



# An introduction to dementia

Never Stand Still

Medicine

Psychiatry

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# **21<sup>st</sup> Century is century of neurodegenerative disease**

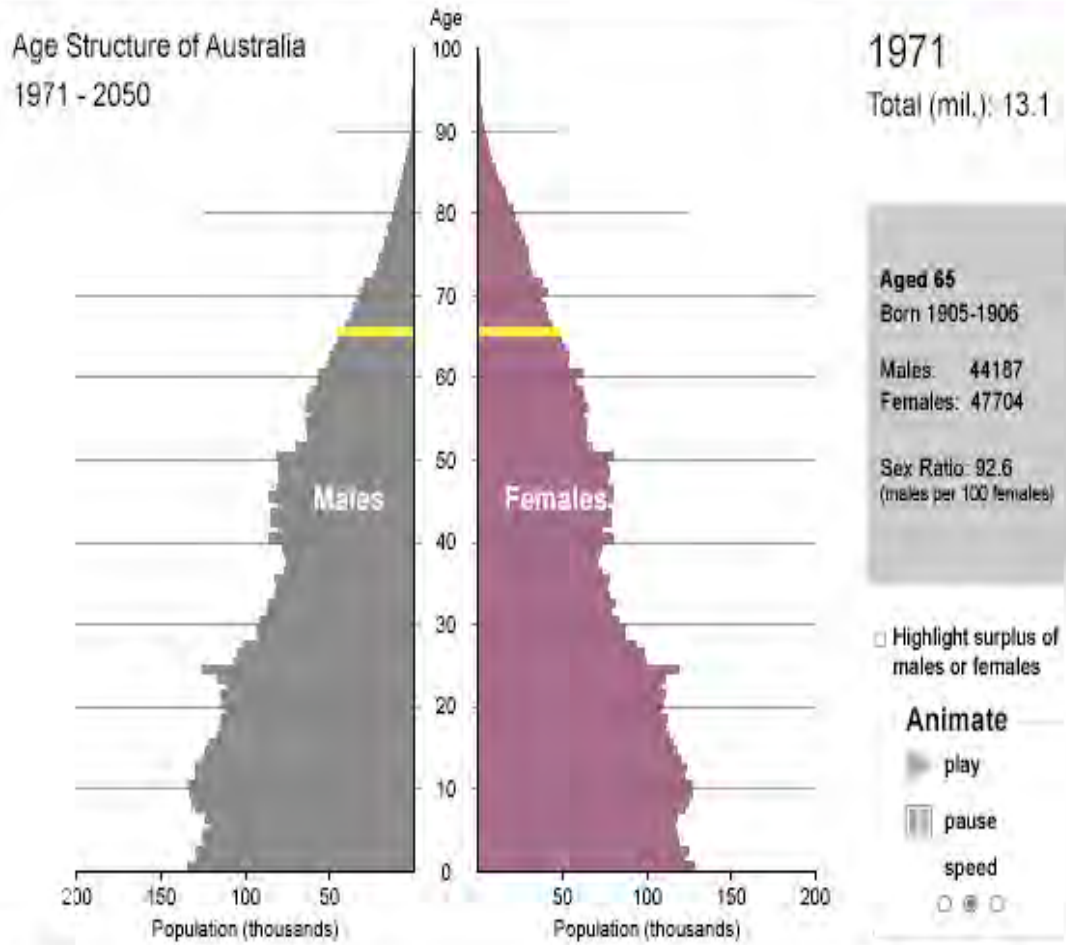
- **19<sup>th</sup> C – infectious disease**
- **20<sup>th</sup> C – heart disease, cancer**
- **21<sup>st</sup> C - neurodegenerative diseases**
  - **Alzheimer's and other dementias**
  - **Cerebrovascular disease/ stroke**
  - **Parkinson's disease**
  - **Macular degeneration**
  - **Balance and gait disorders, falls**



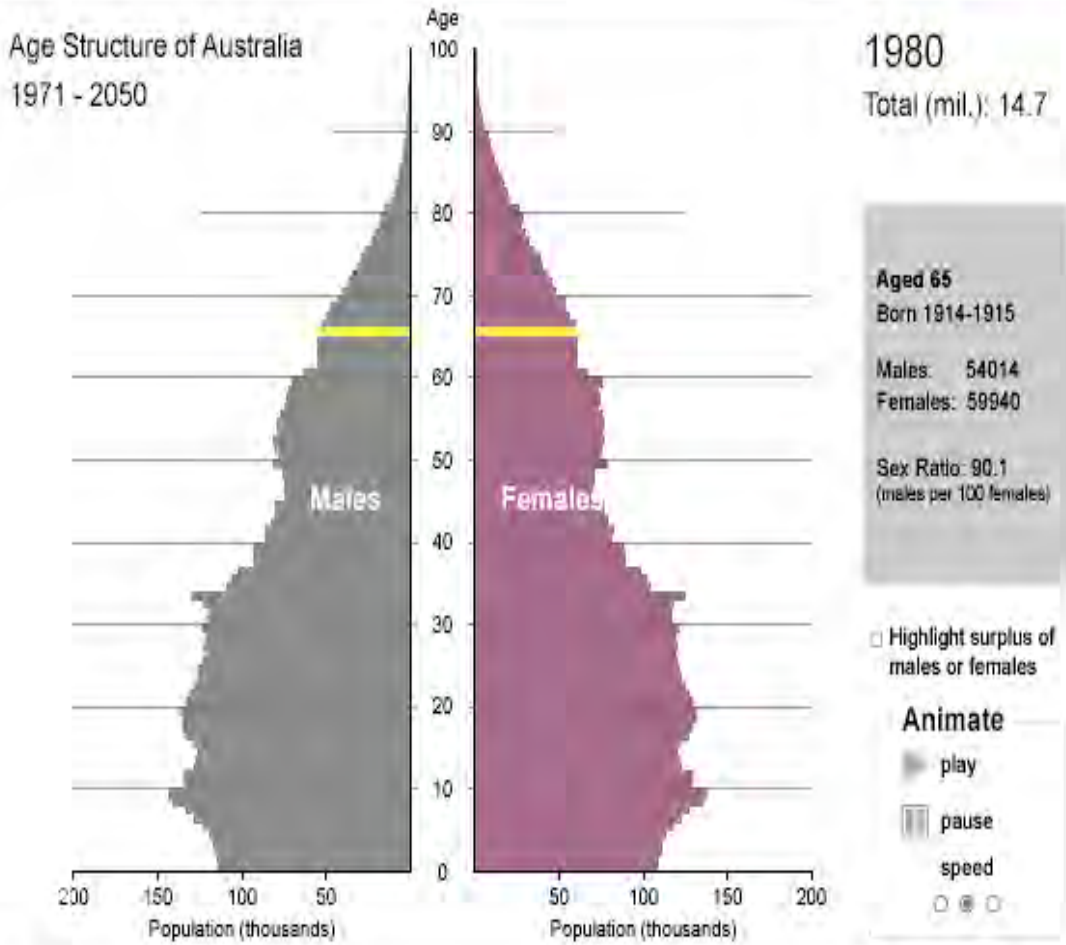
# Our brains . . .

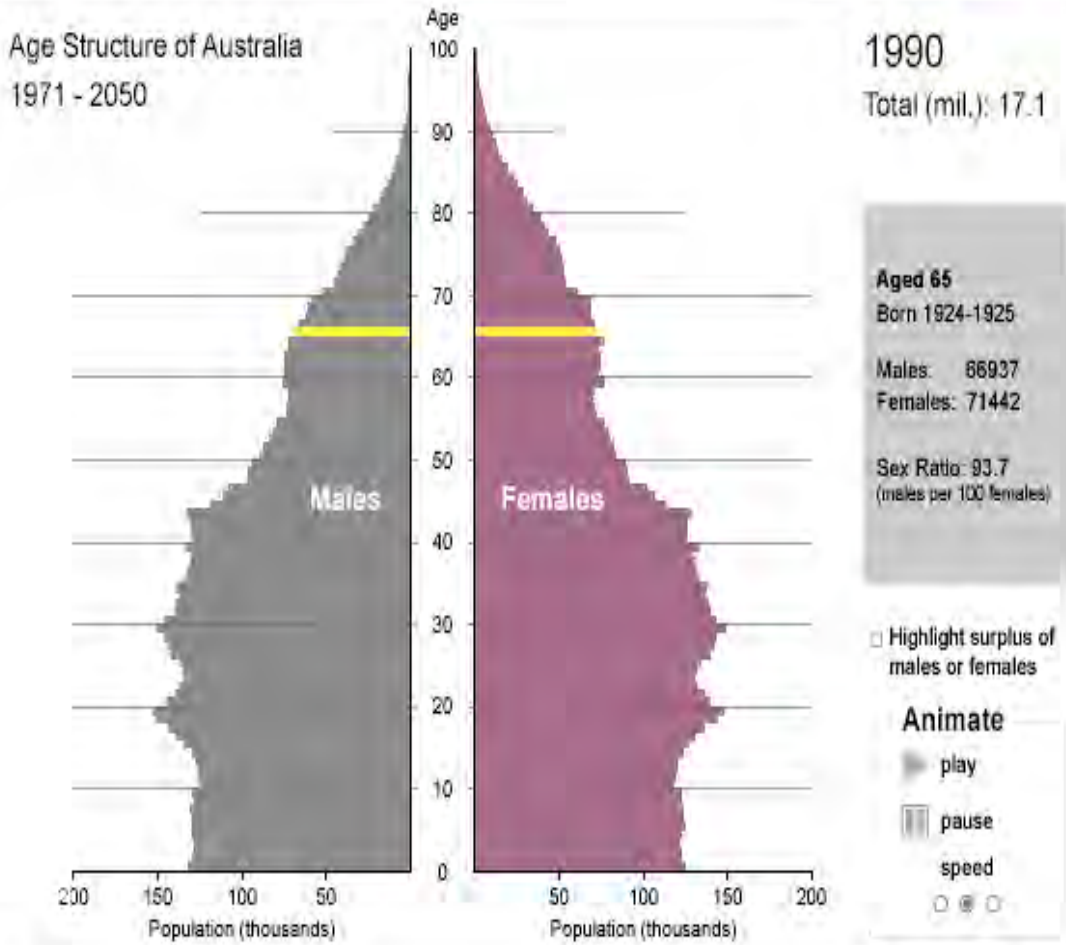
- $\approx 1.3$  Kg of 12% fat, 8% protein, 78% water
- Consume 20% of body's  $O_2$  & almost 20% of blood flow
- Contain about 100 billion neurons, each with 1000 to 10,000 synapses and each neuron is supported by 10-50 support (glial) cells
- Most mysterious of body's organs but now...
- .. more accessible through revolutions in neuroimaging, IT, genomics, other -omics

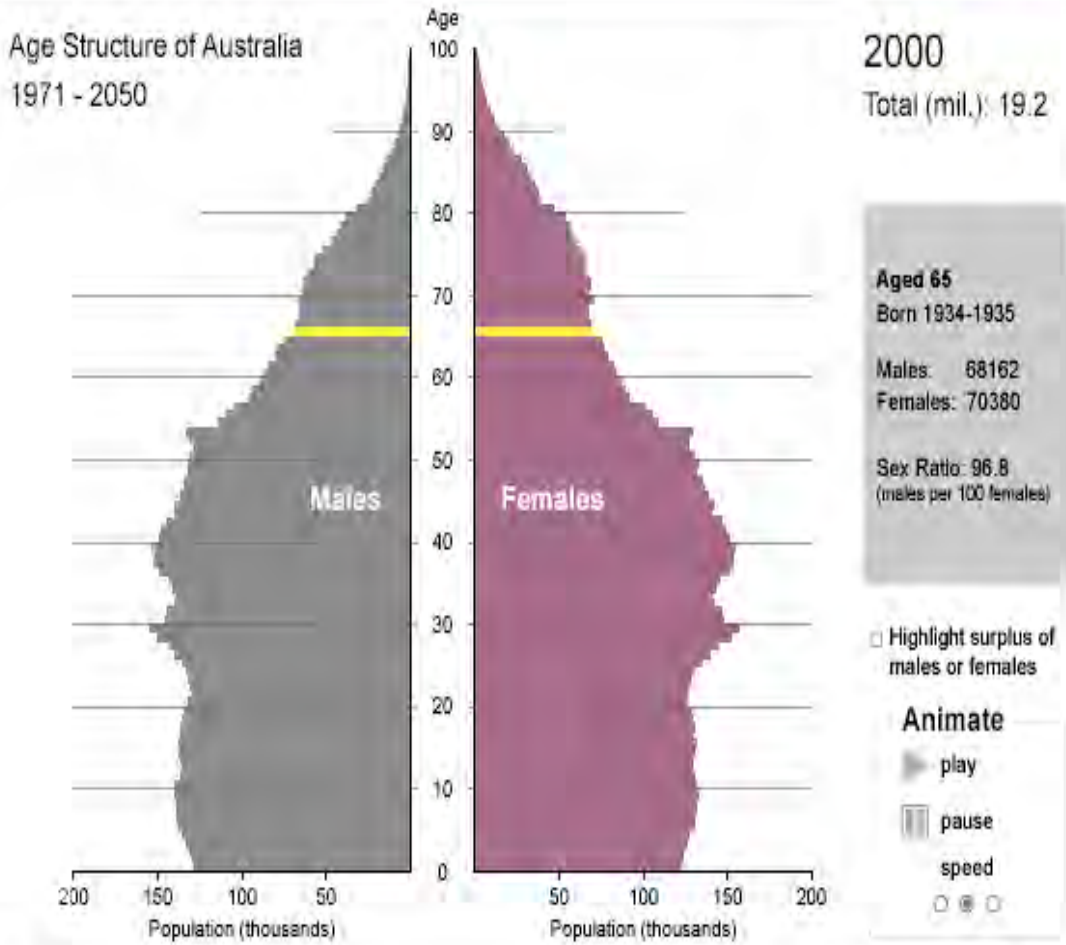




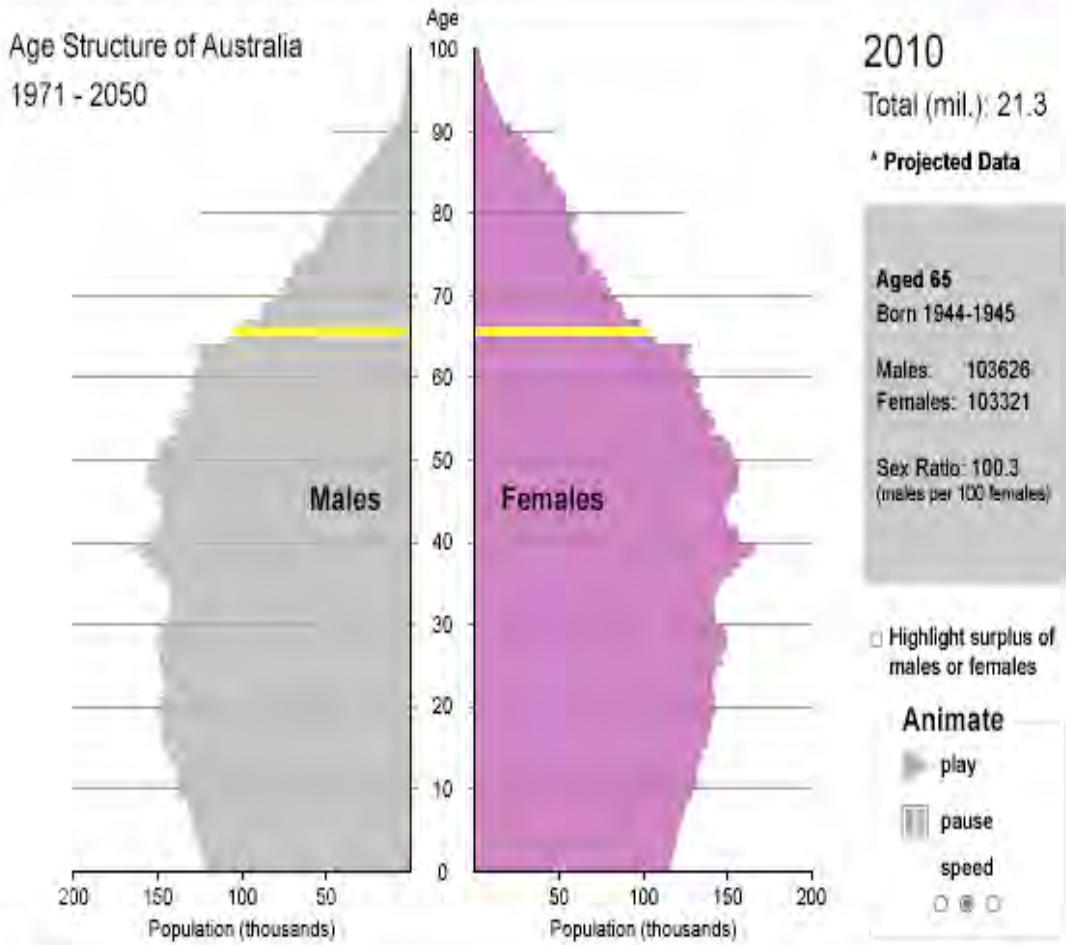




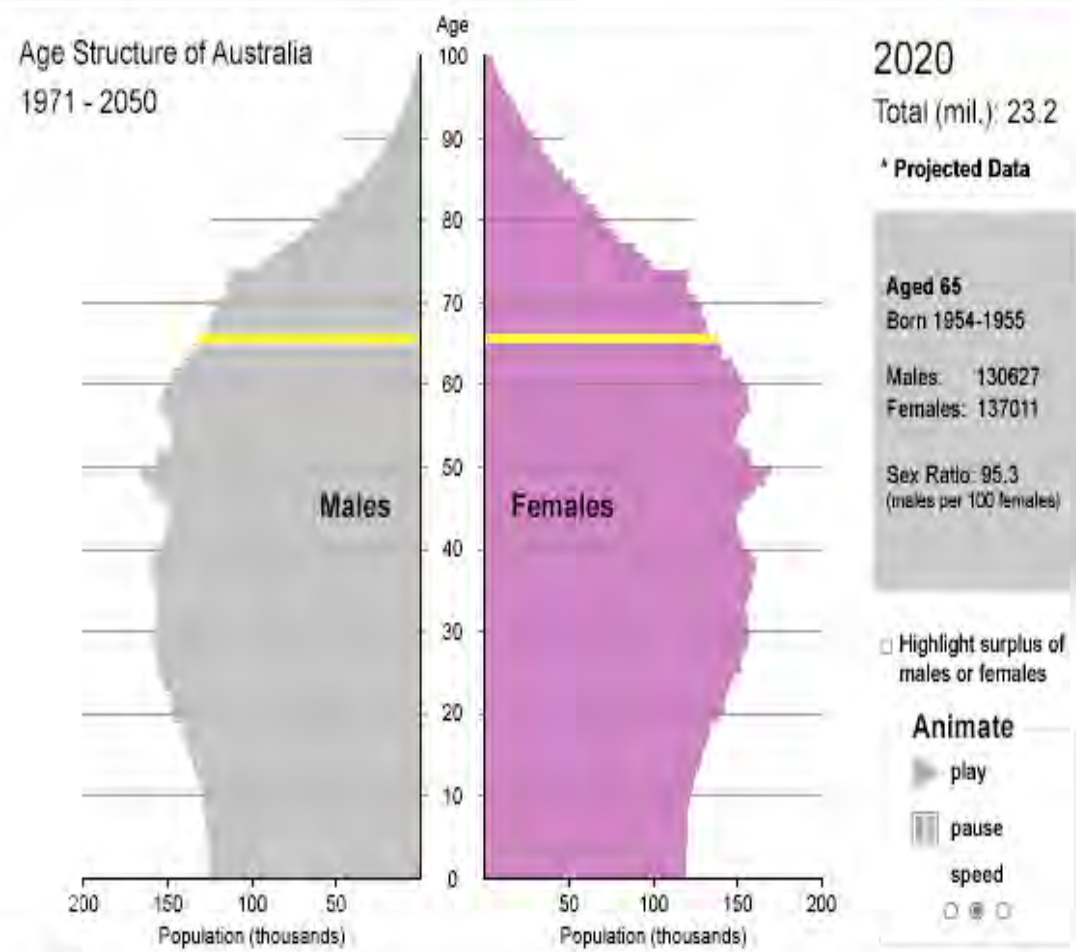


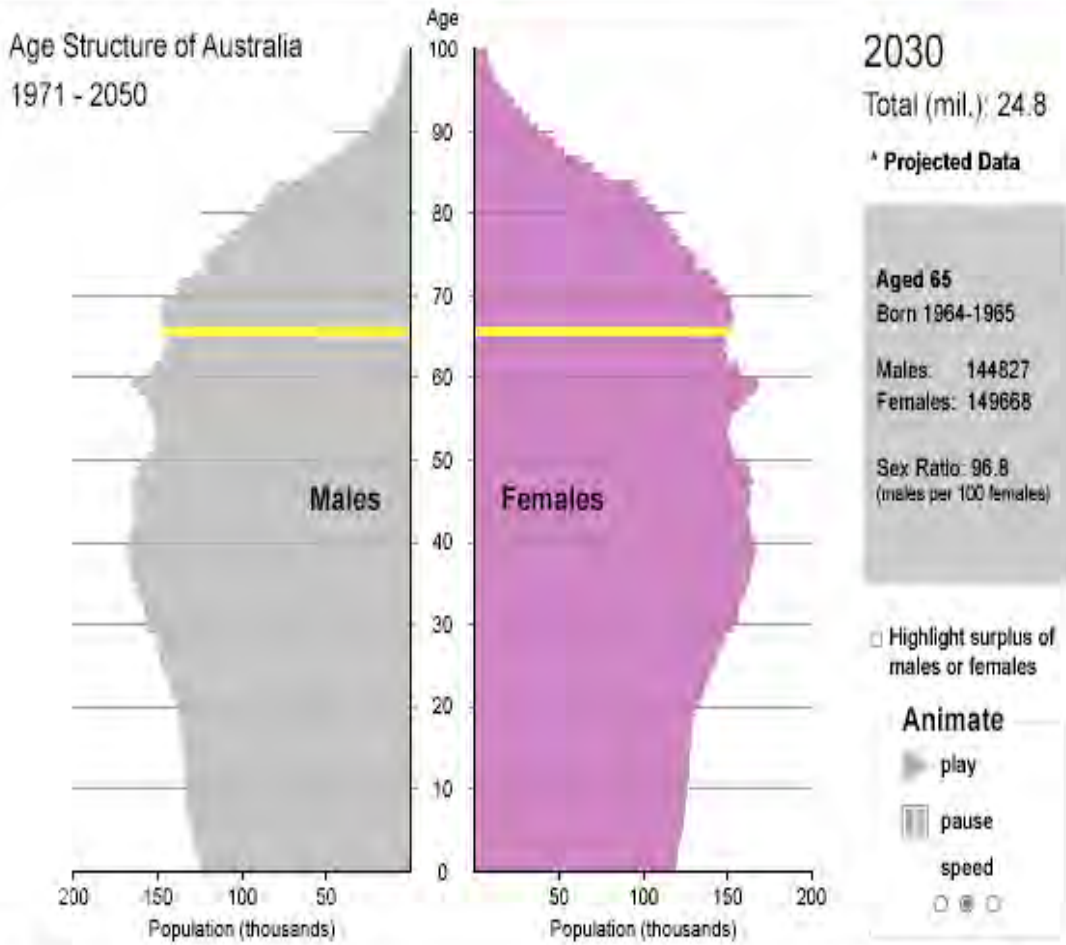


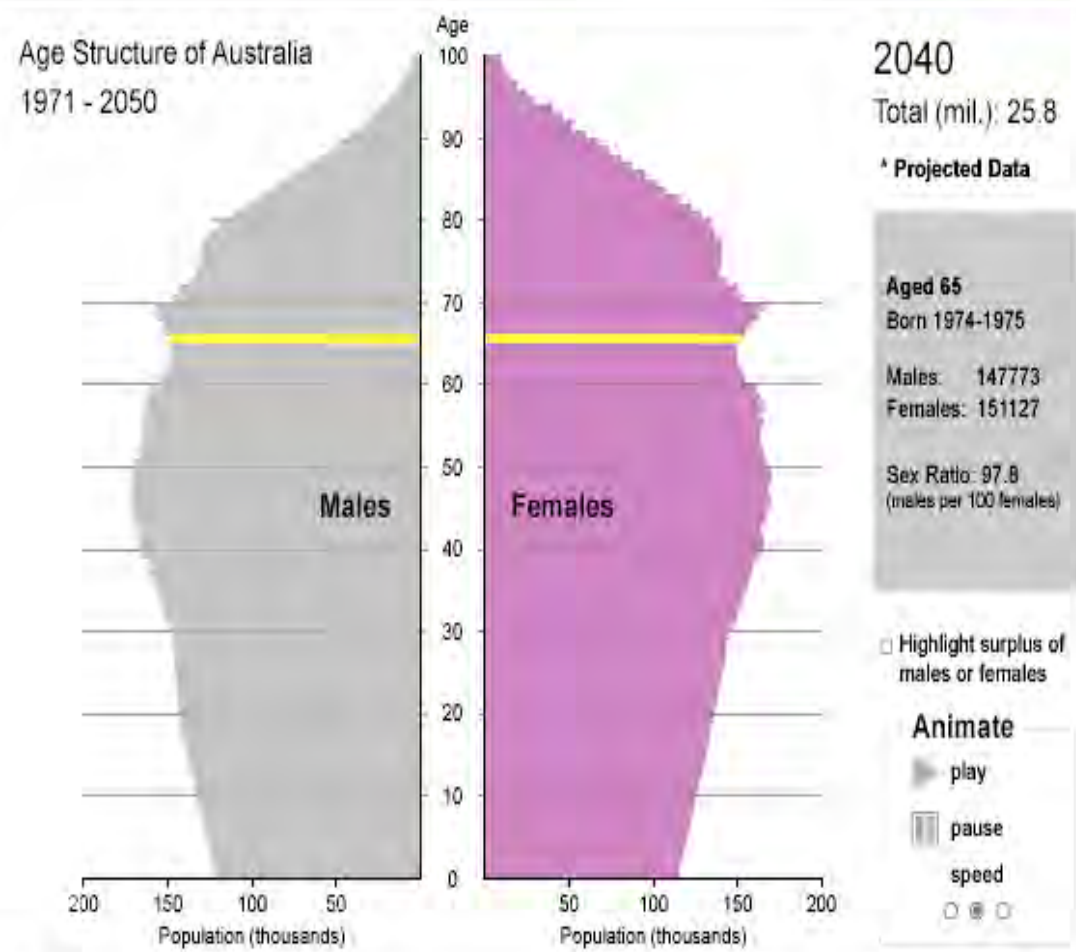




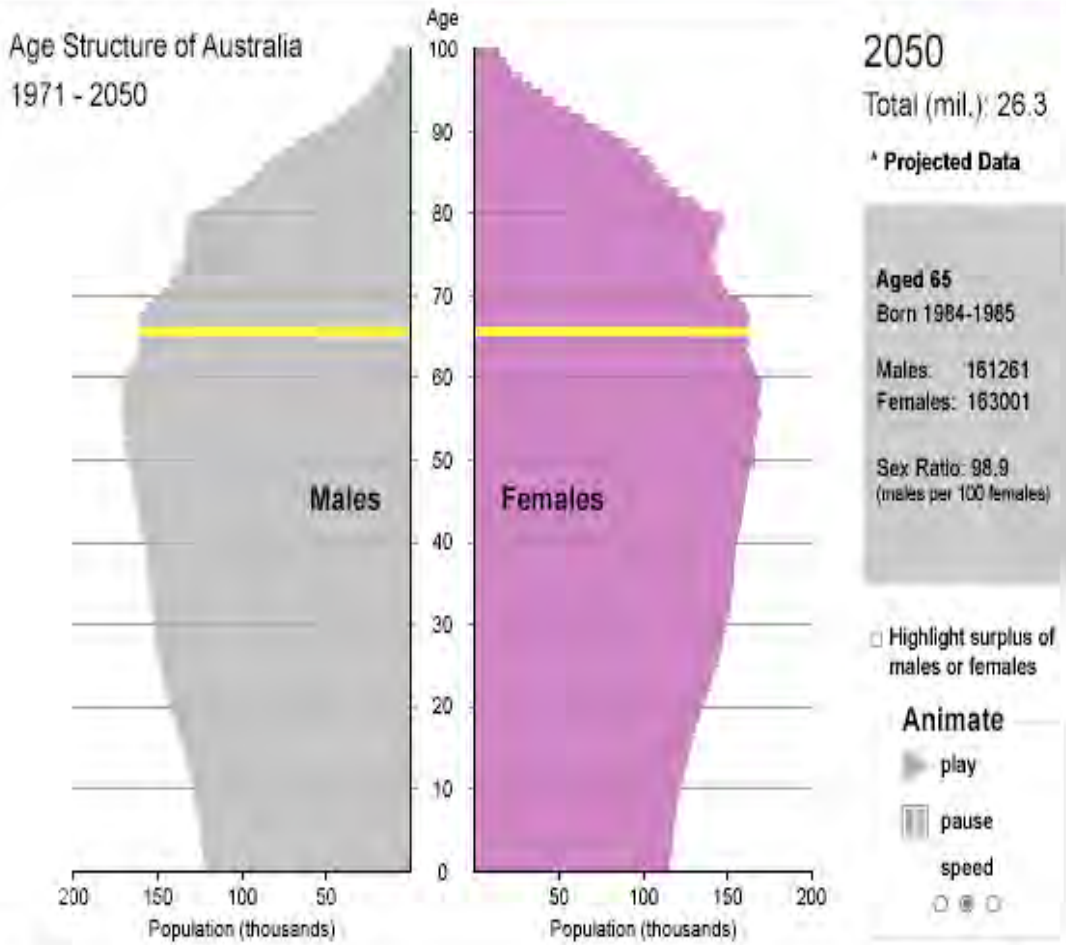














# Australia's ageing population <sup>1</sup>

- By 2050 the population aged ...
  - 65 yo+ will double: 3m → 7.5m (13% → 25%)
  - 85yo + will quadruple: 415,000 → 1.6m
- By 2025: more 65+ yo<sup>s</sup> than > children 0-14 yo
- 30<sup>th</sup> June 2011, 4252 people 100 years or older

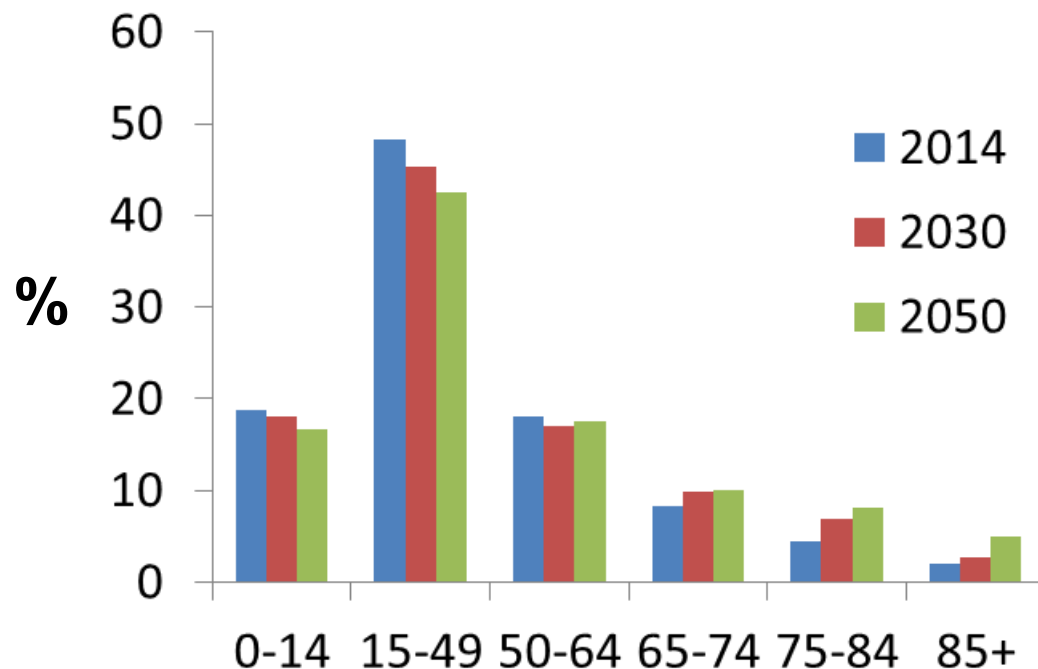
<sup>1</sup> Dementia in Australia, AIHW, 2012



# Australia: Population projections

## Population (approx):

- 2014: 23.5 million
- 2030: 29.0 million
- 2050: 35.3 million

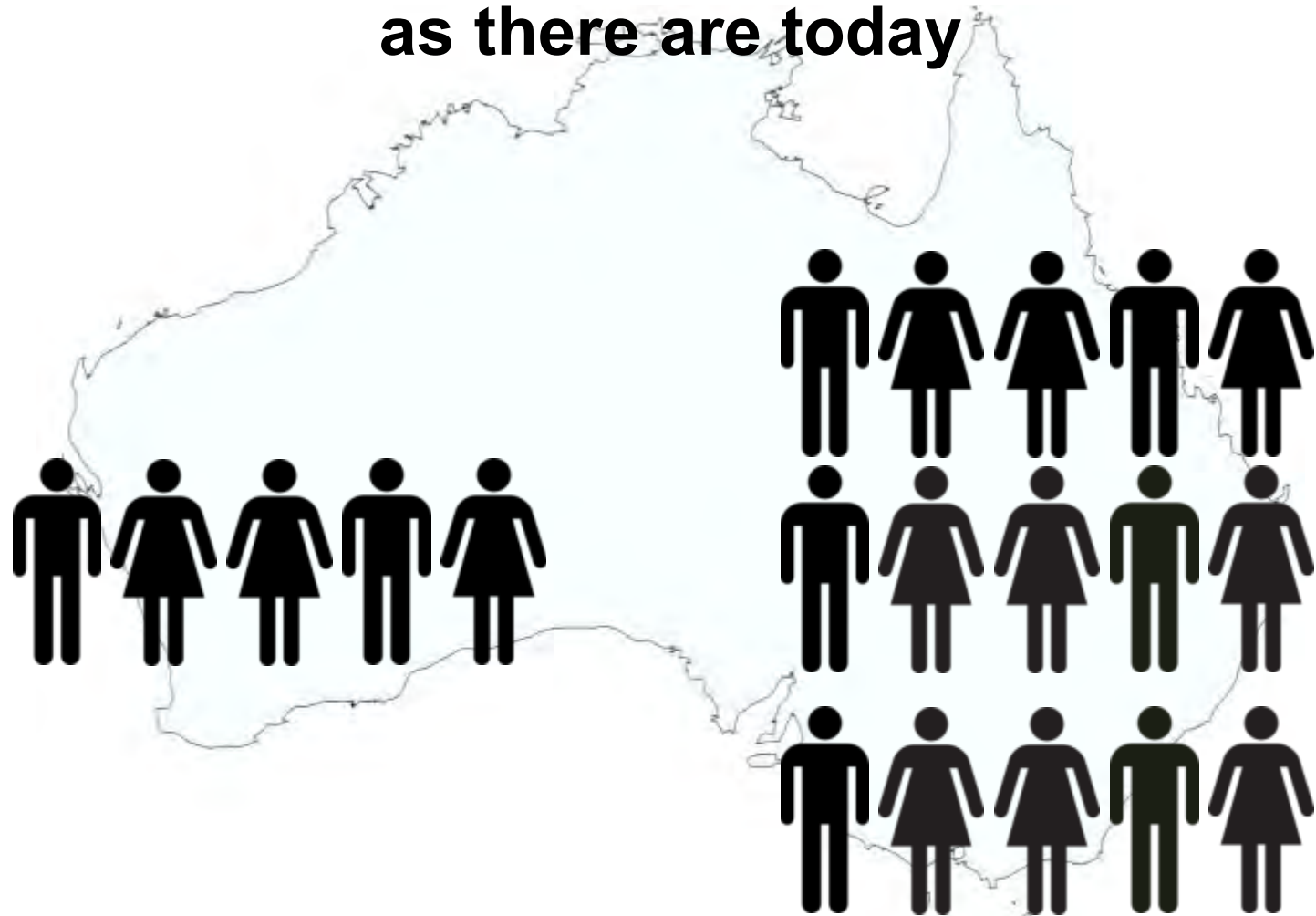


Productivity Commission 2013, *An Ageing Australia: Preparing for the Future*, Commission Research Paper, Canberra.

**In 2030, Australia's population will be  
approx **28.48 million****



**There will be almost 3 times as many centenarians  
as there are today**



**2013: 6,364 centenarians    2030: 18,923 centenarians**



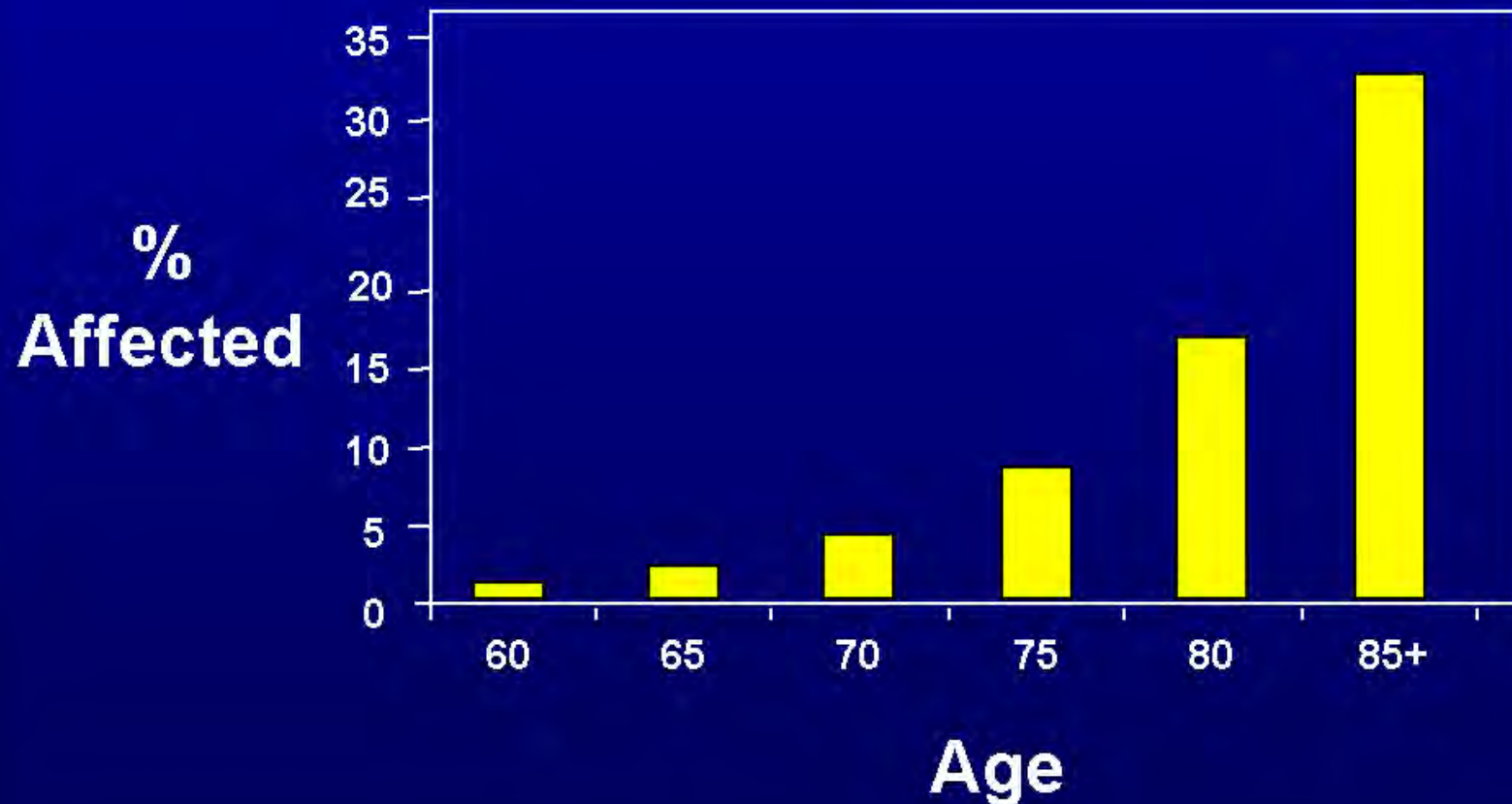
# Costs

- **Cost of health in Australia is  $\approx \leq 10\%$  of GDP or about \$130b and rising above inflation**
- **Drivers – costs, demand, > expensive investigations, medicines and procedures**
- **Dementia costs 0.8% GDP or  $\approx$  \$6b pa.**
- **By 2050, dementia costs  $> 1.8\%$  GDP**

# Prevalence of dementia

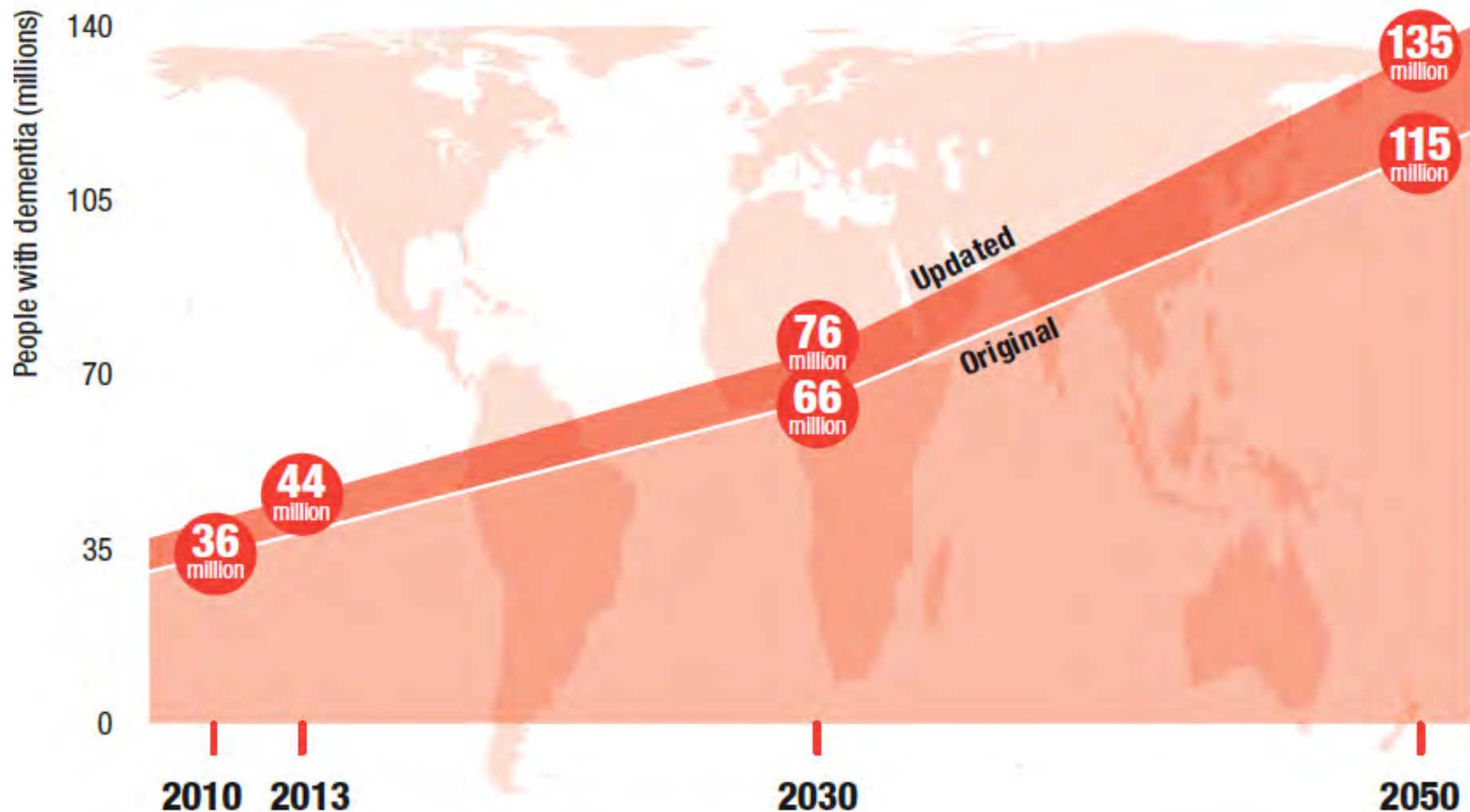
- **> 6% of population  $\geq$  65 years old**
- **20% of persons  $\geq$  80 years**
- **30% of  $\geq$  90 years old**
- **Prevalence doubles every five years after 60**

# Dementia Doubles in Frequency Every 5 Years After Age 60



Evans et al. *JAMA*. 1989.  
Jorm et al. *Acta Psychiatr Scand*. 1987.

# Projections of dementia worldwide



*The Global Impact of Dementia 2013–2050. ADI, 2013.*

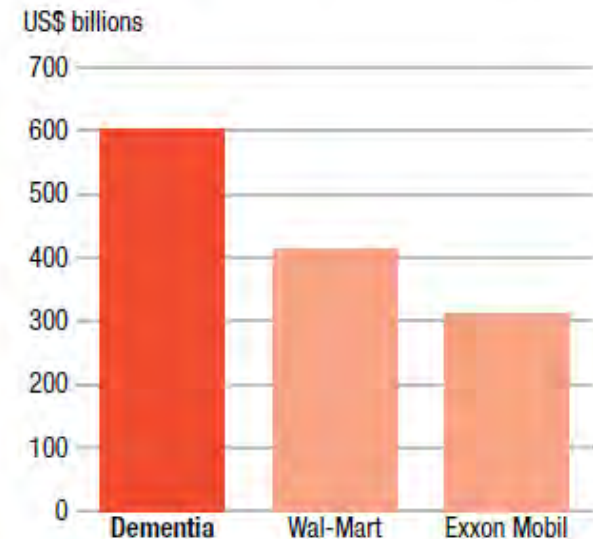




# Global Cost of Dementia

- **Total estimated cost worldwide US\$604 billion in 2010**
- **If dementia were...**
  - a country, it would have the world's 18<sup>th</sup> largest economy
  - a company, it would be the world's largest by annual revenue

Figure 1 Cost of dementia compared to company revenue



**World Alzheimer Report, ADI, 2010**

# Dementia in Australia

- 330,000 people with dementia in 2013
- 74% aged 75+ *but*  $\approx 8\% < 65$  yrs
- 70% live in community
- Projections: 400,000 by 2020; 900,000 by 2050
- 3<sup>rd</sup> leading cause of death
- 4<sup>th</sup> leading cause of disease burden
- 3<sup>rd</sup> leading cause of disability burden; (1<sup>st</sup> in 65+)



\* Dementia in Australia, AIHW, 2012



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# People with dementia and their CGs

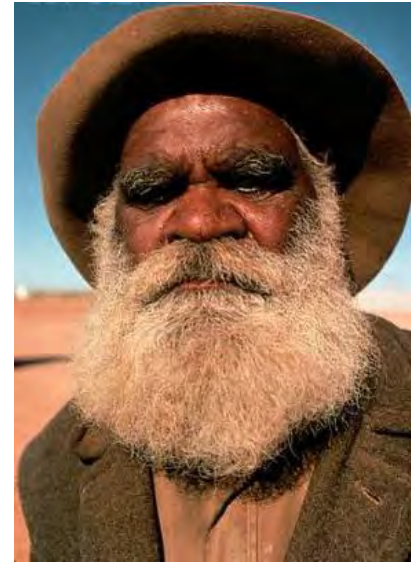
- PWD all over the world have
  - Cognitive decline
  - Functional decline
  - Behavioural disturbances
- CGs all over the world face
  - Stress, depression, burden
  - Financial and social hardship
  - Stigma, ignorance





# Dementia in Australia

- **Aboriginal and Torres Strait Islanders have higher rate**
- **200,000 family carers**
  - **>80% provide >40 hrs pw <sup>1</sup>**
- **Direct health and aged care costs = \$4.9bn <sup>1</sup>**
- **If add unpaid costs of carers > \$6bn pa <sup>2</sup>**
- **0.8% GDP → 1% GDP by 2030<sup>1</sup> → 1.8% by 2050<sup>3</sup>**



<sup>1</sup> Dementia in Australia, AIHW, 2012; <sup>2</sup> Access Economics 2003; <sup>3</sup> Productivity Commission, Caring for Older Australians 2011, 2013

# Bill's story



- 70 y.o. architect
- Married, 3 children + GC
- Mistakes at work
- Admits to anxiety 2 yrs
- Referred for assessment
- Alzheimer's diagnosed



# Bill's story



- **Diagnosis = relief!**
- **Wife grateful**
- **Changes work duties**
- **Starts anti-Alzheimer Rx**
- **Arranges enduring Power of Attorney, e-Guardianship, Will & Advance Directive**
- **Monitors driving**



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# Bill's story



- **Diet, exercise, mental stimulation**
- **Life priority decisions**
  - **more family time**
  - **plans holiday abroad**

# Remember this shopping list

- Milk
- Sausages
- Peas
- Flour
- Oranges
- Steak
- Cheese
- Apple
- Yoghurt
- Sugar



# Dementia definition

- **Loss of at least one cognitive function**
  - memory
  - Language
  - Executive abilities - planning, organisation, abstract thinking, conceptual shift
  - Visuo-spatial abilities
- **Represents a decline**
- **Impairs daily function - occupational or social**

# Dementia - concepts

- Dementia is an umbrella term to describe a syndrome
- Alzheimer's disease is most common
- Some causes reversible - but rare
- Mild Cognitive Impairment
  - intermediate between normal and dementia



# AETIOLOGY OF DEMENTIA

- Over 100 causes
- Alzheimer's disease (AD) up to 50%
  - includes other degenerative dementias
- Vascular (VaD) or multi-infarct dementia (MID) about 15-20%
- Mixed AD and VD about 15%
- Lewy body disease (up to 20%)
- Fronto-temporal dementias
- Alcohol
- Head injury

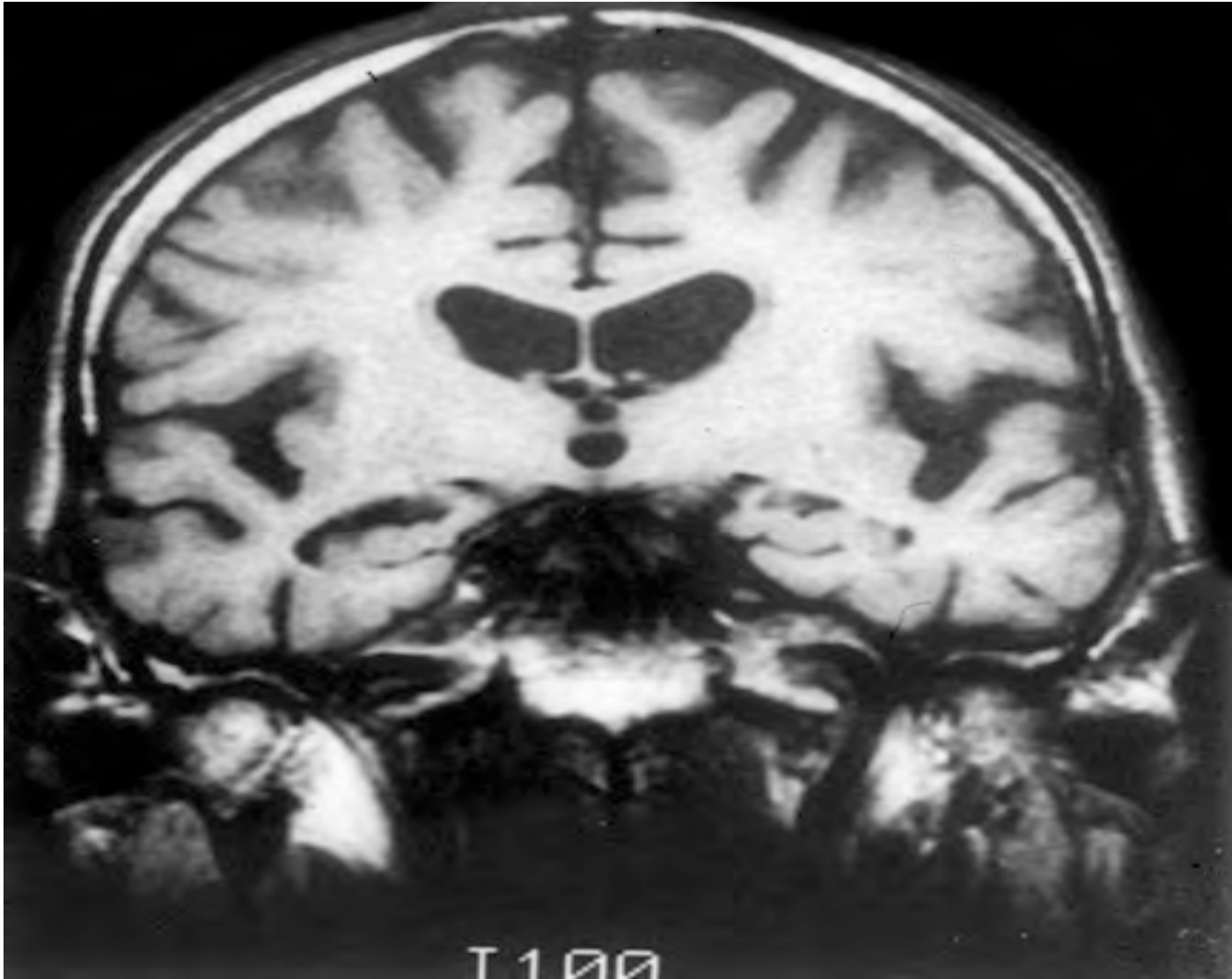


# Potentially reversible or able to be halted causes of dementia

- B12 or folate deficiency
- Thyroid deficiency
- Calcium excess
- Tumours
- Normal pressure hydrocephalus
- Infection eg HIV, syphilis



# MRI: profound atrophy



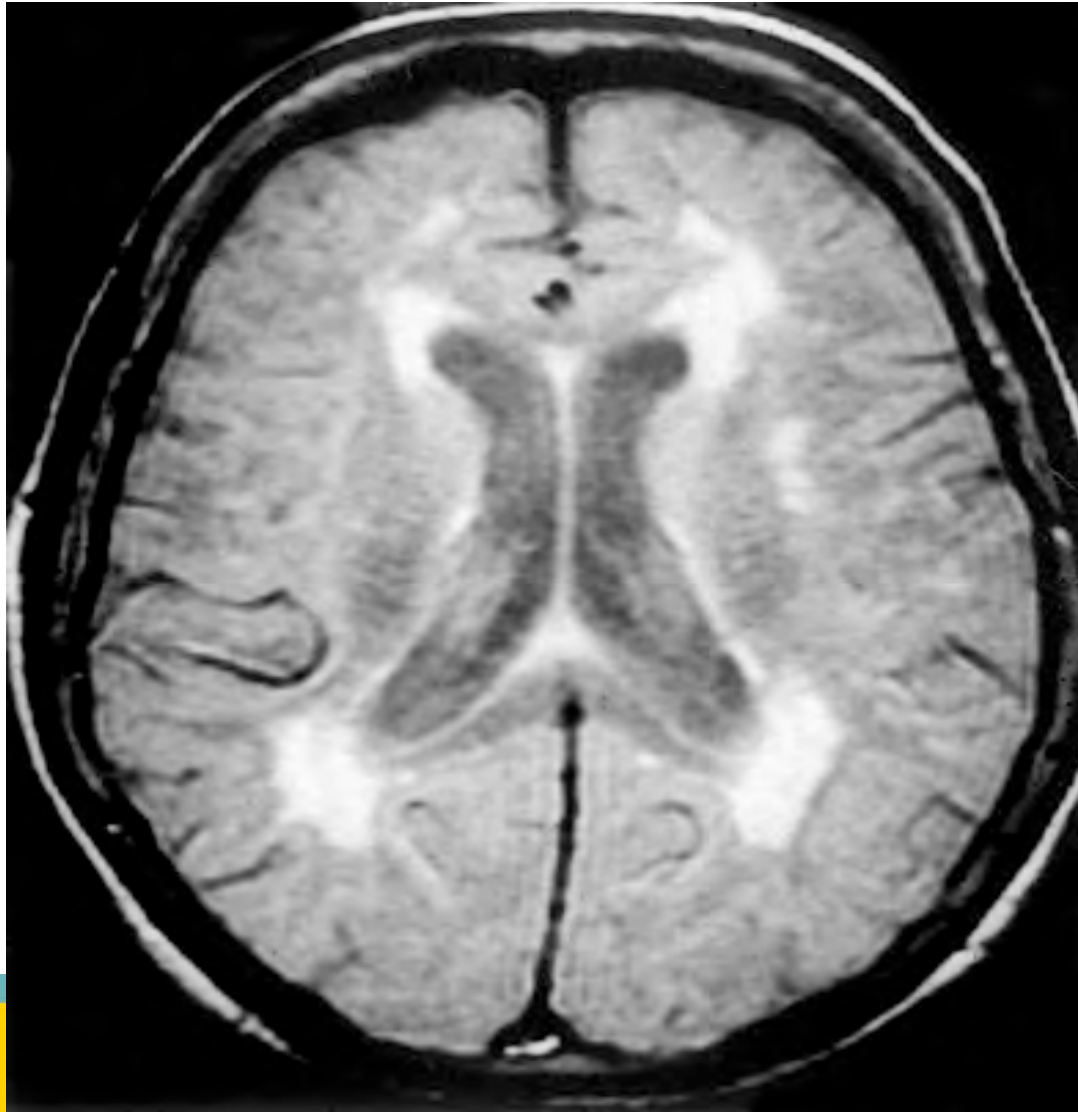
**CHeBA**  
Healthy Brains Positive Ageing



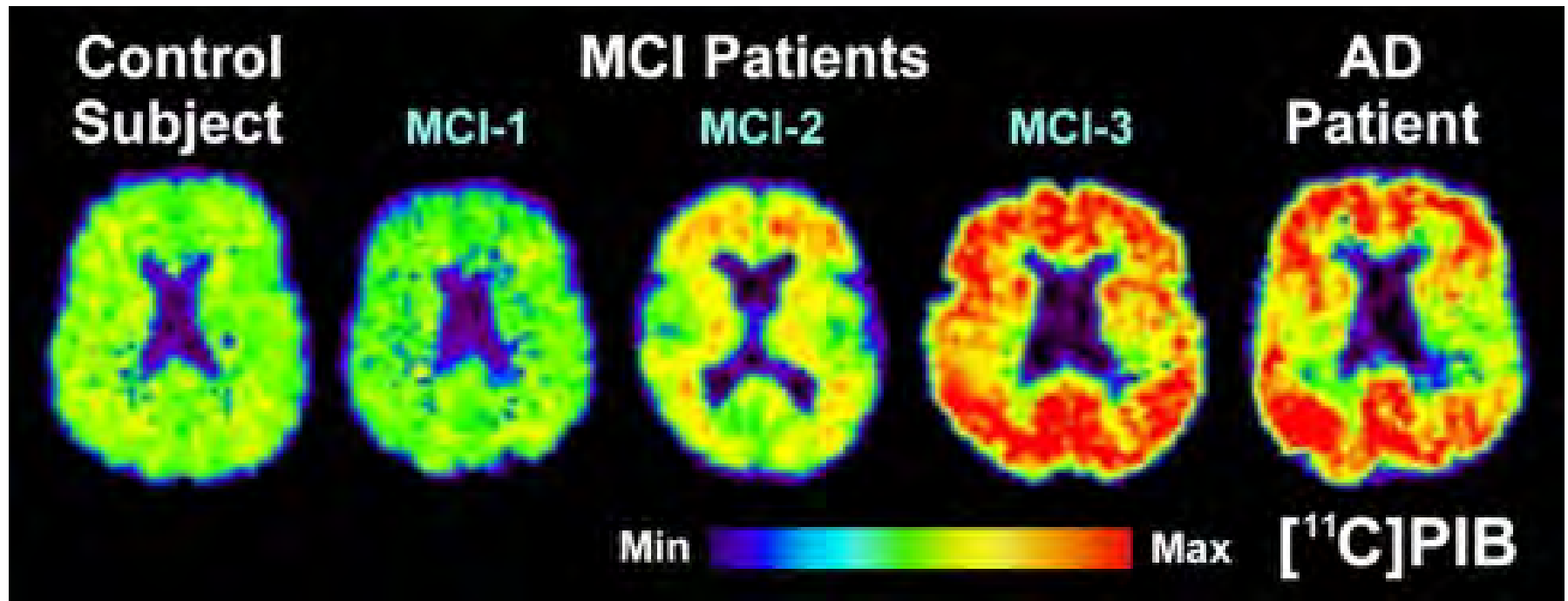
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# MRI scan of brain showing ischaemic changes



# PiB-PET Scans: AD vs MCI vs control



From the online newspaper of Prof Yasser Metwally  
<http://yassermetwally.wordpress.com/dementia-alzheimer-type-and-others/neuroimaging-of-dementia/>

# Early Dementia -Vs- Ageing

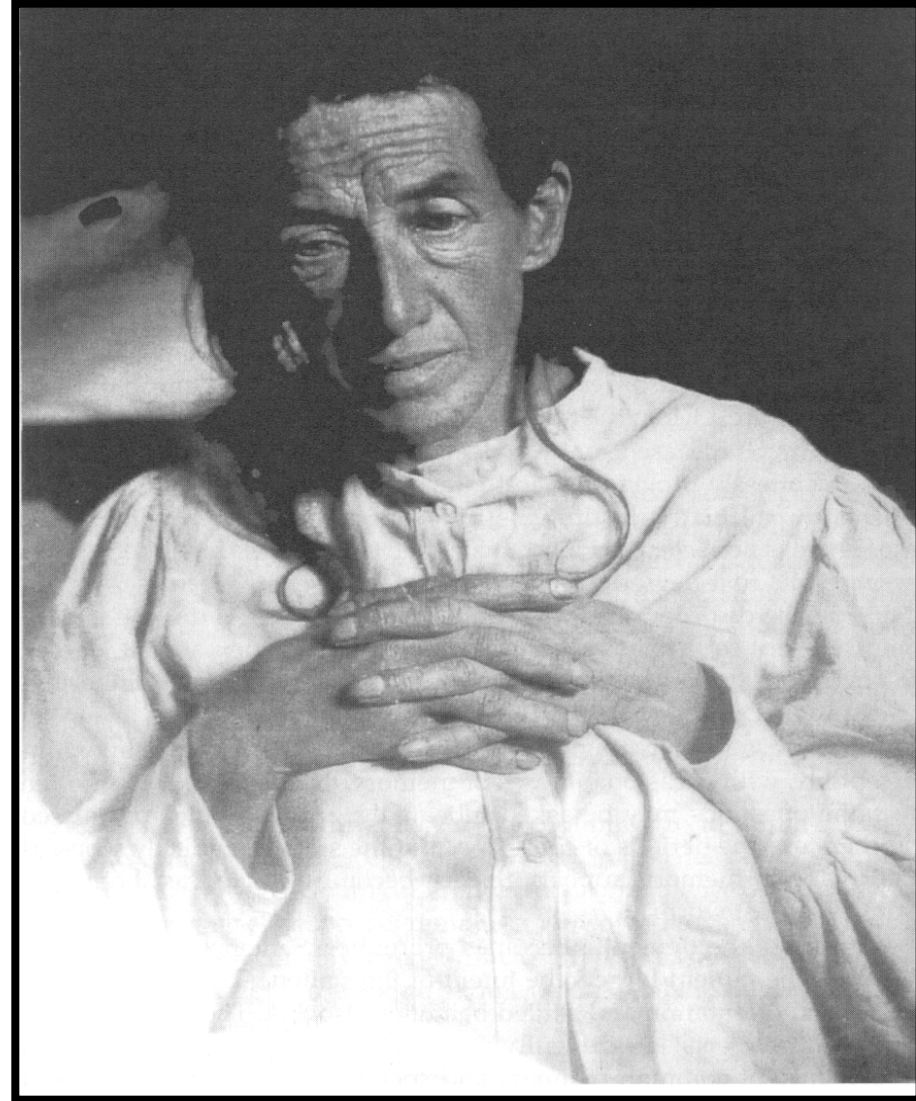
**Suspect early dementia if:**

- **Progressively worse**
- **Difficulty learning even with effort**
- **Events, not just details, forgotten**
- **Interferes with normal function**  
e.g. hobbies, social life, shopping
- **Other cognitive difficulties**
  - **hard to understand a story/follow movie**
  - **difficulty finding words**
  - **can't do calculations**
  - **more disorganised**



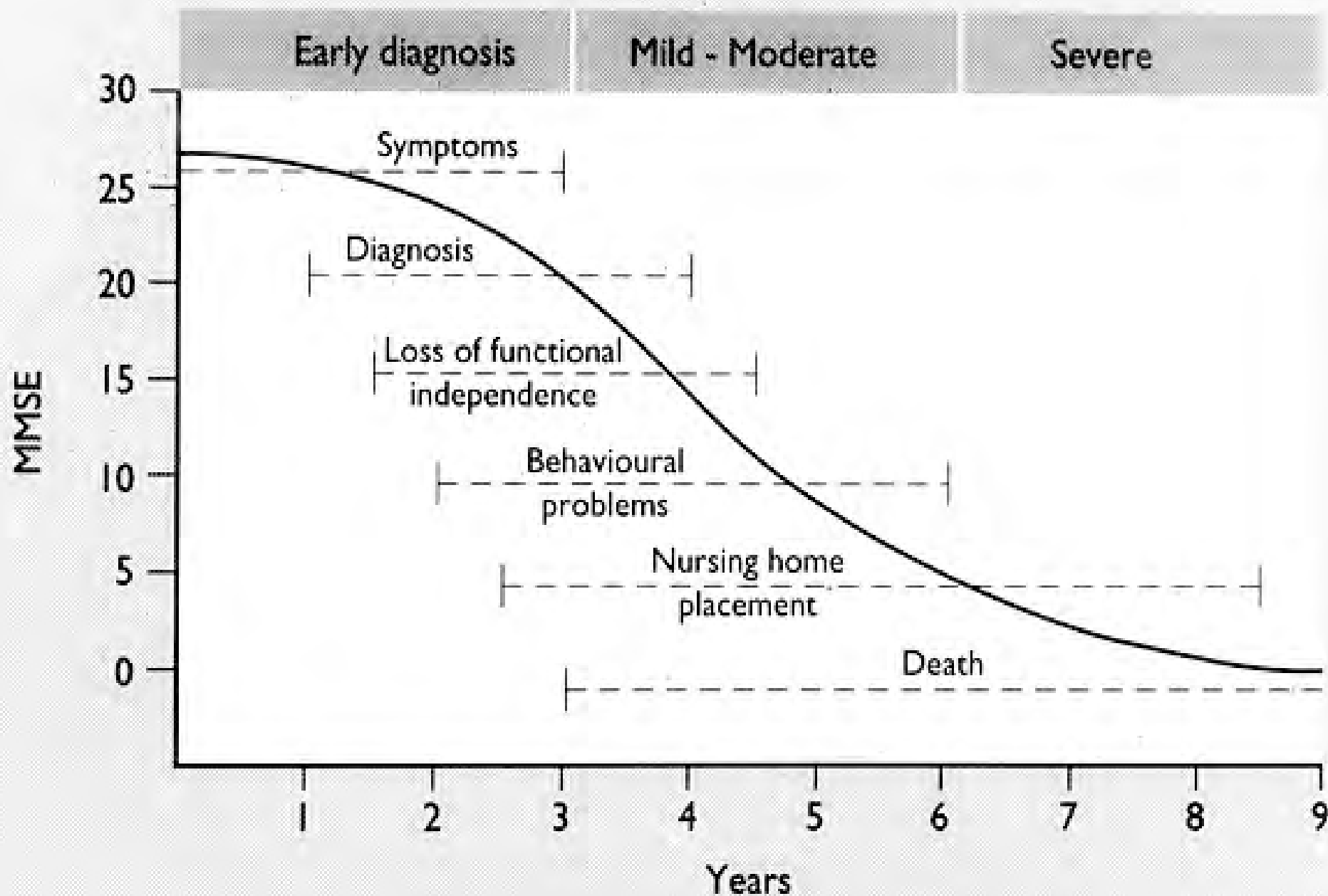
# ***Alzheimer's disease***

- **Memory loss**
- **Language disturbances**
- **Visuospatial deficits**
- **“Dysexecutive”:**  
    **Impaired judgment,  
    motivation**
- **Neuropsychiatric  
symptoms:**  
    **depression, anxiety,  
    sleep disturbance  
    psychosis**



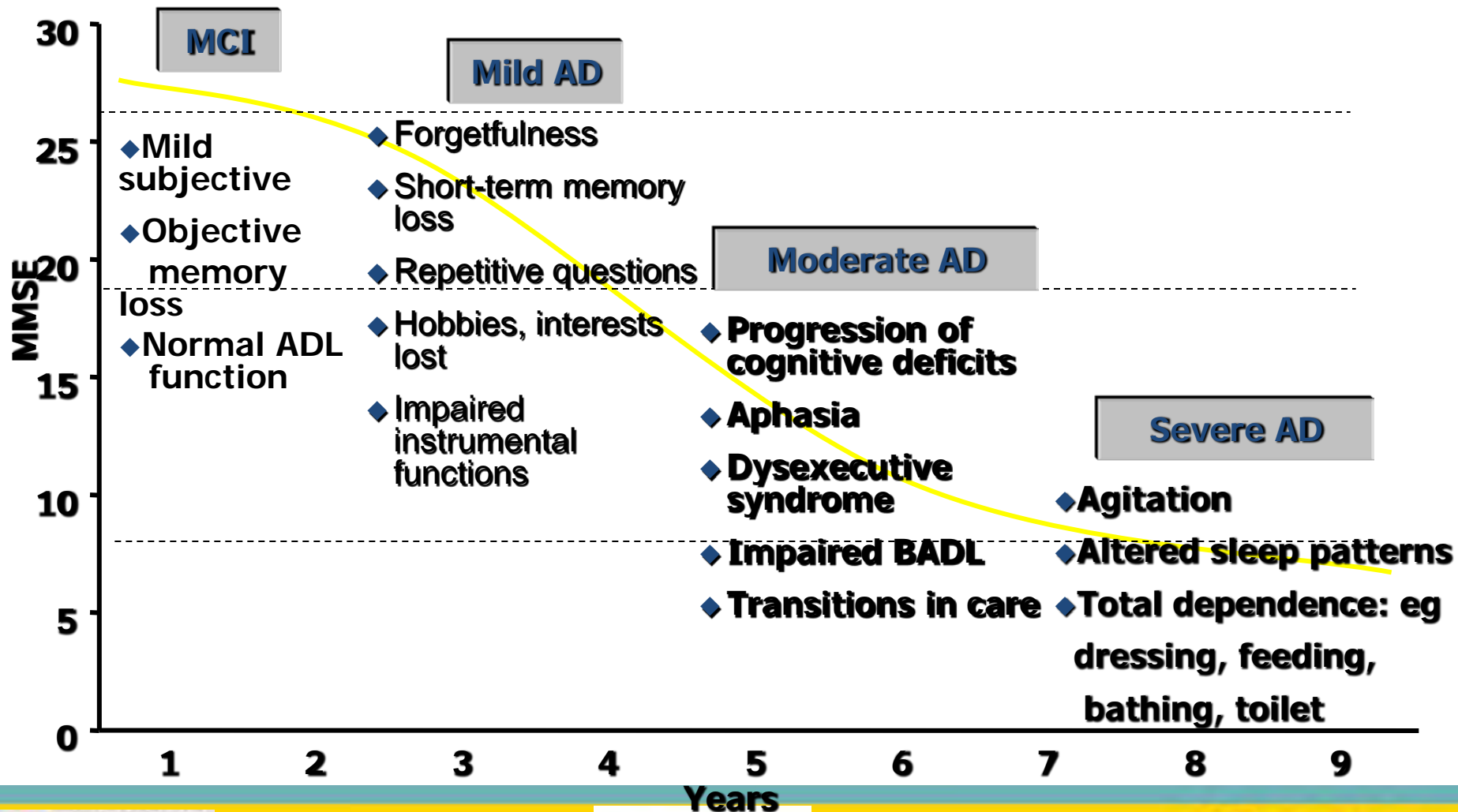
*Alzheimer's original patient: Auguste Deter*

## Natural history of Alzheimer's disease





# Symptom Progression in AD



BADL=basic activities of daily living.

Modified from Feldman et al. *Clinical Diagnosis and Management of Alzheimer's Disease*. 1st ed. 1998.

# Pathology of AD

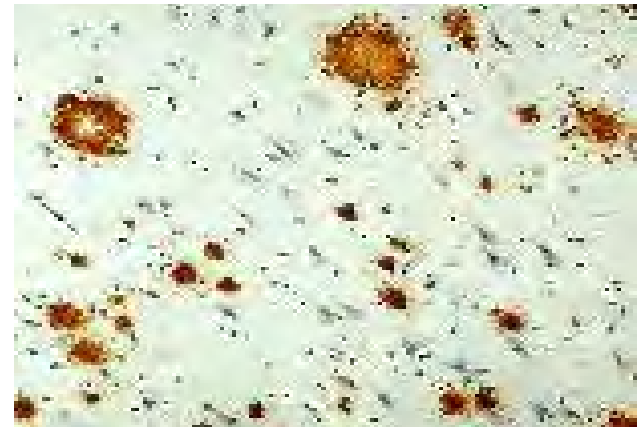
- ***Macroscopic***: atrophy, mostly temporo-parietal and frontal
- ***Microscopic***
  - loss of neurones and synapses
  - neurofibrillary tangles (NFTs)
  - amyloid plaques
  - degeneration

# Pathology of AD

- *Chemistry*

- Build up of abnormal proteins aggregates
  - $A\beta$
  - Tau ( $\tau$ ) protein - phosphorylated
- Loss of neurotransmitters
  - especially acetylcholine (ACh)

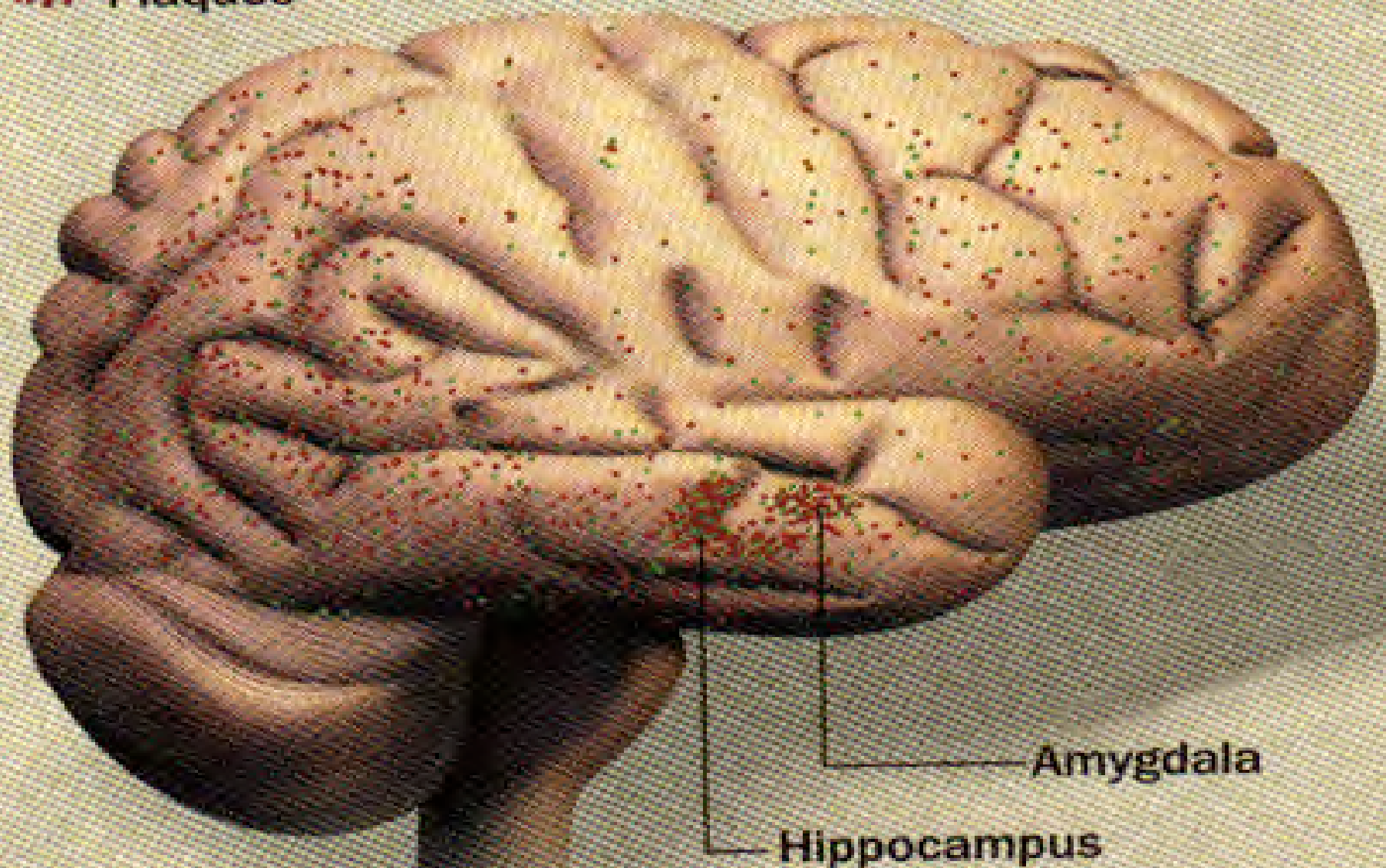
# AD: a progressive CNS disorder with a characteristic pathology



Katzman, 1986; Cummings and Khachaturian, 1996

 Tangles

 Plaques







# Causes of AD unknown - possible factors

## *Genetic*

- **Early onset - Familial AD (FAD), auto dominant**
  - age of onset 40s & 50s, rare
  - mutations on C14, C21, C1
- **Late onset sporadic AD**
  - associated with ApoE4 (gene on C19)

## *Environmental*

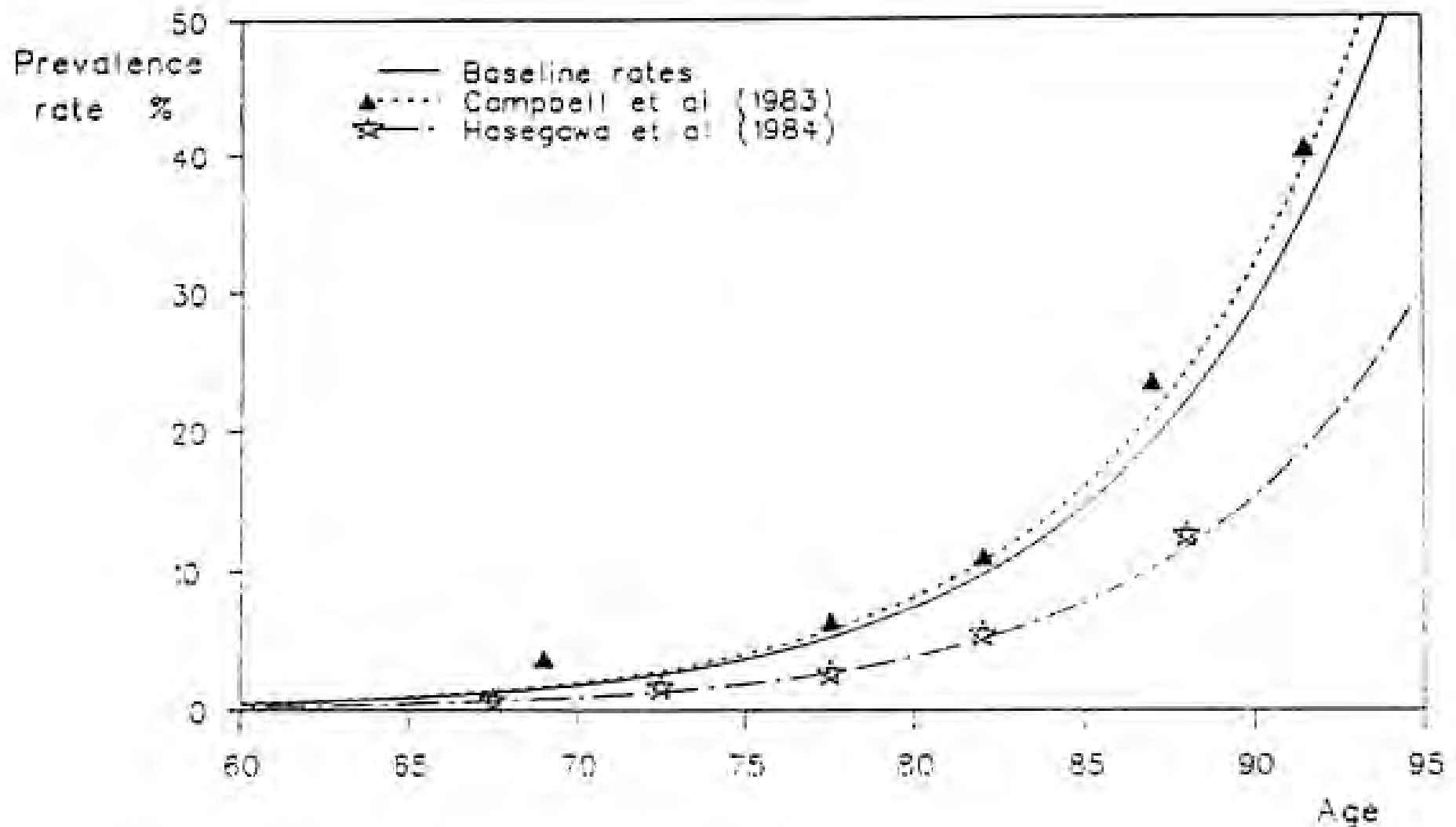


# Strong risk factors for AD

- Age
- Down's syndrome
- Family history
- Certain genes associated with increased risk but do not cause AD eg ApoE4

# Risk factors for A D: 1

Age





**Risk factors  
for AD:  
Down's  
syndrome**



# Less strong risk factors for AD

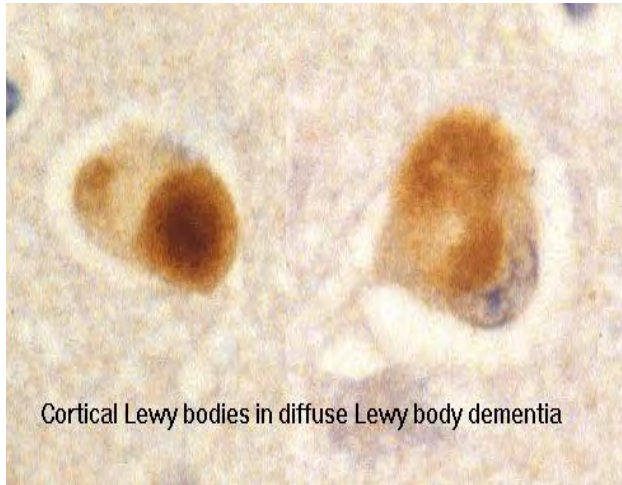
- High blood pressure in mid-life
- High cholesterol in midlife
- Diabetes (Type II)
- Obesity in mid-life
- Current smoking
- Family history of Down's
- Head injury
- ? Depression
- Low education, little cognitive stimulation
- Others – (prob. *not* Aluminium exposure)

# Vascular dementia

- **earlier onset than AD and M>F**
- **sudden onset, stepwise deterioration**
- **history of hypertension**
- **history of strokes**
- **evidence associated atherosclerosis**
- **focal neurological symptoms**
- **focal neurological signs**
- **focal pathology on brain imaging**

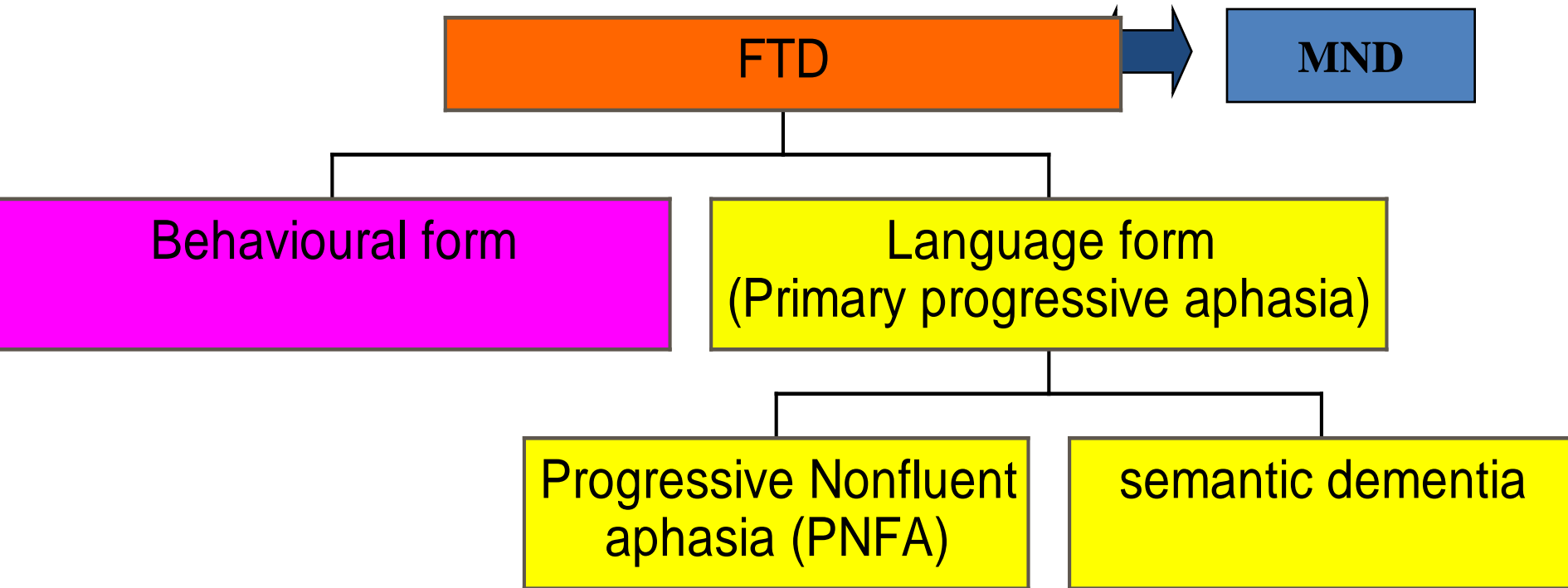
# Lewy Body Dementia

- Dementia
- Lewy bodies diffuse in cortex
- REM Sleep disorder
- Fluctuating cog. impairment ++
- Visual &/or auditory hallucinat<sup>ns</sup>
- Paranoid delusions
- Falls
- Extrapyraxidal features
- Neuroleptic sensitivity
- Visuo-spatial deficits



Cortical Lewy bodies in diffuse Lewy body dementia

# Frontotemporal Dementia



Slide from John Hodges

# Fronto-temporal Dementias (Pick Syndrome)

## *Clinical*

- Onset usually 40-60y.o. (20-80 y. range)
- Up to half cases of pts <65yo
- Usually sporadic but 20% of cases familial with autosomal dominant inheritance
- death occurs sooner than AD
  - esp if with Motor Neuron Disease



# Fronto-temporal dementias

## *On examination*

- **preservation of memory until late**
- **early, prominent personality changes**
- **apathy**
- **irritability**
- **jocularity and euphoria**
- **loss of tact and concern**
- **impaired judgement and insight**

# Can Alzheimer's disease be prevented?



Never Stand Still

Medicine

Psychiatry



# What was that shopping list?

- ***Dairy***
  - Milk
  - Yoghurt
  - Cheese
- ***Staples***
  - Sugar
  - Flour
- ***Butcher***
  - Steak
  - Sausages
- ***Greengrocer***
  - Apple
  - Oranges
  - Peas



# **Prevention: Eliminate v Postpone**

- **Disease elimination**
  - eg smallpox vaccination
  - best prospect is AD vaccine
- **Disease postponement (Brookmeyer R, 1998)**
  - delay AD onset by
  - 2 yrs → ↓ prevalence by 20%
  - 5 yrs → ↓ prevalence by 50%



[yourbrainmatters.org.au](http://yourbrainmatters.org.au)

# Can AD be prevented? May be delayed....

- Look after your heart
- Be physically active
- Mentally challenge your brain
- Follow a healthy diet
- Enjoy social activity

[www.cheba.unsw.edu.au](http://www.cheba.unsw.edu.au)

[www.dementiaresearch.org.au](http://www.dementiaresearch.org.au)





http://www.yourbrainmatters.org.au/



Google AU



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Your Brain Matters



Page



Tools



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NATIONAL DEMENTIA HELPLINE  
**1800 100 500**



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Download BrainyApp today.... And join over 200,000 others looking after their brain health, because Your Brain Matters

**FIND OUT MORE**



Done

Internet

100%





# **Mind your diet**

- **Mediterranean diet**
- **Antioxidants**
- **Tumeric/ curcumin?**
- **Fish? Vegetables?**



An Australian Government Initiative

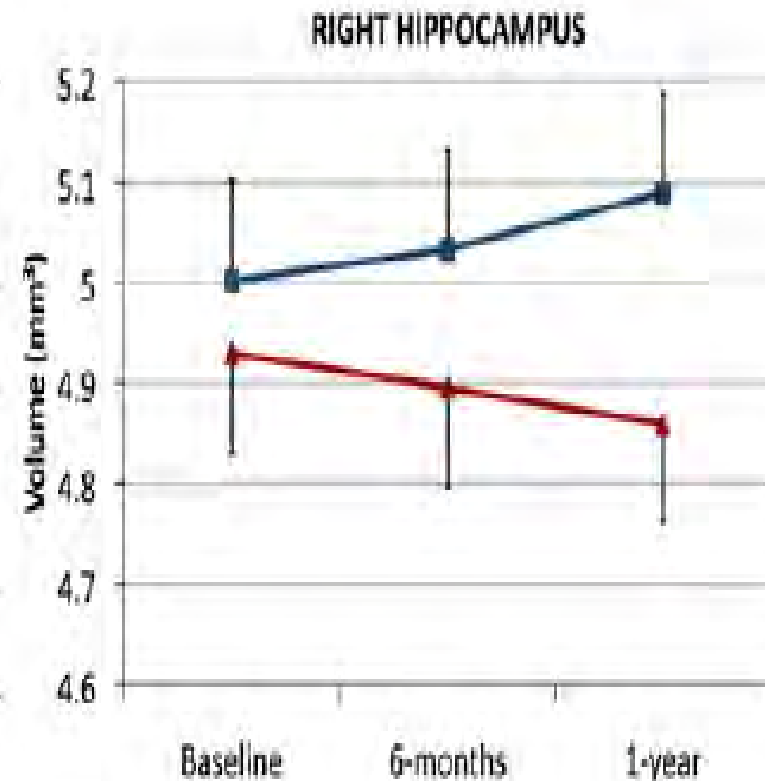
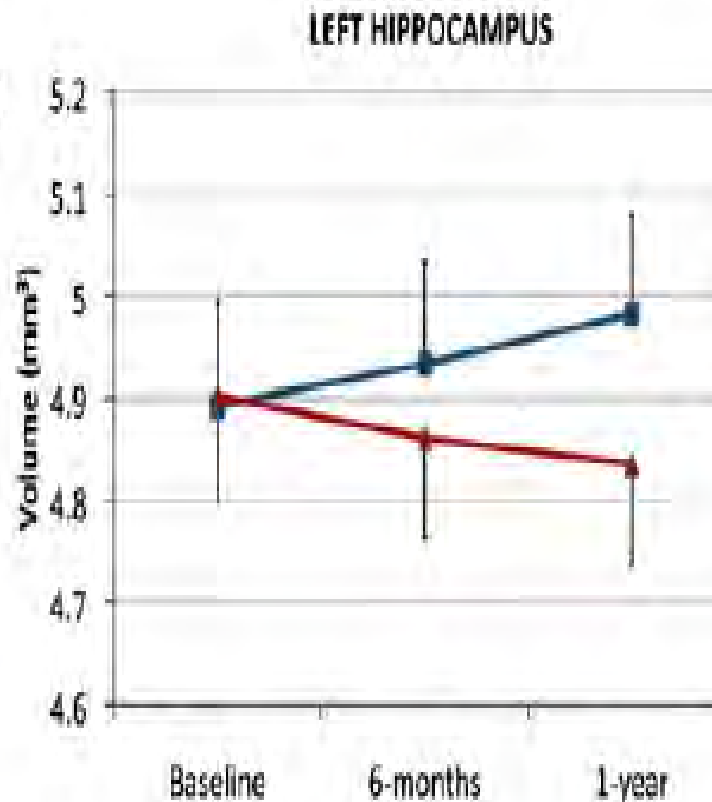
# Mind your Body

- Regular physical exercise



# The power of physical activity

## Hippocampus



Erickson et al., 2011



## **Exercise benefits**

- **Heart disease, blood pressure**
- **Obesity, Diabetes**
- **Sarcopenia, Osteoporosis**
- **Lower levels of biomarkers - CSF and PET PIB in cognitively normal adults<sup>1</sup>**
- **For PWD – behaviour✓; cognition?**

<sup>1</sup>Liang et al, Annals Neurology 2010



# Mental Activity & Dementia

- **Meta-analysis of 22 studies, 29,000 individuals**
- **↑ complex mental activity in late life = ↓ risk of dementia by half; OR = 0.54 (0.49-0.59) <sup>1</sup>**
- **Dose - response relationship evident<sup>1</sup>**
- **Results suggest complex patterns of mental activity in the early, mid- and late-life stages are associated with ↓ dementia incidence<sup>1</sup>**
- **Results held when covariates in source studies were controlled for<sup>2</sup>**

<sup>1</sup>Valenzuela MJ. Sachdev P. (2006). Psychol Med. 36(4): 441-454;

<sup>2</sup>Valenzuela MJ. Sachdev P. (2006) Psychol Med. 36(8): 1065-1073



# Cognitive training

- **Systematic review of RCTs with longitudinal follow-up (>3mths) in healthy elderly<sup>1</sup>**
  - 7 RCTs met inclusion criteria, low quality
  - Strong effect size for cognitive exercise intervention vs wait-and-see controls
  - Longer FU duration (>2yrs) → ES no lower
- **Review of cog. training or rehab in dementia<sup>2</sup>**
  - 11 RCTs, no benefit

Valenzuela & Sachdev (2009) Am J Geriatr Psychiatry 17(3)

Bahar-Fuchs, Clare, Woods – [Cochrane Database Syst Rev.](#) 2013 Jun

5;6:CD003260. doi: 10.1002/14651858.CD003260.pub2.



# The “second patient”



## *Effects on carers*

- High levels of stress
- Physical health suffers
- Social isolation
- Financial hardship

# Alzheimer's Australia

- Support -1 800 100 500 (helpline)
- Counselling, training programs
- Information, brochures, videos
- [www.alzheimers.org.au/](http://www.alzheimers.org.au/)
- Advocacy; Research funding
- *Living with memory loss* program  
980 50 100 or 1-800-100-500
- Dementia Alliance International

[www.dementiaallianceinternational.org/](http://www.dementiaallianceinternational.org/)



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# Drugs for AD

Four drugs approved

- all symptomatic, non curative:

## *Cholinesterase inhibitors*

- Aricept (donepezil)
- Exelon (rivastigmine)
- Reminyl (galantamine)

## *NMDA receptor antagonist*

- Ebixa (memantine)

Souvenaid – Nutraceutical/ Medical food



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# The cutting edge



- **Drugs to prevent AD**
- **Drugs to cure AD**
  - **>200 trials recruiting**
  - **Vaccines, block build up of  $\beta$  amyloid protein**
  - **$\gamma$  and  $\beta$  Secretase prevent  $\beta$  amyloid protein forming**
- **Better ways to help families and people with dementia**
- **Better long term care**
- **Treatment of behavioural and psychological symptoms of dementia**

# Conclusions 1

- **Dementia is common**
- **One in five of people over 80**
- **Main cause is Alzheimer's**
- **For most people cause of AD is unknown**
- **Major public health and economic issue**
- **Planning for future is a priority**





# Conclusions 2

- **Management is complex & continuing**
  - **Patient**
  - **Family**
  - **Medication**
  - **Legal and financial advice**
  - **Practical advice**
- **Pace of research is exciting**



# **Dementia Collaborative Research Centres**

**[www.dementiaresearch.org.au](http://www.dementiaresearch.org.au)**

## **Centre for Healthy Brain Ageing**

**[www.cheba.unsw.edu.au](http://www.cheba.unsw.edu.au)**

**Alz Australia: [www.fightdementia.org.au](http://www.fightdementia.org.au)**

**[www.yourbrainmatters.org.au/](http://www.yourbrainmatters.org.au/)**

**ADI : [www.alz.co.uk](http://www.alz.co.uk)**



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