



An introduction to dementia

Never Stand Still

Medicine

Psychiatry

Professor Henry Brodaty
Dementia Collaborative Research Centre – Assessment and Better Care
Centre for Healthy Brain Ageing
University of New South Wales
h.brodaty@unsw.edu.au



21st Century is century of neurodegenerative disease

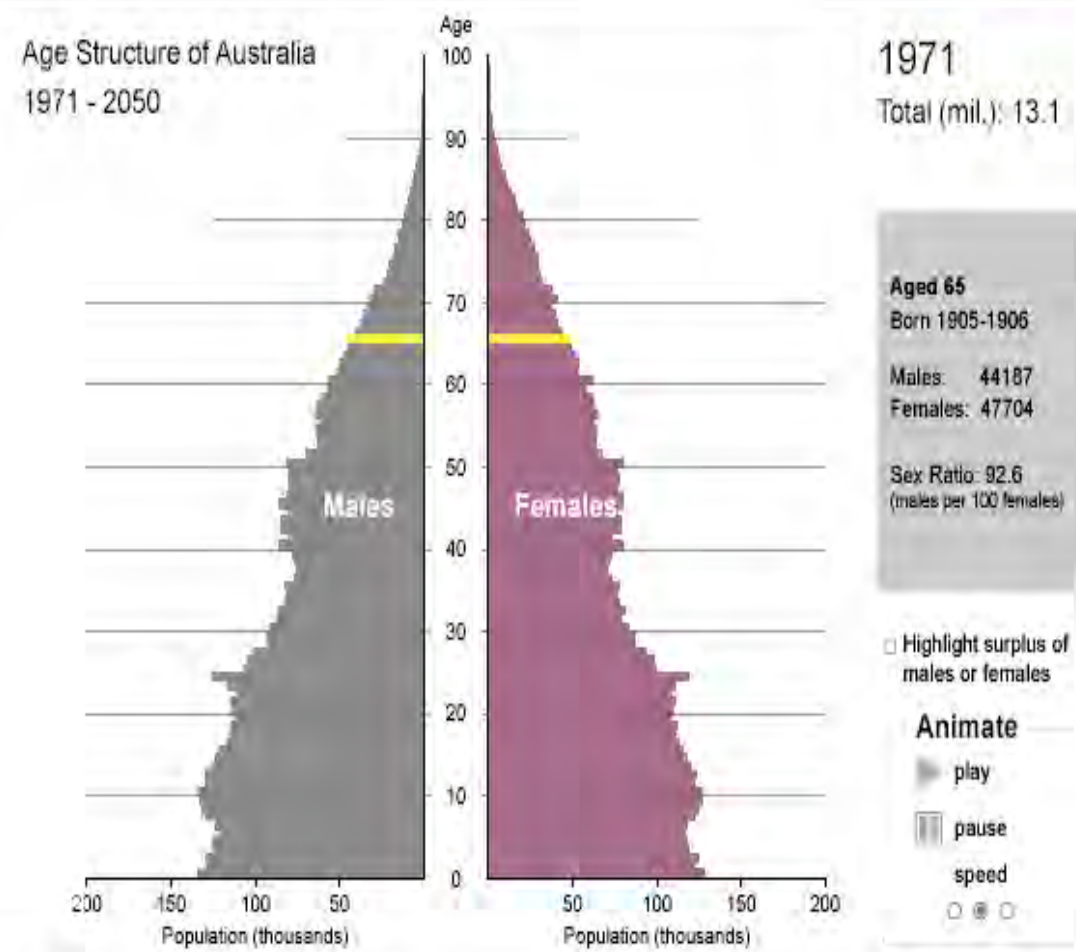
- **19th C – infectious disease**
- **20th C – heart disease, cancer**
- **21st C - neurodegenerative diseases**
 - **Alzheimer's and other dementias**
 - **Cerebrovascular disease/ stroke**
 - **Parkinson's disease**
 - **Macular degeneration**
 - **Balance and gait disorders, falls**

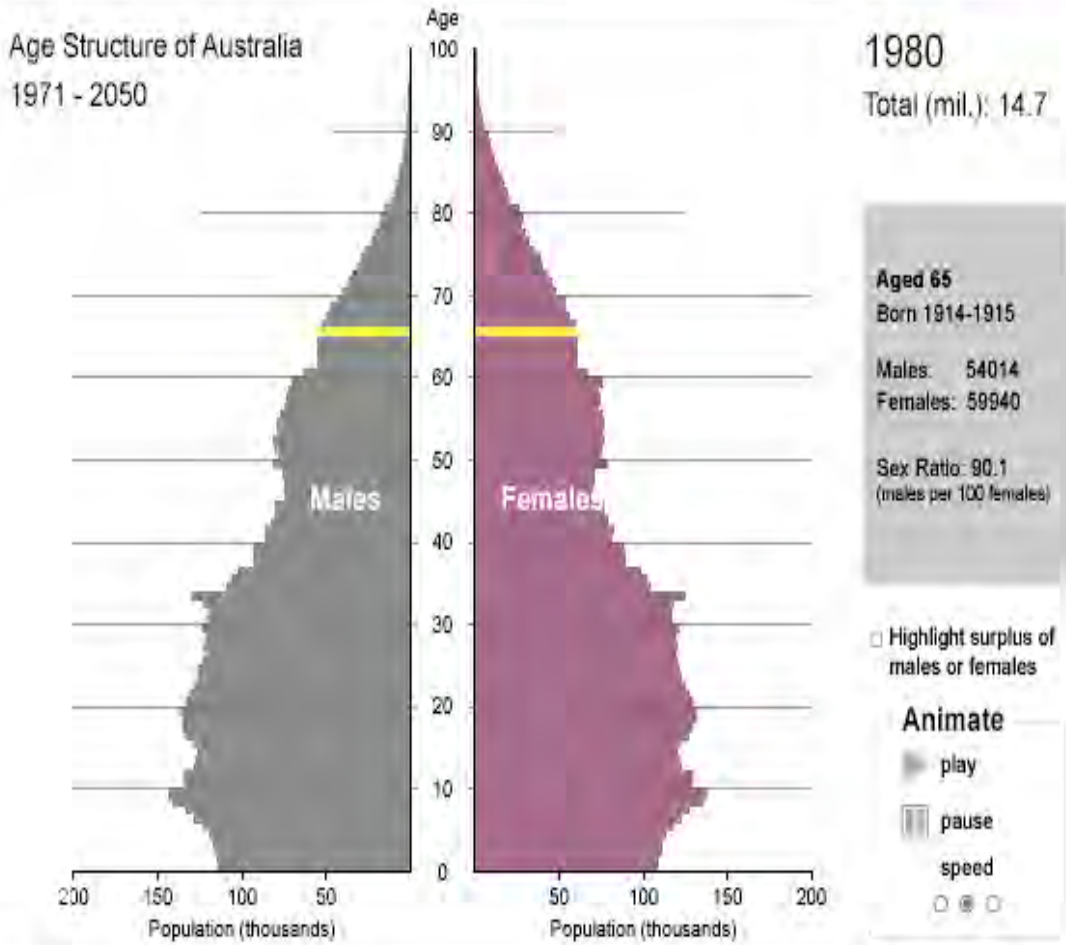


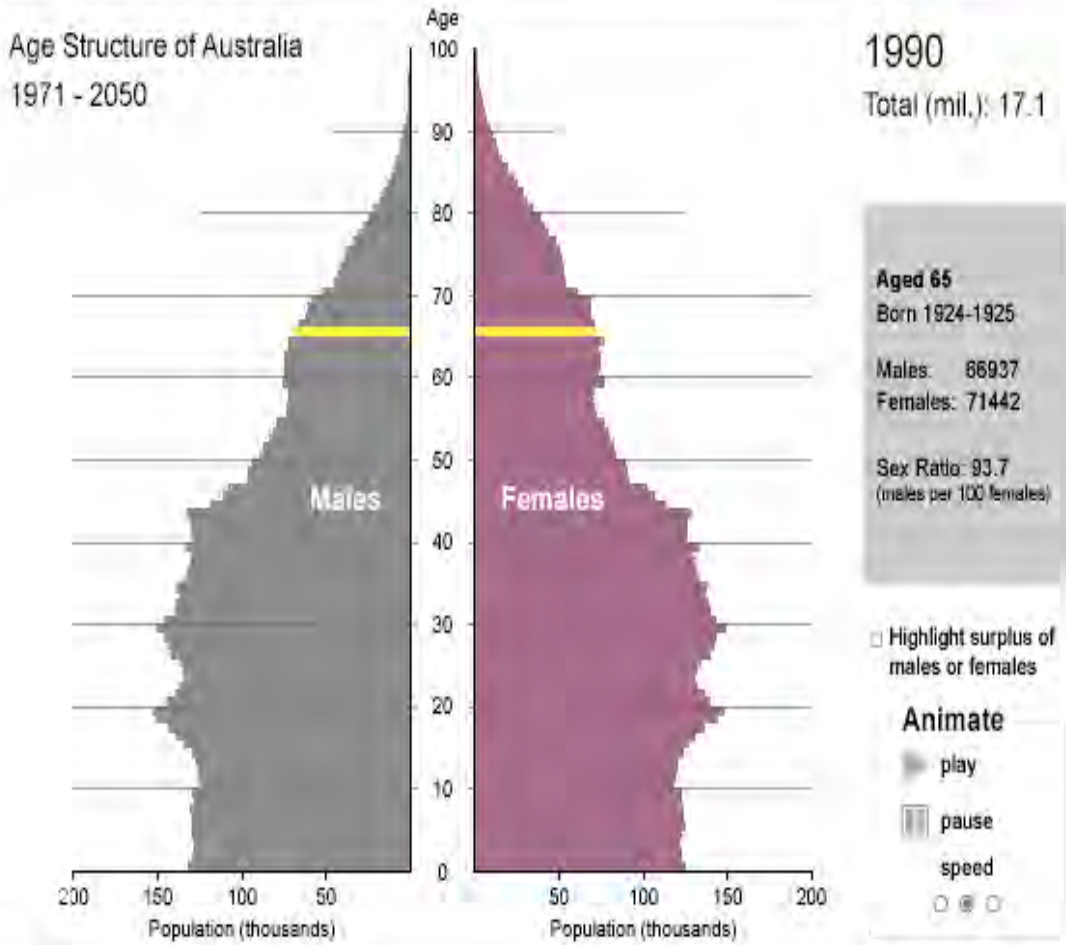
Our brains . . .

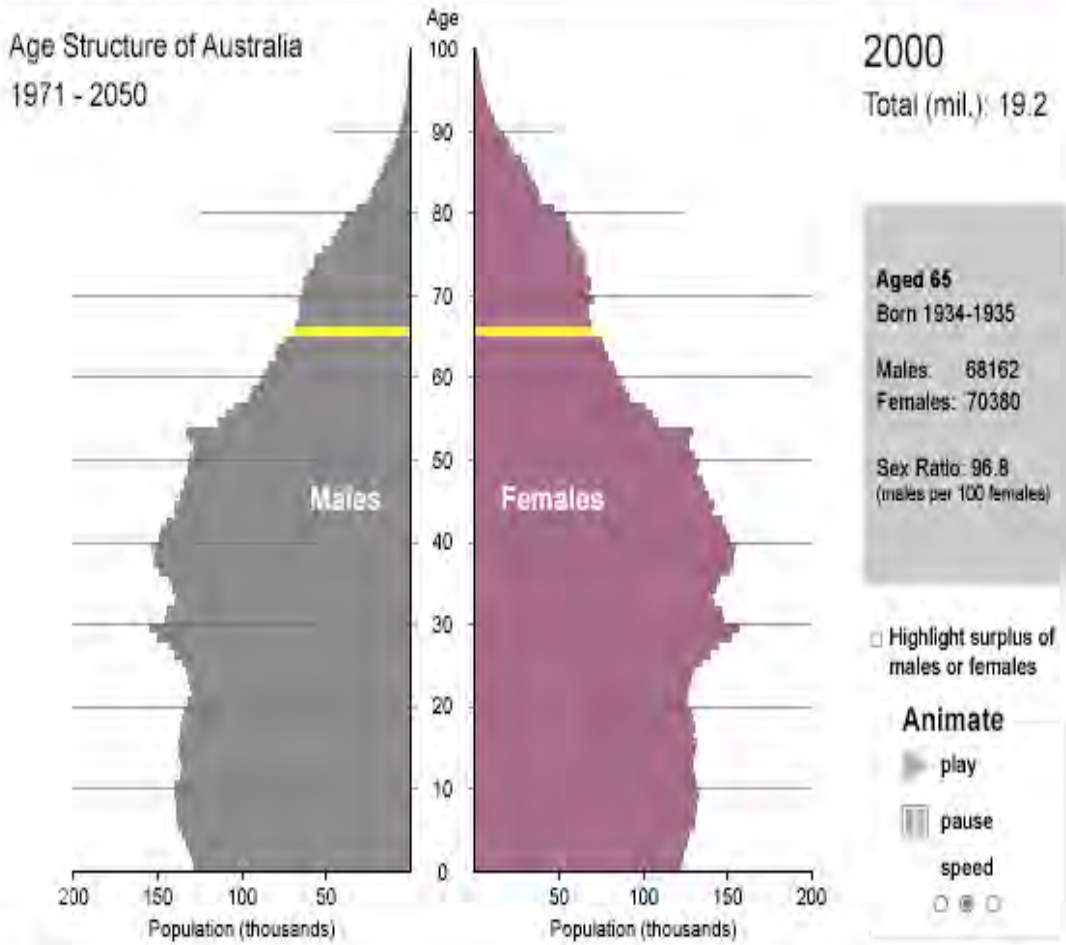
- ≈ 1.3 Kg of 12% fat, 8% protein, 78% water
- Consume 20% of body's O_2 & almost 20% of blood flow
- Contain about 100 billion neurons, each with 1000 to 10,000 synapses and each neuron is supported by 10-50 support (glial) cells
- Most mysterious of body's organs but now...
- .. more accessible through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

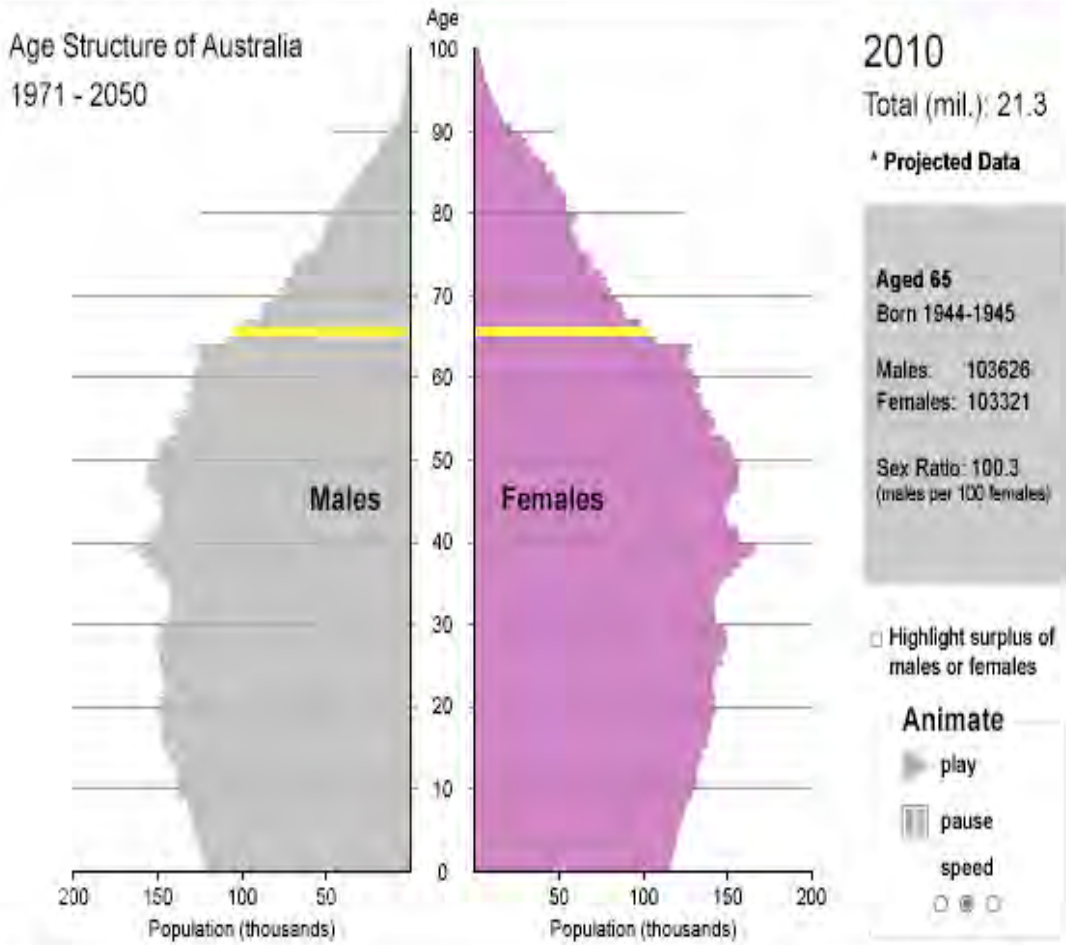


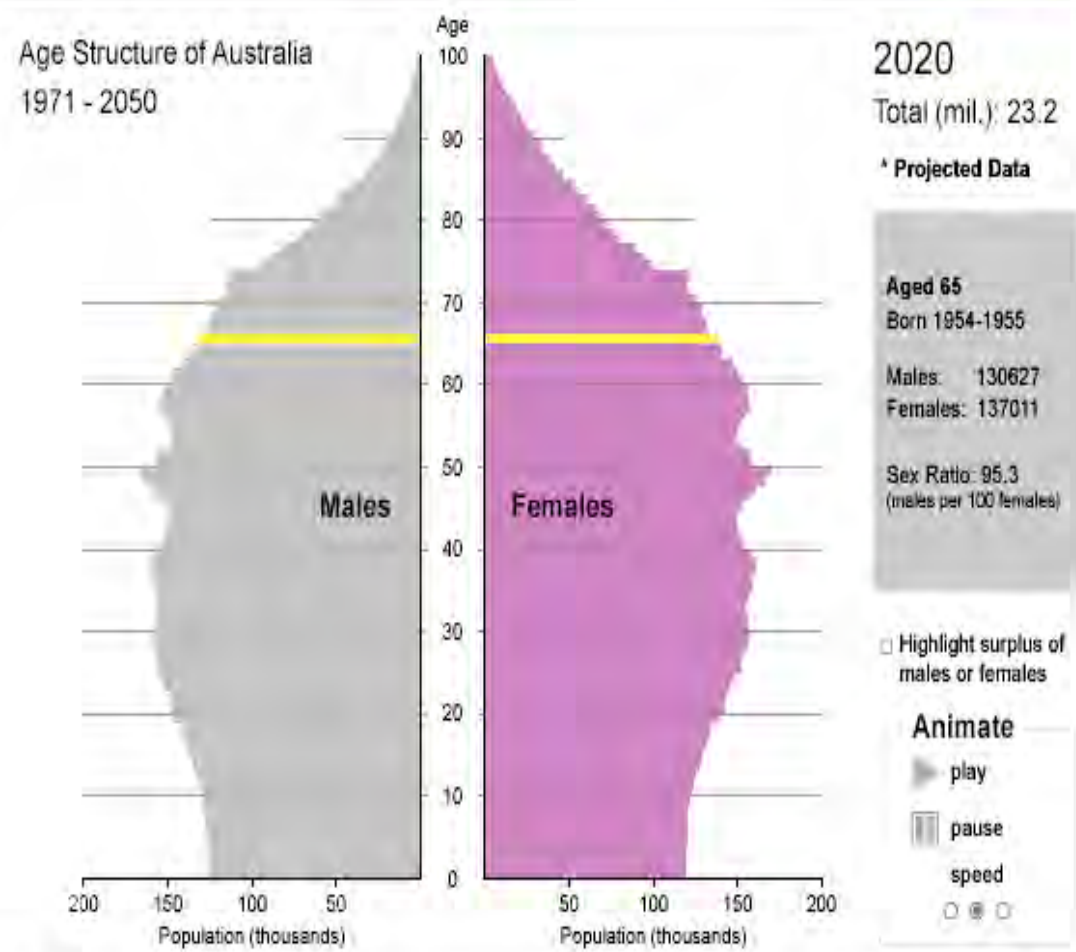


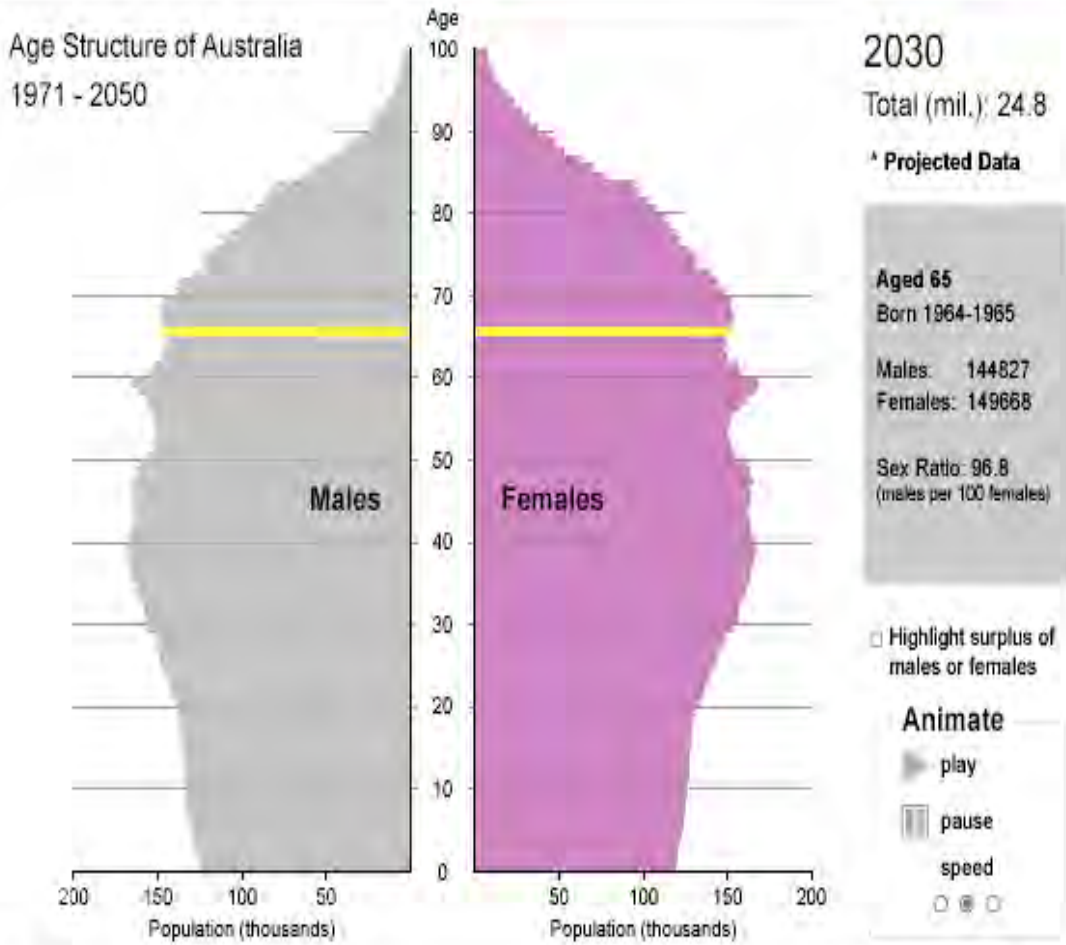


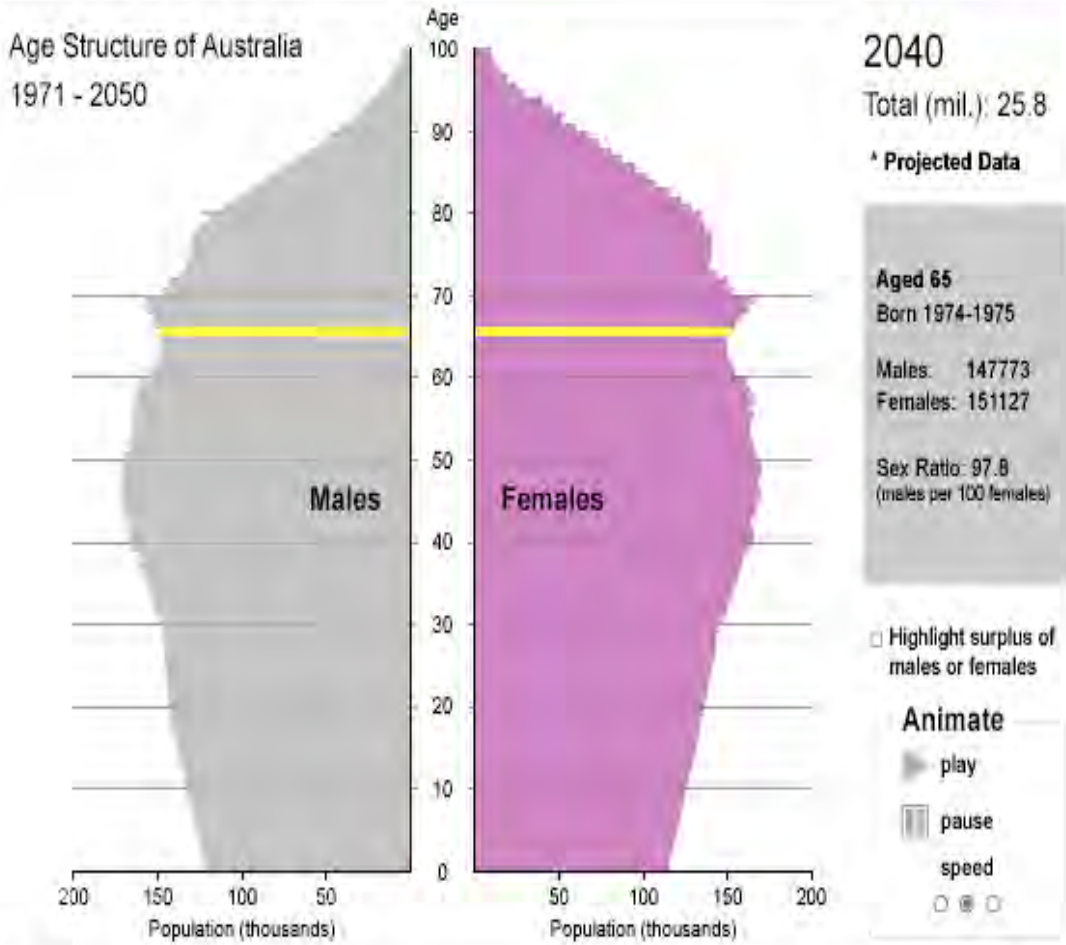


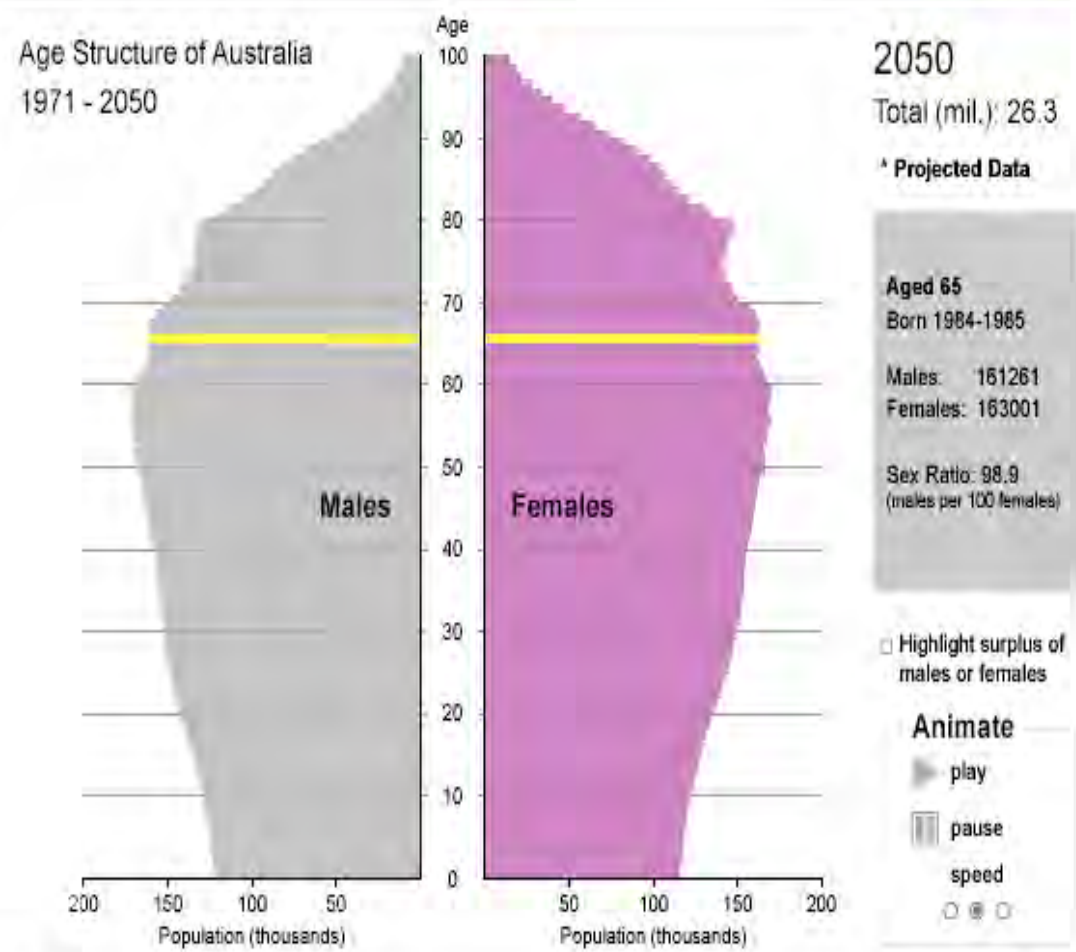












Australia's ageing population ¹

- 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^s than > children 0-14 yo
- 30th June 2011, 4252 people 100 years or older

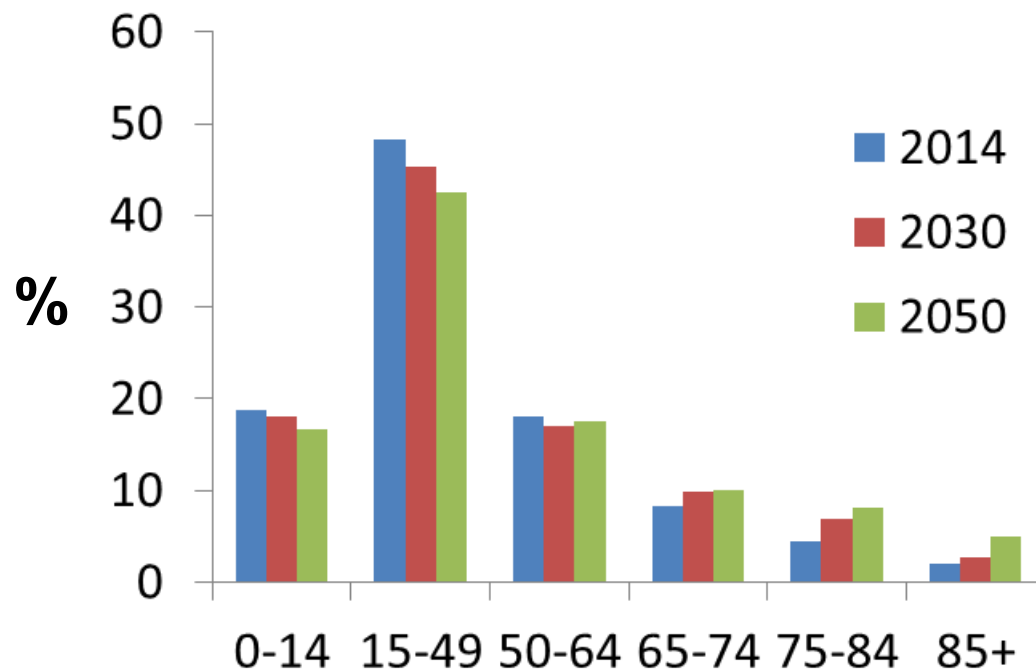
¹ Dementia in Australia, AIHW, 2012



Australia: Population projections

Population (approx):

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

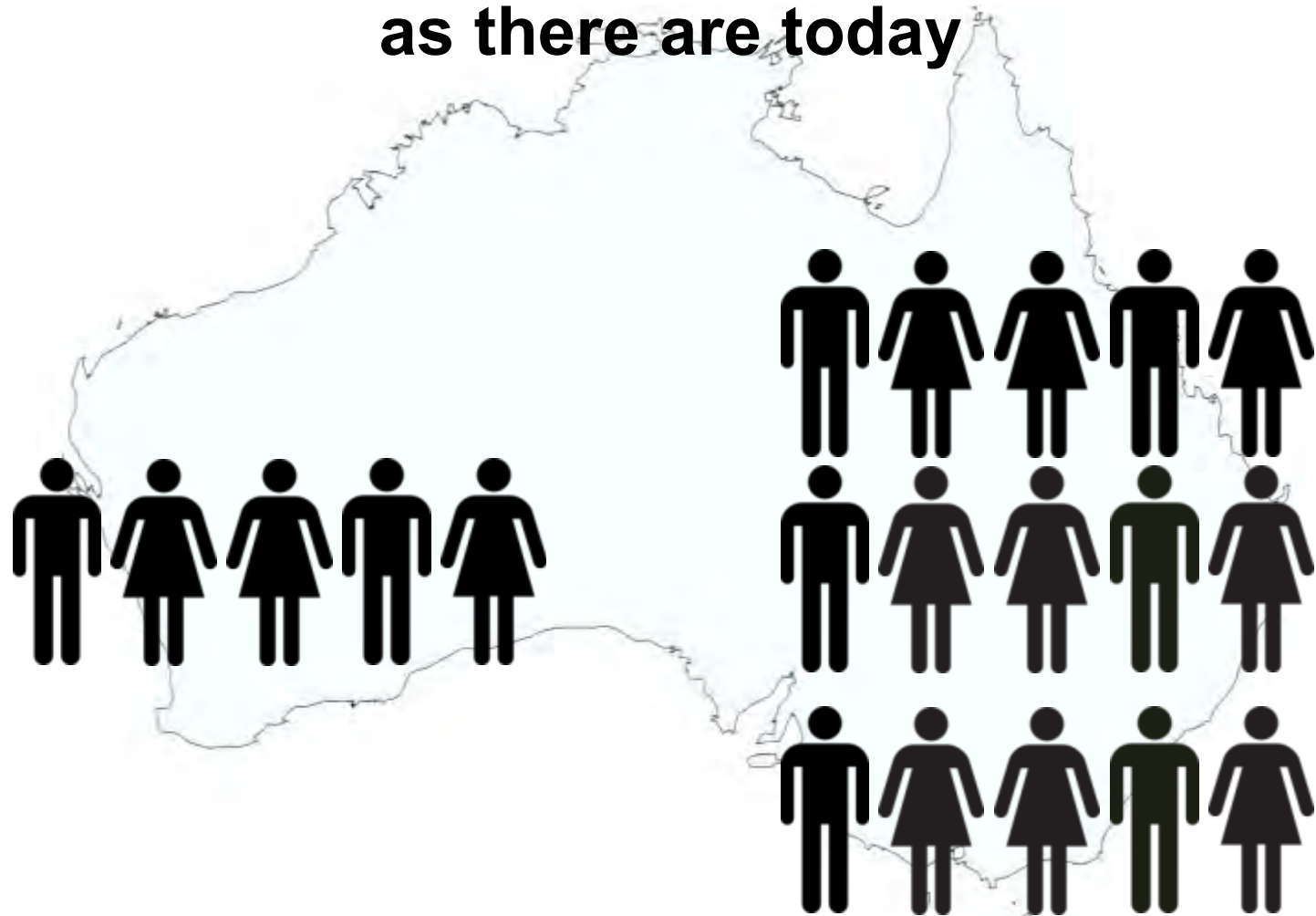


Productivity Commission 2013, *An Ageing Australia: Preparing for the Future*, Commission Research Paper, Canberra.

**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

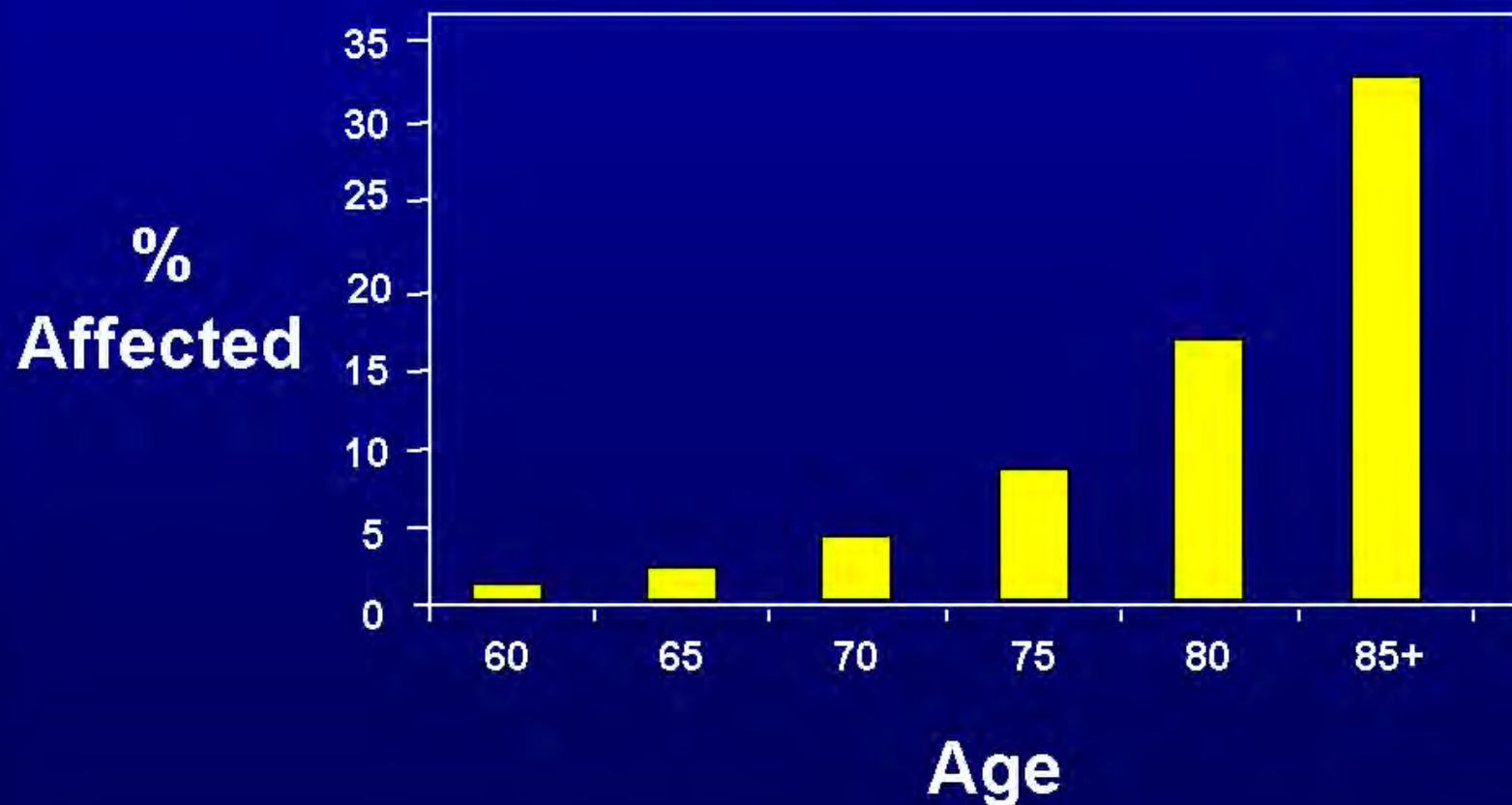
- **Cost of health in Australia is $\approx \leq 10\%$ of GDP or about \$130b and rising above inflation**
- **Drivers – costs, demand, > expensive investigations, medicines and procedures**
- **Dementia costs 0.8% GDP or $\approx$ \$6b pa.**
- **By 2050, dementia costs >1.8% GDP**

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**

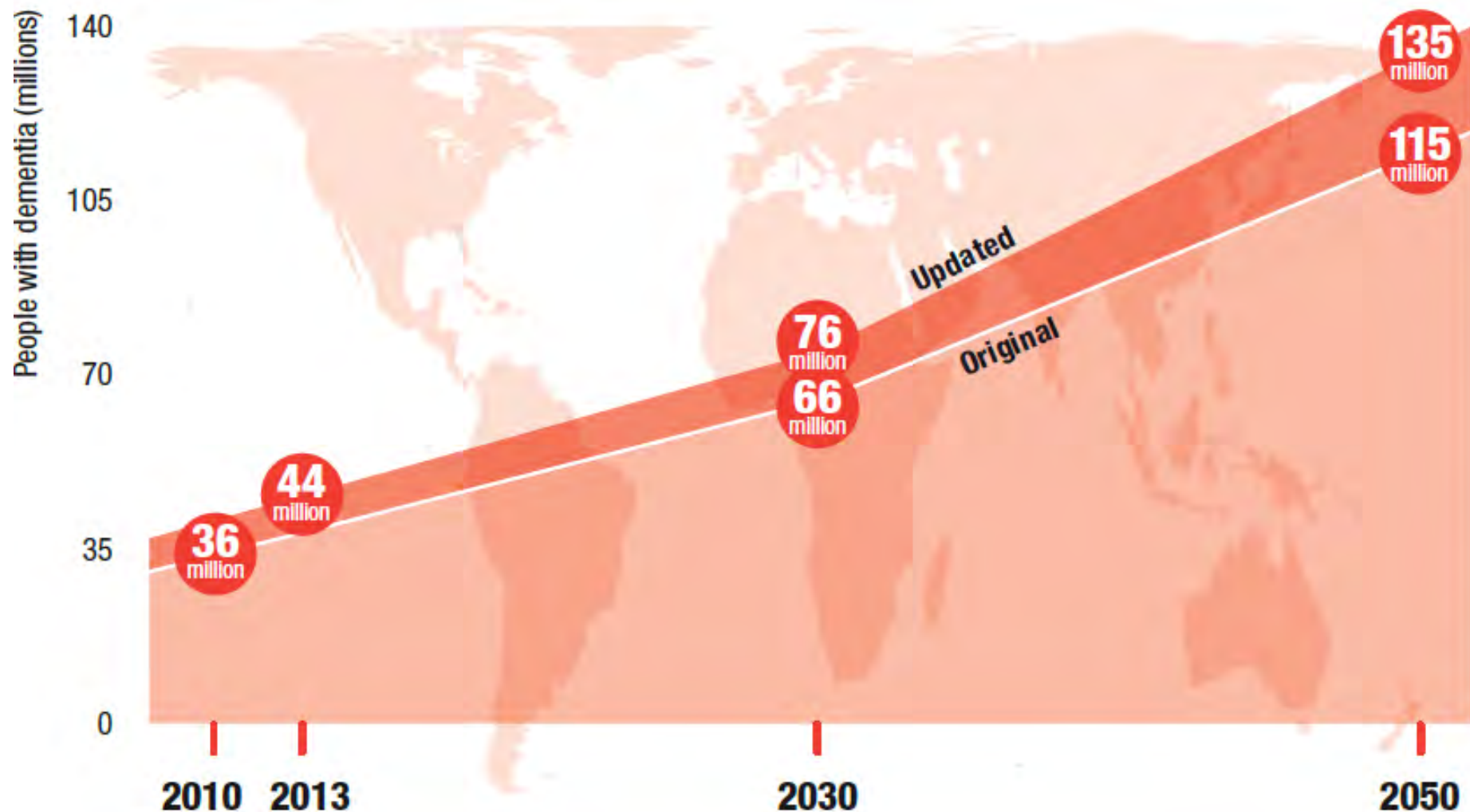


Dementia Doubles in Frequency Every 5 Years After Age 60



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

Projections of dementia worldwide



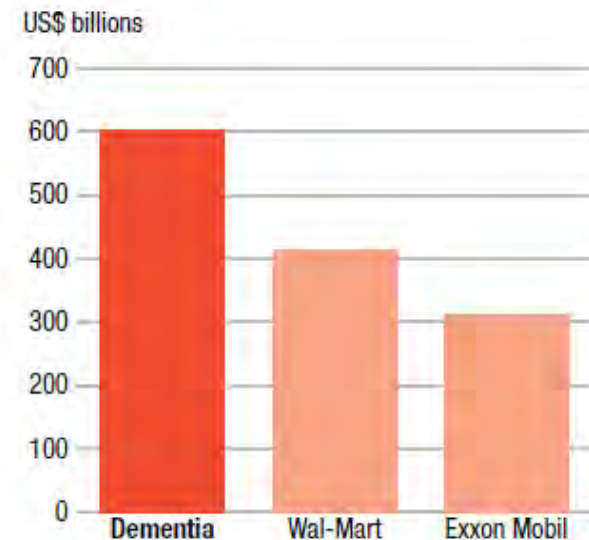
The Global Impact of Dementia 2013–2050. ADI, 2013.



Global Cost of Dementia

- **Total estimated cost worldwide US\$604 billion in 2010**
- **If dementia were...**
 - a country, it would have the world's 18th 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
- 3rd leading cause of death
- 4th leading cause of disease burden
- 3rd leading cause of disability burden; (1st in 65+)



* Dementia in Australia, AIHW, 2012



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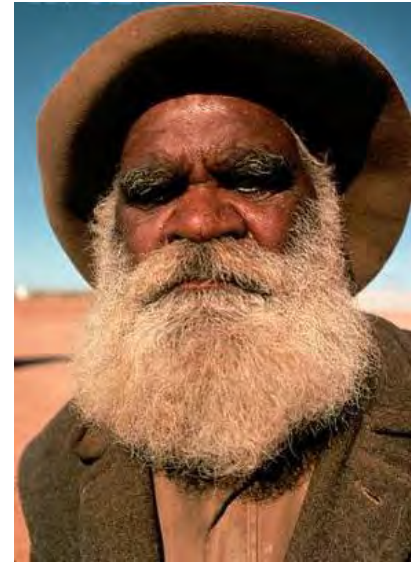
People with dementia and their CGs

- **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 ¹**
- **Direct health and aged care costs = \$4.9bn ¹**
- **If add unpaid costs of carers > \$6bn pa ²**
- **0.8% GDP → 1% GDP by 2030¹ → 1.8% by 2050³**



¹ Dementia in Australia, AIHW, 2012; ² Access Economics 2003; ³ 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

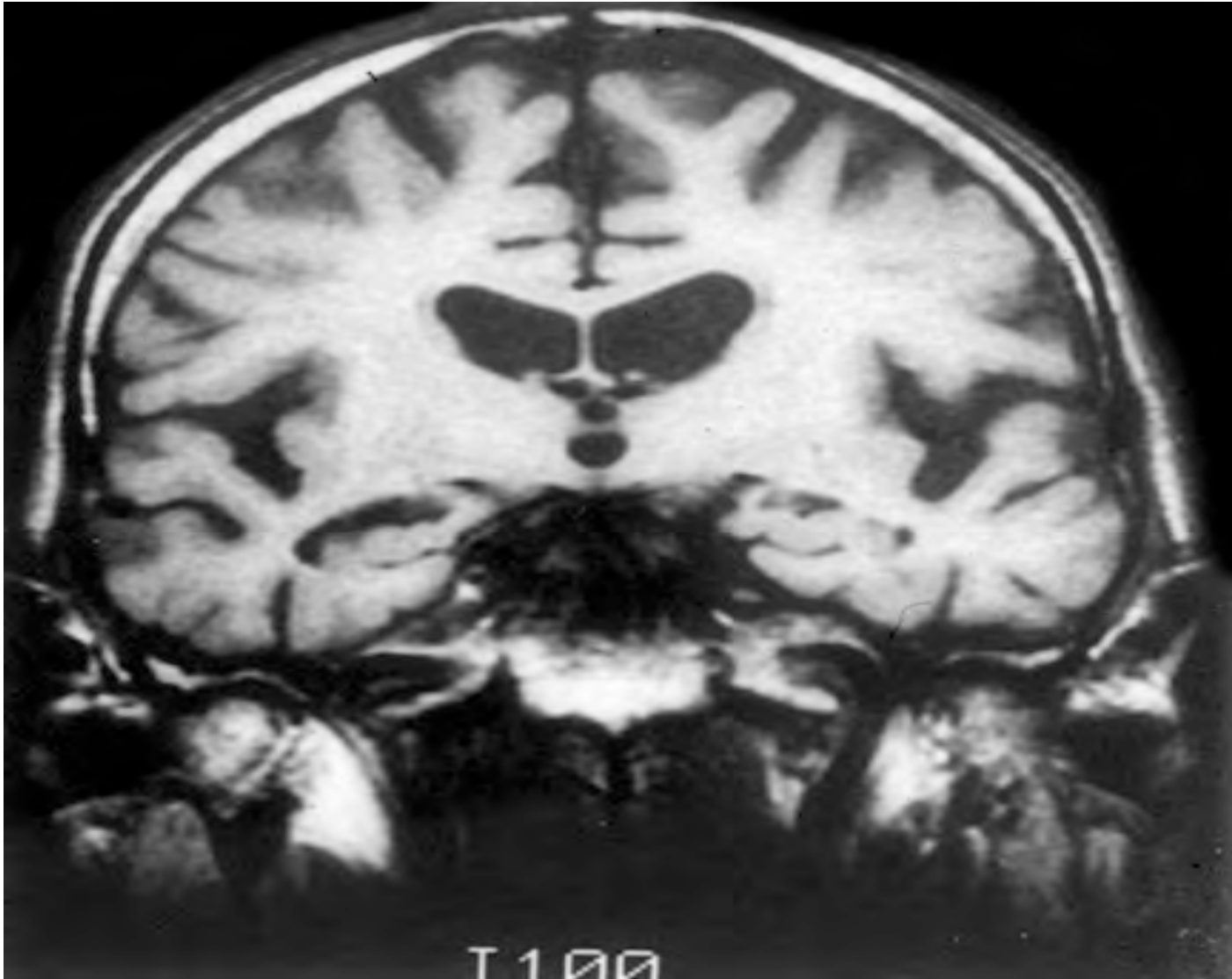


Potentially reversible or able to be halted causes of dementia

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



MRI: profound atrophy

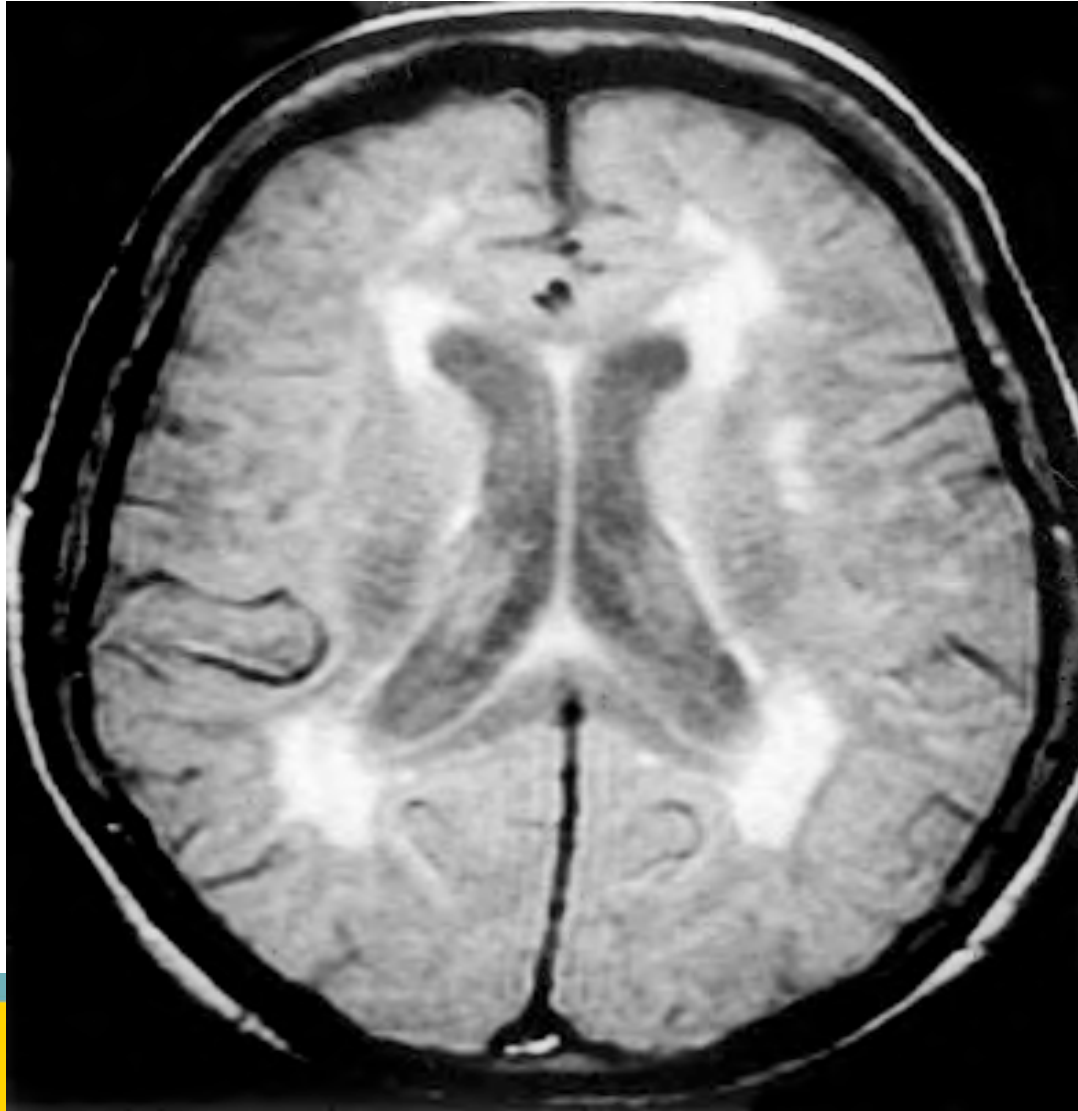


CHeBA
Healthy Brains Positive Ageing

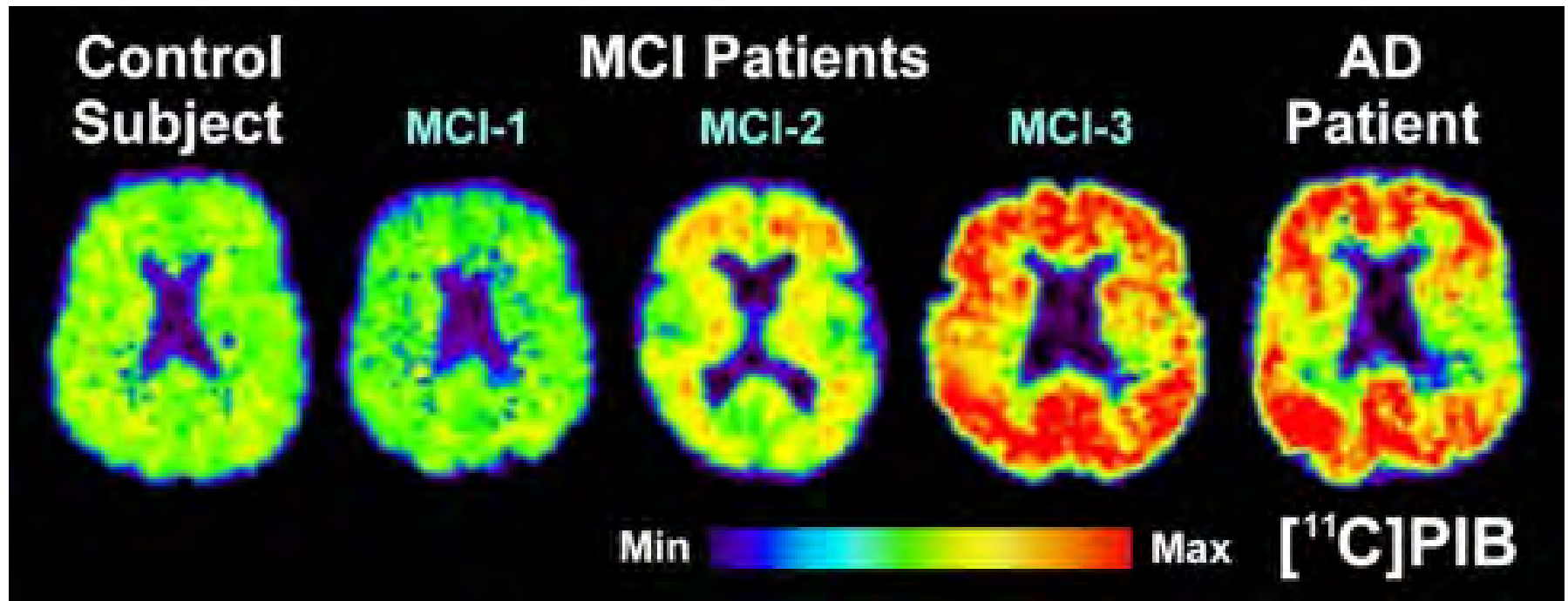


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MRI scan of brain showing ischaemic changes



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

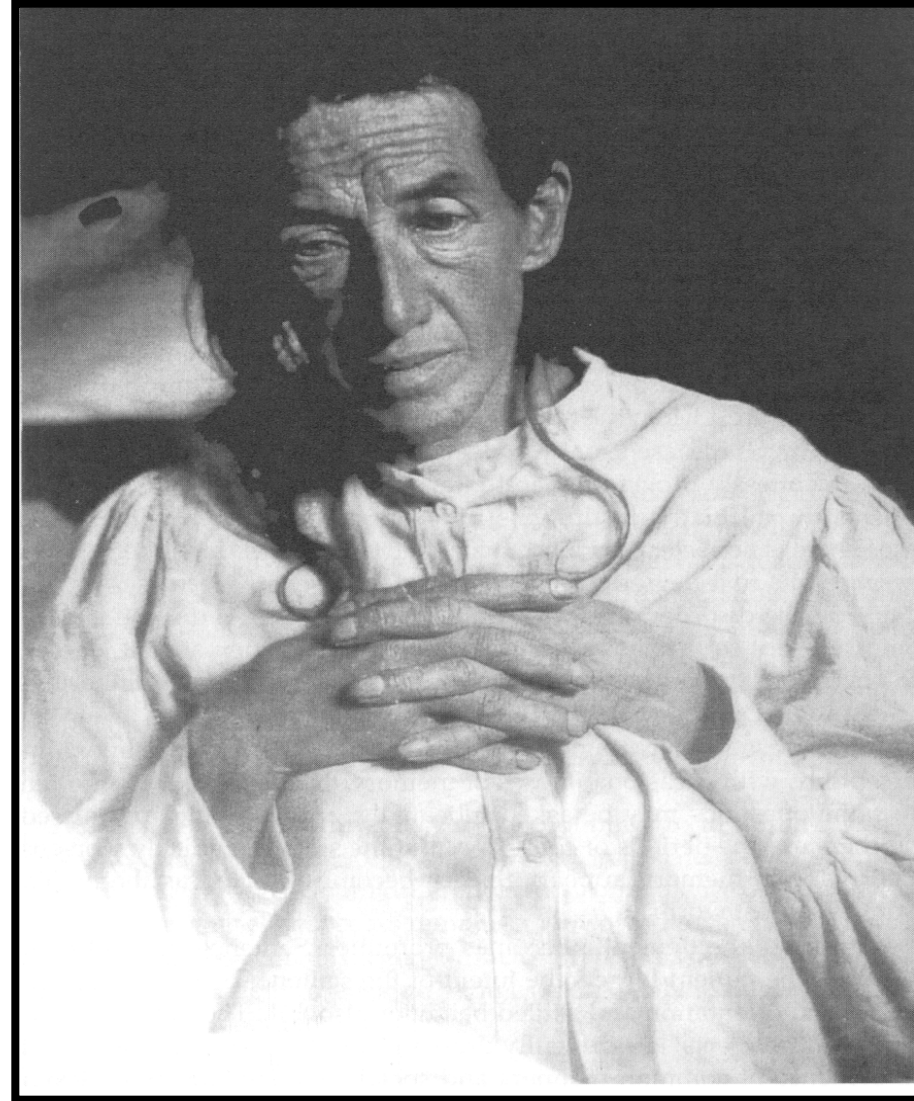
Suspect early dementia if:

- **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**



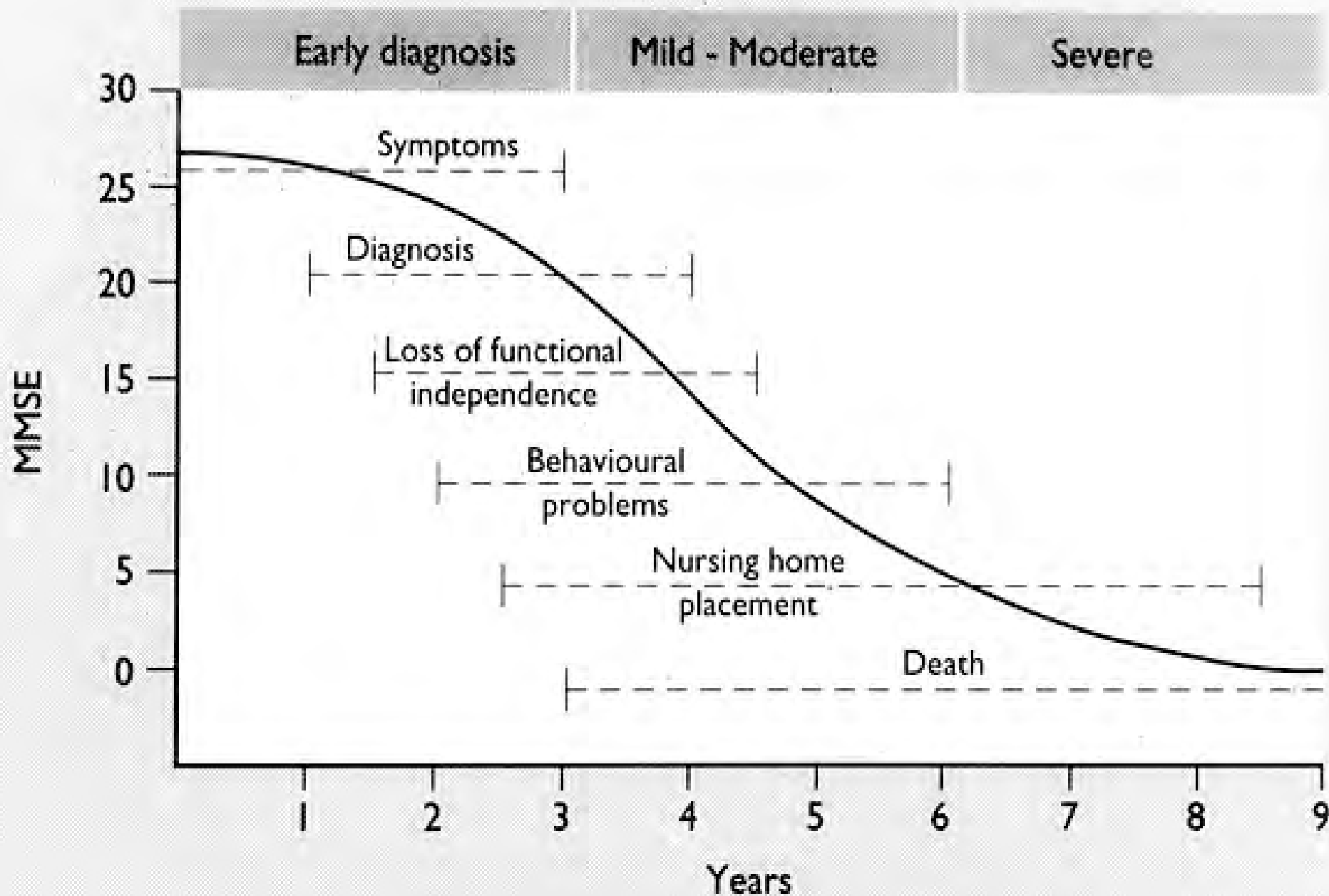
Alzheimer's disease

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

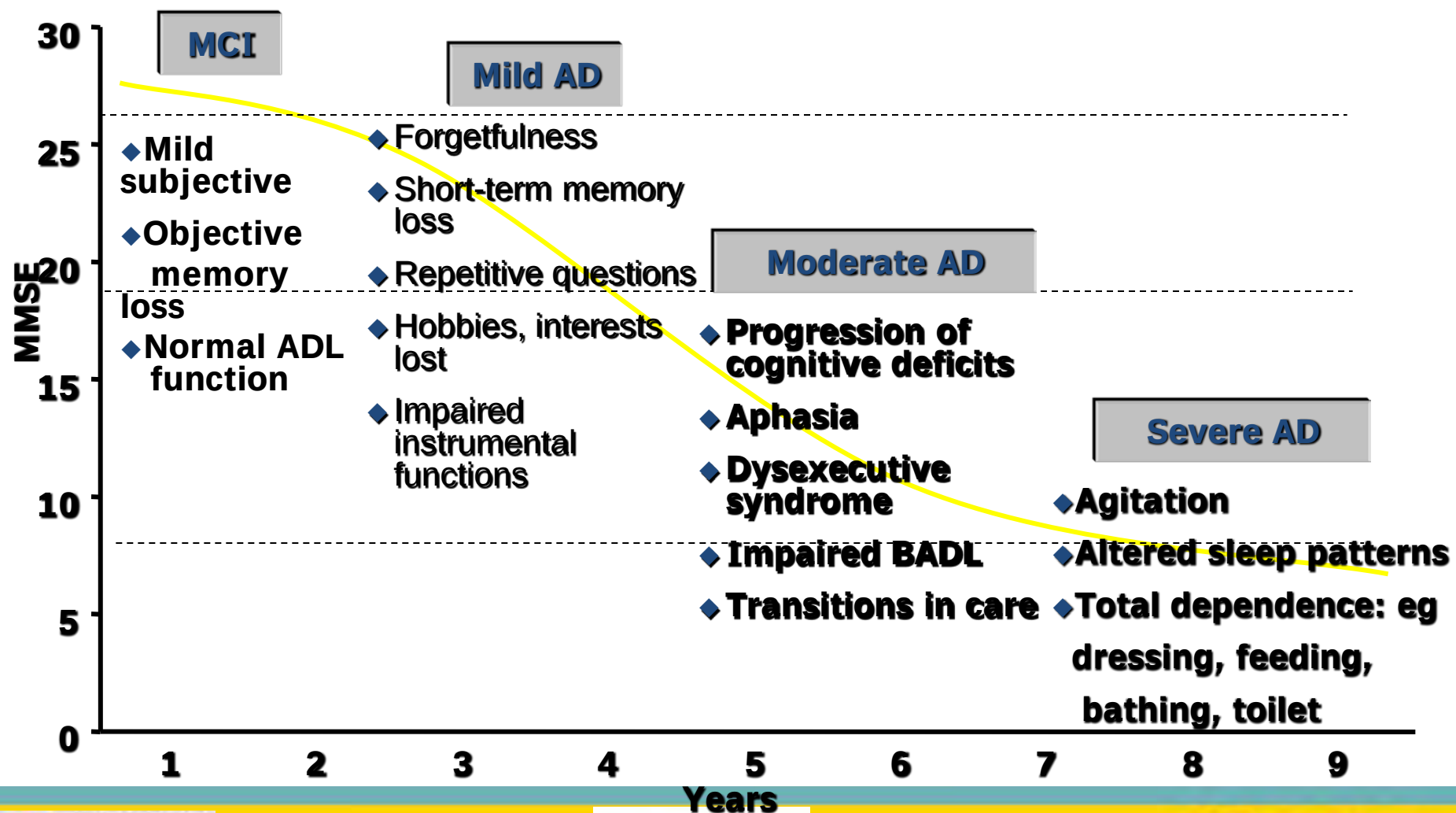


Alzheimer's original patient: Auguste Deter

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

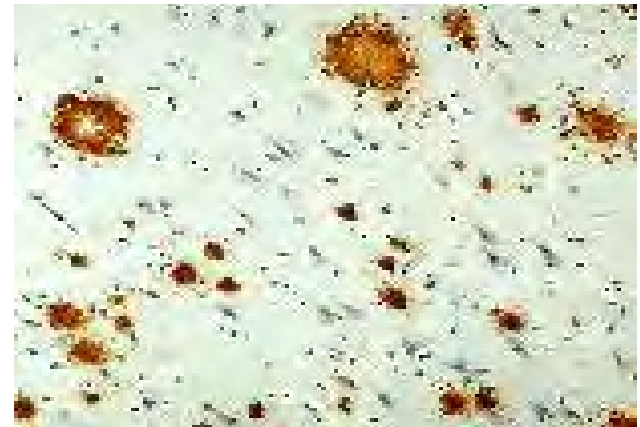
- ***Macroscopic***: atrophy, mostly temporo-parietal and frontal
- ***Microscopic***
 - loss of neurones and synapses
 - neurofibrillary tangles (NFTs)
 - amyloid plaques
 - degeneration

Pathology of AD

- *Chemistry*

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

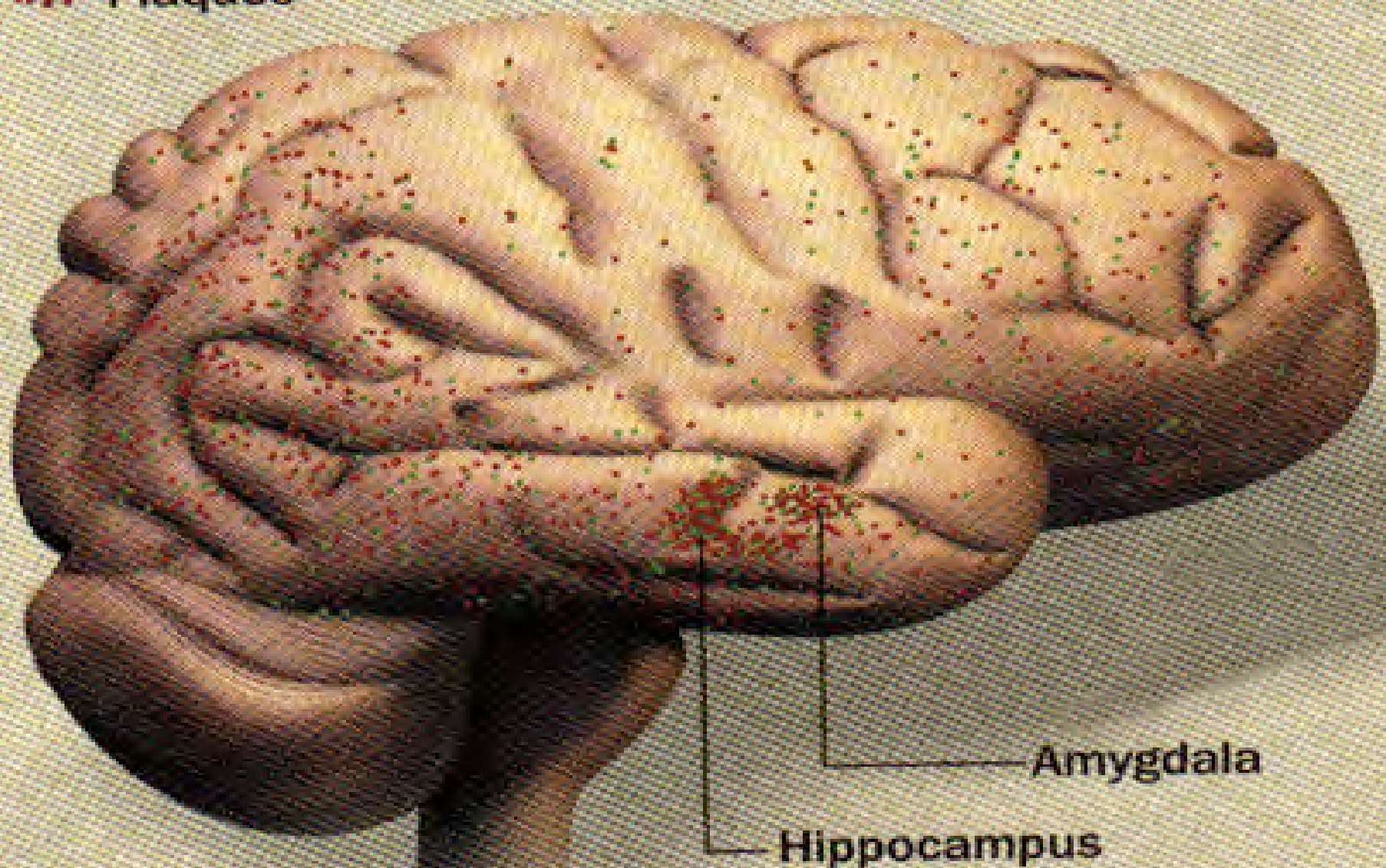
AD: a progressive CNS disorder with a characteristic pathology



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

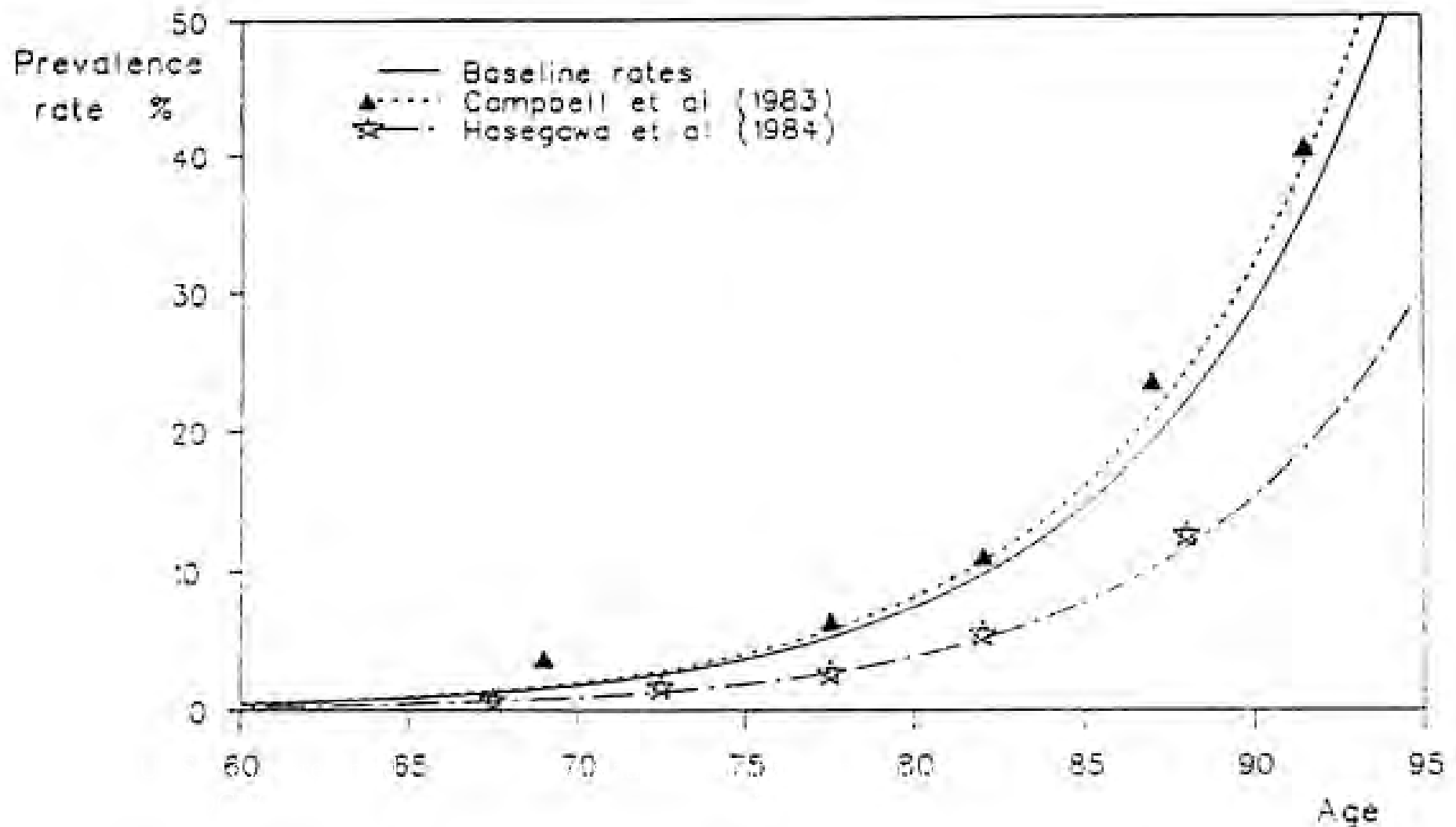


Strong risk factors for AD

- 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

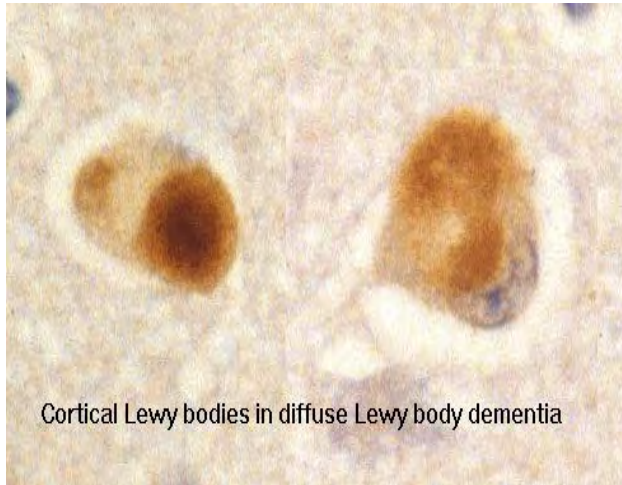
- **High blood pressure in mid-life**
- **High cholesterol in midlife**
- **Diabetes (Type II)**
- **Obesity in mid-life**
- **Current smoking**
- **Family history of Down's**
- **Head injury**
- **? Depression**
- **Low education, little cognitive stimulation**
- **Others – (prob. *not* Aluminium exposure)**

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**

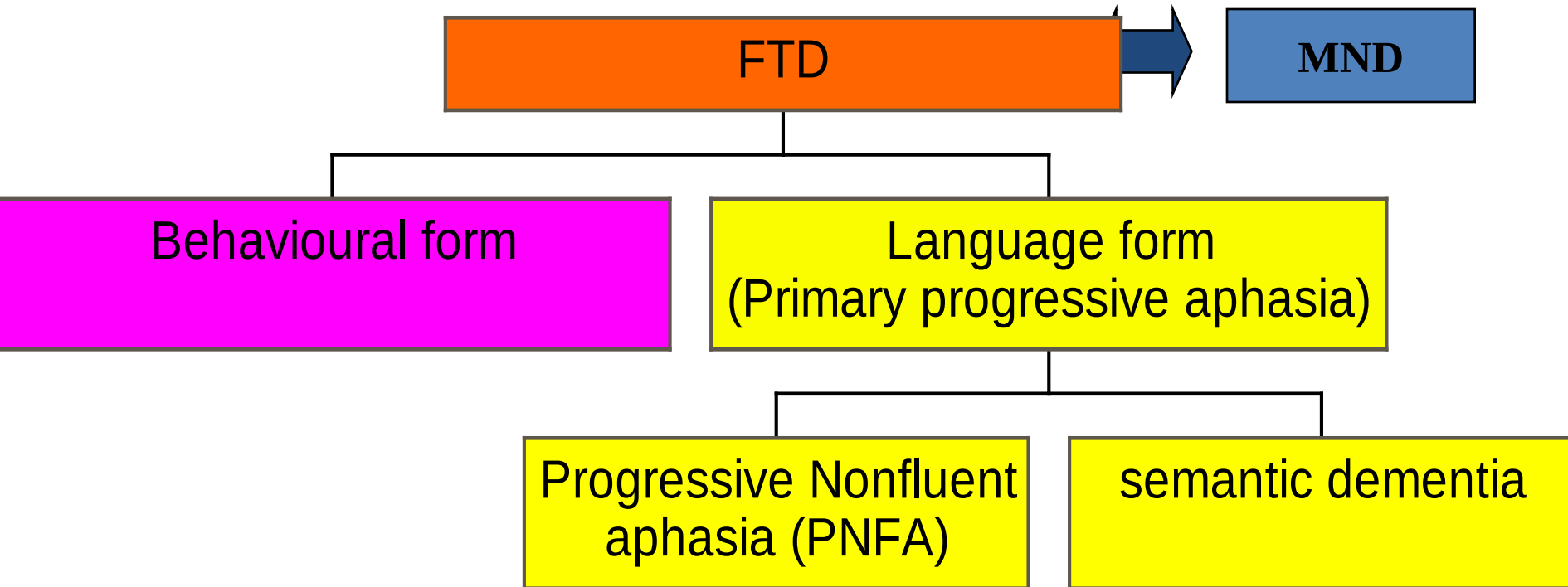
Lewy Body Dementia

- Dementia
- Lewy bodies diffuse in cortex
- REM Sleep disorder
- Fluctuating cog. impairment ++
- Visual &/or auditory hallucinat^{ns}
- Paranoid delusions
- Falls
- Extrapyrarnidal 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

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

www.dementiaresearch.org.au



Search site

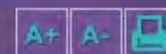


NATIONAL DEMENTIA HELPLINE
1800 100 500



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FIND OUT MORE





Mind your diet

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



An Australian Government Initiative

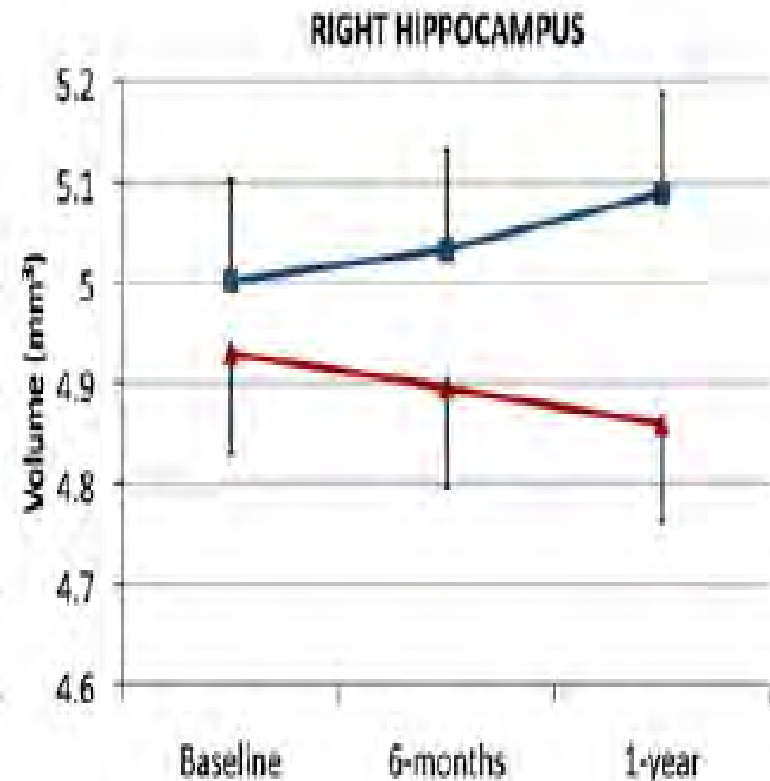
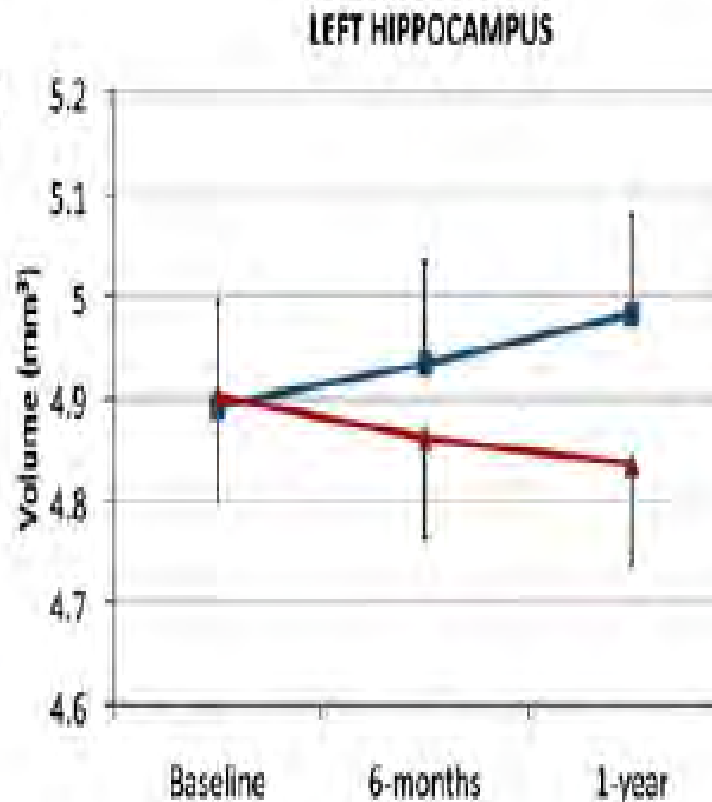
Mind your Body

- 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 adults¹**
- **For PWD – behaviour✓; cognition?**

¹Liang 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) ¹**
- **Dose - response relationship evident¹**
- **Results suggest complex patterns of mental activity in the early, mid- and late-life stages are associated with ↓ dementia incidence¹**
- **Results held when covariates in source studies were controlled for²**

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

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

Cognitive training

- **Systematic review of RCTs with longitudinal follow-up (>3mths) in healthy elderly¹**
 - 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 dementia²**
 - 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/
- Advocacy; Research funding
- *Living with memory loss program*
980 50 100 or 1-800-100-500
- Dementia Alliance International

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 β amyloid protein**
 - **γ and β Secretase prevent β 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

Centre for Healthy Brain Ageing

www.cheba.unsw.edu.au

Alz Australia: www.fightdementia.org.au

www.yourbrainmatters.org.au/

ADI : www.alz.co.uk



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