

Common forms of Cognitive Dysfunction in Older People

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Overview

- The common forms of cognitive impairment are dementia and a syndrome of cognitive impairment associated with ageing which has a lot of different names.
- They both affect really old people
- The common type of dementia are
 1. Mixed
 2. Alzheimers Disease Dementia
 3. Dementia associated with atrophy in very old people
 4. Vascular dementia
 5. Lewy Body dementia
 6. Fronto-temporal dementia

LIFE EXPECTANCY AT BIRTH, Australia

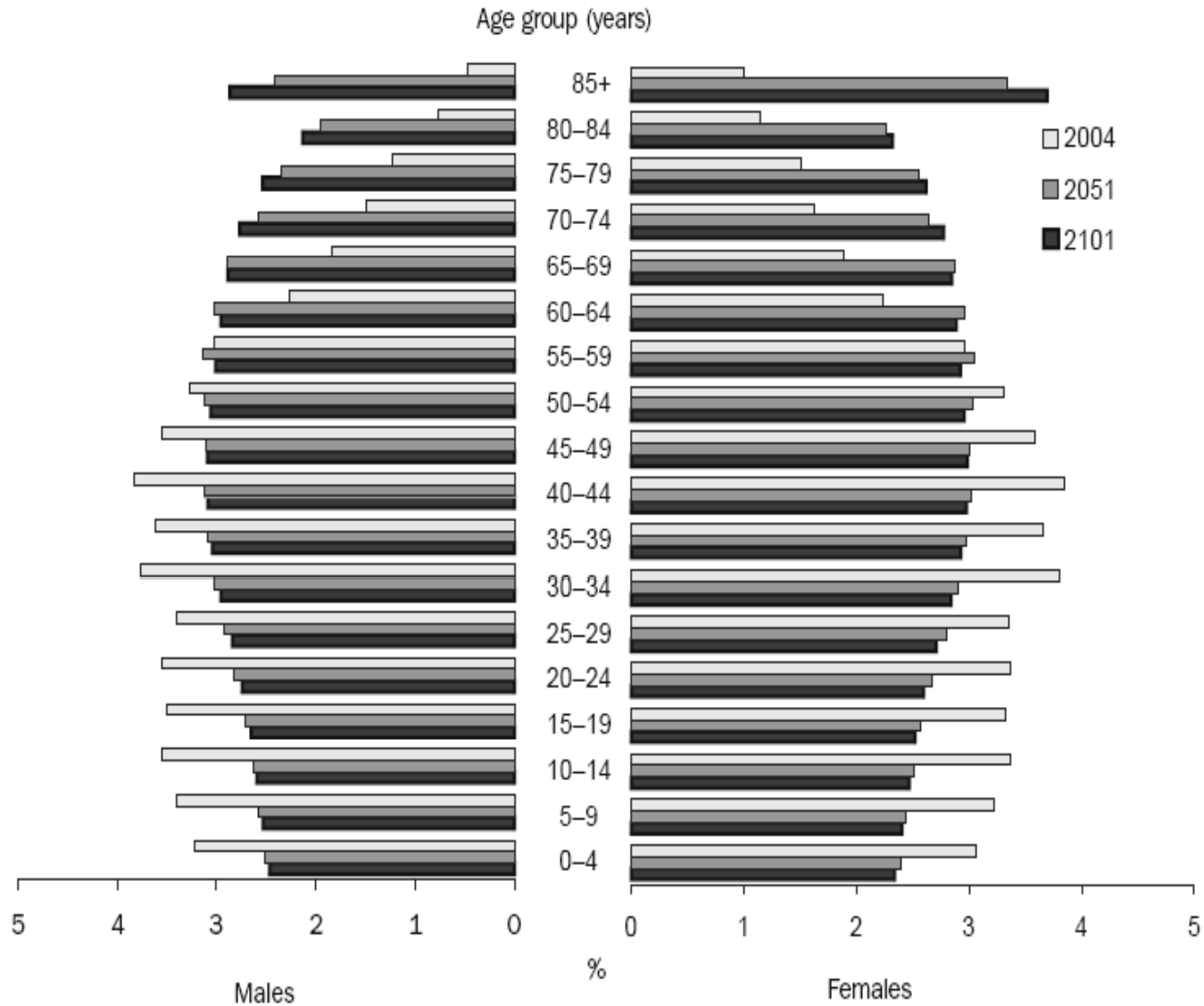


Between 1980–1982 and 2001–2003, life expectancy has improved each year by around 0.30 years for males and 0.25 years for females. This trend has been observed since the early 1970s. For both sexes the smallest increase during this period was recorded between 1995–1997 and 1996–1998 (with male life expectancy increasing by 0.17 years and female life expectancy by 0.15 years) while the largest growth was recorded between

What would happen if there is a constant improvement in life expectancy?

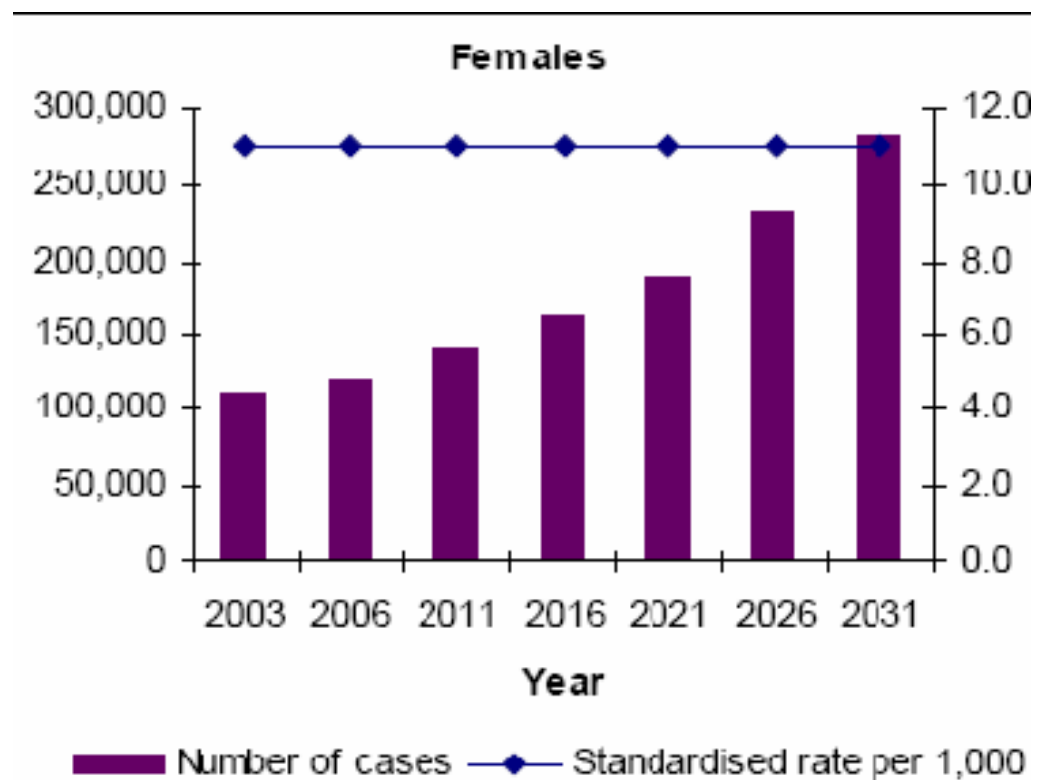
	Men	Women
2005–06	(a) 79.16	(a) 83.89
2010–11	80.66	85.14
2015–16	82.16	86.39
2020–21	83.66	87.64
2025–26	85.16	88.89
2050–51	92.66	95.14

Projected populations – pyramid to coffin?



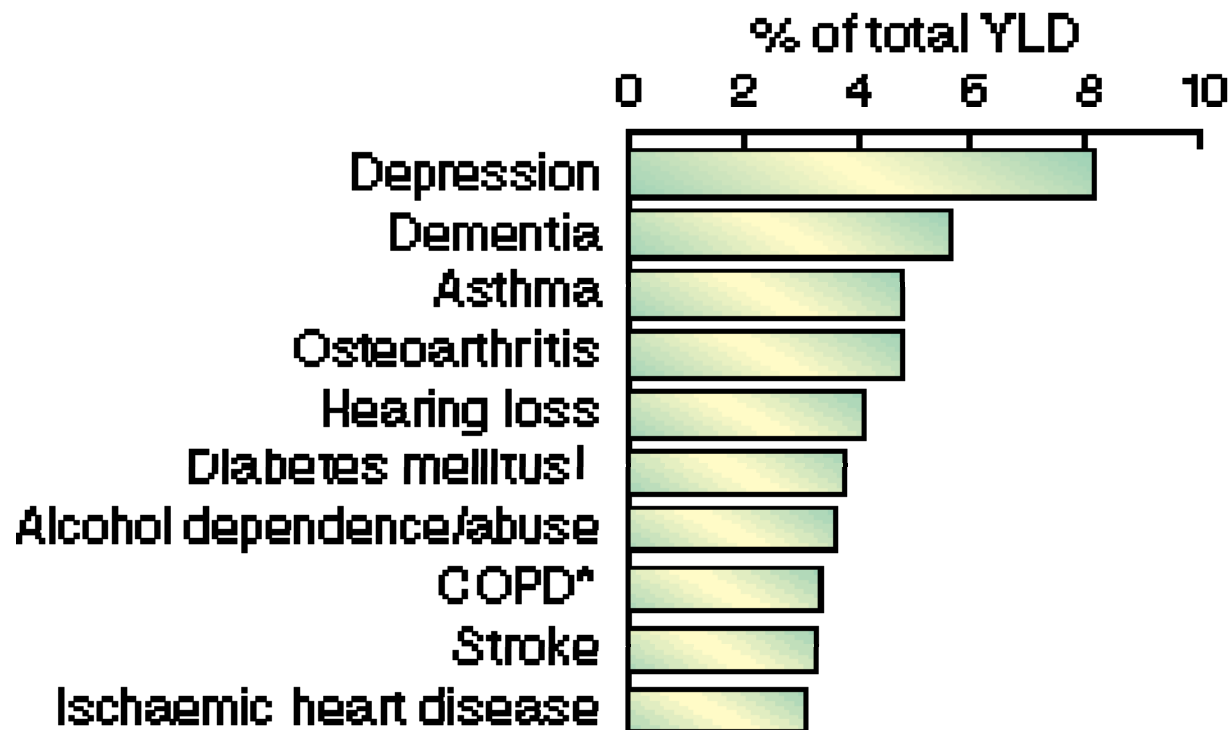
Not just an increase in life expectancy but migration!

Projected number of people with dementia



Source: Calculations by AIHW based on data from Lobo et al. 2000 and Harvey et al. 2003

Years of Life Lost to Disability



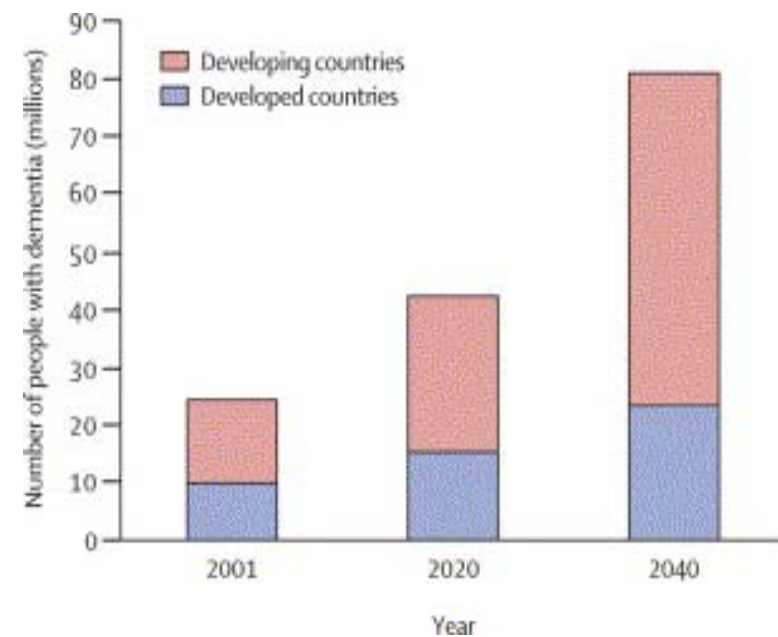
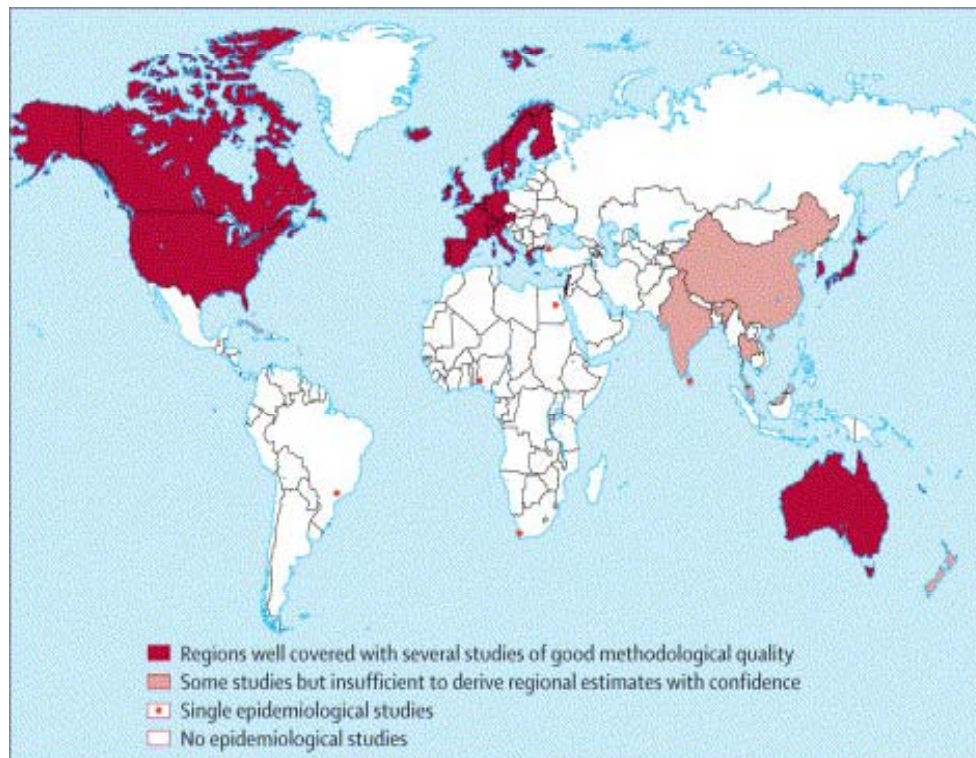
B: Top 10 causes of YLD in Australia, 1996.

2.3**LEADING CAUSES OF DEATH(a), Females—2007(b)**

<i>Underlying Cause of Death</i>	<i>Rank</i>	<i>Females</i>	<i>Total</i>
Ischaemic heart diseases (I20-I25)	1	10 610	22 729
Strokes (I60-I69)	2	6 975	11 491
Dementia and Alzheimer's disease (F01-F03, G30)	3	4 905	7 320
Trachea and lung cancer (C33-C34)	4	2 911	7 626
Breast cancer (C50)	5	2 680	2 706
Chronic lower respiratory diseases (J40-J47)	6	2 593	5 762
Heart failure (I50-I51)	7	2 083	3 444
Diabetes (E10-E14)	8	1 887	3 810
Colon and rectum cancer (C18-C21)	9	1 886	4 107
Diseases of the kidney and urinary system (N00-N39)	10	1 792	3 230

Global prevalence of dementia

Ferri et al, Lancet 2005; 366:2112



	Population (millions), aged ≥60 years (2001)	Consensus dementia prevalence (%) at age ≥60 years	Estimated annual incidence per 1000	New dementia cases (millions) per year, 2001	Number of people (millions) with dementia, aged ≥60 years			Proportionate increase (%) in number of people with dementia	
					2001	2020	2040	2001–2020	2001–2040
Western Europe (EURO A)	89.6	5.4	8.8	0.79	4.9	6.9	9.9	43	102
Eastern Europe low adult mortality (EURO B)	27.4	3.8	7.7	0.21	1.0	1.6	2.8	51	169
Eastern Europe high adult mortality (EURO C)	44.6	3.9	8.1	0.36	1.8	2.3	3.2	31	84
North America (AMRO A)	53.1	6.4	10.5	0.56	3.4	5.1	9.2	49	172
Latin America (AMRO B/D)	40.1	4.6	9.2	0.37	1.8	4.1	9.1	120	393
North Africa and Middle Eastern Crescent (EMRO B/D)	27.5	3.6	7.6	0.21	1.0	1.9	4.7	95	385
Developed western Pacific (WPRO A)	34.5	4.3	7.0	0.24	1.5	2.9	4.3	99	189
China and developing western Pacific (WPRO B)	151.1	4.0	8.0	1.21	6.0	11.7	26.1	96	336
Indonesia, Thailand, and Sri Lanka (SEARO B)	23.7	2.7	5.9	0.14	0.6	1.3	2.7	100	325
India and south Asia (SEARO D)	93.1	1.9	4.3	0.40	1.8	3.6	7.5	98	314
Africa (AFRO D/E)	31.5	1.6	3.5	0.11	0.5	0.9	1.6	82	235
TOTAL	616.2	3.8	7.5	4.6	24.3	42.3	81.1	74	234

Dementia - ICD 10

- Syndrome due to disease of the brain
- Usually chronic and progressive - at least 6 months for a confident diagnosis
- Involves a decline in multiple higher cortical functions including memory.
- Should attempt to avoid false positive diagnoses, especially depression.
- Decline in intellectual functioning affecting personal activities.
- No clouding of consciousness (delirium)

Alzheimer's Disease (ICD 10)

- Primary degenerative cerebral disease with characteristic neuropathological and neurochemical features.
 - Presence of dementia
 - Insidious Onset with slow deterioration
 - Absence of clinical evidence or findings from special investigations to suggest that the mental state may be due to other systemic or brain disease which can induce a dementia
 - Absence of a sudden, apoplectic onset or of neurological signs of focal damage such as hemiparesis, sensory loss, visual field defects and incoordination occurring early in the illness (although these phenomena may be superimposed later)

Vascular Dementia (ICD10)

- General criteria for dementia are met.
- Deficits in higher cognitive functions are unevenly distributed. Thus memory may be quite markedly affected while thinking, reasoning and information processing may show only mild decline.
- Clinical evidence of focal brain damage (≥ 1).
 - Unilateral spastic weakness
 - Unilateral increased tendon reflexes
 - Extensor plantar response
 - Pseudobulbar palsy
- Evidence from history, examination or tests of significant cerebrovascular disease which may be reasonably judged to be aetiologically related to the dementia (eg history of stroke, evidence of cerebral infarction).

Fronto-temporal dementia

- Pick's disease a particular variant of this condition
- Disordered executive functioning (initiation, planning) and disinhibited behaviour
- Relatively little memory disturbance
- Anosognosia is common
- If language disturbance is also present more likely to be Pick's disease

Criteria for Lewy Body Dementia

- Dementia plus two of :
- Fluctuating cognition (chronic delirium)
- Recurrent visual hallucinations (well formed 80%)
- Spontaneous motor features of parkinsonism (75%)
- If these features are present then specificity is high but sensitivity is low (50%).
- Cholinesterase inhibitors may improve apathy, anxiety, hallucinations and delusions.

Alzheimer's Disease & Vascular Dementia - Are they distinct diagnoses?

- Small strokes are a frequent accompaniment of ageing.
- Whether these strokes produce significant cognitive impairment is debatable. Recent studies indicate that leukoariosis is associated with definite and perceptible changes in memory.
- AD and VD may share other risk factors in addition to ageing such as systolic blood pressure.
- Midlife systolic BP has been shown to be associated with cognitive decline, decreased brain volume, and increased white matter hyperintensities.
- This suggests that vascular risk factors may have consequences that are not limited to cerebrovascular disease.

The “Alzheimerization” of dementia

- This is the idea that dementia is nearly all due to Alzheimer’s Disease
- There are comparatively little data to support this.
- Reports have increasingly found less correlation of Alzheimer pathology with dementia than the original report, Blessed et al Br J Psych 1968; 114:797

Association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects

Blessed et al B J Psych 1968; 114:797

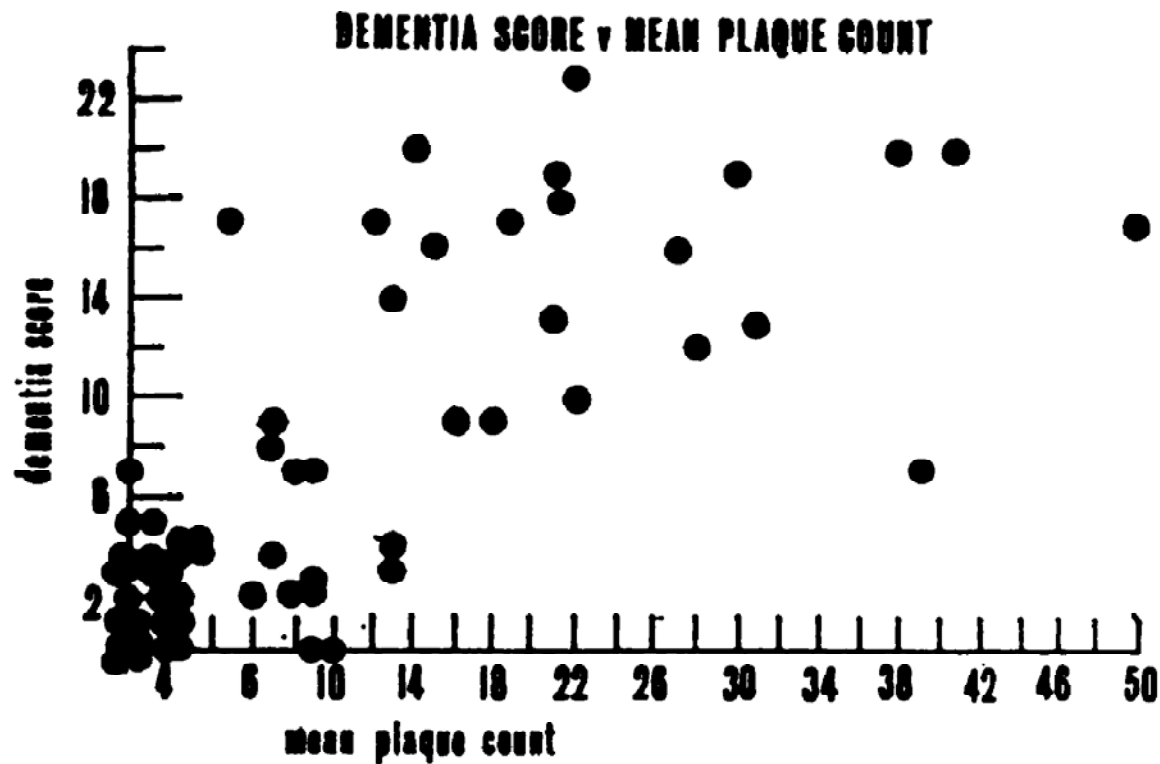
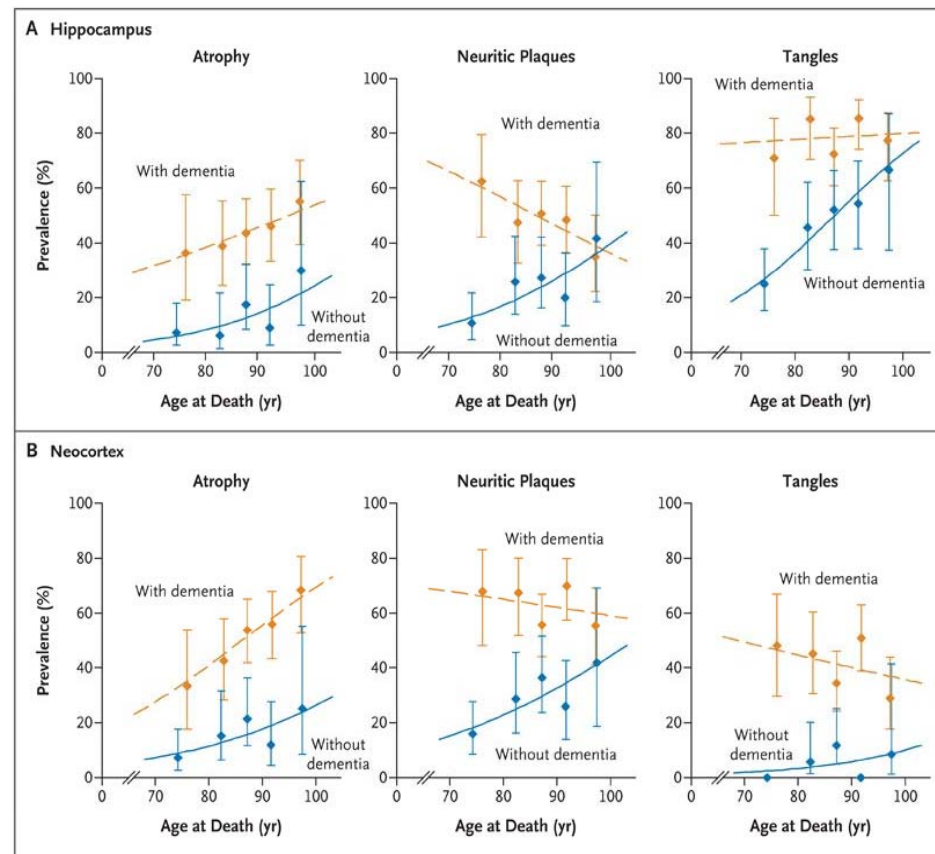


FIG. 3.—Relationship of dementia score to mean plaque count in 60 aged subjects.

Age, neuropathology and dementia

Savva et al N Engl J Med 2009; 360:2302

The association between the presence of dementia and Alzheimer pathology decreases with age



Alzheimer's Disease & Normal Ageing

Are they distinct entities?

- As individuals age, some cognitive abilities decline
 - Particularly reaction time and memory processing.
- It is unclear whether these changes form a continuum with the clinical presentation of people with AD.
- Amyloid plaques and neurofibrillary tangles, the hallmarks of AD, are known to accumulate with ageing in clinically normal individuals.
- Whether such individuals have an early form of AD which may never be expressed clinically during life is unknown.

Cognitive Impairment not Dementia

- In a well-conducted community study, (Graham et al, 1997) the Canadian Study of Health in Ageing, for people > 65 years this entity was more common than dementia (16.8% versus 8%)
- Clearly associated with less burden to the affected individuals and their carers.
- Specific conditions identified included delirium, alcohol use, drug intoxication, depression, psychiatric disease, memory impairment associated with the ageing process and mental retardation.

Mild Cognitive Impairment

- Subjective (objective) memory complaints
- Performance on memory functioning $< 1-1.5$ SD below mean for age
- Not dementia
- At this stage prognosis uncertain
- Conversion rate for clinic attenders 15% c/w community living volunteers, 7.5%.
- 25-40% of those with MCI at 2-3 years no longer impaired in some studies.

Preventing Dementia – An Unobtainable Goal? Wrong!

- It is often said (by all sorts of commentators some of whom should know better) that dementia is an unavoidable consequence of ageing.
- There is now good evidence that treating hypertension reduces the risk of developing cognitive impairment and dementia.

Risk Factors

■ Established

Old age

Down's syndrome

Family history

(some very rare mutations)

APOE genotype - ϵ 4 genotype

Likely

Female

Head injury

Vascular risk

factors - mid-life

hypertension,
AMI etc

Less Likely

- Exposure to electromagnetic radiation
- Exposure to aluminium
- Family history of Down's
- Hyperhomocysteinemia
- Depression

Protective Factors

- ? Likely

Anti-inflammatory Drugs??

Hormone replacement therapy - NO!

Physical Activity

Social engagement

Higher education and intelligence

Ongoing intellectual stimulation

Other dietary factors ? Omega 3, antioxidants

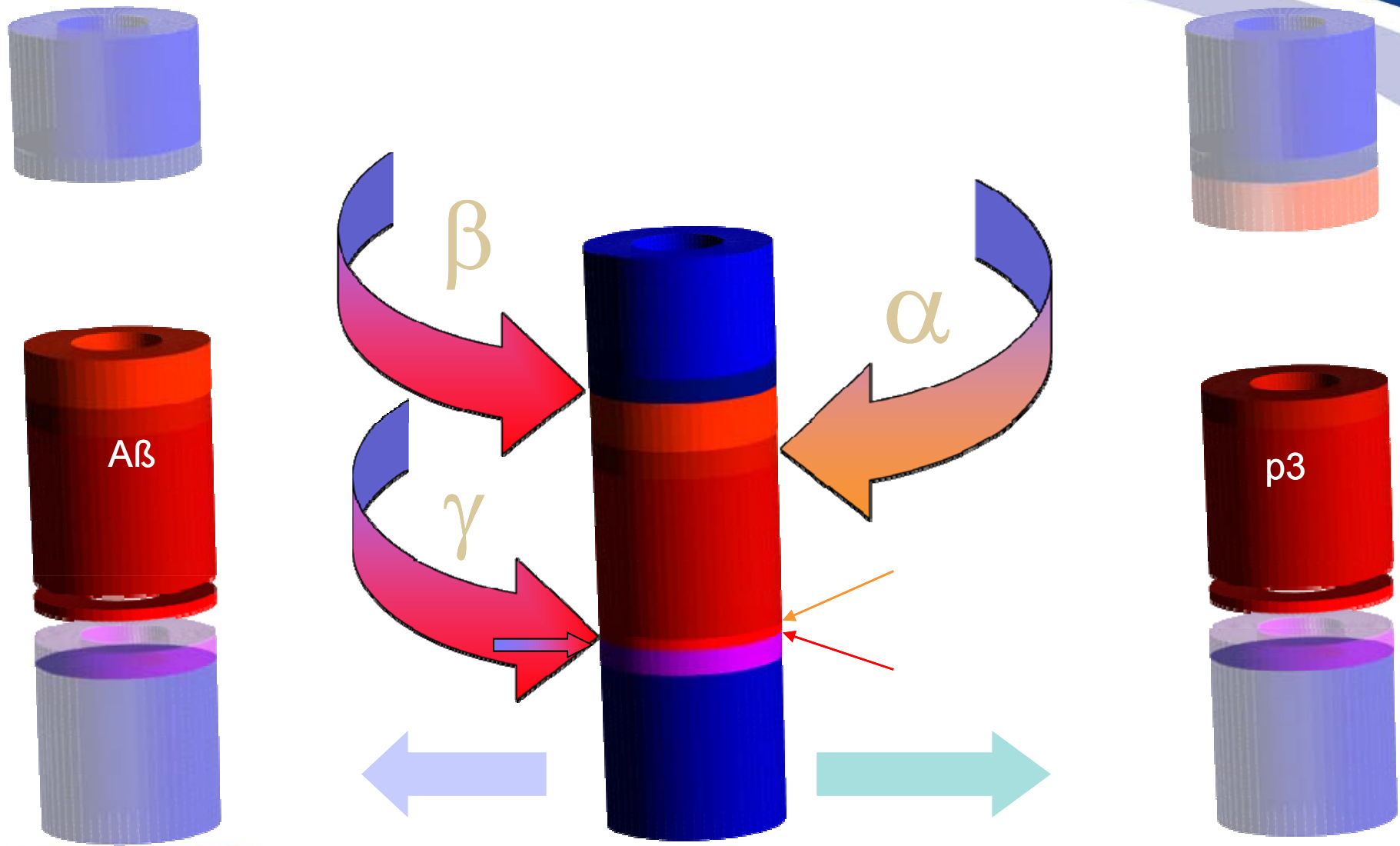
Alcohol

Smoking?? – NOW A RISK FACTOR

Spectrum of Possibilities

1. We will develop a series of interventions which will be effective, cheap and these interventions will not be prone to side-effects. We will then provide these interventions universally e.g. BP treatment, vitamins, physical activity, smoking cessation, cognitive stimulation....
2. The major disease process causing dementia is a single disease process, called Alzheimer Disease. This disease process has a stable pathogenic pathway with specific inhibitors. It is thus possible to devise a specific strategy to target those individuals who are highly likely to develop the disease.

APP Precursor protein (APP) - processing

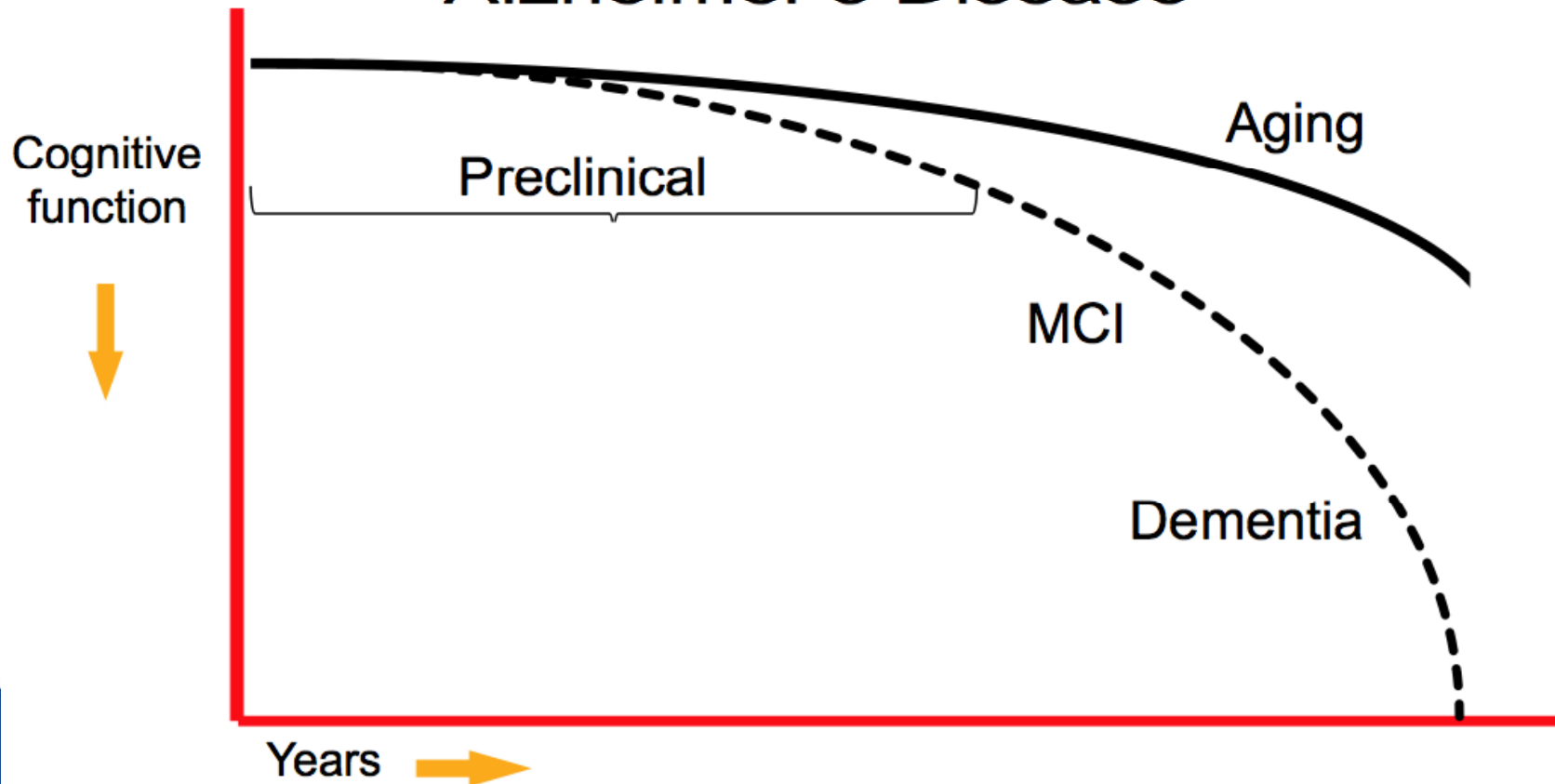


amyloidogenic

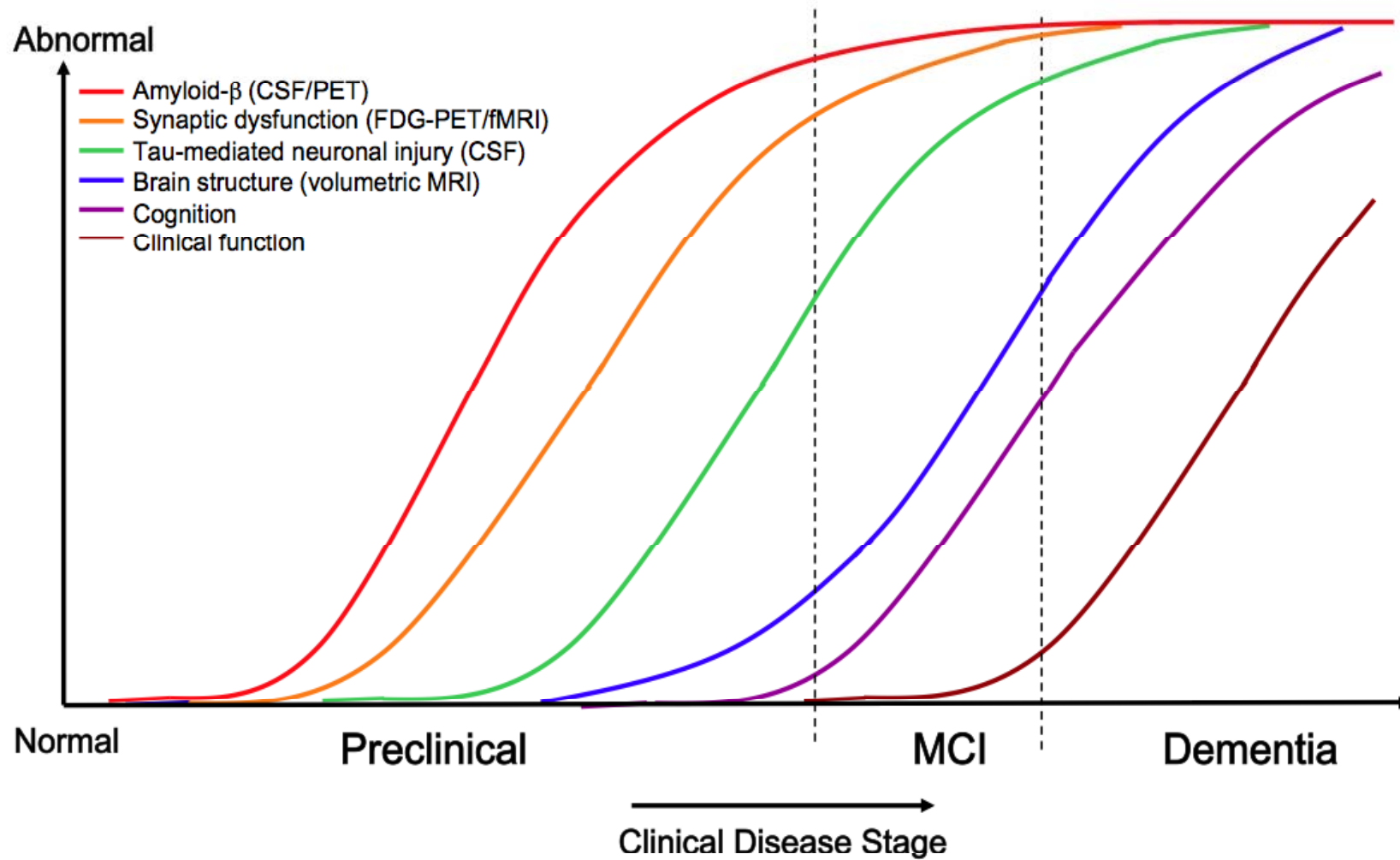
The NIA and Alzheimers Association convened three separate working groups to “address recent advances in AD”

http://www.alz.org/research/diagnostic_criteria/

Alzheimer’s Disease

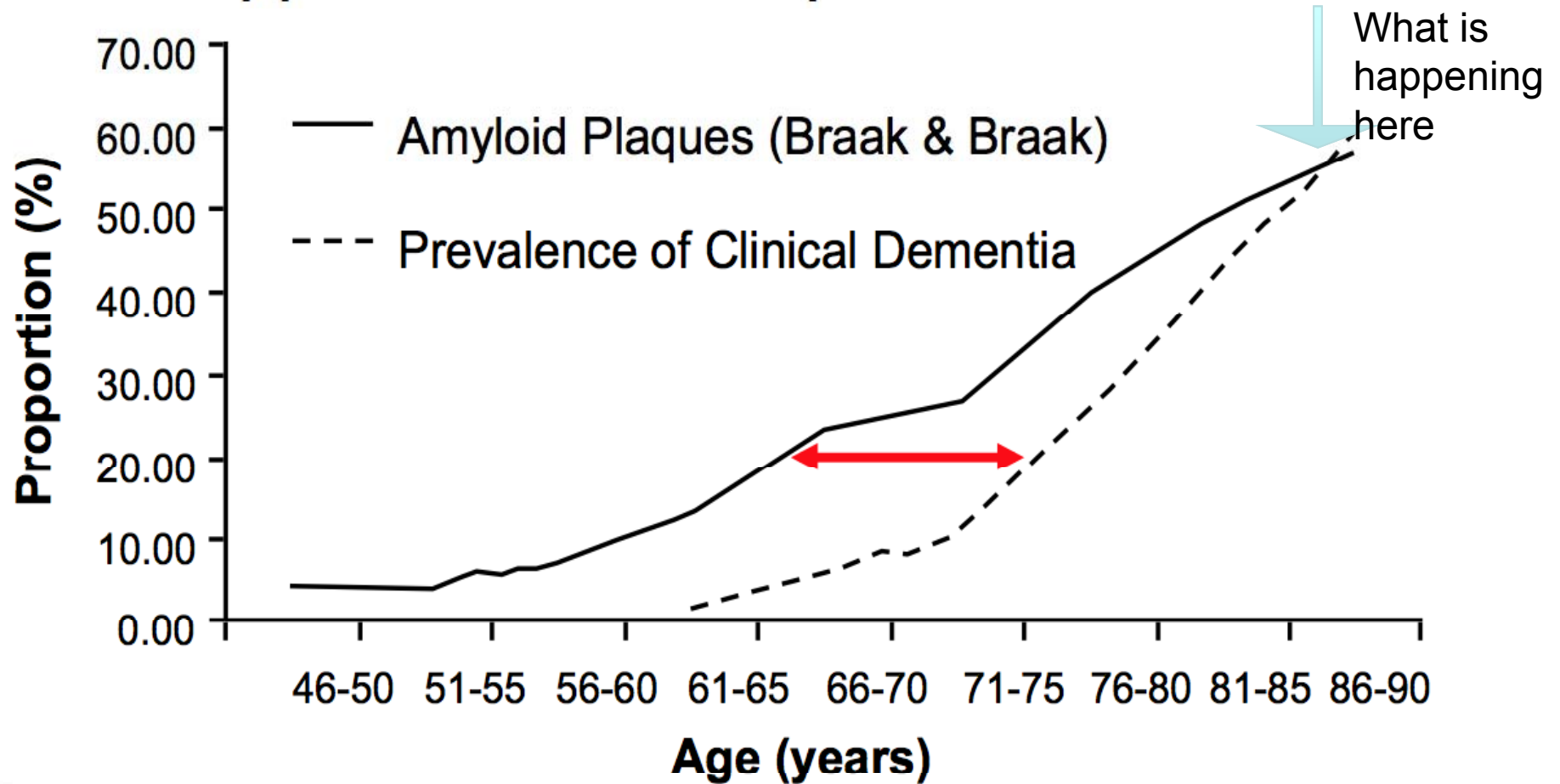


The Evidence Free Zone



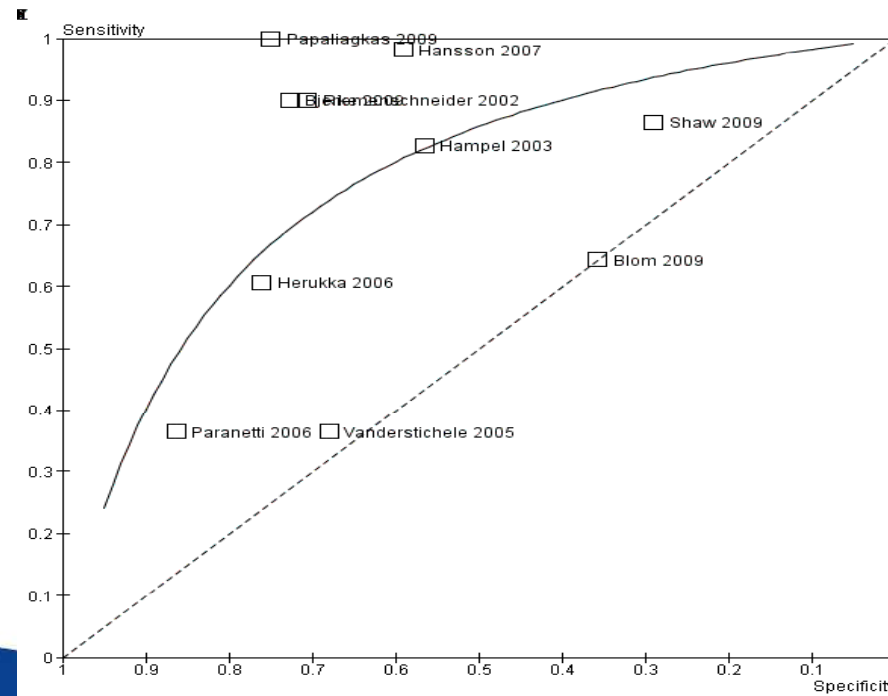
The Evidence Free Zone

Appearance of Plaques vs. Dementia



What does the evidence show? A β 42

Study	TP	FP	FN	TN	Sensitivity	Specificity	Sensitivity	Specificity
Bjerke 2009	18	42	2	112	0.90 [0.68, 0.99]	0.73 [0.65, 0.80]		
Blom 2009	9	9	5	5	0.64 [0.35, 0.87]	0.36 [0.13, 0.65]		
Hampel 2003	24	10	5	13	0.83 [0.64, 0.94]	0.57 [0.34, 0.77]		
Hansson 2007	54	27	1	39	0.98 [0.90, 1.00]	0.59 [0.46, 0.71]		
Herukka 2006	20	11	13	35	0.61 [0.42, 0.77]	0.76 [0.61, 0.87]		
Papaliagkas 2009	4	4	0	12	1.00 [0.40, 1.00]	0.75 [0.48, 0.93]		
Paranetti 2006	4	6	7	38	0.36 [0.11, 0.69]	0.86 [0.73, 0.95]		
Riemenschneider 2002	9	5	1	12	0.90 [0.55, 1.00]	0.71 [0.44, 0.90]		
Shaw 2009	32	113	5	46	0.86 [0.71, 0.95]	0.29 [0.22, 0.37]		
Vanderstichele 2005	4	8	7	17	0.36 [0.11, 0.69]	0.68 [0.46, 0.85]		
Zetterberg 2003	0	0	0	0	Not estimable	Not estimable		



The Kimberley region



65% of the total population of 32,625 live in very remote areas, 47% of the population are Indigenous. Contains over 200 remote Indigenous communities and six larger towns.

Cross-sectional, point prevalence, 367 people, all community members 45 years or older. Selection and training of indigenous health workers.

Assessment with KICA. Within 3 months: clinical assessment of selected participants (100% with scores <37, 50% of 37 and 5% of subjects with 38-40) by geriatrician or psychogeriatrician, then consensus diagnosis.



Dementia Prevalence in Kimberley Indigenous people

Age (yrs)	Dementia numbers (n)		Dementia prevalence rates		Dementia prevalence ratio
	Kimberley	Australia	Kimberley	Australia	
45-59	4	3539	0.021	0.001	21
60-69	12	12322	0.169	0.0085	19.88
70-79	12	49804	0.176	0.04	3.97
80+	17	108713	0.567	0.19	3.06
total	45	174377	0.124	0.026	5.2

Indigenous Australians may be exhibiting a preventable disease 20 years before Non-Indigenous Australians and may reflect a multitude of deleterious risk factors