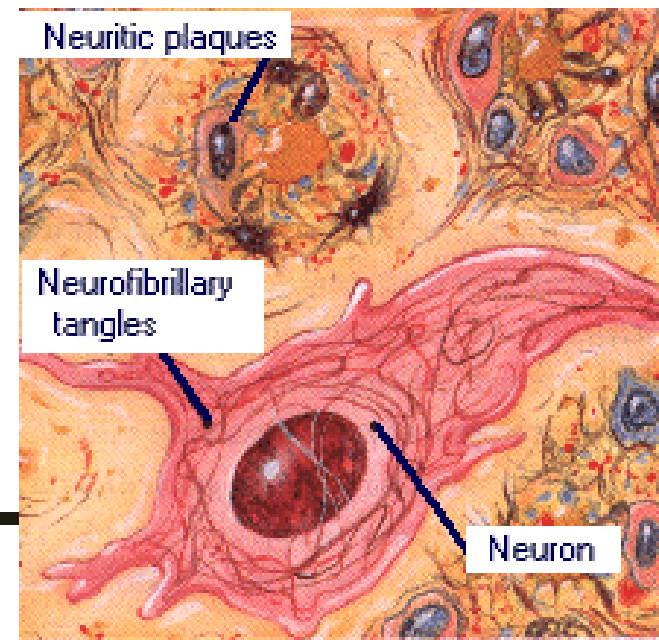
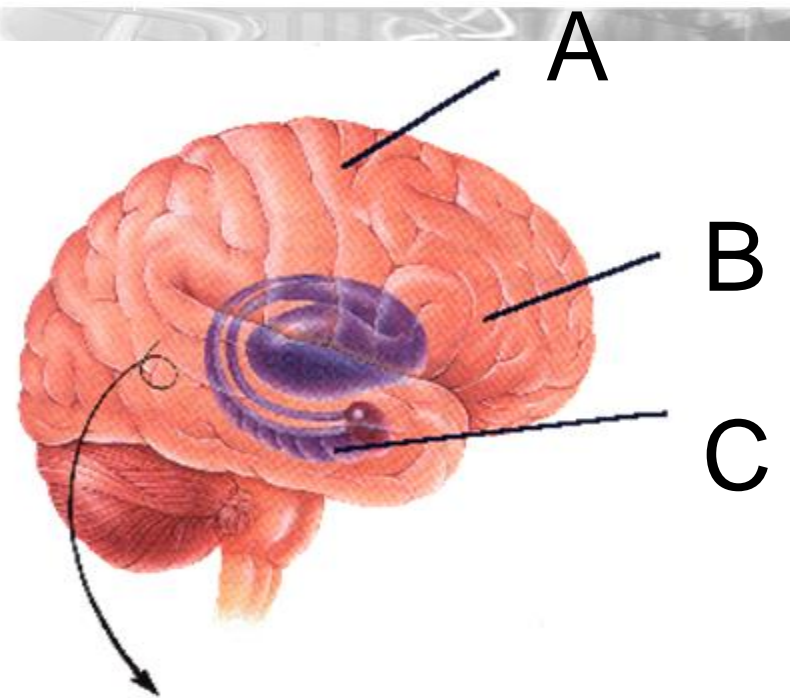
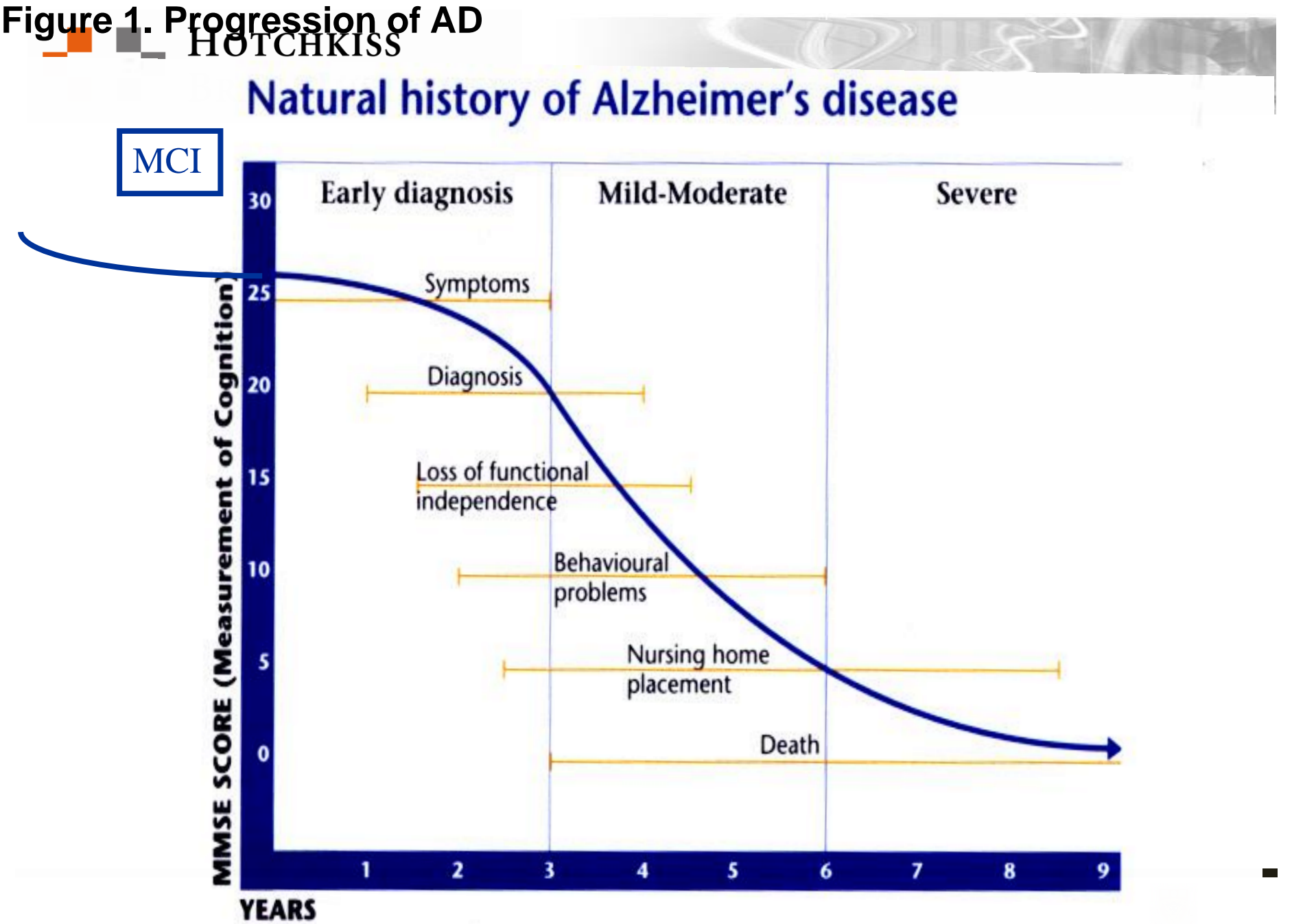


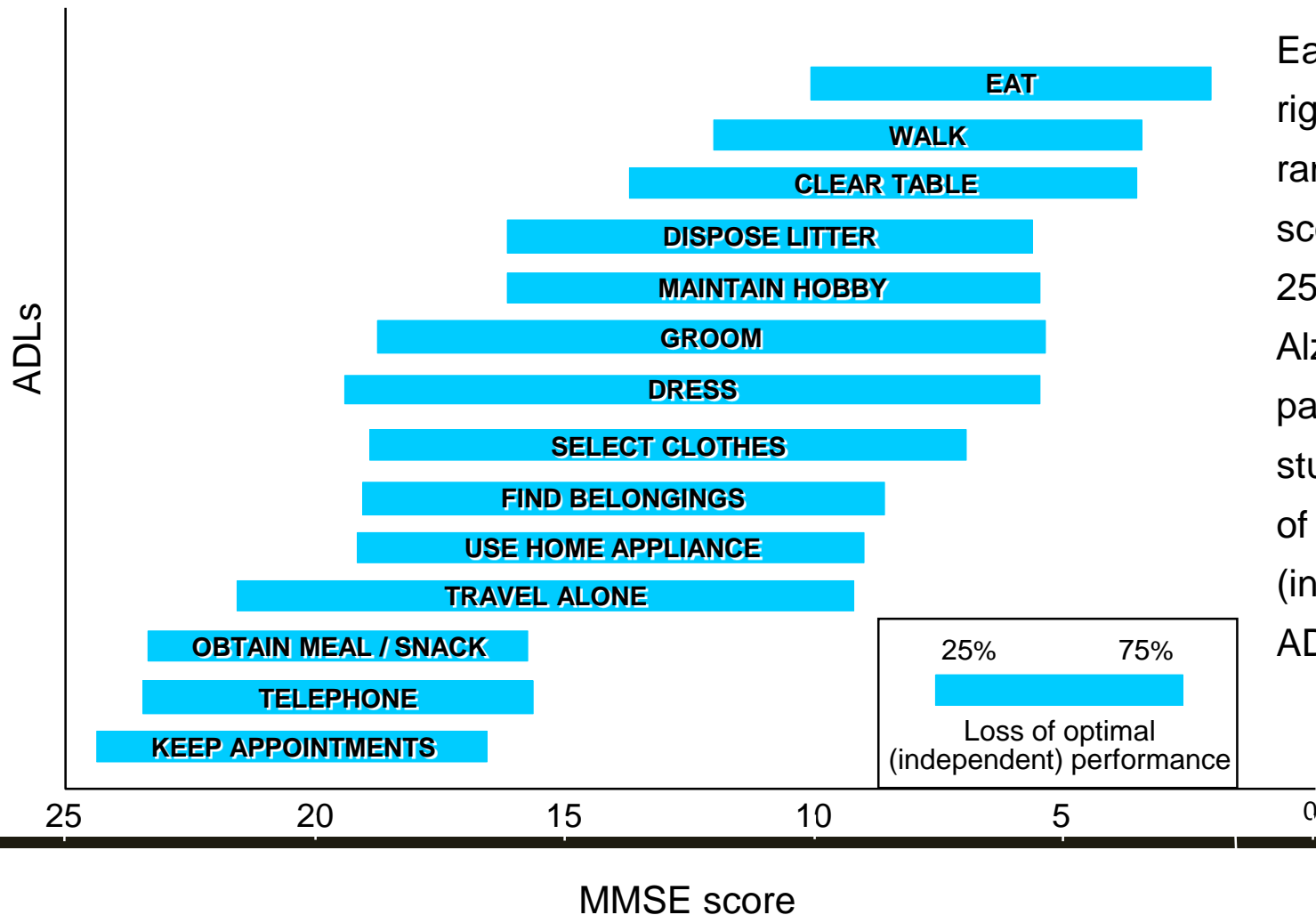
Figure 1. Progression of AD







## Progressive Loss of Activities of Living



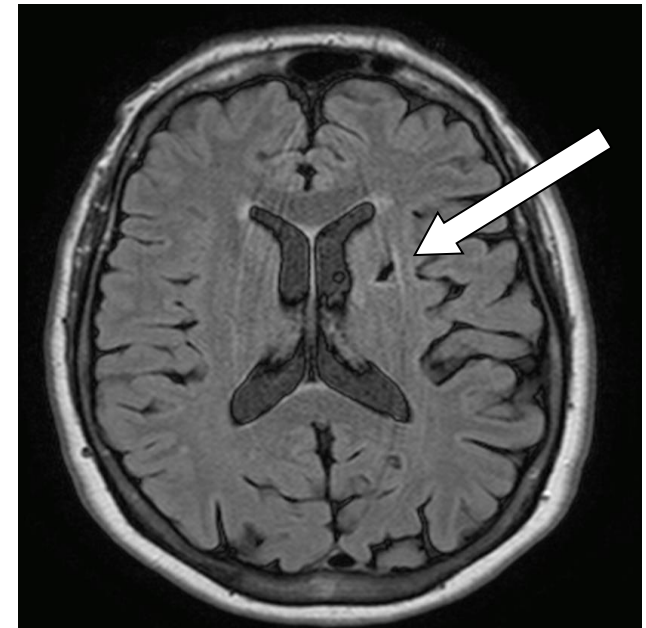
Each bar from left to right represents the range of MMSE scores over which 25–75% of Alzheimer's patients in one study<sup>†</sup> showed loss of optimal (independent) ADL performance





# *Vascular Dementia*

- Some cases are due to effects of stroke.
- Some cases are due to the effects of silent strokes, recognized only when a brain scan is done.
- Risk factors (such as high blood pressure, diabetes, smoking, heart conditions) must be treated.







# ***Fronto-temporal Degeneration (Dementia)—FTD, “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)*

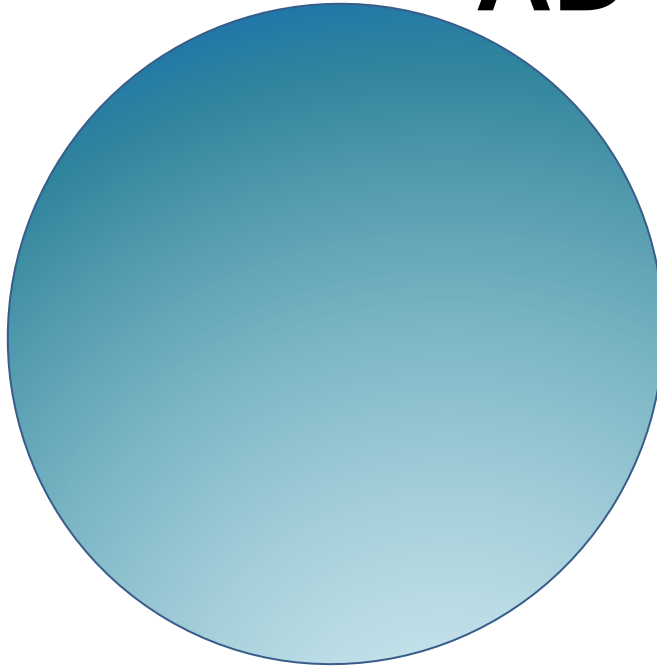
1. Early visual hallucinations
2. Parkinsonism
3. Fluctuation in level of consciousness
  - Sensitivity to the typical and atypical antipsychotic drugs



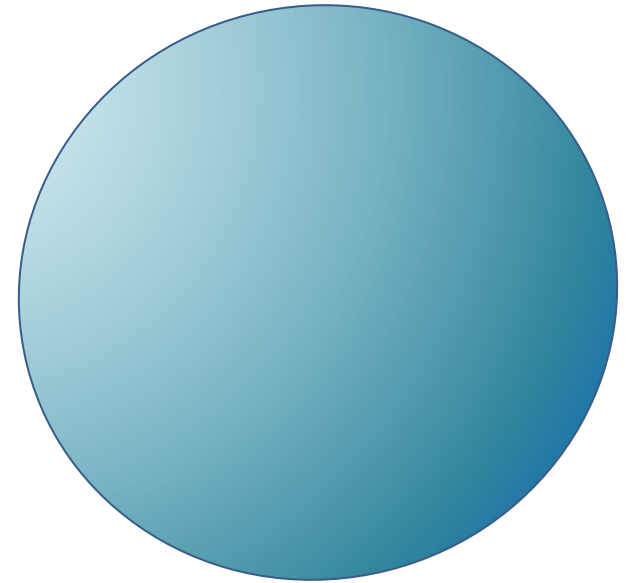


# Mixed Pathologies

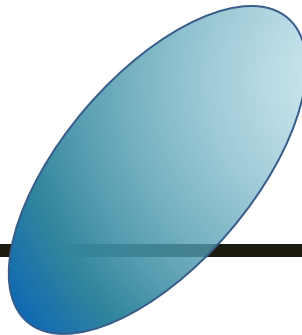
**AD**



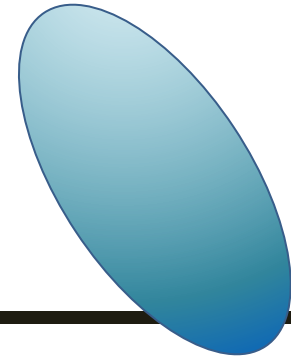
**Vascular**



**Lewy  
Body**



**?**





- **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***





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# 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).

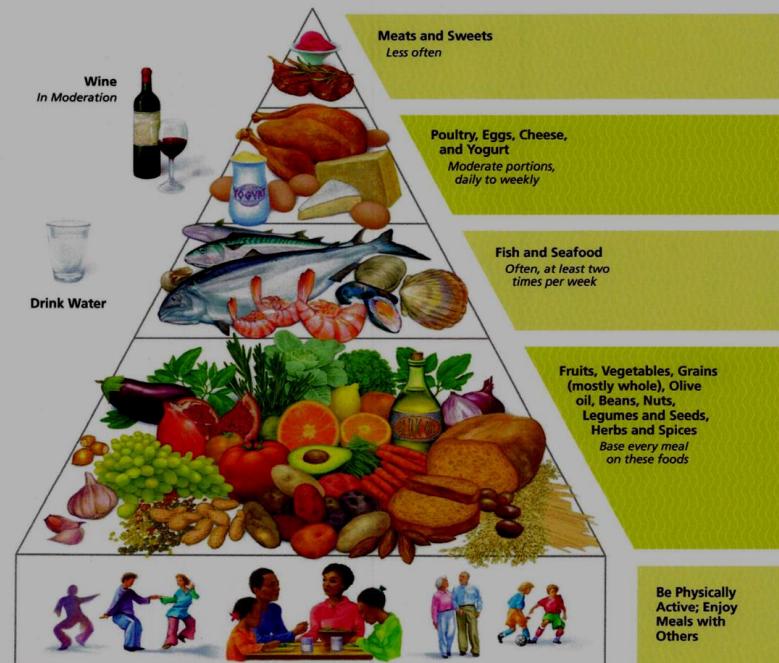


ILLUSTRATION BY GEORGE MIDDLETON

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# 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) which causes early onset dementia (in 40s or 50s): 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.

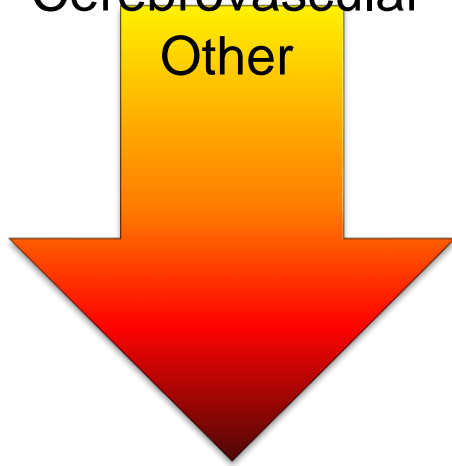


## WHAT CAN I DO TO LOWER MY RISK?

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



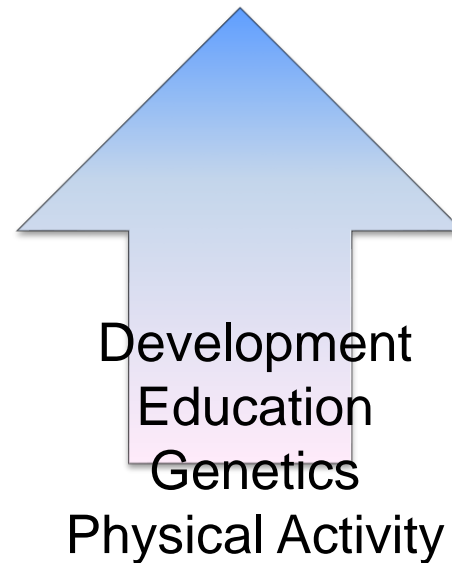
Alzheimer's  
Cerebrovascular  
Other



Pathologies



Cognitive  
Reserve



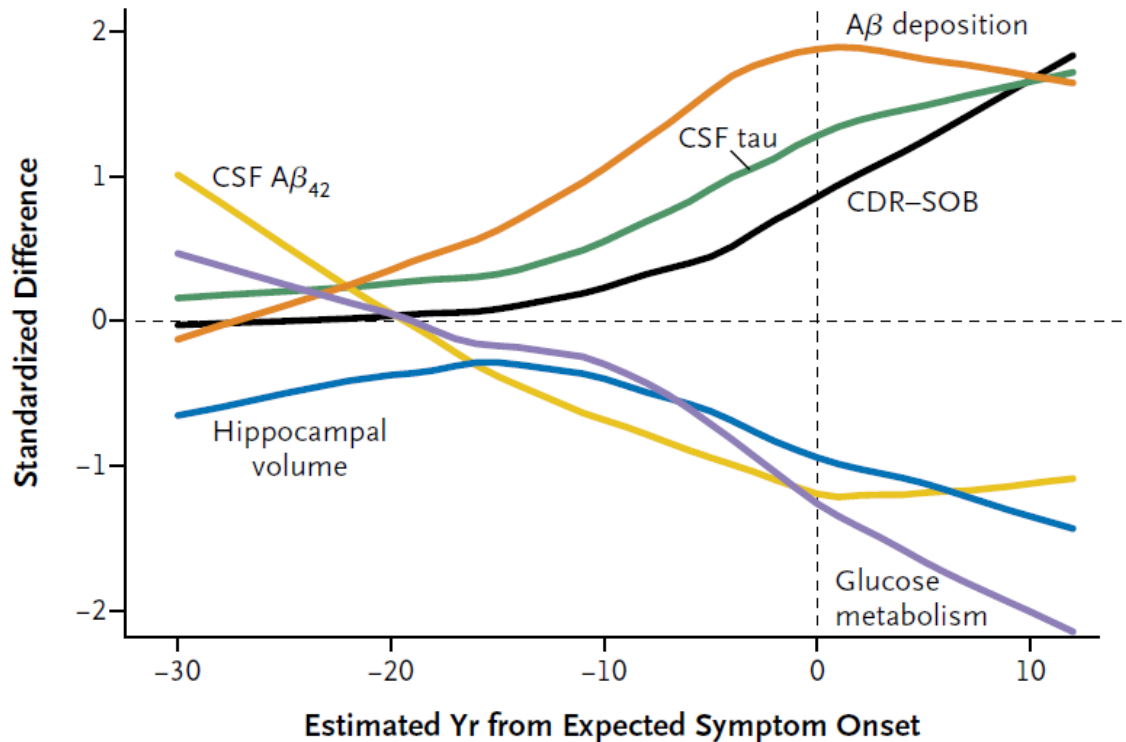
Development  
Education  
Genetics  
Physical Activity





**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



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

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



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# MEDICAL WORK UP FOR COGNITIVE IMPAIRMENT



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## ***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
- *No blood test for Alzheimer's disease—yet!*



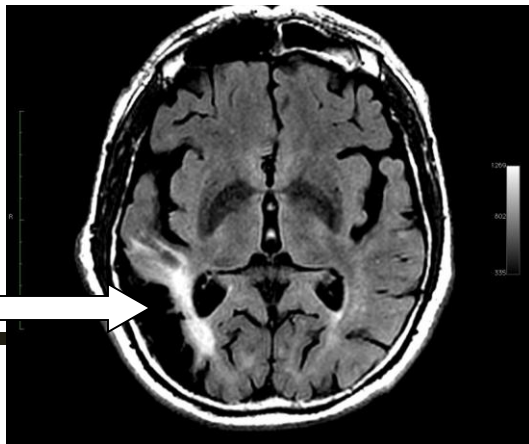


# ***MRI, CT or PET Scan***

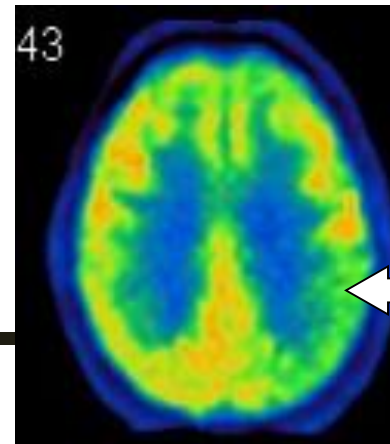
Recommended by guidelines for most but not all clinical scenarios:

- 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.

MRI



PET 43





# ***Current Treatment Options***

## Mild to Moderate Alzheimer Disease

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

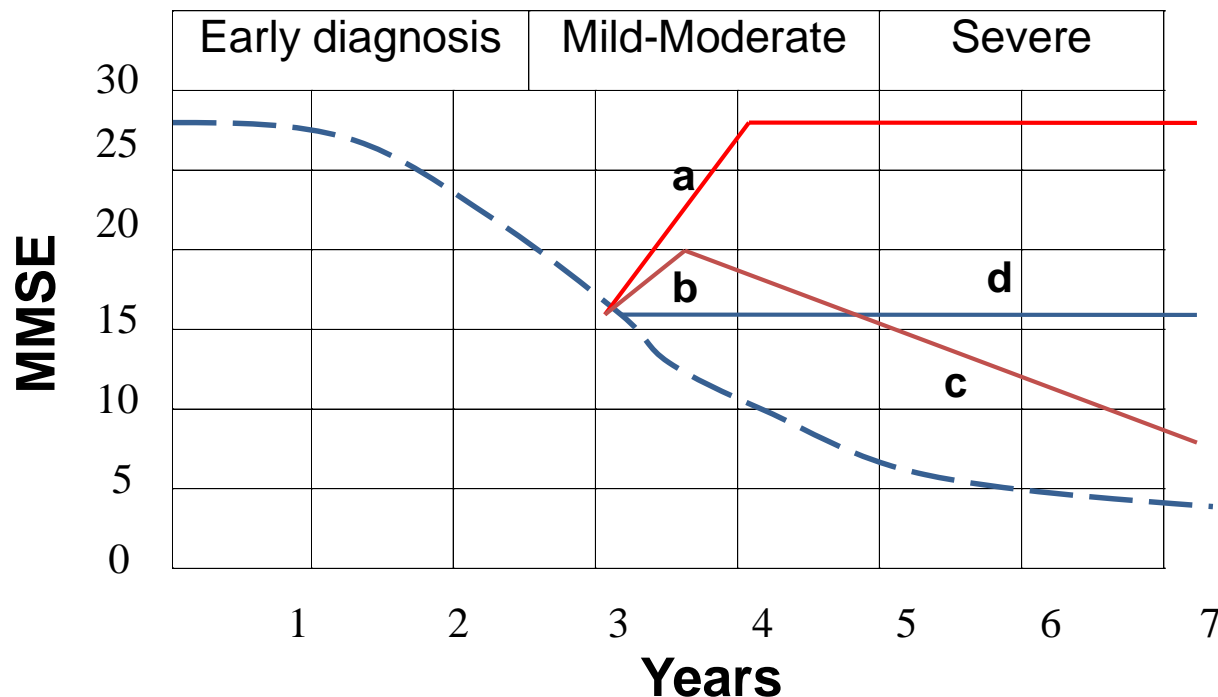
## Moderate to Severe Alzheimer Disease

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





## *Hypothetical Treatment Responses in AD*



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





# TRIALS OF NEW DRUGS

- Symptomatic treatments
  - Act on brain receptors to help restore brain function.
- Disease modifying treatments
  - Prevent progression of disease: a “cure”.
  - Large clinical trials of anti-beta amyloid (anti-plaque) vaccines and drugs (gamma secretase inhibitors) reported as failures in 2012 and 2013.



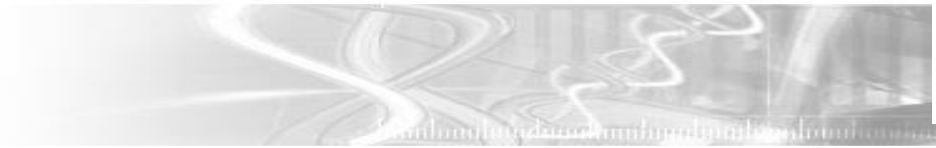


# Canada's National Research Strategy for Dementia



Funded beginning September 2014

32.5 million dollar effort involving all of Canada's major  
research universities



## What CCNA Will Do

- Enroll participants with Alzheimer's disease, vascular cognitive impairment, fronto-temporal dementia, and Lewy body disease.
  - To understand the prognosis and causes
  - To develop diagnostic tests.
  - New ideas for treatments.
- Laboratory research into causes and new drug approaches.
- Impact of dementia on quality of life and caregiving.



# Participant Assessments in the COMPASS-ND Study

## 1. Recruitment Into CCNA



Note: Can be recruited into OBI, CIMA-Q as well

## 2. Informed Consent Signed



Shared consent procedures

## 3. History, Physical, Cognitive Evaluation



- iPad/tablet clinical data (upload)
- Web-based computerized intake
- Assess inclusion/exclusion criteria
- Demographics, medical/surgical history
- Physical/Neurological examination

## 4. Questionnaires



- mental health
- Social
- psychiatric

## 5. Psychometric Testing



- National battery

## 6. Biosamples



### 6a. Blood



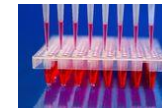
### 6b. Saliva



### 6c. CSF



## 7. Sample Processing



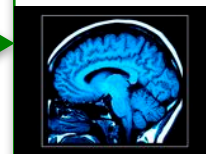
## 8. Sample Shipping to Biobank



## 9. MRI Imaging Acquisition



## 10. MRI IT and Databasing



C-Brain

LORIS

## 11. Brain Donation Program and Follow-up in Clinic





## RESEARCH AT THE UNIVERSITY OF CALGARY

- CCNA study (to start in early 2016).
- Blood test for Alzheimer's disease: blood test and lumbar puncture (spinal tap) (ongoing).
  - We also need controls without Alzheimer's disease to have blood test and lumbar puncture.
- Clinical trials: mild cognitive impairment or mild Alzheimer's disease, both symptomatic and disease-modifying treatments.

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Please call 403-944-1594 if you are interested in learning more.



## RESEARCH STUDIES

- Involve more visits and tests.
- Not all who are screened are eligible.
- No guarantee of direct benefit.
- Clinical trials: experimental drugs with potential side effects

*Ask the researcher:*

What does the research involve?

What are the risks?

Would anything else about my medical care change?

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Please call 403-944-1594 if you are interested in learning more.



## 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.
- Healthier living may prevent dementia.





## 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)**

Please call 403-944-1594 if you are interested  
in learning more about research on dementia.



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