Assessment of People with Dementia

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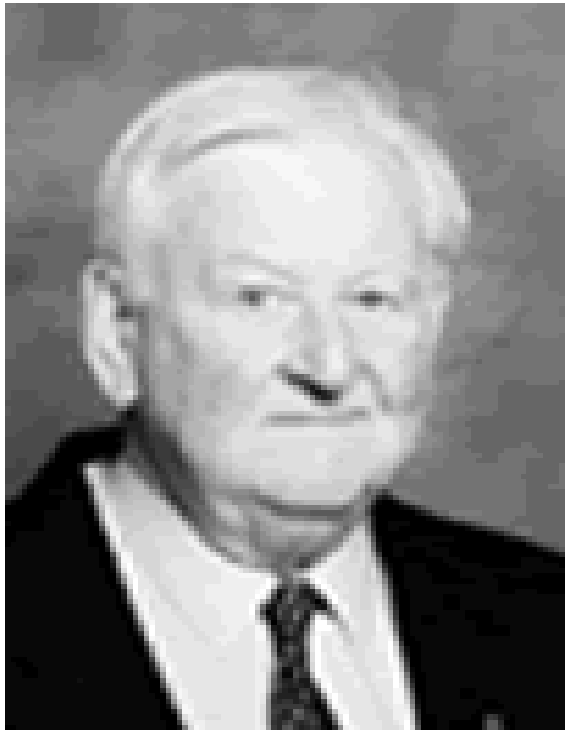
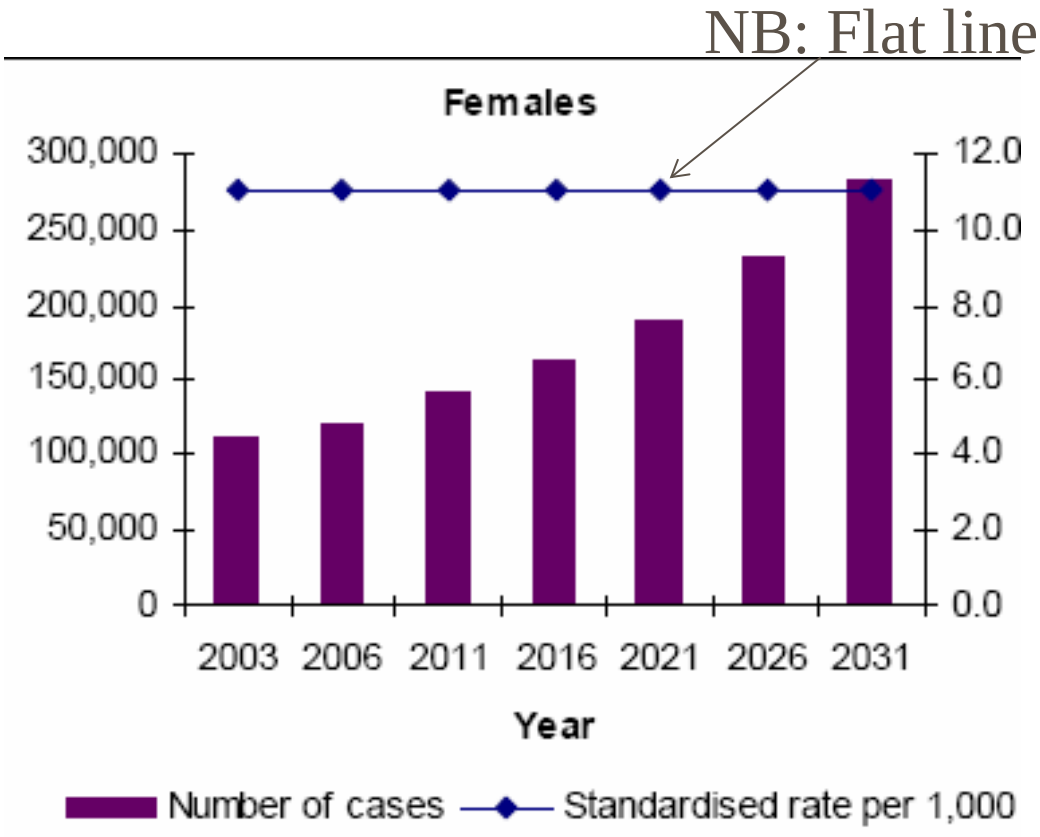
THE UNIVERSITY OF WESTERN AUSTRALIA

WESTERN AUSTRALIAN CENTRE FOR HEALTH AGEING

Inaugural David Simmons Address



Projected number of people with dementia



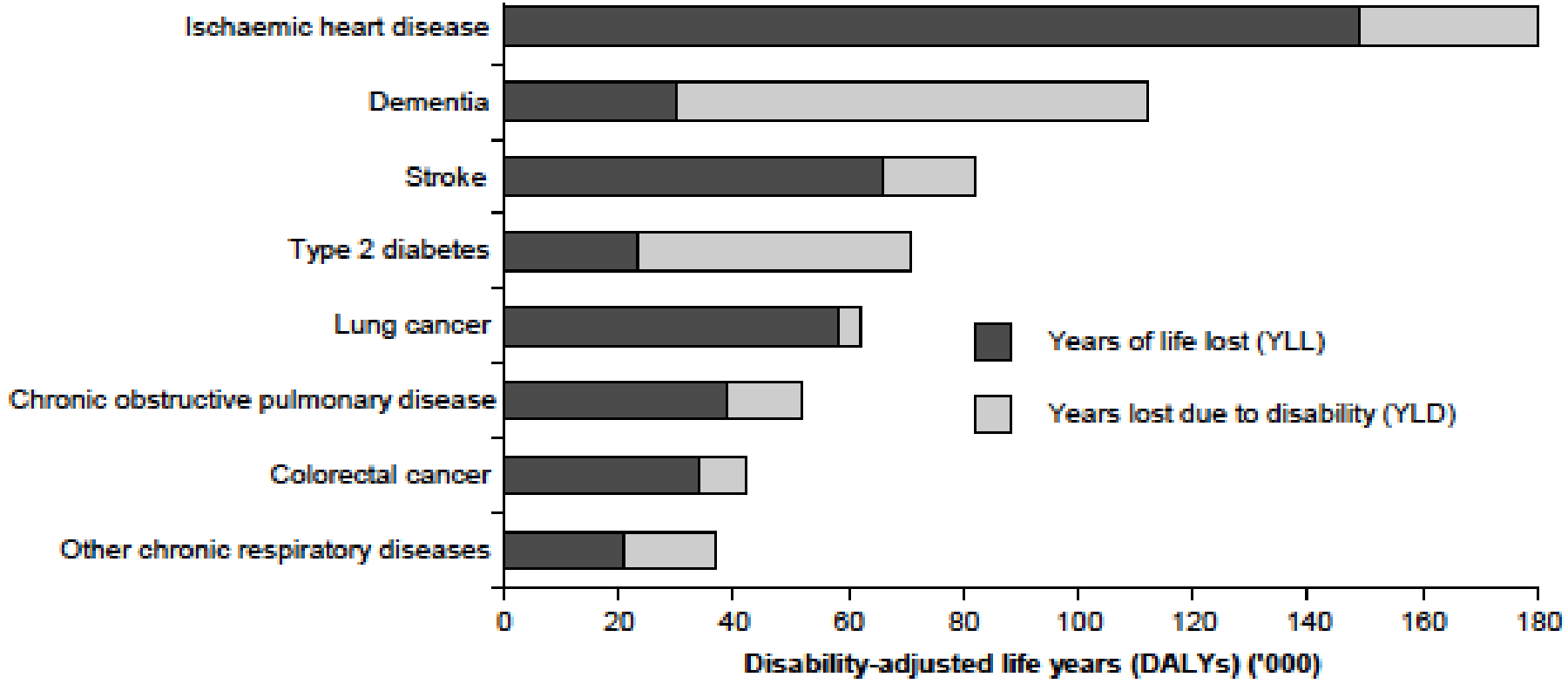
Source: Calculations by AIHW based on data from Lobo et al. 2000 and Harvey et al. 2003

Cause of Death in Australia

	Males		Females		Persons	
Cause of death (ICD-10 code)	Number	Rank	Number	Rank	Number	Rank
Ischaemic heart diseases (I20–I25)	11,704	1	10,004	1	21,708	1
Cerebrovascular diseases (I60–I69)	4,333	3	6,871	2	11,204	2
Dementia (F01, F03, G30)	2,920	6	6,083	3	9,003	3
Trachea, bronchus and lung cancer (C33–C34)	4,934	2	3,165	4	8,099	4
Chronic lower respiratory diseases (J40–J47)	3,224	5	2,898	5	6,122	5

Source: ABS 2012b.

Years of Life Lost by Condition



Note: Data for this figure are shown in Appendix Table A2.6.

Sources: AIHW projection of burden of disease based on rates from Begg et al. (2007) and population data for 2011 (ABS 2012a).

Figure 2.6: Leading causes of burden of disease by fatal and non-fatal components, for people aged 65 and over, 2011

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 ($\geq$ 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).

Frontotemporal 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.

Mild Cognitive Impairment

- Subjective memory complaints
- Performance on memory functioning or other mental function below average for age
- Not dementia – no functional impairment
- At this stage prognosis uncertain

In one study > 20% improved in cognitive function over 2 years and these changes correlated with improvements in brain structure Song et al J Neurol Neurosurg Psychiatry 2013; 84:71

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.

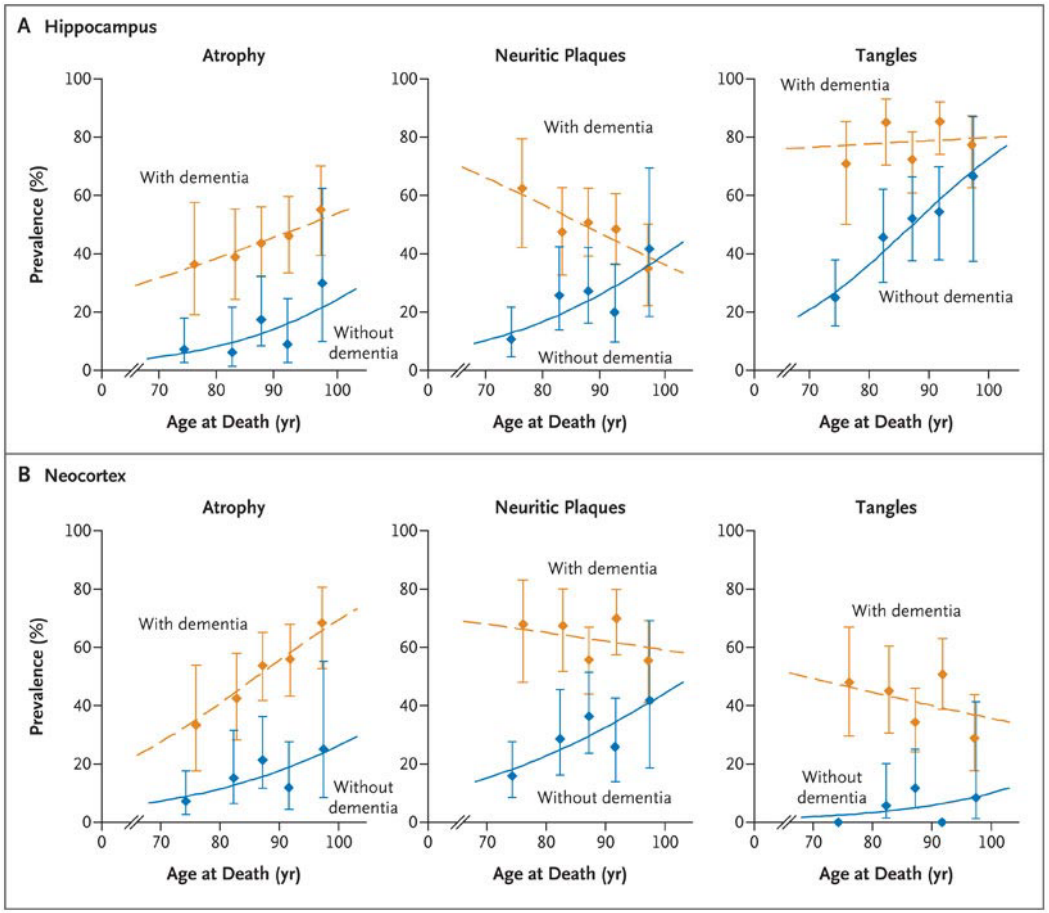
The “Alzheimerization” of dementia

- 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

Dementia or Cognitive Frailty?

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



- 5 separate pathologies associated with “Alzheimers-type dementia”
- Plaques and tangles
- Microvascular Lesions
- Atrophy
- Hippocampal sclerosis
- Cortical Lewy Bodies

(White L 2009)

Dementia or Cognitive Frailty?

- Amyloid as the “cause” of Alzheimers dementia Masters et PNAS 1985
- Hopes were raised that within 10 years, effective interventions that alter disease progression would be available.
- Some 29 years later, such hopes are somewhat diminished.
- Interventions based on this hypothesis were duly tested and removed amyloid protein from the brain.
- They did not result in any clinical improvement, and in one trial of a gamma secretase inhibitor, semagacestat, worsening.
- The most parsimonious explanation is that amyloid accumulates as part of the brain’s repair mechanism.
- Not all people progress to dementia from MCI and that some actually improve over time Song et al J Neur, Neurosurg Psych 2013
- Would explain high rates in Indigenous Australians, effects of physical activity, education, dementia following delirium etc

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.

Operational Research Criteria for Defining Preclinical AD

1. Biomarker evidence of amyloid-β accumulation (Stage 1 = asymptomatic cerebral amyloidosis)

a. Elevated tracer retention on PET amyloid imaging and/or low Aβ42 on CSF assay

2. Biomarker evidence of synaptic dysfunction and or early neurodegeneration (Stage 2 = evidence of amyloid positivity + presence of one or more additional AD markers)

a. Elevated CSF tau or phospho-tau

b. Hypometabolism in an AD-like pattern (i.e. posterior cingulate, precuneus, and/or temporo-parietal cortices) on FDG-PET

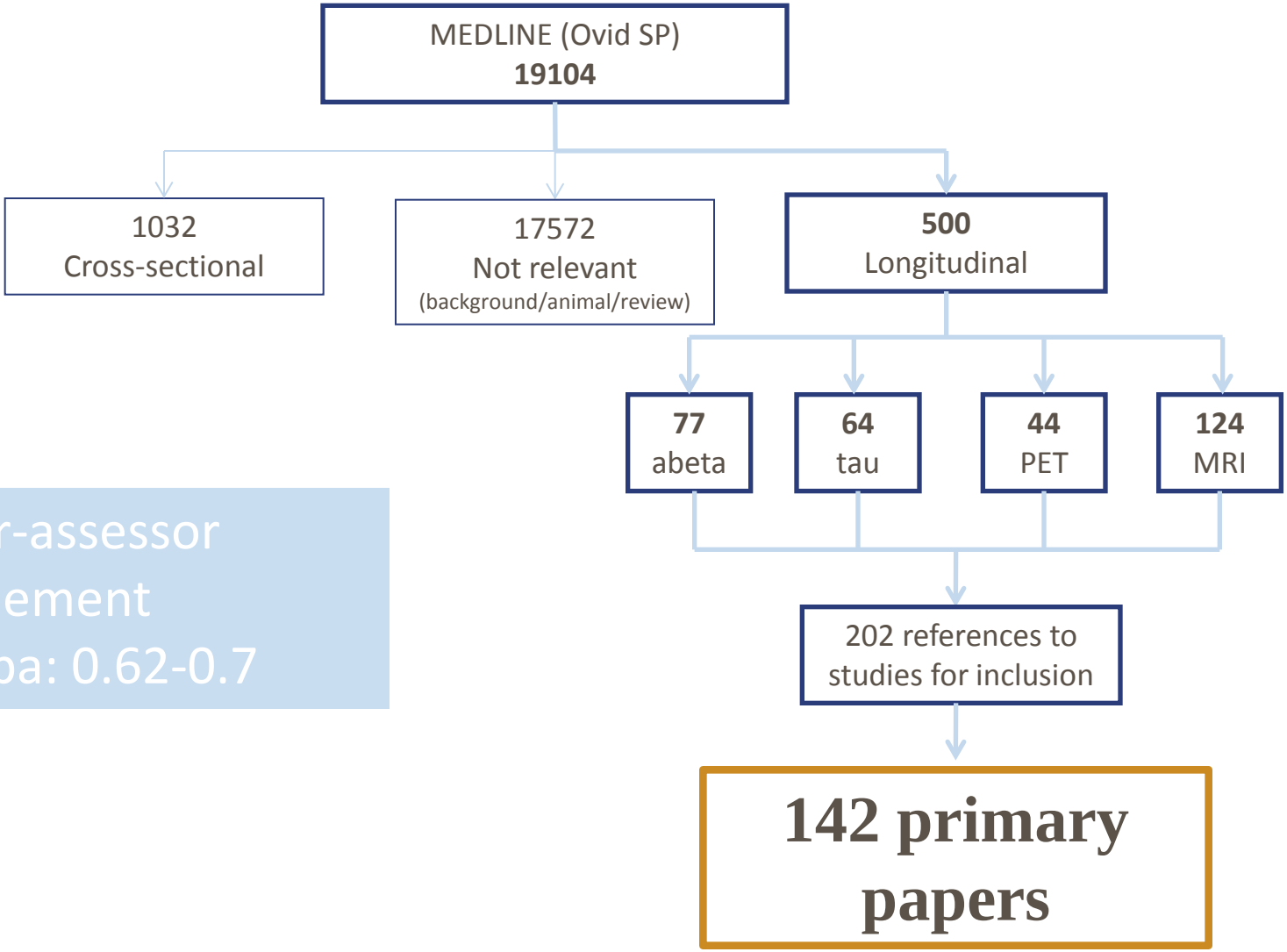
c. Cortical thinning/grey matter loss in AD-like anatomic distribution (i.e. lateral and medial parietal, posterior cingulate and lateral temporal cortices) and/or hippocampal atrophy on volumetric MRI

3. Evidence of subtle cognitive decline, but does not meet criteria for MCI or dementia (Stage 3 = amyloid positivity + markers of neurodegeneration + very early cognitive symptoms)

a. Demonstrated cognitive decline over time on standard cognitive tests, but not meeting criteria for MCI

b. Subtle impairment on challenging cognitive tests

Results: search



Inter-assessor agreement
Kappa: 0.62-0.7

THE COCHRANE COLLABORATION®

Plasma and cerebrospinal fluid amyloid beta for the diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI) (Review)

Ritchie C, Smailagic N, Noel-Storr AH, Takwoingi Y, Flicker L, Mason SE, McShane R

THE COCHRANE COLLABORATION®

Main results

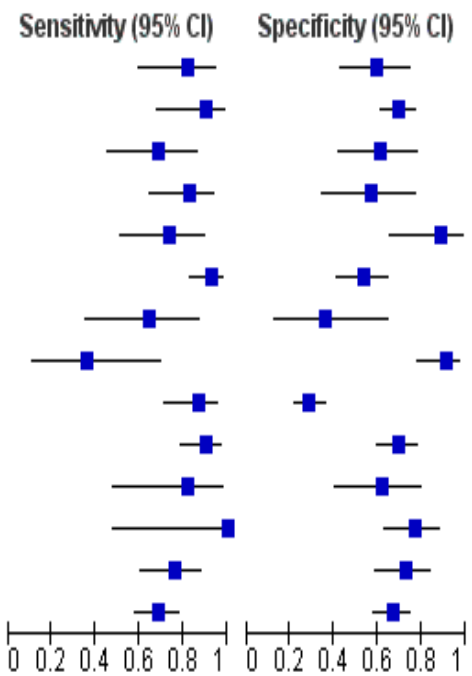
Alzheimer's disease dementia was evaluated in 14 studies. Of the 1349 participants included in the meta-analysis, 436 developed Alzheimer's dementia. Individual study estimates of sensitivity were between 36% and 100% while the specificities were between 29% and 91%..... At the median specificity of 64%, the sensitivity was 81% (95% CI 72 to 87).

Authors' conclusions

.. From our review, the measure of abnormally lowCSF Aß levels has very little diagnostic benefit …..We conclude that when applied to a population of patients with MCI, CSF Aß levels cannot be recommended as an accurate test for Alzheimer's disease.

Study results of cerebrospinal amyloid beta 42 for detection of Alzheimer's disease dementia.

Study	TP	FP	FN	TN	Abeta 42 Threshold	Threshold Unit of measurement	Sensitivity (95% CI)	Specificity (95% CI)
Galluzzi 2010	18	17	4	25	500.0	ng/l	0.82 [0.60, 0.95]	0.60 [0.43, 0.74]
Bjerke 2009	18	43	2	99	512.0	ng/l	0.90 [0.68, 0.99]	0.70 [0.61, 0.77]
Zetterberg 2003	15	12	7	19	532.0	ng/l	0.68 [0.45, 0.86]	0.61 [0.42, 0.78]
Hampel 2004	24	10	5	13	679.0	ng/l	0.83 [0.64, 0.94]	0.57 [0.34, 0.77]
Chiasserini 2010	17	2	6	16	741.0	ng/l	0.74 [0.52, 0.90]	0.89 [0.65, 0.99]
Hansson 2007	53	36	4	41	0.64	ng/ml	0.93 [0.83, 0.98]	0.53 [0.42, 0.65]
Blom 2009	9	9	5	5	82.0	pM	0.64 [0.35, 0.87]	0.36 [0.13, 0.65]
Parnetti 2006	4	4	7	40	500.0	pg/l	0.36 [0.11, 0.69]	0.91 [0.78, 0.97]
Shaw 2009	32	113	5	46	192.0	pg/ml	0.86 [0.71, 0.95]	0.29 [0.22, 0.37]
Hertze 2010	47	33	5	75	209.0	pg/ml	0.90 [0.79, 0.97]	0.69 [0.60, 0.78]
Monge-Argiles 2011	9	10	2	16	320.0	pg/ml	0.82 [0.48, 0.98]	0.62 [0.41, 0.80]
Papaliagkas 2009	5	11	0	37	472.0	pg/ml	1.00 [0.48, 1.00]	0.77 [0.63, 0.88]
Kester 2011	32	16	10	42	495.0	pg/ml	0.76 [0.61, 0.88]	0.72 [0.59, 0.83]
Vos 2013	62	41	29	82	500.0	pg/ml	0.68 [0.58, 0.78]	0.67 [0.58, 0.75]



THE COCHRANE COLLABORATION®

What additional information does this provide and what is its value?

Can we diagnose Alzheimers Disease before clinical symptoms? Preclinical AD

1. Amyloid-β accumulation PET amyloid imaging and/or low Aβ42 on CSF assay

2. Biomarker evidence of synaptic dysfunction and or early neurodegeneration (Stage 2 = evidence of amyloid positivity + presence of one or more additional AD markers)

a. Elevated CSF tau or phospho-tau

b. Hypometabolism in an AD-like pattern

c. Cortical thinning/grey matter loss in AD-like anatomic distribution and/or hippocampal atrophy on volumetric MRI

3. Evidence of subtle cognitive decline

How do we apply this? Schneider Lancet Neurology 2013

The AIBL investigators postulate a17-year preclinical period for AD, consisting of a presymptomatic phase of about 13 or 14 years until episodic memory impairment, and a symptomatic, pre-dementia phase of 4 years, on average. ..It is evident that a substantial majority will die earlier than in 17 years and not develop dementia.

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

- Cerebral microinfarcts are also a frequent accompaniment of ageing.
- Whether these microinfarcts 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 chronic high systolic blood pressure may have consequences that are not limited to cerebrovascular disease.

Early or Timely Diagnosis?

- A diagnosis should be made as soon as possible in every individual case - Driven by personal and professional experiences of delays in access to diagnosis and support.
- Currently no high quality evidence that diagnosis before the usual point of clinical presentation leads to long term improvements for people with dementia and their families. “policy cart before the research horse.”
- “Early” versus “screening”
- Potential harms of premature diagnosis
  - Diversion of resources from activities of proven value
  - Misclassification of substantial numbers of people
  - Overdiagnosis and overtreatment
  - Raising levels of anxiety in the population, particularly among older people.

Assessment and Management of Dementia

- Assessment is closely interlinked with management.
- There has been an increase in interest in this area because of the cholinesterase inhibitors.
- These symptomatic treatments for Alzheimer's Disease mandate the need for comprehensive assessment of people with Alzheimer's Disease and their carers.
- These assessments have the potential to provide more benefit than the medications themselves though better access to services and general support.

Domains of Assessment

- Cognition
- Functioning
  - Activities of daily living
  - Instrumental Activities of Daily Living
- Informant information
  - Related to cognitive decline
  - Abnormal behaviour
- Carer Assessment
  - (Medical) Type of dementia & medical co-morbidities

TYPE OF COGNITIVE SCREENING INSTRUMENTS AVAILABLE

Brief Screening

There are many but there does not appear to be major differences

TEST	PERS. INFO	ORIENTATION	STM	LTM	ATT	OTH
MSQ	◆	◆		◆		
BLESSED						
IMC Test	◆	◆	◆	◆	◆	
AMTS	◆	◆	◆	◆	◆	
MMSE		◆	◆		◆	◆
SPMS	◆	◆		◆	◆	
OBS	◆	◆	◆	◆		◆

Functional Tools

- Can be divided into
  - Activities of Daily Living (ADL) such as mobility, dressing, bathing, feeding, continence and eating.
  - Instrumental Activities of Daily Living (IADL) such as telephone, shopping, cooking, housekeeping, washing, use of transport, handling medications and finances.
- There is generally an heirachial relationship between ADL and IADL with those people who cannot do ADL very unlikely to be able to do IADL but many people who cannot do IADL are able to do some activities of ADL.
- This information is required for the diagnosis of dementing process and often the information concerning IADL clinches the diagnosis in uncertain cases.

Functional Tools (cont'd)

- You need to this information for other reasons; planning of service requirements, level of institutional care etc.
- The commonly used instruments are all good and share many common items.
- Most ACATs use some type of ADL or IADL
- One of the major national issues is the degree ACATs involve themselves in assessment and case management

Informant Scales

- This has been a relatively neglected area but in people with dementia the history must be taken from an informant, usually the primary carer, so as to be valid.
- These tools based on the assessment of cognitive decline from an informant.
- These tests may be particularly useful to standardise the information obtained in those people who score in the “normal” range on cognitive tests but the carers are concerned because of deteriorating cognitive function.
- The most easily applied is the IQCODE.

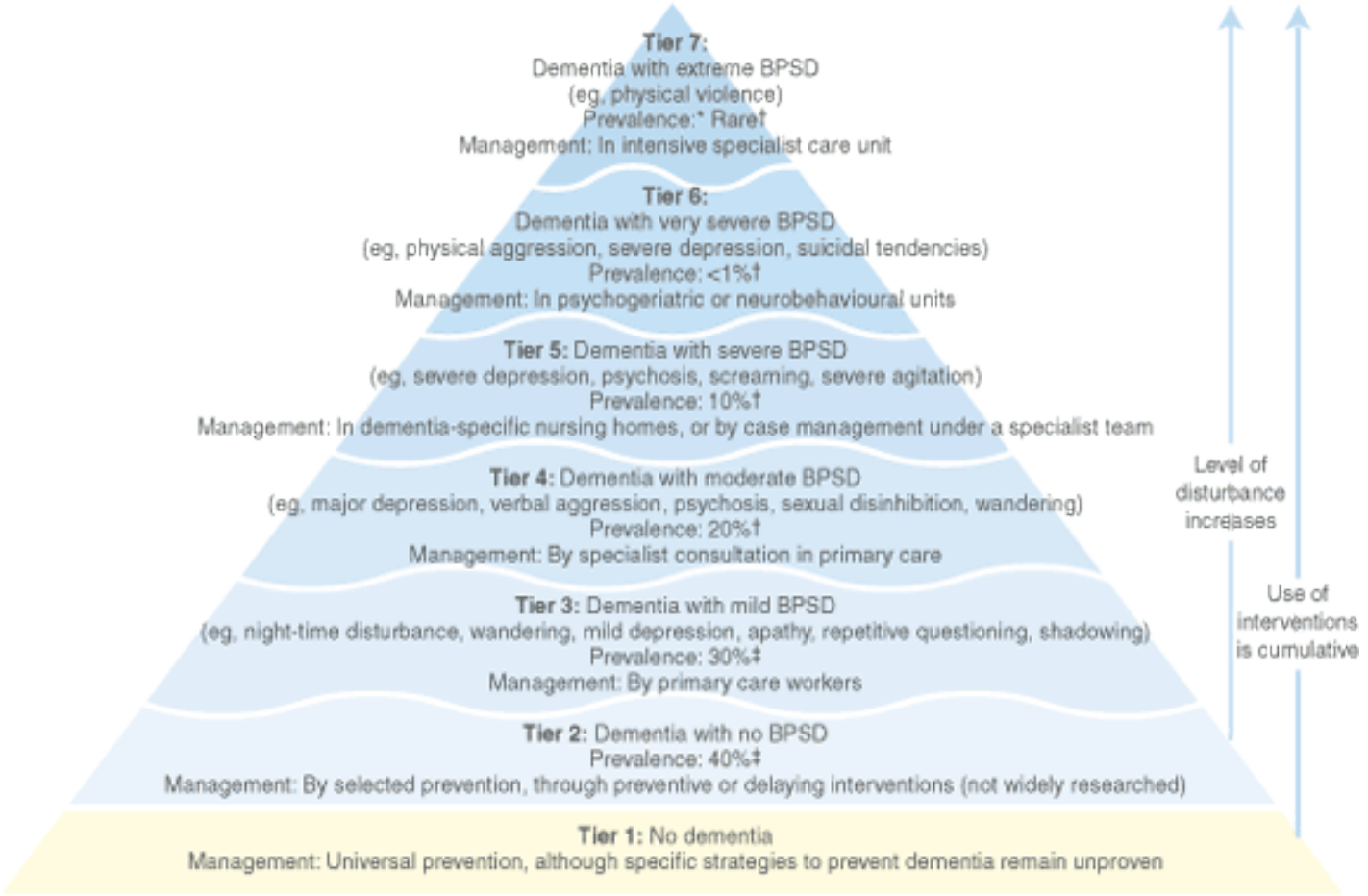
Informant Scales - Behaviour

You want information on

- Social interaction
- Delusions
- Hoarding
- Sleep disturbance
- Inappropriate urination
- Repeats the same question
- Hallucinations (any type)
- Wandering
- Yelling
- Emotional lability
- Resists help in bathing, dressing and eating
- Physically hits, swings or pushes

Brodaty et al

MJA 2003 178: 231-234



Noncognitive Symptoms in Alzheimer's Disease

- Personality changes often occur before obvious cognitive impairment - Range from progressive passivity to marked hostility.
- Decreased emotional expression, increased stubbornness, diminished initiative, greater suspiciousness.
- Delusions in up to 50% of patients with paranoid delusions being the most common.
- Hallucinations, usually visual in up to 25% of patients.
- Depression and anxiety in up to 40% of patients.
- The Behavioural Rating Scale (BRS) from the CERAD has been proposed as a useful scale.
- The Neuropsychiatry Inventory (NPI) has been used often.

Dementia - Diagnostic Protocol

There are two main uses for this information:

Case Identification	**Severity and Impact Profile**
Positive	Cognition Informant information on
If: Short history, acute illness, depression	Cognitive decline ADL and IADL Carer evaluation
More intensive medical assessment is mandatory	? Depression, behaviour

Dementia is mainly a condition of older people – residential care

- An estimated 298,000 Australians had dementia in 2011. This figure increased from the previous estimations, no major increase in new studies.
- 62% were women, 74% were aged 75 and over, and 30% lived in residential care.
- The number of people with dementia doubles every 5 years after the age of 60 years.
- The proportion of people in residential care with dementia was likely to be an underestimate because it is based on the ACFI more likely 40% one of the highest fractions in the world

Dementia in Residential Care

- This is the commonest health condition
- The standard of care is far from ideal with general practitioners poorly resourced
- There is major problems with access to specialist support for patients in residential care
- There major issues in training and competencies around assessment and management

Cholinesterase inhibitors for Alzheimer's disease
(Birks J Cochrane review)

- The results of 13 randomized, double blind, placebo controlled trials demonstrate that treatment for periods of 6 months - one year, with donepezil, galantamine or rivastigmine for people with mild, moderate or severe dementia due to Alzheimer's disease produced improvements in
  - cognitive function, on average -2.7 points (95%CI -3.0 to -2.3),
  - Global clinical state
  - Measures of activities of daily living and behaviour.
- No evidence to suggest the effects are less for patients with severe dementia or mild dementia,
- There is evidence of more adverse events in patients treated with a ChEI c/w placebo.

Donepezil for mild cognitive impairment (Review)
Cochrane: Birks, Flicker

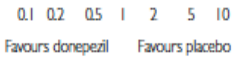
Analysis 01.12. Comparison 01 donepezil (10mg/day) vs placebo, Outcome 12 Number who progress to AD or another dementia after 1 year of treatment

Review: Donepezil for mild cognitive impairment

Comparison: 01 donepezil (10mg/day) vs placebo

Outcome: 12 Number who progress to AD or another dementia after 1 year of treatment

Study	Donepezil n/N	Placebo n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
Thal 1999	16/253	38/259		100.0	0.39 [0.21, 0.72]
Total (95% CI)	253	259		100.0	0.39 [0.21, 0.72]
Total events: 16 (Donepezil), 38 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.99 p=0.003					



Analysis 01.13. Comparison 01 donepezil (10mg/day) vs placebo, Outcome 13 Number who progress to AD or another dementia after 3 years of treatment

Review: Donepezil for mild cognitive impairment

Comparison: 01 donepezil (10mg/day) vs placebo

Outcome: 13 Number who progress to AD or another dementia after 3 years of treatment

Study	Donepezil n/N	Placebo n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
Thal 1999	63/253	73/259		100.0	0.84 [0.57, 1.25]
Total (95% CI)	253	259		100.0	0.84 [0.57, 1.25]
Total events: 63 (Donepezil), 73 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.84 p=0.4					

Delirium ? Precursor to dementia

- Clouded state of consciousness
- Problems in sustaining attention
- Sensory misperceptions
- Disturbed thinking
- Hyper and hypo activity with disturbance in sleep wake cycle
- Onset is rapid
- Condition fluctuates

Causes of Delirium

- Manifold but…
- Surgery - (multifactorial)
- Drug toxicity or withdrawal
- Infection - Urine, chest or intra-abdominal
- Fluid and electrolyte imbalance
- Renal or hepatic failure

Dementia Disclosure Analogous to cancer

- You see a 75 year old male patient with normal cognitive function and a central mass on chest X-ray.
- Sputum cytology reveals non small cell lung cancer
- Do you discuss with his wife whether he can “take” the diagnosis and then collude to shield him from the diagnosis?
- He dies without ever knowing the diagnosis
- This was STANDARD treatment for patients with cancer before 1960. Oken D. What to tell cancer patients. A study of medical attitudes. Journal of the American Medical Association1961;175:1120–8.

Should the Doctor Tell the Patient that the Disease is Cancer?*

Victor A. Gilbertsen, M.D.

and Owen H. Wangensteen, M.D.

VICTOR A. GILBERTSEN, M.D.

ADVANTAGES OF KNOWING DIAGNOSIS
354 Patients; 330 Replies

	% Indicating Advantage	
	Series A	Series B
Understanding Illness	67	60
Planning Follow-up Medical Care	66	48
Making for Peace of Mind	42	55
Decrease in Worry about Health	32	18
Planning Religious Matters	30	17
Planning Own Future	26	29
Planning Family Future	26	21
Planning Financial Matters	26	21

Fig. 6

SOUNDING BOARD

Should Patients with Alzheimer's Disease Be Told Their Diagnosis?

Margaret A. Drickamer, M.D., and Mark S. Lachs, M.D., M.P.H.

N Engl J Med 1992; 326:947-951April 2, 1992

Why disclose dementia diagnosis?

- Patient has a right to know (or not to know)
- Helps to avoid later confusion and ambiguity
- Starting point for sharing information
- Fosters a collaborative relationship between the patient and healthcare professional
- Makes future communications easier
- Enables patient and carer to plan for the future
- Enables patient to start sorting out legal, financial and practical issues
- Maintains openness in the relationship with the patient

Foy et al, 2007

Memory Clinics 1

- Memory clinics were first set up in the United States of America in the 1970s to provide an outpatient diagnostic, treatment and advice service for people with memory impairment.
- A survey of 20 memory clinics in the British Isles (Wright & Lindesay 1995) revealed that
  - Most clinic ran on a weekly basis with dementia as their primary focus.
  - Most ran on a multidisciplinary model with psychiatrists, geriatricians and psychologists most frequently being involved.
  - A mean of 2.4 patients were seen each week.
  - Regular follow-up was provided in only 30% of clinics.
  - 95% of clinics provided advice and information to patients and their relatives
  - On average 75% of the clinics' referrals suffered from a form of dementia and 47% from probable Alzheimer's disease
- There is a low diagnostic yield of reversible dementias in such clinics (Brodaty 1990)

A Randomised Trial of a Memory Clinic

- Work performed by Dina LoGiudice in conjunction with Waltrowicz, Brown, Burrows, Ames and Flicker (Int J Geriatr. Psych 1999 626-632).
- Aim of this project was to evaluate the impact of a MC on the psychosocial health status and burden of carers of those with cognitive impairment.
- 50 patients with mild to moderate cognitive impairment and their carers were recruited.
- The majority were recruited from ACATs although some were recruited through other community services.
- Carers had to have at least weekly contact with the person with dementia.

Randomised Trial of a MC

- Results (Adjusted for age of patient and baseline status)
- There were no significant benefits for psychological morbidity, burden, and dementia knowledge.
- Significant benefits on the Functional Limitation profile - psychosocial and social interaction subscales at 6 months (10.3 [4, 16.7]) but was only maintained for social interaction at 12 months.
- This suggests there are subtle benefits in some outcomes of even “low dosage” interventions aimed at caregivers even if they are already receiving reasonable service provision.

People with Dementia and Hospitals

The problem is Comorbidity (Draper et al 2011)

- Dementia was the principal diagnosis for 6% of hospital admissions of people with dementia.
- The most common principal diagnoses for those stays were lower respiratory tract infections (8%), fractured femur (6%), urinary tract infections (6%), head injury (3%) and stroke (3%).
- Patients with dementia spent longer in hospital (17 days) than those without dementia (9 days).
- Differences in length of stays were even more pronounced among younger patients.

A Shared Care Model for Dementia

- Assume an average ACAT region services 100,000 Australians. In that catchment about 114 GPs.
- There will be approximately 1350 people with dementia.
- Each GP would have on average 12 people with dementia to look after (assuming a survival of 5 years) ~ 2 new people with dementia per year
- The memory service would have to be able to provide diagnostic services for ~250 new cases per year and provide support to GPs for the others including 400 people in residential care.

IS THIS SO HARD?