

Research In Dementia in Australia

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Professor of Psychogeriatrics &
Director, Primary Dementia
Collaborative Research Centre,
UNSW; & Aged Care Psychiatry
POW Hospital, Sydney

Auguste D in 2006??

- How would she be treated today?
- Use of cholinesterase inhibitor, memantine, atypical antipsychotics
- Multidisciplinary Mx
- Carer support and training
- Managed at home



MAURER K, ... AMES D et al. (2006) Has treatment for Alzheimer's disease changed over the last 100 years? *Lancet*, 368: 1619-1621.

Health R&D: Benefits vs Costs

- Returns on money spent on health R&D in Australia are 5 – 8 fold annually
- e.g. R&D that reduced cancer deaths by 20% = saving of \$184bn to Australia
- Investment in health R&D = biggest source of rising living standards
- R&D is the greatest hope to reduce burden of chronic diseases of ageing which are set to place unprecedented demands on Australian health care system

ASMR; Access Economics 2003: Exceptional Returns

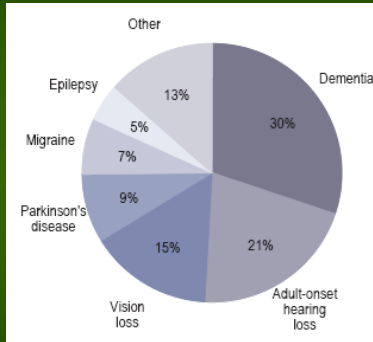
The Cost of Dementia In Australia

- Total cost of dementia (direct & indirect) = AU \$6 576 million in 2002



Access Economics 2003

Burden of Disease: Dementia



Neurological & sense disorder burden (DALYs) expressed as proportions of total

- 5th (women) & 11th (men) cause of total burden (DALYs)
- 7th cause of mortality burden in women
- 3rd (women) & 5th (men) cause of incident non-fatal burden

AIHW 2007: The burden of disease & injury in Australia 2003

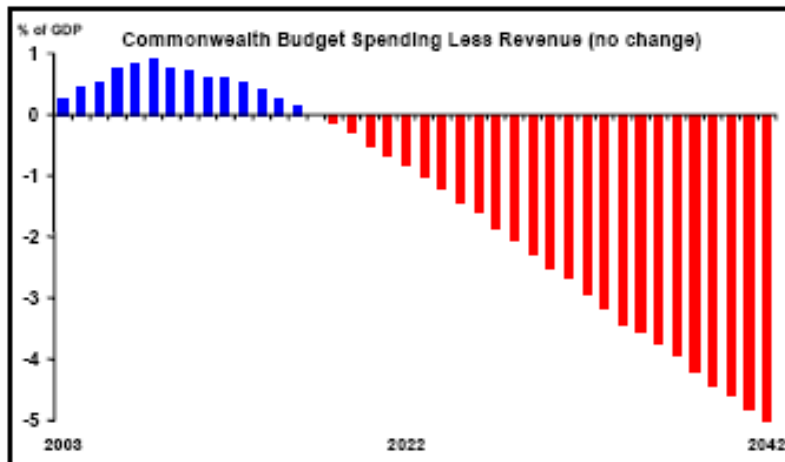
Direct Costs 1993-1994: Disease Comparisons

- Circulatory \$3.7 b
- Cancer \$1.9 b
- Dementia \$1.4 – 1.5 b*

*estimated direct cost based on underestimation of NH costs in 1993-94

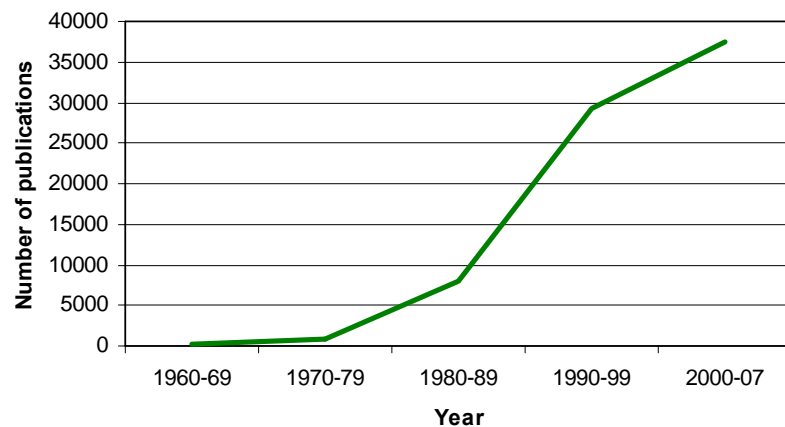
Access Economics 2003

Projected Financial Impact of Dementia with No Revenue Increase



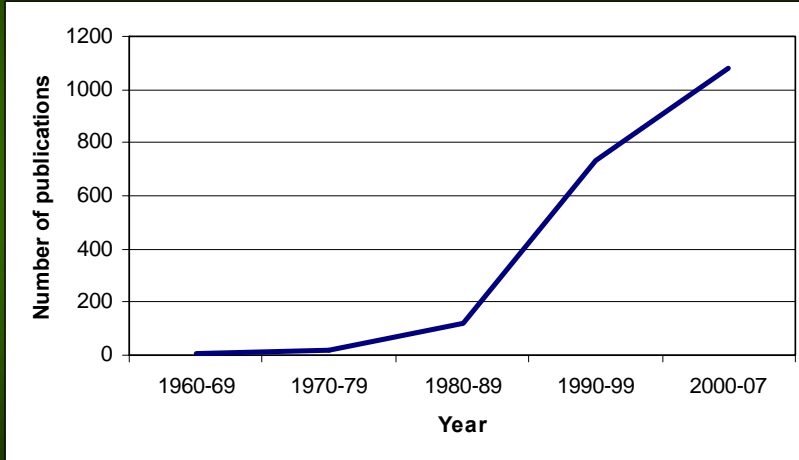
Access Economics 2003

The Increase in World Wide Dementia Research: 1960-2007*



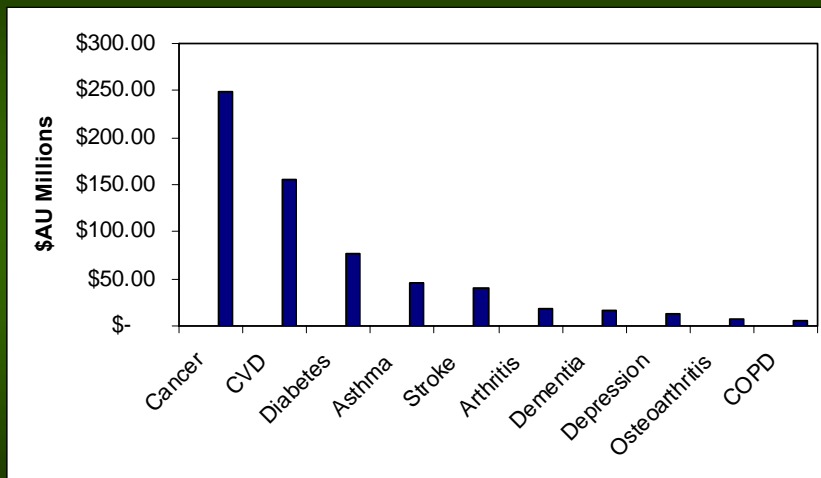
*Medline and PsycINFO searched for abstracts with 'dementia' or 'Alzheimer\$'

The Increase in Australian Dementia Research: 1960-2007*



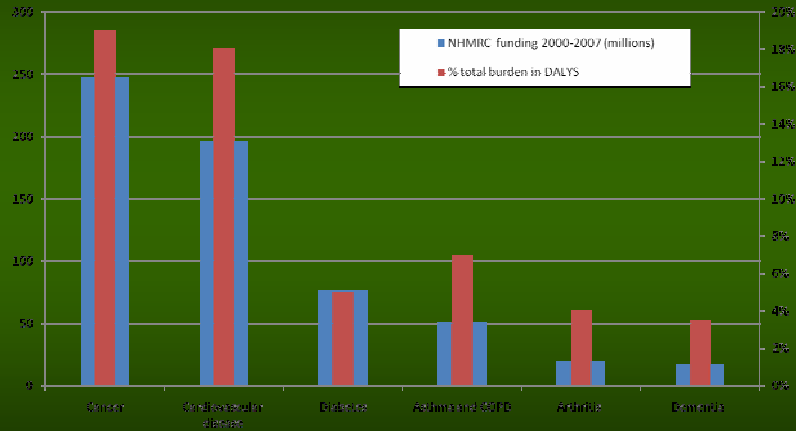
*Medline and PsycINFO searched for abstracts with 'dementia' or 'Alzheimer\$' and 'Australia\$' or 'Australia' or 'Australian' in the author address

NHMRC Grants Awarded: 2000-07

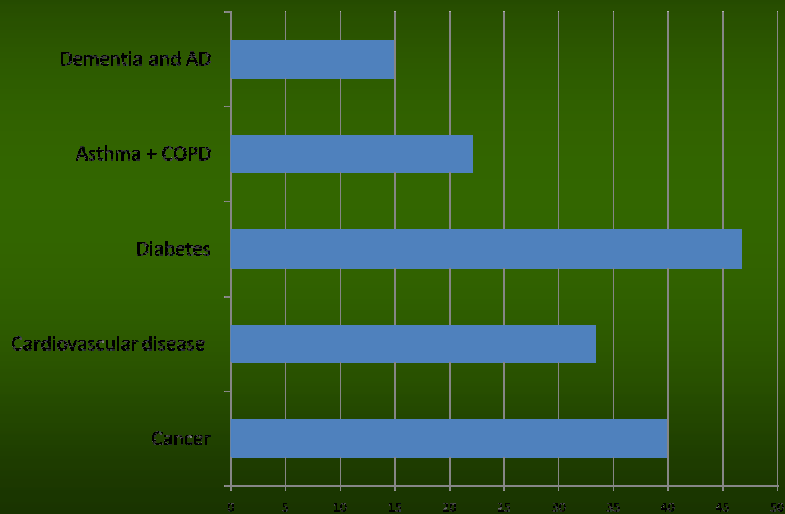


Calculated from NHMRC data

NHMRC funding and % of Australian disease burden



Proportion of funding to proportion of burden ratio



Spending on research

- **\$\$ on medical & health research per year**
 - In Australia 0.255% of GDP
 - In USA 0.6% of GDP
- **NHMRC funding for dementia in 2006:**
AUD\$0.54 per Australian
- **NIH funding for dementia in 2006:**
AUD\$2.57 per US American
- **Annual rates of return to Australia health R&D were \$5 for every \$1 spent on R&D**
(Australian Society for Medical Research, 2003)

Dementia: A National Health Priority

- **Australian government initiative announced in 2005**
- **\$320.9m including \$26m for research over 3 years, including:**
 - Two rounds of NHMRC grants \$16m
 - Three Dementia Collaborative Research Centres total of \$7m over 3 y



Fields of research

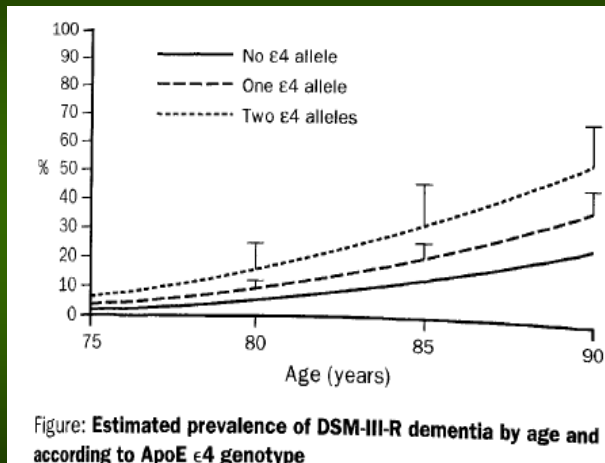
- Epidemiology
- Diagnosis
 - Instruments
 - GP training
- Pathology
- Therapeutics
- Carers
- BPSD & Nursing homes
- Clinical research
- Legal aspects
- Special populations
 - Aboriginal people
 - CALD

Epidemiology

- Henderson
- Jorm
 - Eurodem
 - Canberra
 - Path through life
 - Honolulu Asian Aging Study
- Broe – Sydney Older Persons' Study
- Memory and Ageing Study
- AIBL

Scott Henderson

ϵ 4 allele is a risk factor for dementia, but not sufficient for its development



Henderson AS et al (1995) Apolipoprotein E allele epsilon4, dementia, and cognitive decline in a population sample. *Lancet*. 346:1387-1390

Tony Jorm



- Dementia prevalence rates double every 5.1 years¹
- Cognitive deficits frequently present 3-6 years prior to dementia onset²

¹ Jorm AF et al. (1987) The prevalence of dementia: a quantitative integration of the literature. *Acta Psychiatrica Scandinavica*. 76(5):465-79

² Jorm AF et al. (2005) Cognitive deficits 3 to 6 years before dementia onset in a population sample: The Honolulu-Asia Aging Study. *JAGS*. 53(3): 452-455

Eurodem: Depression & AD

- Hx of depression associated with AD
- Association held for episodes of depression more both ≥ 10 yrs before AD onset, & ≤ 10 yrs following onset
- No association was found with anti-depressant treatment or death of spouse, death of a child and divorce.

Jorm AF. et al. (1991). Psychiatric history and related exposures as risk factors for Alzheimer's disease: a collaborative re-analysis of case-control studies. EURODEM Risk Factors Research Group. Int J Epidemiology. 20 (Suppl 2) :S43-47

PATH Through Life study



- 20 year longitudinal study of 7,485 community residents aged 20-24, 40-44 and 60-64 randomly selected from the Electoral Rolls of Canberra and Queanbeyan
- Follow-up every 4 yrs
- Aims to investigate the causes of 3 classes of common mental health problems:
 1. Anxiety and depression
 2. Alcohol and other substance abuse
 3. Cognitive functioning and dementia

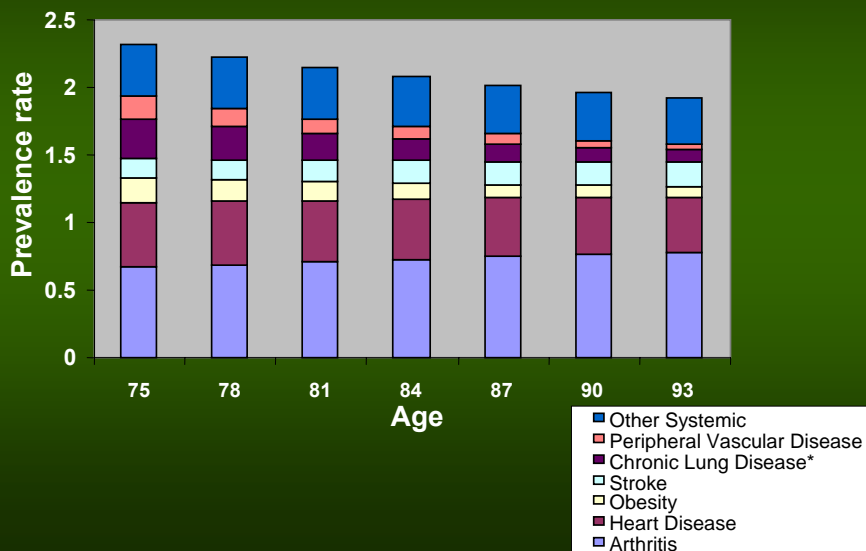
Professor Tony Broe



- Epidemiological studies in Scotland
- Sydney Older Persons Study (SOPS)
- Rise of neurodegenerative disorders with age and relative reduction in systemic disorders
- Mix of pathologies in late age

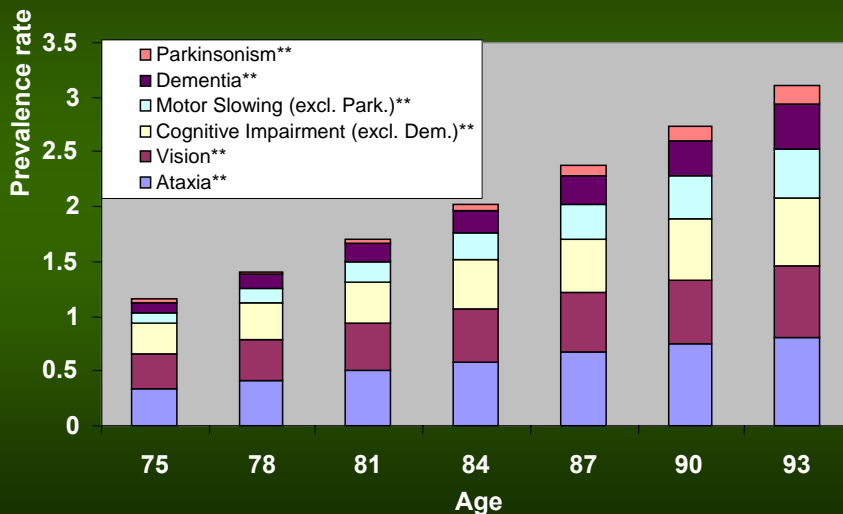
Systemic diseases: Prevalence

(N=522. Age trends: * $p < 0.05$; ** $p < 0.01$)



Neurodegenerative disorders: Prevalence

(N=522. Age trends: * $p < 0.05$; ** $p < 0.01$)



The Australian Biomarker and Imaging Lifestyle (AIBL) Flagship Study of Ageing



David Ames

- 3 yr prospective longitudinal Study of 1000 volunteers (60 yrs+)
- Not cognitive impaired, (600), MCI (200), AD (200)
- Aims:
 - To improve understanding of causes and diagnosis of AD
 - To examine lifestyle and diet factors that may influence the onset of AD
 - To help develop Rxx & preventative strategies

<http://www.aibl.nnf.com.au/page/home>



Memory and Ageing Study



- To determine prevalence of mild cognitive impairment, MCI, in 1000 community dwellers
- Electoral Roll, 70-90 years
- Follow-up 12 months and every 2 years
- To determine incidence of MCI
- To examine disease burden of MCI
- To determine progression of MCI

¹ Brodaty, Sachdev, Broe, Draper, Trollor, Slavin, Kochan, Schnier, Schofield

² Sachdev, Brodaty, Andrews NHMRC Program grant

Memory and Ageing Study

- What predicts healthy cognitive ageing?
- What predicts cognitive decline?
 - Genes
 - Past and present life style
 - Diet
 - MRI scan findings
 - Neuropsychological performance
 - Physical signs eg walking, smell
 - Subtle signs noted by other person (CICAQ)

Diagnosis

- Amyloid β protein in blood (Ralph Martins)
- MRI, PET with PIB
- **New diagnostic instruments**
- GP training (Pond)

Measurement tools

- IQCODE
- PAS
- COGSTATE
- GPCOG
- RUDAS
- KICA
- Abbey Pain Scale

IQCODE¹ & Short IQCODE²

- **IQCODE (26 items) & Short IQCODE (16 items):**
 - Informant questionnaire
 - Assesses changes in patient's cognitive performance over previous 10 yrs
 - Rated on a 5 point scale from “much improved” to “much worse”
 - Lower scores better

¹Jorm AF, Scott R, Jacomb PA. (1989). *International Journal of Geriatric Psychiatry*. 4(1): 35-39; ²Jorm AF. (1994) *Psychological Medicine*. 24(1):145-153

Examples of Short IQCODE Items

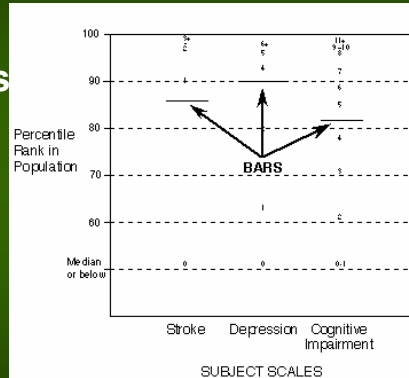
Compared with 10 yrs ago, how is this person at:

1. Remembering things about family & friends e.g. occupations, birthdays, addresses?
2. Remembering things that have happened recently?
3. Recalling conversations a few days later

Responses on 5-point scale ranging from much improved to much worse

Psychogeriatric Assessment Scale (PAS)

- Assesses dementia and depression on scales
- Subject interview, 3 scales
 - Stroke
 - Depression
 - Cognitive Impairment
- Informant i/view, 3 scales
 - Stroke
 - Cognitive Decline
 - Behaviour change
- Gives results as a percentile rank within the population



http://www.mhri.edu.au/pas/User_Guide/User_Guide.html#Using%20Summary%20Profile



- A/Prof David Darby - Chief Medical Officer
- CogState = a range of computerised cognitive tests to measure reaction time, attention, visual memory & learning, social cognition, verbal memory & learning, planning and problem solving
- Used to determine the effect of drugs etc on cognition
- Used in > 30 clinical trials

<http://cogstate.com/>

General Practitioners Assessment of Cognition (GPCOG)

- Designed for GPs; for efficiency in screening
- Two sections:
 - Cognitive Testing (range 0-9; 6 items, ↑ better)
 - Informant interview (6 items, ↑ better)
- <4.5 minutes to administer; several languages
- Informant can be contacted by telephone
- If cognitive score is > 8 or < 5, informant interview not needed
- Valid and reliable, sensitivity/specificity > 0.85

Brodaty H. et al. (2002). The GPCOG: A new screening test for dementia designed for general practice. *Journal of the American Geriatrics Society*. 50(3): 530-534

RUDAS

- Designed to be free of cultural bias
- 10 minutes to administer
- Items divided into:
 - Memory
 - Visuospatial Orientation
 - Praxis
 - Visuoconstructional Drawing
 - Language

Storey JE. et al. (2004). The Rowland Universal Dementia Assessment Scale (RUDAS): A multicultural cognitive assessment scale. *Int Psychogeriatrics*. 16(1): 13-31

Kimberley Indigenous Cognitive Assessment tool (KICA)

Difficulties associated with cognitive testing of older indigenous Australians:

- **Limited access to formal education**
- **English is often 3rd or 4th language**
- **Indigenous languages generally oral**
- **Different concepts of number, time & space**
- **Inappropriate to discuss personal/family issues**
- **Poor vision highly prevalent**

LoGiudice D et al. (2006) International Psychogeriatrics. Vol. 18(2); pp 269-280.



Prof Nicola Lautenschlager
University of Western Australia

Prof Leon Flicker
University of Western Australia



Kimberley Indigenous Cognitive Assessment tool (KICA)

- KICA-Cog: 16 questions
- Score: 0 – 39 (31/32; sens = 97, spec = 82)
- Higher scores better
- 30 – 40 minutes to administer
- Walmajarri language specific to Kimberley
- Orientation, free & cued recall, language, verbal fluency, copying sequence pattern & ideational praxis

LoGiudice D et al. (2006) *International Psychogeriatrics*. Vol. 18(2); pp 269-280.

Examples of KICA Items

- Hold up 3 items in turn: comb, pannikin (cup) & matches, and ask “What do you call this?”, “What is this one for?”
- “Tell me the names of all the animals that people hunt” – time: 1 minute
- “I’ll show you some pictures, you tell me what they are”: boy, emu, crocodile, billy on fire, bicycle

GP training



Dimity Pond leading an NHMRC funded consortium from 4 universities to answer these Qs:

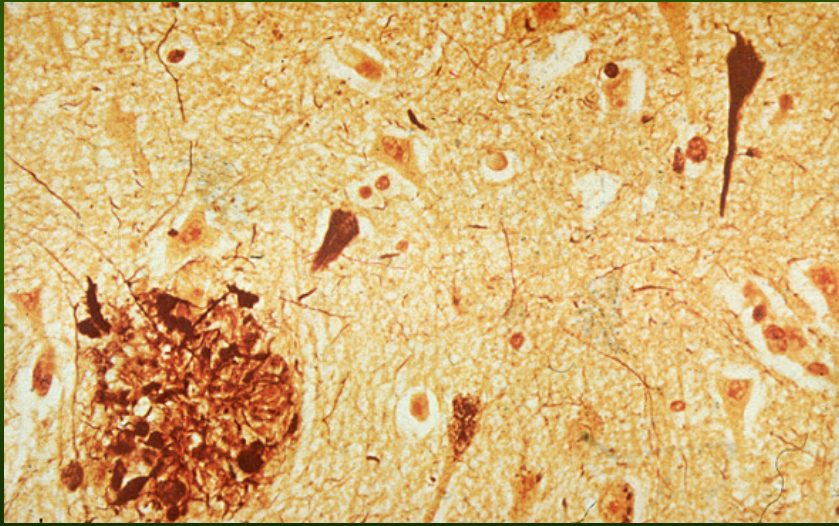
1. Does GP training improve:
 - Diagnosis rate
 - Adequacy of management
2. Does earlier diagnosis lead to positive outcome?

Abbey Pain Scale

- Measures pain in PWD
- 6 items:
 - Vocalisation; Facial expression; Change in body language; Behavioural change; Physiological change; Physical change
- Measured on 4-pt scale for severity (absent to severe)



Pathology



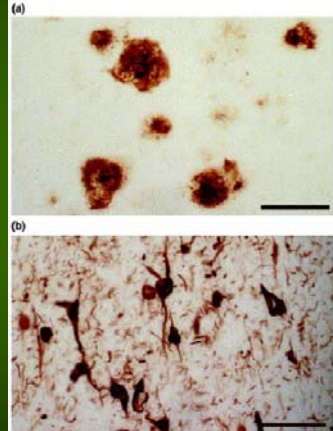
Colin Masters, Laureate Professor



- Masters and his team were among the first to isolate & characterise amyloid in AD
- Masters championed the amyloid theory of AD
- > 800 papers on amyloid published annually

Colin Masters: Landmark Paper

Characterised the cerebral amyloid prNn that forms the plaque core in AD and in aged individuals with Down syndrome



Masters CL. et al. (1985) *Amyloid plaque core protein in Alzheimer disease and Down syndrome*. Proceedings of the National Academy of Sciences of the United States of America. 82(12):4245-9 TIMES CITED: 1900



Ashley Bush, Professor
Pathology and Psychiatry
Mental Health Research Institute;
U Melb

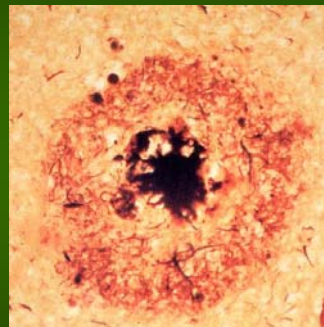
- Novel insight into metabolic processes underlying age-related neurodegenerative diseases
- Disruption in metabolism of critical biological metal ions, such as Cu and zinc
- Uncovered interactions of biometals (Cu, Zn & Fe) & β -amyloid that contributes to both oxidation damage and amyloid accumulation in AD

Therapeutics

- AC4R
- PBT2 (Bush, Masters, Ritchie, Ames)
- Testosterone (Martins)
- Current drug trials in Australia

PBT2: 2nd Generation Clioquinol

- Designed to modify the course of AD by preventing metal-dependent aggregation, deposition & toxicity of A β
- FDA Phase: Phase II/IIa/IIb



Ritchie CW. et al. (2003). Metal-protein attenuation with iodochlorhydroxyquin (clioquinol) targeting Abeta amyloid deposition and toxicity in Alzheimer disease: a pilot phase 2 clinical trial. *Archives of Neurology*. 60(12):1685-1691

The Australasian Consortium of Centres for Clinical Cognitive Research (AC4R)

- Peak body representing Dementia Research Centres in Australasia
- Goal is to bring together all centres throughout Australasia involved in treatment studies for dementia
- 80 members in 2006
- Geriatric medicine, neurology, psychiatry, psychopharmacology, psychogeriatrics, neurobiology, nuclear medicine and neuropathology

AC4R: drug trials in Australia

- Rosiglitazone (recruiting)
- Lecoatan (ongoing, recruitment closed)
- PBT2 (successor to clioquinol) (start soon)
- High dose, slow release donepezil (soon)
- Xaliproden (completed, results awaited)
- Memantine (soon)
- Leuprolide (abandoned, financial problems)

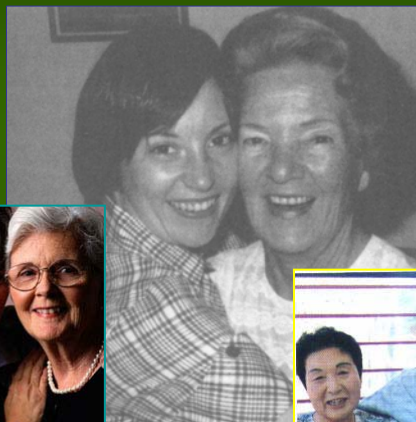
Testosterone & Dementia



- Are ↓ testosterone levels a causative factor in cognitive decline with ageing?
- Interaction between testosterone and APOE ε4
- ↑ testosterone associated with better general cognition in non- ε4 carriers
- ε4 carriers: ↑testosterone associated with ↓ executive functioning, working memory & attention

Burkhardt MS ... Martins RN et al. (2006) Interaction between testosterone and apolipoprotein E epsilon4 status on cognition in healthy older men. *Journal of Clinical Endocrinology & Metabolism*.91(3); 1168-1172

Advances with carers

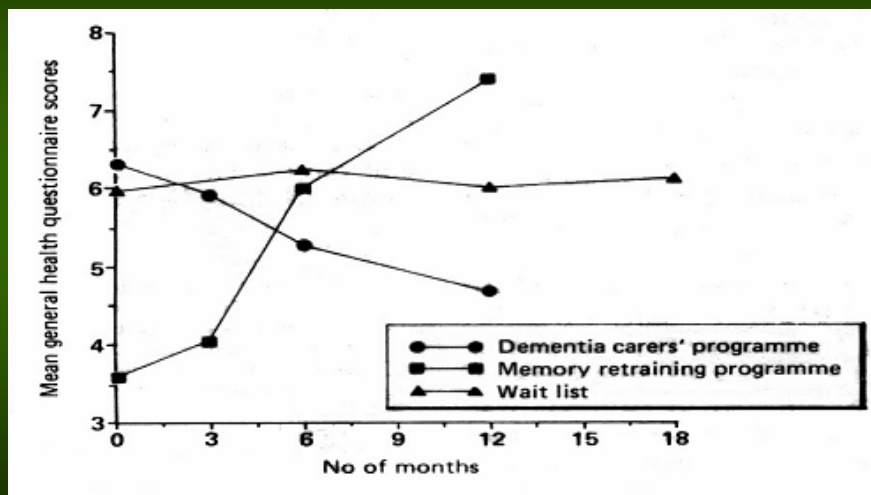


The Dementia Carers Program

- Ten day intensive residential program
- For persons with dementia and carers
- Intensive, comprehensive, extensive
- Counselling, skills & communication training, knowledge, mutual support
- Involve PWD and extended family
- Follow-up 2nd → 6th weekly by tel and quarterly in person for a year

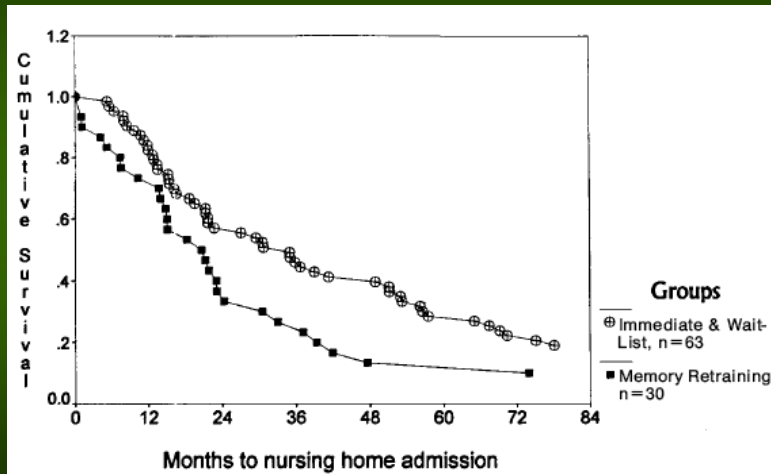
Brodaty and Gresham (1989), *BMJ*; 299: 1375-1379
Brodaty H. et al. (1997) *IJGP* 12:183-92

The Dementia CGs' Program Results: GHQ



Brodaty and Gresham (1989)

7 yr survival at home for patients of Carers undertaking Dementia Carer Training



Brody H. et al. (1997) The Prince Henry Hospital dementia caregivers' training programme. *International Journal of Geriatric Psychiatry*. 12(2):183-92

Meta-analysis of psychosocial interventions for CGs

- CG interventions can reduce CG psychological morbidity (ES = 0.3) and help people with dementia stay at home longer
- Significant benefits in CG psychological distress, knowledge
- Success predicted by involvement of patients and their families, by “dose” of intervention
- Flexibility and constant therapist appear important

Brody H. et al (2003) Meta-analysis of psychosocial interventions for caregivers of people with dementia. *JAGS*; 51(5): 657-664

The three country study: Aricept ± counselling



Manchester, UK - Alistair Burns

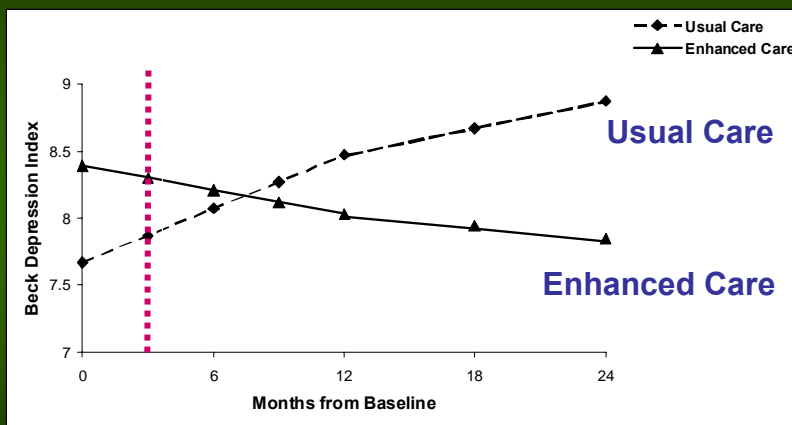


New York, USA - Mary Mittelman



Sydney, Australia - Henry Brodaty

The 3 Country Study: Caregiver Depression



The treatment group started off more depressed than control group and ended up less depressed

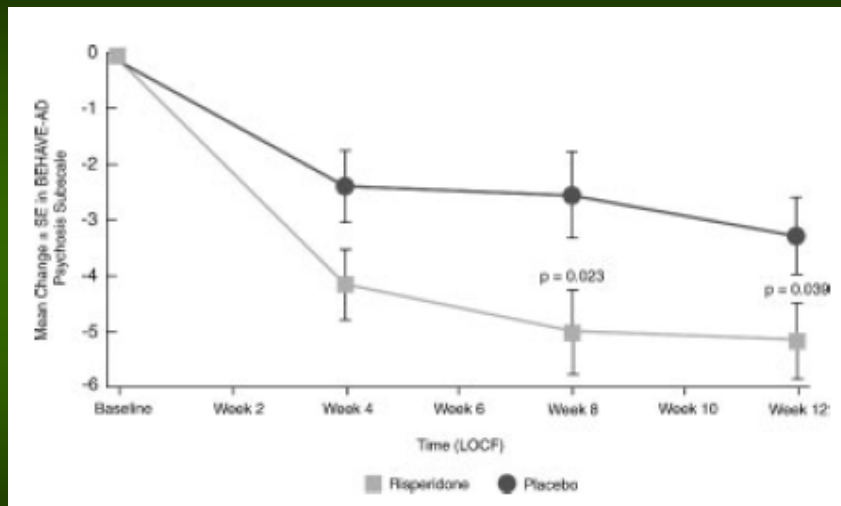
Behavioural and Psychological Symptoms of Dementia (BPSD) & Nursing Homes

BPSD in Sydney NHs

- >90% of NH residents exhibited ≥ 1 behavioural disturbance
- Psychosis = 60%, depressed mood = 42% & activity disturbances or aggression = 82%
- Rates higher if
 - NH larger; more residents in room
 - residents younger
 - residents more functionally impaired
 - chart diagnosis of psychosis

Brodsky, Draper, Low et al. (2001). Psychosis, depression & behavioural disturbances in Sydney nursing home residents: prevalence and predictors. *Int J of Ger Psych* 16(5): 504-512

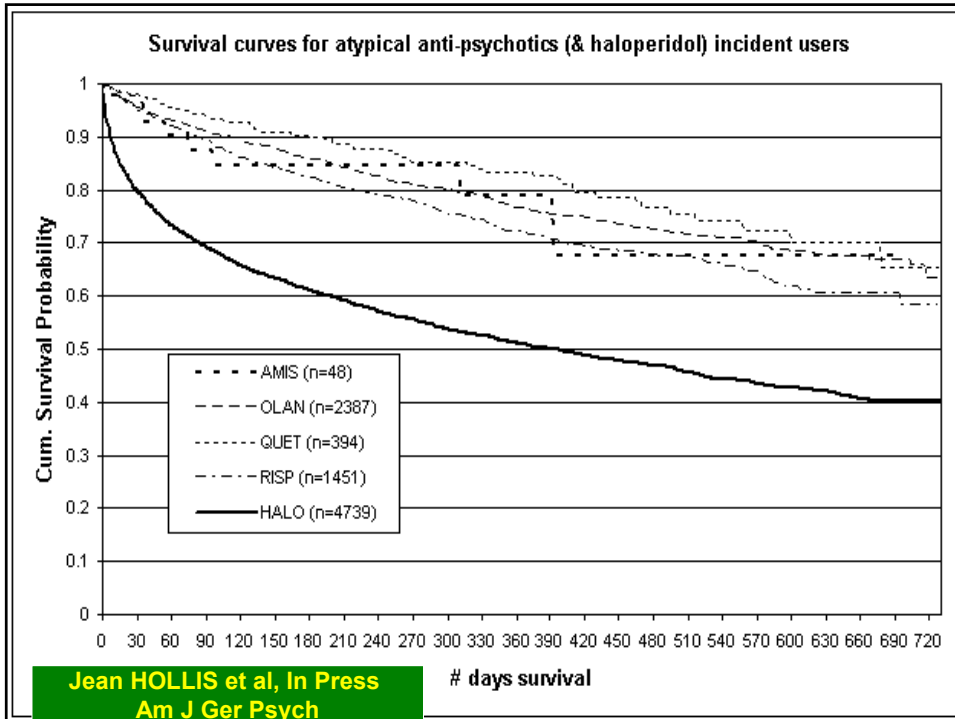
BPSD – risperidone trial



Brody H. et al. (2005). Risperidone for psychosis of Alzheimer's disease and mixed dementia: Results of a double-blind, placebo-controlled trial. *International Journal of Geriatric Psychiatry*. 20(12); 1153-1157

Risks of antipsychotics

- Australian RIS trial 1st to report increased risk of stroke with antipsychotics
- Many studies since demonstrated increased risk of stroke and of death
- Risk of death appears higher with typical antipsychotics



High Rates of Psychotropic Use in NHs

- 47.2% \geq 1 psychotropic drug regularly¹
- Compared to 1988, \downarrow hypnotics (11.3%) & anxiolytics (4.1%), but \uparrow antidepressants (20.5%)¹
- Psychotropics = 51.5%²
- Multiple psychotropics = 22.7%²
- Antidepressants = 19.8%²

¹Snowdon J. et al. (2006); ²Draper B. et al. (2001)

Dementia Care Mapping



Professor
Lynn Chenoweth

- Prospective RCT comparing
 - DCM
 - Person-centred care (PCC)
 - Usual care (UC)
- Primary outcome = CMAI
- PCC > DCM > UC

Clinical research

Kaarin Anstey: Cognition and falls

- MMSE & verbal reasoning at baseline predicted rate of falling over 8 yrs
- ↓ verbal ability, processing speed, & immediate memory associated with increases in risk & rates of falling



Anstey KJ et al (2006) An 8-year prospective study of the relationship between cognitive performance and falling in very old adults. *JAGS*. 54(8):1169-1176

PRIME

- Prospective naturalistic study
- Data base of patients attending 8 memory clinics around Australia (Ames, Boundy, Brodaty, Clarnette, Davies, Woodward, Kurrle, Mander)
- Target = 1000 patients with longitudinal data over 2 years
- Sponsored by Janssen but drug prescribing remains independent
- Participating clinicians can request analysis of data for research thro' SAC

Legal aspects

- **Darzins P, Strang D, Molloy W**
 - **Who Can Decide?: The Six Step Capacity Assessment Process**
- **Peisah C**
 - **Description of family disputes in cases coming before guardianship tribunal**
 - **Competency to marry**

Economic/ Social

- **Access Economics report 2003**
- **Access Economics report 2006 for Asia-Pacific**
- **Alzheimer Australia Prevention of AD strategy “Mind your mind”**

Research only in Australia

- EACH, EACH-D, CACPs
- CALD
- Indigenous people
- Nursing Homes



Research gaps

- Culturally and Linguistically Diverse (CALD)
- Aboriginal people with dementia
 - KICA
 - Broe T (in progress)
 - Abbey J (in progress)
- Developmental disability
- Young onset dementia
- PWD in rural and remote communities

CALD in Australia

Most common non-English languages are:

- Italian
- Greek
- Cantonese
- Arabic
- Vietnamese
- Mandarin

CALD in Australia

- 15% speak a language other than English
- Australians speak over 200 languages (including > 45 Indigenous languages)



Indigenous Australians and Dementia

- Aboriginal and Torres Strait Island people = 2.4% of Australian population¹
- Poorer quality of health than non-indigenous Australians¹
- Reduced life expectancy (~ 20 years)¹
- 50 yrs+ used to plan health care for elderly indigenous Australians

¹Health & Ageing Factbook 2006

Indigenous Australians and Dementia

- 10% of 65yr+ diagnosed with dementia¹
- Cerebrovascular disease and alcohol abuse are major contributors¹



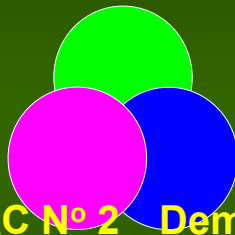
¹Henderson & Jorm (1998)



Dementia Collaborative Research Centres



Assessment and Better Care Outcomes Primary Dementia CRC



Dementia CRC N° 2

Dementia CRC N° 3

Prevention, Risk Reduction and Early Detection

Consumers, Carers and Social Research

CRCs

- UNSW
 - U Syd
 - U Newcastle
 - UTS
 - AIHW
 - Hammond
 - Monash
 - Melb U
 - **Alz Australia**
- ANU
 - U Canberra
 - Melb U
 - Edith Cowan Uni
 - U Qld
 - Alz Australia (Vic)**
- QUT
 - Hammond
 - Latrobe
 - Griffith
 - Alz Australia**

An Australian Government Initiative

DCRC
Dementia Collaborative
Research Centres

Sydney, Australia | 17-18 September, 2007

First National Dementia Research Forum

Translating Research into Practice

Australian Government Dementia: A Health Priority Initiative

Auguste D in 2106??

- How will she be treated in 100 years time
- National Framework and policies ✓
- World leader in community care
- Research improving



MAURER K, ... AMES D et al. (2006) Has treatment for Alzheimer's disease changed over the last 100 years? [Lancet](#), 368: 1619-1621.

Funding Opportunities

- NHMRC, ARC
- Alzheimer's Australia
- Pfizer Neuroscience Grants
- Rebecca Cooper Foundation
- Gerontology
- CRCs



Auguste D in 2106??

- Australia punching above weight but...
- Still behind compared to other conditions & countries
- Research is
 - Academics
 - Government
 - \$\$ - NGOs, Philanthropy
 - You
 - Exciting



Help plant the seeds of dementia research and care for the next 100 years

- **THANKS** to Louisa Gibson and Lee-Fay Low
- **CRC** www.dementia.unsw.edu.au
- **Dept Old Age Psychiatry, UNSW and POWH**
[//adfoap.med.unsw.edu.au](http://adfoap.med.unsw.edu.au)
- **Alzheimer's Australia**
www.alzheimers.org.au
- **Alzheimer's Disease International**
www.alz.co.uk