NARI
NATIONAL AGEING RESEARCH INSTITUTE LTD
Bringing research to life

POSTERA CRESCAM LAUDE
THE UNIVERSITY OF MELBOURNE

Emeritus Professor David Ames

AO BA MD BS FRCPsych FRANZCP

UoM Academic Unit for Psychiatry of Old Age

National Ageing Research Institute, Howard Florey Research Institute, St George's Hospital, and Epworth Camberwell
dames@unimelb.edu.au

Dementia and Alzheimer's disease – a psychiatrist's view

We heard a rumour that Ralph Fiennes might be on the flight

Conflict of interest declaration

- I have received honoraria for talks/consultancies, assistance with conference attendance, and/or financial support of research from Astra-Zeneca, Eisai, Eli Lilly, Forrest, GSK, Janssen-Cilag, Lundbeck, Novartis, Pfizer, Roche, Sandoz, Sanofi-Aventis, Servier, SmithKlineBeecham, Voyager, Wyeth **but not for 5 years** (darn it)
- Investigator on numerous AD drug trials - currently PI for Florey site for Eli Lilly Amaranth study.
- Former Editor-in-Chief *International Psychogeriatrics* 2003-11
- Member International Psychogeriatric Association, Geelong Football Club, 3 Wagner societies, der Förderverein der Osterfestspiele Salzburg, Glyndebourne Festival Society, Medical Advisory Panel of ADI and former (unpaid) medical advisor to Alzheimer’s Australia

William Beattie Smith
1853 – 1921

- Born Walker, Northumberland, England, son of a surgeon. Educated Campsie House School, Musselburgh, Scotland, and University of Edinburgh. Licentiate RCP, Edinburgh (1876), and licentiate (1876) and fellow (1879) RCS, Edinburgh,studied mental diseases under Thomas Smith Clouston, the outstanding teacher of his day. Practised Stockton-upon-Tees. 1881 he visited Australia and was appointed RMO Ararat Lunatic Asylum, then promoted to deputy medical superintendent at Yarra Bend Lunatic Asylum. In 1888 returned as medical superintendent to Ararat and developed a small wine-growing industry. In 1899 he became superintendent at the Kew Lunatic Asylum. Encouraged better conditions and treatment for patients.

- He recommended in 1887 a systematic plan of nurse teaching and insisted that attendants have uniforms. Concerned at the lack of knowledge of mental diseases among GPs, he began instruction for medical students at Kew in 1899; attendance was compulsory but there was no exam.
- He was forthright, autocratic disciplinarian who never feared to accept responsibility or to force innovations. He took offence easily, was impatient with his superiors and colleagues and caustic in his communication. In 1900 he came into conflict with the government pathologist and resigned 1902 after a disagreement with the chief secretary. He went into private practice as Melbourne's first full-time alienist. He continued to lecture to Medical Students until 1907 and to serve on a committee to advise the chief secretary, which played a part in the reform of the Lunacy Act in 1903 and 1914, when voluntary treatment was introduced sixteen years before England did so.
- Beattie Smith died, unmarried, of arteriosclerotic heart disease at his East Melbourne home on 12 December 1921, and is buried in Brighton cemetery. He left £1000 to the University of Melbourne for an annual lecture on insanity, to be named after him. By 1994 the sum had grown to $6500. The lecture has been held since 1925.

- William Beattie Smith bequeathed "to the University of Melbourne £1000" and directed “that the annual interest on same be used to establish ‘a few’ annual lectures on the early treatment of insanity as I consider the practitioner and the public are in need of much education in regard to this subject."
- The income is devoted to the provision in each year of a few lectures on the early treatment of mental illness having regard to causation, pathology, symptoms, diagnosis, prognosis, therapeusis, control and prevention or any of these. Such lectures may be directed in any year wholly or in part specially to medical practitioners or specially to the public.
- 1925-2017 -114 lectures by 83 lecturers including my mentors Herbert Bower, Brian Davies, Anthony Mann and Ed Chiu and on topics relating to Old age psychiatry or dementia 2 lectures by Herbert Bower 1963 (Sociological and Psychiatric Aspects of Old Age in Western Society), and one each by Ross Anderson 1987 (the Choroid Plexus and Dementia), Ed Chiu 2002 (Silly Old Buggers: Ageing Mental Health and Society) and Henry Brodaty 2007 (the Rise and Surprise of Old Age Psychiatry)

SENILE DEMENTIA? - ISN'T THAT WHEN ELDERLY CLIENTS DISAGREE WITH YOU ABOUT WHAT'S BEST FOR THEM?

What is dementia?

An acquired decline in higher mental function occurring in an alert patient, due to organic brain disease, producing decline in multiple higher mental functions (memory, intellect, personality) which results in significant impairment in social or occupational functioning.

Most dementia is irreversible and progressive.

Prevalence doubles every 5 years from ages 60 to 90

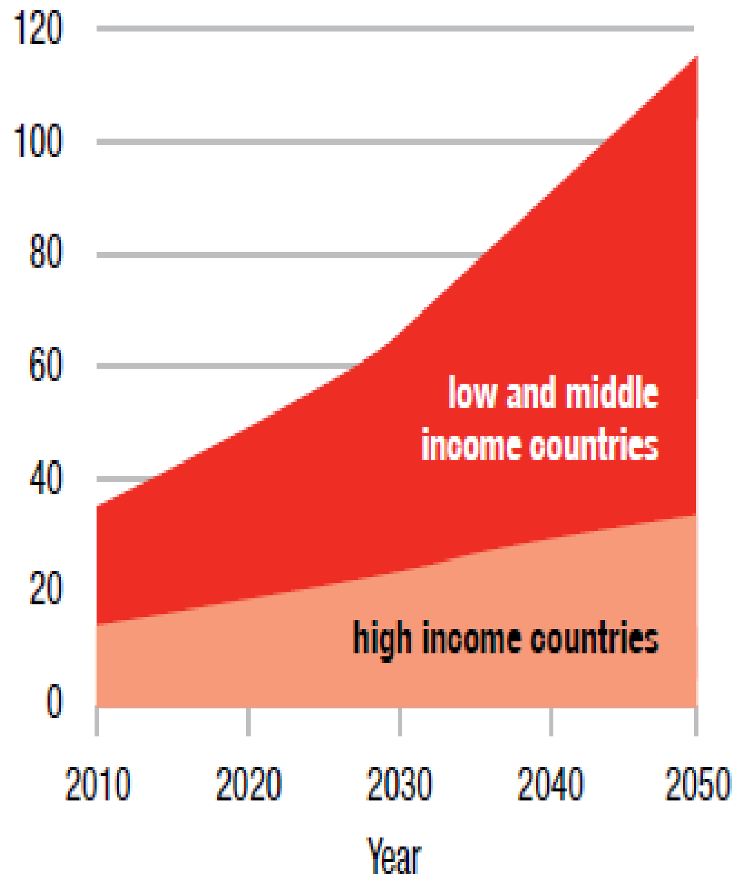
7 or 8 out of 10 die without dementia

Now Major Neurocognitive Disorder USA DSM5

OLD MOTHER HUBBARD
WENT TO THE CUPBOARD...

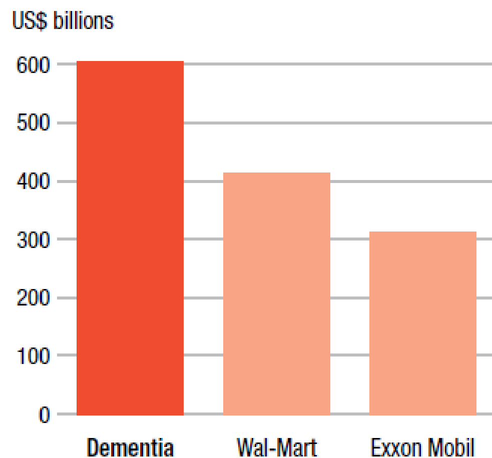
Geoff Thompson

Growth of numbers of people with dementia



- **The World Alzheimer Report (2009) estimated:**
  - **35.6 million people living with dementia worldwide in 2010**
  - **Increasing to 65.7 million by 2030**
  - **115.4 million by 2050**

Worldwide cost of dementia



- The societal cost of dementia is enormous.
- Dementia affects every health and social care system in the world.
- The economic impact on families is insufficiently appreciated.
- The total estimated worldwide costs of dementia were US$604 billion in 2010.
- These costs were around 1% of the world's GDP

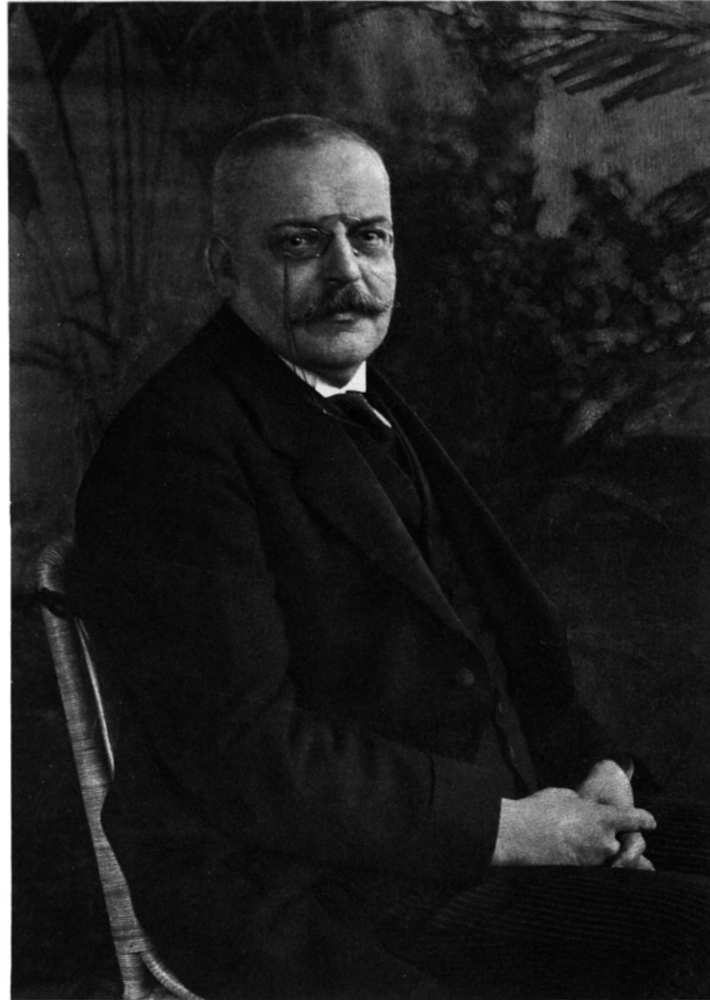
  0.24% in low income

  1.24% in high income

Mild Cognitive Impairment MCI

- Historically concept evolved since 1962 through benign senescent forgetfulness, age associated memory impairment, CIND etc
- 1.5 SD below the age & education adjusted mean on at least one neuropsychological test
- Complaint of memory impairment
- Substantially intact ADL & not demented
- Intermediate state between healthy cognition and dementia
- In clinic based studies 10-20% annual rate of AD dementia development
- One third never progress to develop dementia

Alois Alzheimer (1864-1915)



Verlag von Julius Springer, Berlin. Hel. Meisenbach Riffarth & Co. Berlin.

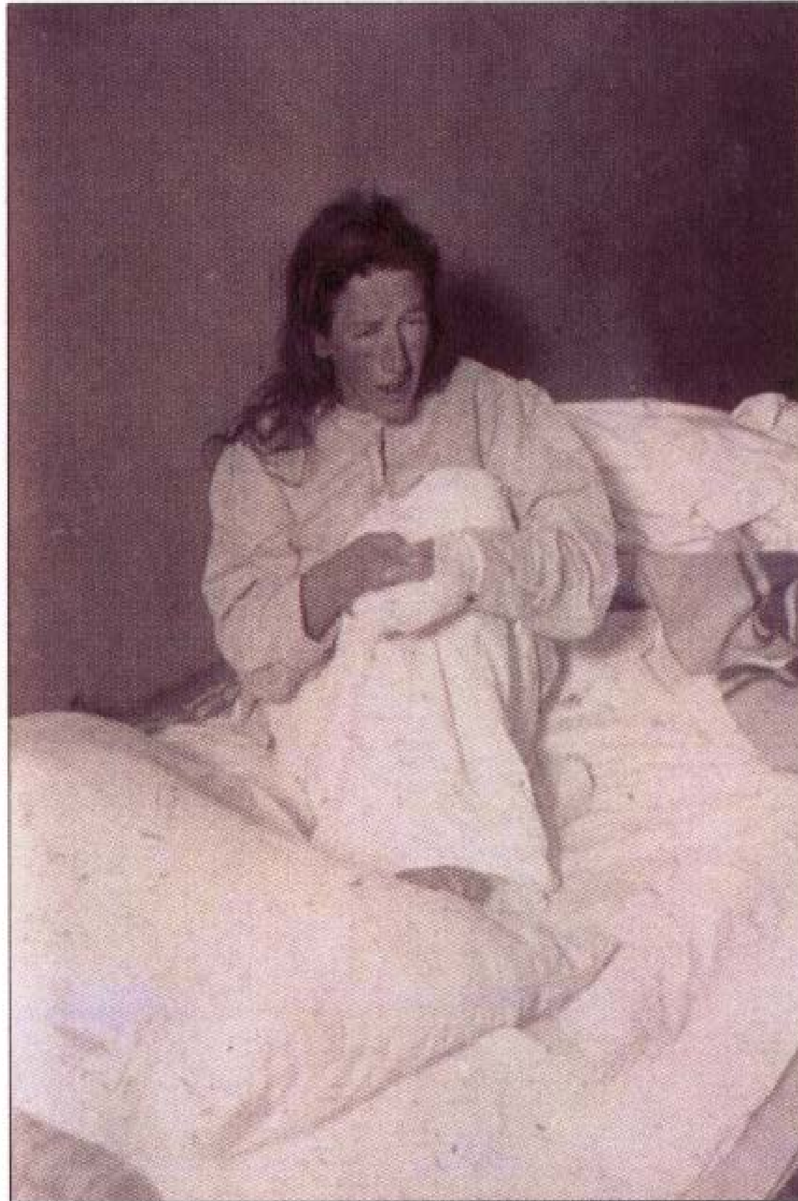
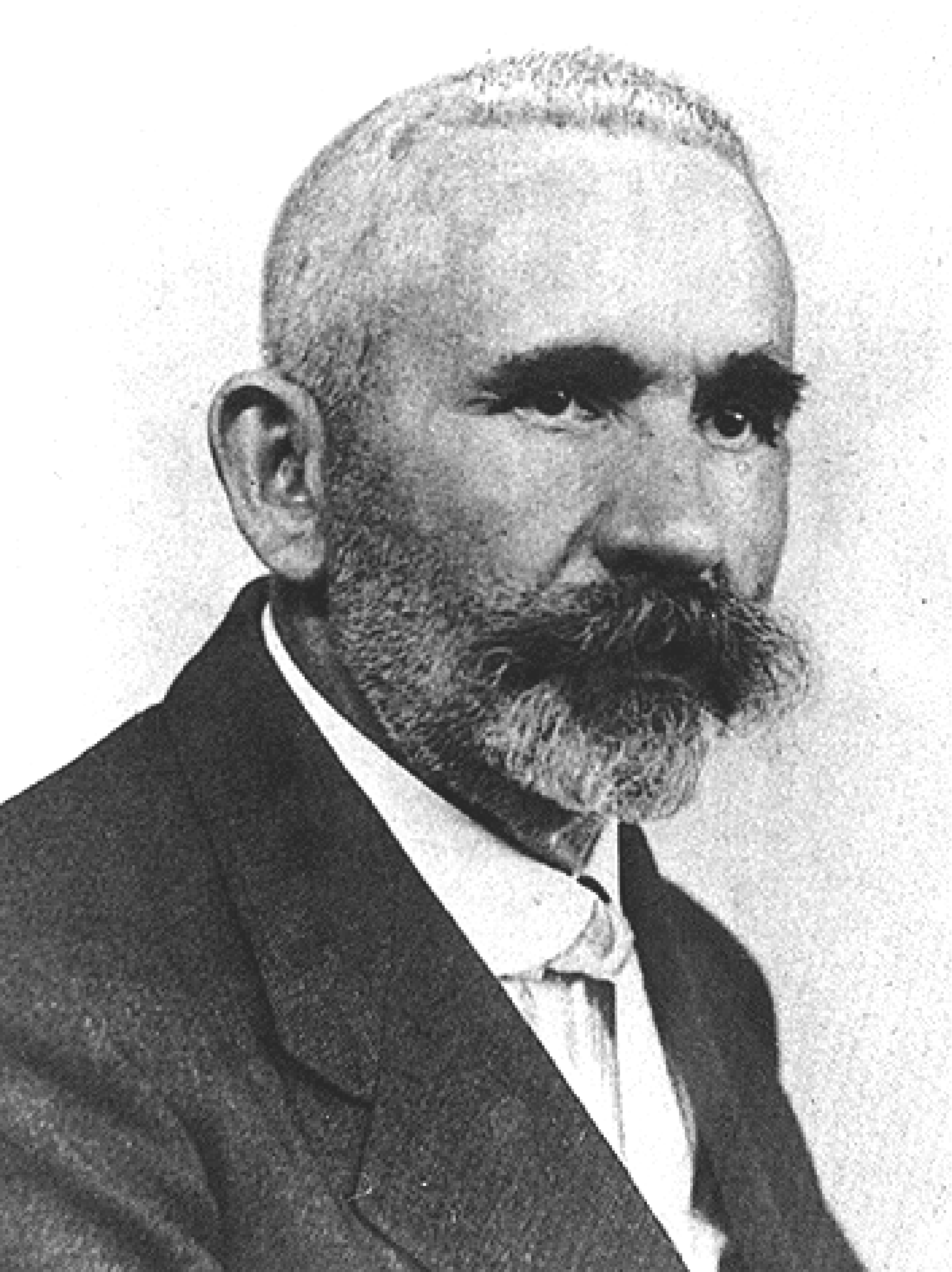


Figure: Auguste D, June 18, 1902 at asylum for the insane and epileptics in Frankfurt on Main

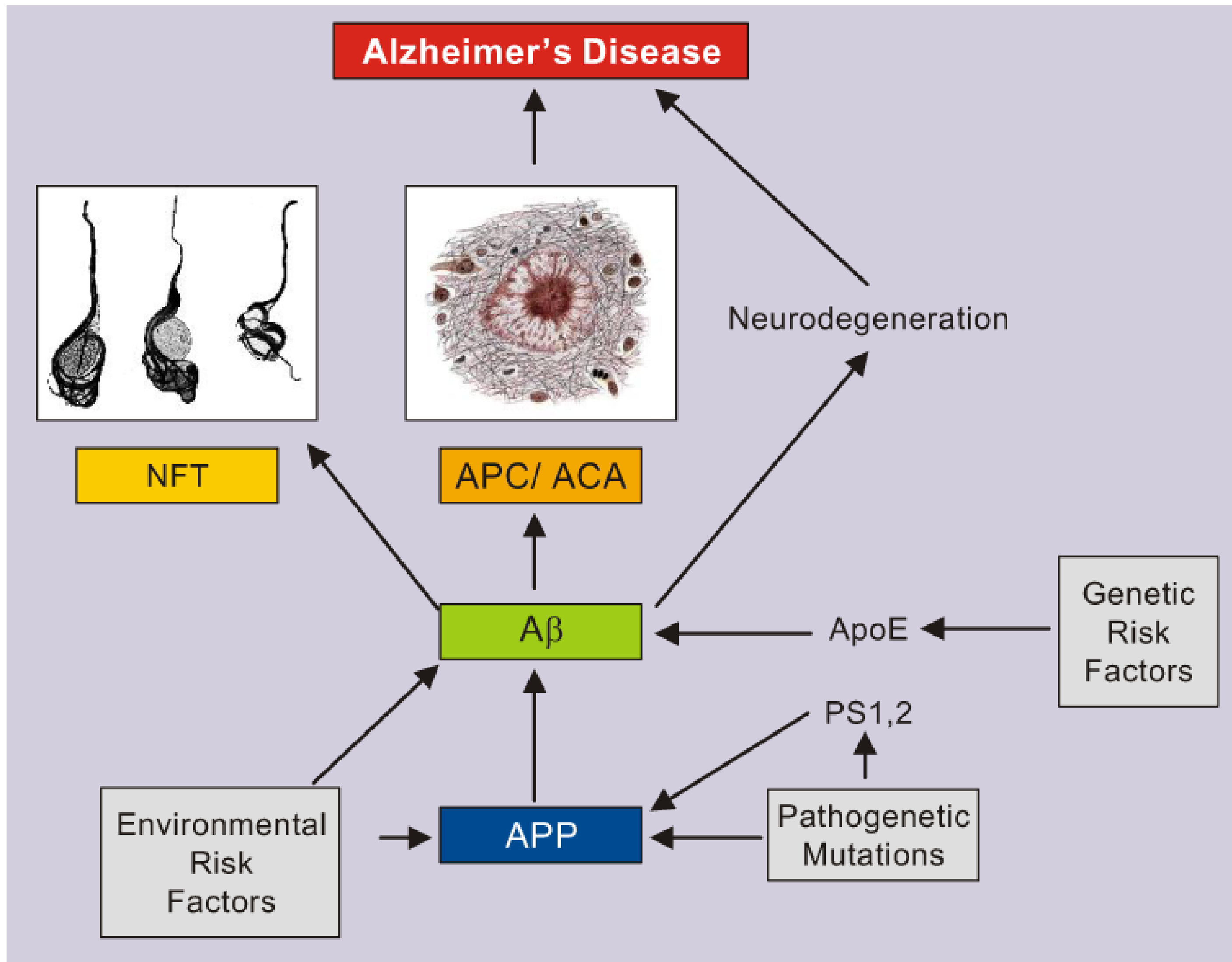


Emil Kraepelin

Alzheimer's disease

- Causes or contributes to 50-80% of all dementias
- Characterised by insidious onset and slow steady progression of deficits – 30 year incubation
- Initially new learning is affected, later praxis, language and some frontal functions will deteriorate
- Pathological hallmarks are plaques (amyloid) between cells and tangles (tau) within neurons
- Appears related to breakdown of amyloid precursor protein leading to amyloid production
- Main risk factors are unmodifiable – age, family history, APOE ε4, female sex, but potentially modifiable may include head injury and vascular risk factors – maybe depression and hearing impairment too
- No perfect diagnostic test (even amyloid imaging imperfect); clinical diagnosis correlates 80-90% with autopsy findings in experienced hands
- Typical course 7-10 years from onset of dementia to death

The amyloidocentric theory of Alzheimer's disease

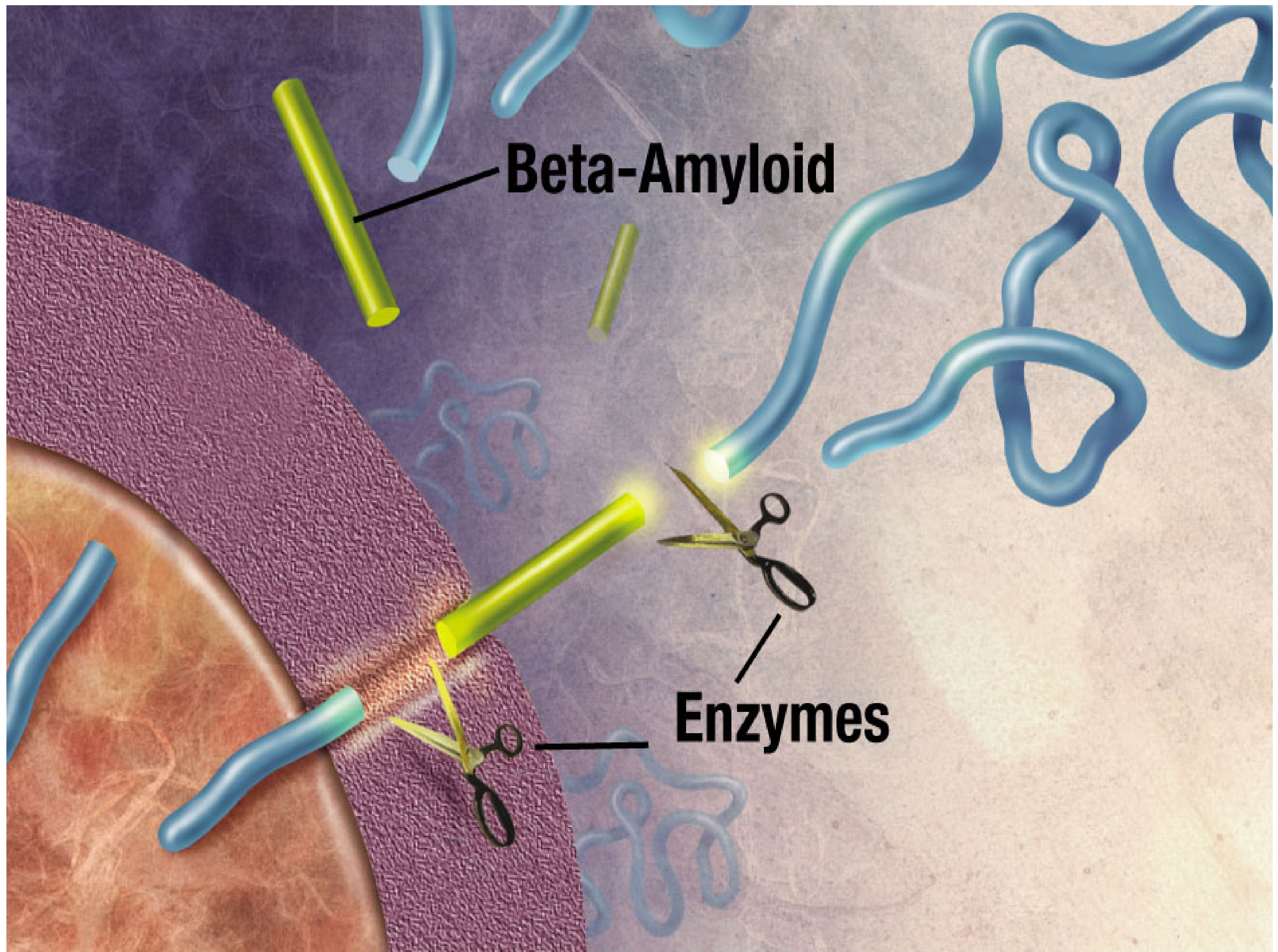


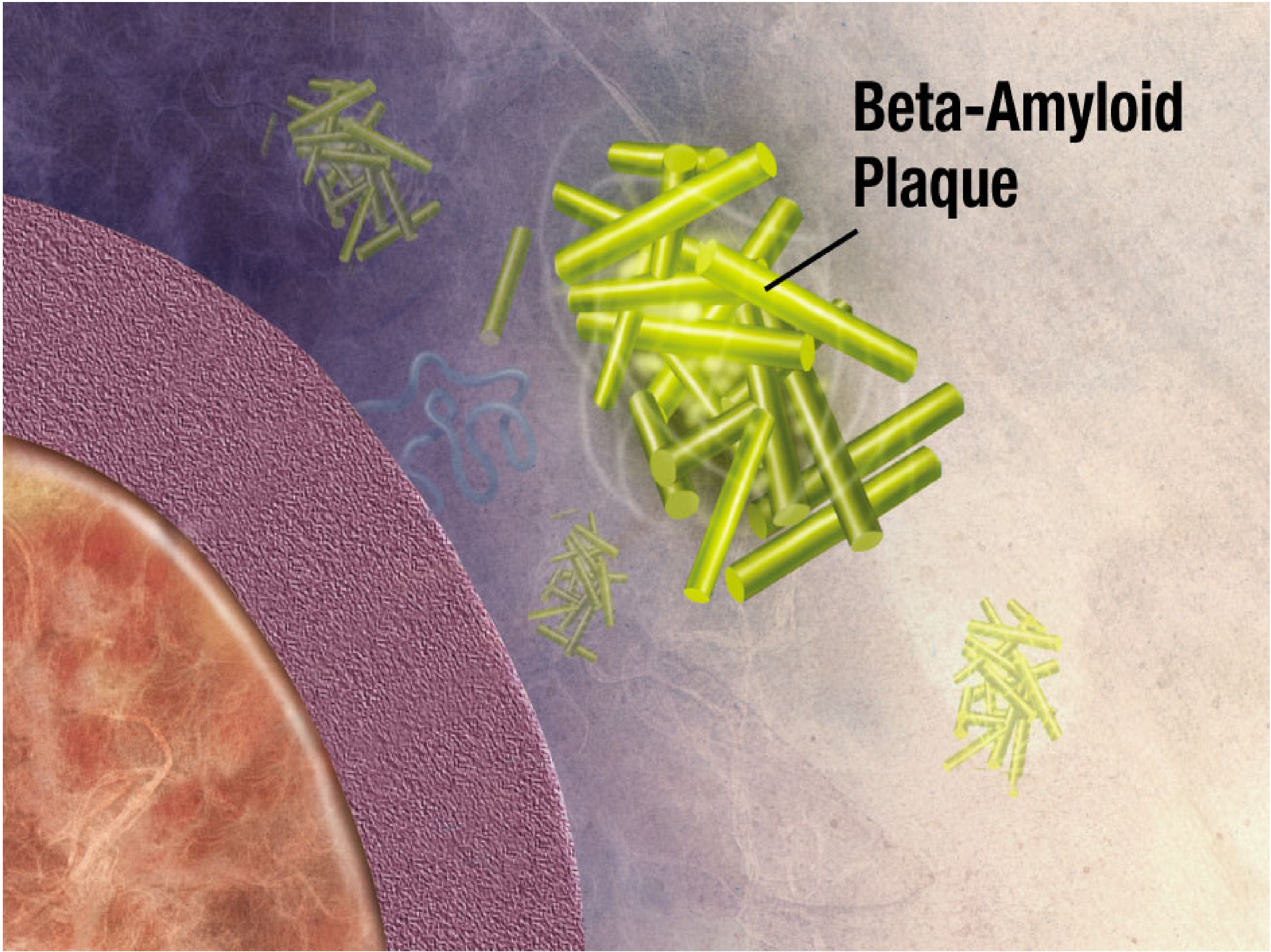
Amyloid Plaque Formation

Cell Membrane

APP Molecule

Cell Interior


Beta-Amyloid
Enzymes


Beta-Amyloid
Plaque

Compelling evidence for the Aβ theory of AD

- Aβ is the major macromolecule in the AD plaque
- Mutations in APP and gamma-secretase (PS1, PS2) cause AD
- Correlations of AD with PiB-PET and CSF A $beta_{42}$ (🡇)
- Pathologic lesions of AD occur in Down's Syndrome (APP triplication)
- Zn / Cu interactions with A beta explain the selective topography of AD in the excitatory glutamatergic system
- ApoE polymorphism – the only major genetic risk factor - may act through Aβ clearance pathway
- Preliminary evidence of 1-2% loss of clearance capacity of Aβ in sporadic AD (Bateman)
- Preliminary evidence that therapeutic targeting of Aβ is effective (e.g. aducanumab)
- **Alternate theories not developed**

Creation of academic posts in Old Age Psychiatry 1989-1990 – Chiu, Ames, O'Connor

- So what have we been doing about it since then?

- Services including Memory Clinic
- Assessment instruments
- Treatment studies
- Carers
- BPSD/Neuropsychiatric symptoms
- Biomarkers including imaging and genetics
- AIBL study
- Diet and Lifestyle
- Lancet Dementia Commission
- Education and training
- The future

Research on Services

AMES D, FLYNN E & HARRIGAN S. (1994) Prevalence of psychiatric disorders among inpatients of an acute geriatric hospital. Australian Journal on Ageing, 13: 8-11.

•

AMES D & TUCKWELL V. (1994) Psychiatric disorders among elderly patients in an acute general hospital. Medical Journal of Australia, 160: 671-675.

•

SNOWDON J, **AMES D**, CHIU E & WATTIS J. (1995) A survey of psychiatric services for elderly people in Australia. Australian and New Zealand Journal of Psychiatry, 29: 207-214.

•

MOSS F, WILSON B, HARRIGAN S & **AMES D**. (1995) Psychiatric diagnoses, outcomes and lengths of stay of patients admitted to an acute psychogeriatric unit. International Journal of Geriatric Psychiatry, 10: 849-854.

•

LOGIUDICE D, WALTROWICZ W, McKENZIE S, **AMES D** & FLICKER L. (1995) Prevalence of dementia among patients referred to an aged care assessment team and associated stress in their carers. Australian Journal of Public Health, 19: 275-280.

•

LOGIUDICE D, WALTROWICZ W, MCKENZIE S, **AMES D**, BURROWS C, BROWN K & FLICKER L. (1997) Health care costs of people referred to an aged care assessment team: the effect of cognitive impairment. Australian and New Zealand Journal of Public Health, 21: 311-316.

Dementia in the General Hospital

- **Psychiatric disorders among elderly patients in a general hospital.** Ames D, Tuckwell V.
- Of 495 enrolled patients, 204 were aged over 65 years; 167 could be interviewed; 18% showed evidence of organic mental impairment, 27% were depressed and 2% had other psychiatric disorders. Some mental state findings were recorded on admission for only 25% of patients, 52% of patients were prescribed hypnotic or psychotropic drugs and 30% of the psychiatric disorders identified by the survey were mentioned in the discharge summary.

- Screening for psychiatric disorders in this setting was not routine. The frequency of such disorders makes it desirable to conduct prospective evaluation of the use of brief cognitive and depression screening instruments on admission to hospital.

- March 1988 Melbourne’s first Memory Clinic founded by Leon Flicker & David Ames, support from NARI and UoM Dept Psychiatry
- First 100 patients - mean age 75.5 years and 75 were women: 74 met DSM-IIIR criteria for dementia and a further 13 had other organic brain syndromes.
- Of the next 577 patients seen mean age was 72.9 years and 60.8% were female. Over 40% fulfilled ICD-10 diagnostic criteria for dementia in Alzheimer's disease. A further 24% had another dementing illness.
- Clinic formed model for statewide CADMS clinics introduced in 1998

Memory Clinics

AMES D, FLICKER L & HELME R. (1992) A memory clinic at a geriatric hospital: rationale, routine and review of the first 100 patients. Medical Journal of Australia, 156: 618-622.

•

LOGIUDICE D, WALTROWICZ W, BROWN K, BURROWS C, **AMES D** & FLICKER L. (1999) Do memory clinics improve the quality of life of carers? A randomised pilot trial. International Journal of Geriatric Psychiatry, 14: 626-632.

•

LOGIUDICE D, HASSETT A, COOK R, FLICKER L & **AMES D**. (2001) Equity of access to a memory clinic in Melbourne? Non-English speaking background attendees are more severely demented and have increased rates of psychiatric disorders. International Journal of Geriatric Psychiatry, 16: 327-334.

•

STRATFORD JA, LOGIUDICE D, FLICKER L, COOK R, WALTROWICZ W & **AMES D**. (2003) A memory clinic at a geriatric hospital: a report on 577 patients assessed with the CAMDEX over 9 years. Australian & New Zealand Journal of Psychiatry, 37: 319-326. *

•

BRODATY H, WOODWARD M, BOUNDY K, **AMES D** & BALSHAW R, on behalf of the PRIME study group. (2011) Patients in Australian memory clinics: baseline characteristics and predictors of decline at 6 months. International Psychogeriatrics, 23: 1086-1096 doi: 10.1017/S1041610211000652 .

MASTWYK M, **AMES D**, ELLIS KA, CHIU E & DOW B. (2014) Disclosing a dementia diagnosis: what do patients and family consider important? International Psychogeriatrics, 26: 1263-1272. doi: 10.1017/S1041610214000751.

•

MASTWYK M, DOW B, ELLIS K & **AMES D.** (2016) Why attend a memory clinic? What do patients and their families want and/or expect? Australasian Journal on Ageing, 35: 220-224. doi:10.1111/ajag.12257

•

CROSS AJ, JOHNSON G, WOODWARD M, **AMES D**, BRODATY H, ILOMÄKI J & ELLIOTT RA, (2016) Potentially inappropriate medications and anticholinergic burden in older people attending a memory clinic. Drugs and Ageing, 33: 37-44. doi: 10.1007/s40266-015-0332-3.

•

CONNORS MH, **AMES D**, BOUNDY K, CLARNETTE R, KURRLE S, MANDER A, WARD J, WOODWARD M & BRODATY H (2016) Mortality in Mild Cognitive Impairment: a longitudinal study in memory clinics. Journal of Alzheimer's Disease, 54: 149-155. doi: 10.3233/JAD-160148.

•

CROSS AJ, GEORGE J, WOODWARD MC, **AMES D**, BRODATY H & ELLIOTT RA. (2017) Dietary supplement use in older people attending memory clinics in Australia. Journal of Nutrition, Health and Aging, 21: 46-50. doi: 10.1007/s12603-016-0742-x.

•

CONNORS M, **AMES D,** WOODWARD M & BRODATY H. (2017) Mild Cognitive Impairment and driving cessation: a three year longitudinal study. Dementia and Geriatric Cognitive Disorders, 44: 63-70. doi: 10.1159/000478740.

•

CROSS AJ, JOHNSON G, WOODWARD MC, **AMES D**, BRODATY H, WOLFE R, CONNORS MH & ELLIOTT RA. (2017) Potentially inappropriate medication, anticholinergic burden and mortality in people attending memory clinics. Journal of Alzheimer's Disease, 60: 349-358. doi: 10.3233/JAD-170265.

•

An Australian Government Initiative

StV

Helping Australians with dementia,
and their carers

Assessment Instruments

1. **AMES D**, ASHBY D, FLICKER L, SNOWDON J, WEST C & WEYERER S. (1992) Jim who? Recall of national leaders by elderly people in three countries. International Journal of Geriatric Psychiatry, 7: 437-442.
2. **AMES D**, FLYNN E, TUCKWELL V & HARRIGAN S. (1994) Diagnosis of psychiatric disorder in elderly general and geriatric hospital patients: AGECAT & DSMIIIR compared. International Journal of Geriatric Psychiatry, 9: 627-633.
3. O'CONNOR DW, BLESSED G, COOPER B, JONKER C, MORRIS JC, PRESNELL IB, **AMES D**, KAY DW, BICKEL H, SCHAUFELE M, WIND A, COATS M & BERG L. (1996) Cross-national interrater reliability of dementia diagnosis and factors associated with disagreement. Neurology, 47: 1194-1199.
4. FLICKER L, LOGIUDICE D, CARLIN J & **AMES D**. (1997) The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry, 12: 203-209.
5. SHAH A, CHIU E & **AMES D**. (1997) The relationship between two scales measuring aggressive behaviour among elderly nursing home residents. International Journal of Geriatric Psychiatry, 12: 628-631.
6. KNAFELC R, LOGUIDICE D, HARRIGAN S, COOK R, FLICKER L, MACKINNON A & **AMES D.** (2003) The combination of cognitive testing and an informant questionnaire in screening for dementia. Age and Ageing, 32: 541-547.
7. GERMANO C, KINSELLA G, STOREY E, ONG B & **AMES D.** (2008) The episodic buffer and learning in early Alzheimer's disease. Journal of Clinical and Experimental Neuropsychology, 30: 627-638. LOWNDES G, SALING M, **AMES D,** CHIU E, GONZALEZ L & SAVAGE G. (2008) Recall and recognition of verbal paired associates in healthy aging. Journal of the International Neuropsychological Society, 14: 591-600.
8. LOWNDES G, SALING M, **AMES D**, CHIU E, GONZALEZ L & SAVAGE G. (2008) Recall and recognition measures of paired associate learning in healthy aging. Aging, Neuropsychology and Cognition, 15: 506-522.
9. WOODWARD M, BRODATY H, BOUNDY K, **AMES D,** BLANCH G, BALSHAW R ON BEHALF OF THE PRIME STUDY GROUP. (2010) Does executive impairment define a frontal variant of Alzheimer's disease? International Psychogeriatrics, 22: 1280-1290. doi: 10.1017/S1041610210001596.
10. McBRIDE,S, GOOD N, SZOEKE C, **AMES D,** MARTINS R, MASTERS C, MARUFF P, ROWE C, SAVAGE G, ELLIS K, AND THE AIBL RESEARCH GROUP. (2011) A web-based normative data tool for assessing cognitive performance in healthy older Australians. Medical Journal of Australia, 194 (Suppl. 4): S12-S14.
11. PIKE KE, KINSELLA GJ, ONG B, MULLALY E, RAND E, STOREY E, **AMES D,** SALING M, CLARE L & PARSONS S. (2012). Names and numberplates: quasi-everyday associative memory tasks for distinguishing amnestic mild cognitive impairment from healthy ageing. Journal of Clinical and Experimental Neuropsychology, 43: 269-278.
12. DELPRADO J, KINSELLA G, ONG B, PIKE K, **AMES D**, STOREY E, SALING M, CLARE L, MULALLY E & RAND E. (2012) Clinical measures of prospective memory in amnestic mild cognitive impairment. Journal of the International Neuropsychological Society, 18: 295-304. doi.org/10.1080/13803395.2011.633498
13. LIM YY, ELLIS K, HARRINGTON K, **AMES D**, MARTINS R, MASTERS C, ROWE C, SZOEKE C, DARBY D, & MARUFF P. (2012) Use of the COGSTATE brief battery in the assessment of Alzheimer's disease related cognitive impairment in the Australian Imaging, Biomarkers and Lifestyle (AIBL) study. Journal of Clinical and Experimental Neuropsychology, 34: 345-358. doi: 10.1080/13803395.2011.643227.
14. LIM YY, HARRINGTON K, **AMES D**, ELLIS KA, LACHOVITSZKI R, SNYDER P & MARUFF P. (2012) Short term stability of verbal memory impairment in mild cognitive impairment and Alzheimer's disease measured using the International Shopping List Test. Journal of Clinical and Experimental Neuropsychology, 34: 853-863. doi: 10.1080/13803395.2012.689815.
15. PIKE KE, KINSELLA GJ, ONG B, MULLALY E, RAND E, STOREY E, **AMES D,** SALING M, CLARE L & PARSONS S. (2013) Is the WMS-IV verbal paired associates as effective as other memory tasks in discriminating mild cognitive impairment from normal aging? The Clinical Neuropsychologist, 27: 908-923. doi: 10:1080/13854046.2013.809149.
16. MARUFF P, LIM YY, DARBY D, ELLIS KA, PIETRZAK RH, SNYDER PJ, BUSH AI, SZOEKE C, SCHEMBRI A, **AMES D**, & MASTERS CL. (2013) Clinical utility of the Cogstate brief battery in identifying cognitive impairment in mild cognitive impairment and Alzheimer's disease. BMC Pharmacology and Toxicology, 1: 30.
17. LIM YY, VILLEMAGNE V, LAWS S, PIETRZAK R, **AMES D**, FOWLER C, RAINEY-SMITH R, SNYDER P, BOURGEAT P, MARTINS RN, SALVADO O, ROWE CC, MASTERS CL & MARUFF P on behalf of the AIBL research group. (2016) Performance on the Cogstate Brief Battery is related to amyloid levels and hippocampal volume in very mild dementia. Journal of Molecular Neuroscience, 60: 362-370. doi: 10.1007/s12031-016-0822-8.
18. HARRINGTON K, LIM YY, **AMES D**, HASSENSTAB J, RAINEY-SMITH S, ROBERTSON J, SALVADO O, MASTERS CL, MARUFF P and the AIBL Research Group. (2017) Using robust normative data to investigate the neuropsychology of cognitive aging. Archives of Clinical Neuropsychology, 32: 142-154. doi: 10.1093/arclin/acw106. ***This paper won the 2017 Nelson Butters Award for Research Contributions to Clinical Neuropsychology, presented by the National Academy of Neuropsychology for the best paper of the year in the journal Archives of Clinical Neuropsychology. This was the second year in a row that these authors won the award.***
19. WEINBORN M, BUCKS RS, SOHRABI HR, RAINEY-SMITH SR, BROWN BM, GARDENER S, GOZT A, CHRISTENSEN D, SAVAGE G, LAWS S, TADDEI K, MARUFF P, ROBERTSON JS, ELLIS KA, **AMES D**, MASTERS CL, ROWE CC & MARTINS RN for the AIBL research group (2018) Trajectories of irregular word reading ability as a proxy for premorbid intelligence in Alzheimer's disease, Mild Cognitive Impairment and healthy aging: a longitudinal study. Psychological Assessment, in press, accepted 30/11/17.

•

Drug Treatment Studies

DAVIES B, ANDREWES D, STARGATT R, **AMES D**, TUCKWELL V & DAVIS S. (1990) Tetrahydroaminoacridine in Alzheimer's disease. International Journal of Geriatric Psychiatry, 5: 317-321.

AMES D, BHATHAL P, DAVIES B, FRASER J, GIBSON P & ROBERTS S. (1990) Heterogeneity of hepatic reactions to THA. Australian and New Zealand Journal of Medicine, 20: 193-195.

BALSON R, GIBSON P, **AMES D** & BHATHAL P (1995). Tacrine-induced hepatotoxicity: tolerability and management. CNS Drugs, 4: 168-181.

BURNS A, ROSSOR M, HECKER J, GAUTHIER S, PETIT H, MÖLLER H-J, ROGERS SL, FRIEDHOFF LT, and the **INTERNATIONAL DONEPEZIL STUDY GROUP+** (1999) The effects of donepezil in Alzheimer's disease – results from a multinational trial. Dementia and Geriatric Cognitive Disorders, 10: 237-244. +International Dementia Study Group includes **D. AMES**.

FELDMAN H, GAUTHIER S, HECKER J, VELLAS B, SUBBIAH P, WHALEN E AND **INTERNATIONAL DONEPEZIL STUDY GROUP+** (2001) A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease. Neurology, 57: 613-620. +International Dementia Study Group includes **D. AMES**.

BRODATY H, **AMES D,** BOUNDY L, HECKER J, SNOWDON, J, STOREY E & YATES M. (2001). Pharmacological treatment of cognitive deficits in Alzheimer's disease. Medical Journal of Australia, 175: 324-329.

GAUTHIER S, FELDMAN H, HECKER J, VELLA B., **AMES D**, SUBBIAH P & WHALEN E. (2002). Efficacy of Donepezil on behavioural symptoms in patients with moderate to severe Alzheimer's disease. International Psychogeriatrics, 14: 389-404.

BRODATY H, **AMES D,** SNOWDON J, WOODWARD, M, KIRWAN J, CLARNETTE R, LEE E, LYONS B & GROSSMAN F. (2003). A randomized placebo controlled trial of Risperidone for the treatment of agitation and psychosis of dementia. Journal of Clinical Psychiatry, 64: 134-143.

RITCHIE CW, BUSH AI, MACKINNON A, MACFARLANE S, MASTWYK M, MACGREGOR L, KIERS L, CHERNY R, LI Q, TAMMER A, CARRINGTON D, MAVROS C., VOLITAKIS I, XILINAS M, **AMES D**, DAVIS S, BEYREUTHER K, TANZI RE & MASTERS CL. (2003) Metal-protein attenuation with iodochlorhydroxyquin (Clioquinol) targeting Aß amyloid deposition and toxicity in Alzheimer's disease: a pilot Phase 2 clinical trial. Archives of Neurology, 60: 1685-1691.

RITCHIE CW, **AMES D**, CLAYTON T & LAI R. (2004) Meta-analysis of randomized trials of the efficacy and safety of donepezil, galantamine and rivastigmine for the treatment of Alzheimer's disease. American Journal of Geriatric Psychiatry, 12: 358-369.

AMES D, BALLARD R, CREAM J, SHAH A, SUH G-H & McKEITH I. (2005) For debate: should novel antipsychotics ever be used to treat the behavioral and psychological symptoms of dementia (BPSD)? International Psychogeriatrics, 17: 3-29. doi:10.1017/S104161020521102-X

BRODATY H, **AMES D**, SNOWDON, J, WOODWARD, M, KIRWAN J, CLARNETTE R, LEE E & GREENSPAN A. (2005) Risperidone for psychosis of AD: results of a double-blind, placebo controlled trial. International Journal of Geriatric Psychiatry, 20: 1153-1157.

BRODATY H, WOODWARD, M, BOUNDY K, BARNES N & ALLEN G, for the NATURE Investigators+ (2006) A naturalistic study of galantamine for Alzheimer's disease. CNS Drugs, 20: 935-943. +The NATURE Investigators includes **D. AMES**.

MAURER K, CUMMINGS J, McKEITH I, **AMES D** & BURNS A. (2006) Has treatment for Alzheimer's disease changed over the last 100 years? Lancet, 358: 1619-1621.

KATONA C, LIVINGSTON G, COOPER C, **AMES D**, BRODATY H & CHIU E on behalf of the Consensus Group (2007) Consensus Statement: International Psychogeriatric Association consensus statement on defining and measuring treatment benefits in dementia. International Psychogeriatrics, 19: 345-354. doi: 10.1017/S1041610207005145.

TILLER J, **AMES D,** BRODATY H, BYRNE G, CHAWLA S, HALLIDAY G, SNOWDON J, HEPWORTH G, McARDLE P & SCHWEITZER I. (2008) Antipsychotic use in the elderly: what doctors say they do, and what they do. Australasian Journal on Ageing, 27: 134-142.

LANNFELT L, BLENNOW K, ZETTERBERG H, BATSMAN S, **AMES D**, HARRISON J, MASTERS C, TARGUM S, BUSH A, MURDOCH R, WILSON J & RITCHIE C, on behalf of the PBT2-201-Euro study group. (2008) Safety, efficacy and biomarker findings of PBT2 in targeting Aβ as a modifying therapy for Alzheimer's disease: a phase IIa randomised, double-blind placebo controlled trial. Lancet Neurology, 7: 779-786. doi:10.1016/S1474-4422(08)70167-4

AMES D, KADUSZKIEWICZ H, VAN DEN BUSSCHE H, ZIMMERMANN T, BIRKS J & ASHBY D. (2008) For Debate: is the evidence for the efficacy of cholinesterase inhibitors in the symptomatic treatment of Alzheimer's disease convincing or not? International Psychogeriatrics, 20, 259-292. doi:10.1017/S1041610207006680

SZOEKE C, CAMPBELL S, LAUTENSCHLAGER N, YASTRUBETSKAYA O & **AMES D**. (2010) What's the future of treatment for Alzheimer's disease? Medicine Today, 11 (6): 18-32.

COOPER C, MUKADAM N, KATONA C, LYKETSOS CG, BLAZER D, **AMES D,** RABINS P, BRODATY H, DE MENDONÇA LIMA C & LIVINGSTON G. (2013) Systematic review of the effectiveness of pharmacological interventions to improve quality of life and wellbeing in people with dementia. American Journal of Geriatric Psychiatry, 21: 173-183. doi: 10.1097/JGP.0b013e31823e31a2.

•

Plus 2 Lazabemide studies, and studies of efficacy of Milameline, Rasagaline, Servier compound for MCI (poison), Xaliproden, Rosiglitazone, Memantine, Lilly Ɣsecretase inhibitor, Dimebon, Lundbeck compound and Amaranth β-secretaase inhibitor in AD/MCI.

Carers

WALTROWICZ W, **AMES D**, McKENZIE S & FLICKER L. (1996) Burden and stress on relatives (informal carers) of dementia sufferers in psychogeriatric nursing homes. Australian Journal on Ageing, 15: 115-118.

•

LOGIUDICE D, KERSE N, BROWN K, GIBSON SJ, BURROWS C, **AMES D**, YOUNG D & FLICKER L. (1998) The psychosocial health status of carers of persons with dementia: a comparison with the chronically ill. Quality of Life Research, 7: 345-351.

•

LOGIUDICE D, WALTROWICZ W, BROWN K, BURROWS C, **AMES D** & FLICKER L. (1999) Do memory clinics improve the quality of life of carers? A randomised pilot trial. International Journal of Geriatric Psychiatry, 14: 626-632.

•

MOORE K, OZANNE E, DOW B, & **AMES D**. (2013) How do family carers respond to the behavioral and psychological symptoms of dementia? International Psychogeriatrics, 25: 743-753. doi: 10.1017/S1041610213000070.

•

DOW B, MOORE K, RUSSELL M, **AMES D,** CYARTO E, HAINES T, HILL, LAUTENSCHLAGER NT, K, McKENZIE L, WILLIAMS S & LOI S. (2013) Improving mood through physical activity for carers and care recipients: protocol for a randomised trial (IMPACCT). Journal of Physiotherapy, 59: 125.

•

BRODATY H, WOODWARD M, BOUNDY K, **AMES D** & BALSHAW R. (2014) Prevalence and predictors of burden in caregivers of people with dementia. American Journal of Geriatric Psychiatry, 22: 756-765. doi: 10.1016/j.jagp.2015.05.004

•

LOI S, DOW B, MOORE K, HILL K, RUSSWLL M, CYARTO E, MALTA S, **AMES D** & LAUTENSCHLAGER N. (2015) Attitudes to aging in older carers – do they have a role in their wellbeing? International Psychogeriatrics, 27: 1893-1901. doi: 10.1017/1041610215000873

•

LOI S, DOW B, MOORE K, HILL K, RUSSELL M, CYARTO E, MALTA S, **AMES D** & LAUTENSCHLAGER NL. (2016) Factors associated with depression in older carers. International Journal of Geriatric Psychiatry, 34: 293-301. doi: 10.1002/gps.4323.

•

POZZEBON M, DOUGLAS J & **AMES, D.** (2016) Spouses' experience of living with a partner diagnosed with a dementia: a synthesis of the qualitative research. International Psychogeriatrics, 28: 537-556 doi: 10.1017/S1041610215002239.

•

POZZEBON M, DOUGLAS J & **AMES D**. (2016) "It was a terrible, terrible journey": an instrumental case study of a spouse's experience of living with a partner diagnosed with semantic variant primary progressive aphasia. Aphasiology, 31: 375-387. doi: 10.1080/02687038.2016.1230840

Behavioural and Psychiatric Symptoms of Dementia AKA Neuropsychiatric symptoms

MARTIN C, McKENZIE S & **AMES D**. (1994) Disturbed behaviour in dementia sufferers: a comparison of three nursing home settings. International Journal of Geriatric Psychiatry, 9: 393-398. *

- SHAH A, CHIU E & **AMES D**. (2000) Aggressive behaviour and environmental characteristics in Australian nursing homes. Aging and Mental Health, 4: 43-47.

- SHAH A, CHIU E, **AMES D**, HARRIGAN S & MCKENZIE D. (2000) The characteristics of aggressive subjects in Australian (Melbourne) nursing homes. International Psychogeriatrics, 12: 145-161.

- 10/66 Research Group (FERRI C, **AMES D,** PRINCE M. et al.) (2004) Behavioral and Psychological Symptoms of Dementia in developing countries. International Psychogeriatrics, 16: 441-459.

- O'CONNOR D, **AMES D**, GARDNER B & KING M. (2009) Psychosocial treatments of behaviour symptoms in dementia: a systematic review of reports meeting quality standards. International Psychogeriatrics, 21: 225-240. doi:10/1017/S1041610208007588.

- O'CONNOR D, **AMES D**, GARDNER B & KING M. (2009) Psychosocial treatments of psychological symptoms in dementia: a systematic review of reports meeting quality standards. International Psychogeriatrics, 21: 241-251. doi:10.1017/S1041610208008223.

- PIETRZAK R, SCOTT JC, NEUMEISTER A, LIM YY, MARUFF P, **AMES D**, ELLIS KA, HARRINGTON K, LAUTENSCHLAGER NT, SZOEKE C, MARTINS RN, MASTERS CL, VILLEMAGNE V & ROWE C for the AIBL RESEARCH GROUP. (2014) Anxiety symptoms moderate the effect of cerebral amyloid on memory decline in healthy older adults: a three year prospective cohort study. British Journal of Psychiatry, 204: 400-401.

- BRODATY H, CONNORS MH, XU J, WOODWARD M & **AMES D**, on behalf of the PRIME study group. (2015) The course of neuropsychiatric symptoms in dementia: a three year longitudinal study. Journal of the American Medical Directors' Association, 16: 380-387. doi: 10.1016/j.jamda.2014.12.018.

- PIETRZAK R, LIM YY, NEUMEISTER A, **AMES D**, ELLIS KA, HARRINGTON K, LAUTENSCHLAGER NT, RESTREPO C, MARTINS RN, MASTERS CL, VILLEMAGNE V, ROWE C & MARUFF P for the AIBL RESEARCH GROUP. (2015) Aβ, anxiety, and cognitive decline in preclinical Alzheimer's disease: anxiety symptoms moderate the effect of cerebral amyloid on memory decline in healthy multicentre, prospective cohort study. JAMA Psychiatry, 72: 284-291. doi: 10.1001/jamapsychiatry.2014.2476.

- HOLMES SE, ESTERLIS I, MAZURE CM, LIM YY, **AMES D**, RAINEY-SMITH S, MARTINS RN, SALVADO O, DORÉ V, VILLEMAGNE V, ROWE CC, LAWS S, MASTERS CL, MARUFF P, PIETRZAK RH & the AIBL RESEARCH GROUP (2017) β-amyloid, APOE and BDNF genotype, and depressive and anxiety symptoms in cognitively normal older women and men. American Journal of Geriatric Psychiatry, 24: 1191-1195.

HARRINGTON K, GOULD E, LIM YY, **AMES D**, PIETRZAK R, REMBACH A, RAINEY-SMITH S, MARTINS RN, SALVADO O, VILLEMAGNE VL, ROWE CC, MASTERS CL, MARUFF P & the AIBL RESEARCH GROUP. (2017) Amyloid burden and incident depressive symptoms in cognitively normal older adults. International Journal of Geriatric Psychiatry, 32: 455-463. doi: 10.1002/gps.4489.

- CONNORS M, **AMES D**, WOODWARD M & BRODATY H. (2018), Psychosis and clinical outcomes in Alzheimer's disease: a longitudinal study. American Journal of Geriatric Psychiatry, 26: 304-313.

- PERIN S, HARRINGTON K, LIM YY, ELLIS KA, **AMES D**, PIETRZAK R, SCHEMBRI A, RAINEY-SMITH S, SALVADO O, LAWS S, MARTINS RN, VILLEMAGNE VL, ROWE CC, MASTERS CL & MARUFF P for the AIBL RESEARCH GROUP. (2018) Amyloid burden and incident depressive symptoms in preclinical Alzheimer's disease. Journal of Affective Disorders, 229: 269-274. doi: 10.1016/j.jad.2017.12.101.

- CONNORS M, SEEHER KM, CRAWFORD J, **AMES D**, WOODWARD M & BRODATY H. (2018) The Stability of neuropsychiatric sub-syndromes in Alzheimer's disease. Alzheimer's and Dementia, in press, accepted 8/2/18.

'Some people feel they've entered a dark, claustrophobic place from which there's no escape. They feel like a trapped rat. Hope you're not one of those.'

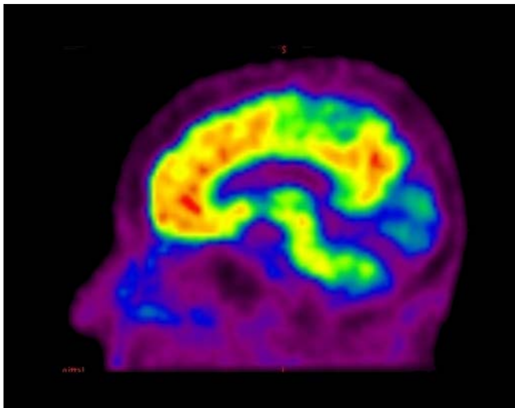
Imaging Research Phase 1

- **AMES D**, DOLAN R & MANN A. (1990) The distinction between depression and dementia in the very old. International Journal of Geriatric Psychiatry, 5: 193-198.
- O'BRIEN JT, DESMOND P, **AMES D**, SCHWEITZER I, TUCKWELL V & TRESS B. (1994) The differentiation of depression from dementia by temporal lobe magnetic resonance imaging. Psychological Medicine, 24: 633-640.
- DESMOND P, TRESS B, **AMES D**, O'BRIEN J, CLEMENT J, CLEMENT P, SCHWEITZER I, ROBINSON G & TUCKWELL V. (1994) Volumetric and visual assessment of the mesial temporal structures in Alzheimer's disease. Australian and New Zealand Journal of Medicine, 24: 547-553.
- O'BRIEN J, **AMES D**, DESMOND P, SCHWEITZER I, HARRIGAN S & TRESS B. (1996) A magnetic resonance imaging study of white matter lesions in depression and Alzheimer's disease. British Journal of Psychiatry, 168: 477-485.
- O'BRIEN J, **AMES D**, DESMOND P, SCHWEITZER I & TRESS B. (1996) Clinical and magnetic resonance imaging correlates of hypothalamic-pituitary-adrenyl axis function in depression and Alzheimer's disease. British Journal of Psychiatry, 168: 679-687.
- O'BRIEN J, DESMOND P, **AMES D**, SCHWEITZER I & TRESS B. (1997) Magnetic resonance imaging correlates of memory impairment in the healthy elderly: association with medial temporal lobe atrophy but not white matter lesions. International Journal of Geriatric Psychiatry, 12: 369-374.
- O'BRIEN J, DESMOND P, **AMES D**, SCHWEITZER I, CHIU E & TRESS B. (1997) Temporal lobe Magnetic Resonance Imaging can differentiate Alzheimer's disease from normal ageing, depression, vascular dementia and other causes of cognitive impairment. Psychological Medicine, 27: 1267-1275.
- SWANN A, O'BRIEN J, **AMES D**, SCHWEITZER I, DESMOND P & TRESS B. (1997) Does hippocampal atrophy on MRI predict cognitive decline? A prospective follow-up study. International Journal of Geriatric Psychiatry, 12: 1182-1188.
- O'BRIEN JT, **AMES D,** SCHWEITZER I, TRESS B, DESMOND P, BINNS D, LICHTENSTEIN M & DAVIS S. (2001) Combined Magnetic Resonance Imaging and Single-Photon Emission Tomography Scanning in the Discrimination of Alzheimer's Disease from age-matched controls. International Psychogeriatrics, 13: 149-161.

Biomarkers and Genetics

- BUSH A, MARTINS R, RUMBLE B, MOIR R, FULLER S, MILWARD E, CURRIE J, **AMES D**, WEIDEMANN A, FISCHER P, MULTHAUP G, BEYREUTHER K & MASTERS C. (1990) The amyloid precursor protein of Alzheimer's disease is released by human platelets. Journal of Biological Chemistry, 265: 15977-15982.
- O'BRIEN JT, SCHWEITZER I, **AMES D** & COLMAN P. (1996) Enhanced adrenal sensitivity to adrenocorticotrophic hormone (ACTH) is evidence of HPA axis hyperactivity in Alzheimer's disease. Psychological Medicine, 26: 7-14.
- KWOK JBJ, QIAO-XIN LI, HALLUPP M, WHYTE S, **AMES D**, BEYREUTHER K, MASTERS CL & SCHOFIELD PR. (2000) Novel Leu723Pro amyloid precursor protein mutation increases amyloid β42 (43) peptide levels and induces apoptosis. Annals of Neurology, 47: 249-253.
- FLICKER L & **AMES D**. (2005) Metabolic and endocrinological causes of dementia. International Psychogeriatrics, 17 (Supp.1): S79-S92.
- LEE T, MOSING M, WRIGHT M, HENRY J, TROLLOR J, LAMMEL A, **AMES D,** MARTIN N, WRIGHT M, & SACHDEV P. (2012) Genetic influences on five measures of processing speed and their covariation with general cognitive ability in the elderly: the Older Australians Twins study. Behaviour Genetics, 42: 96-106. doi: 10.1007/s10519-011-9474-1.
- SACHDEV P, LEE T, WEN W, **AMES D**, BATOULI A, BOWDEN J, BRODATY H, CHONG E, CRAWFORD J, KANG K, MATHER K, LAMMEL A, SLAVIN M, THALAMUTHU A, TROLLOR J, WRIGHT MJ & THE OATS TEAM. (2013) The contribution of twins to the study of cognitive ageing and dementia: the Older Australian Twins Study. International Review of Psychiatry, 25, 738-747.
- KANCHIBHOTLA S, MATHER KA, THALAMUTU A, ZHUANG L, SCHOFIELD PR, KWOK JBJ, **AMES D**, WRIGHT MJ, WEN W, TROLLOR J & SACHDEV P. (2014) Genetics of microstructure of corpus callosum in older adults. PLOS ONE, 9 (12): e113181. doi: 10.1371/journal.pone.0113181.
- DAVIES G, ARMSTRONG N, …., **AMES D**, …. & DEARY I. (2015) Genetic contributions to variation in general cognitive function: a meta-analysis of genome-wide association studies in the CHARGE consortium (N = 53,949). Molecular Psychiatry, 20: 183-192. doi: 10.1038/mp.2014.188.
- LAZARUS J, MATHER KA, ARMSTRONG NJ, SONG F, POLJAK A, THALAMUTHU A, LEE T, KOCHAN NA, BRODATY H, WRIGHT MJ, **AMES D**, SACHDEV PS & KWOK JBJ. (2015) DNA methylation in the Apolipoprotein-A1 gene is associated with episodic memory performance in healthy older individuals. Journal of Alzheimer's Disease, 44: 175-182. doi: 10.3233/JAD-141314.
- BORAXBEKK CJ, **AMES D**, KOCHAN NA, LEE T, THALAMUTHU A, WEN W, ARMSTRONG NJ, KWOK JB, SCHOFILED PR, REPPERMUND S, WRIGHT MJ, TROLLOR JN, BRODATY H, SACHDEV P & MATHER K. (2015) Investigating the influence of KIBRA and CLSTN2 genetic polymorphisms on cross-sectional and longitudinal measures of memory performance and hippocampal volume in older individuals. Neuropsychologia, 78: 10-17.
- LUPTON MK, STRIKE L, HANSELL NK, WEN W, MATHER KA, ARMSTRONG NJ, THALAMUTU A, McMAHON KL, DE ZUBICARAY GI, ASSAREH AH, SIMMONS A, PROITSI P, POWELL JF, MONTGOMERY GW, HIBAR DP, WESTMAN E, TSOLAKI M, KLOSZEWSKA I, SOININEN H, MECOCCI P, VELAS B, LOVESTONE S, THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE, BRODATY H, **AMES D,** TROLLOR JN, MARTIN NG, THOMPSON PM, SACHDEV PS & WRIGHT M. (2016) The effect of increased genetic risk for Alzheimer's disease on hippocampal and amygdala volume. Neurobiology of Aging, 40: 68-77.
- SACHDEV P, THALAMUTU A, MATHER K, **AMES D**, WRIGHT M, WEN W. & the OATS collaborative research team. (2016) White matter hyperintensities are under strong genetic influence Stroke, 47: 1422-1428.
- MATHER KA, THALAMUTHU A, OLDMEADOW C, SONG F, ARMSTRONG NJ, POLJAK A, HOLLIDAY E, McEVOY M, KWOK JB, ASSAREH AA, REPERMUND S, KOCHAN NA, LEE T, **AMES D**, WRIGHT M, TROLLOR JN, SCHOFIELD PW, BRODATY H, SCOTT R, SCHOFIELD PR, ATTIA J & SACHDEV PS. (2016) Genome wide significant results identified for plasma apolipoprotein H levels in middle-aged and older adults. Scientific Reports, 6: 23675. doi: 10.1038/srep23675.
- ADAMS HHH, HIBAR DP, …, ALMASY L, **AMES D**, …& THOMPSON PM. (2016) Novel genetic loci underlying human intracranial volume identified through genome-wide association. Nature Neuroscience, 19: 1569-1582.
- HIBAR DP, ADAS HH, …, **AMES D**,…. IKRAM MA. (2017) Novel genetic loci associated with hippocampal volume. Nature Communications, 8: 13624.

The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing – an example of Australian research on Alzheimer's disease



AIBL: Two site collaborative study 2006-2018 – CSIRO $3M initiative 2005

Study is conducted at two sites: Perth (40%) and Melbourne (60%).

CSIRO Preventative Health Flagship
University of Melbourne
Neurosciences Australia Ltd (NSA)
Edith Cowan University (ECU)
Mental Health Research Institute (MHRI)
National Ageing Research Institute (NARI)
Austin Health
University of WA (UWA)
CogState Ltd.
Charles Gairdner Hospital
Alzheimer's Australia
Macquarie University

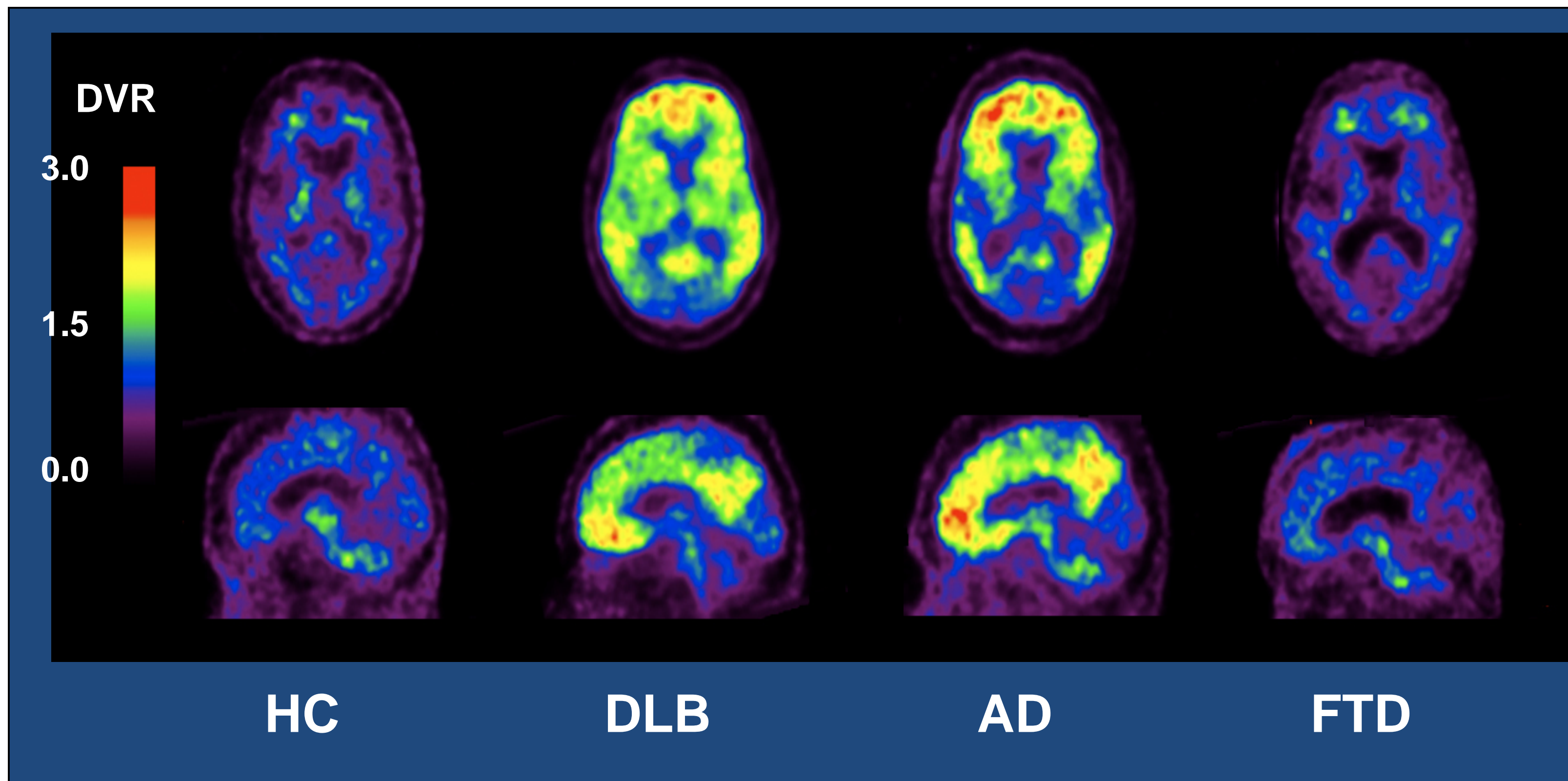
The Australian Imaging Biomarkers and Lifestyle Study of Ageing

Commenced 2006
Amyloid PET + MRI with follow-up in 288 of the 1112 original participants.

Now in 1,515 of 2,135 participants (November 2017)

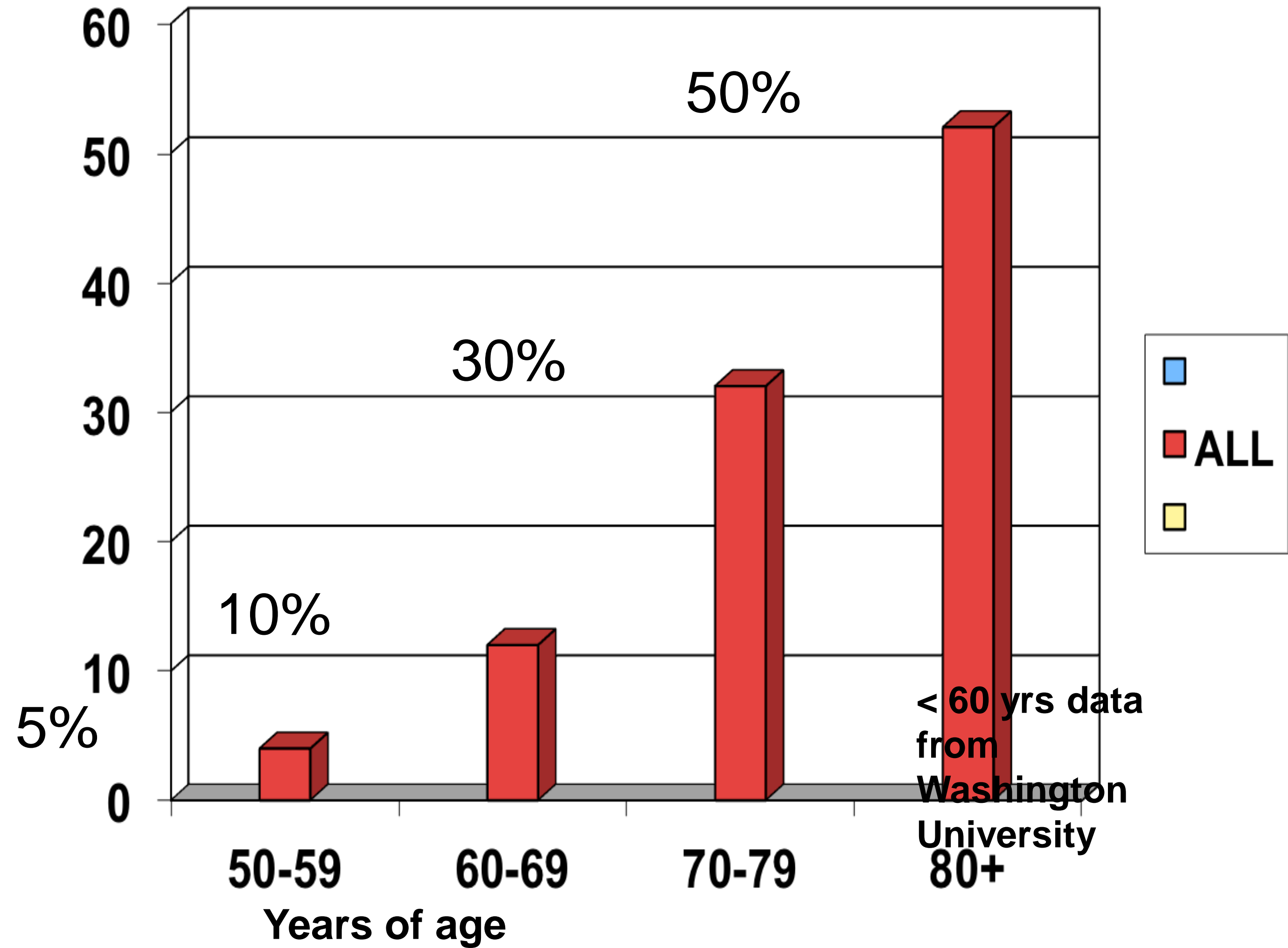
Imaging Beta-amyloid Burden in Aging and Dementia

Beta-amyloid PET inventors: **Chet Mathis, William Klunk (***University of Pittsburgh)*
First Publication 2004.



Rowe CC, et al. Neurology 2007
(919 citations)

% of healthy population who have plaques



Austin Health

Rowe CC, et al. Neurobiology of Aging. 2010 (611 citations)

aibl

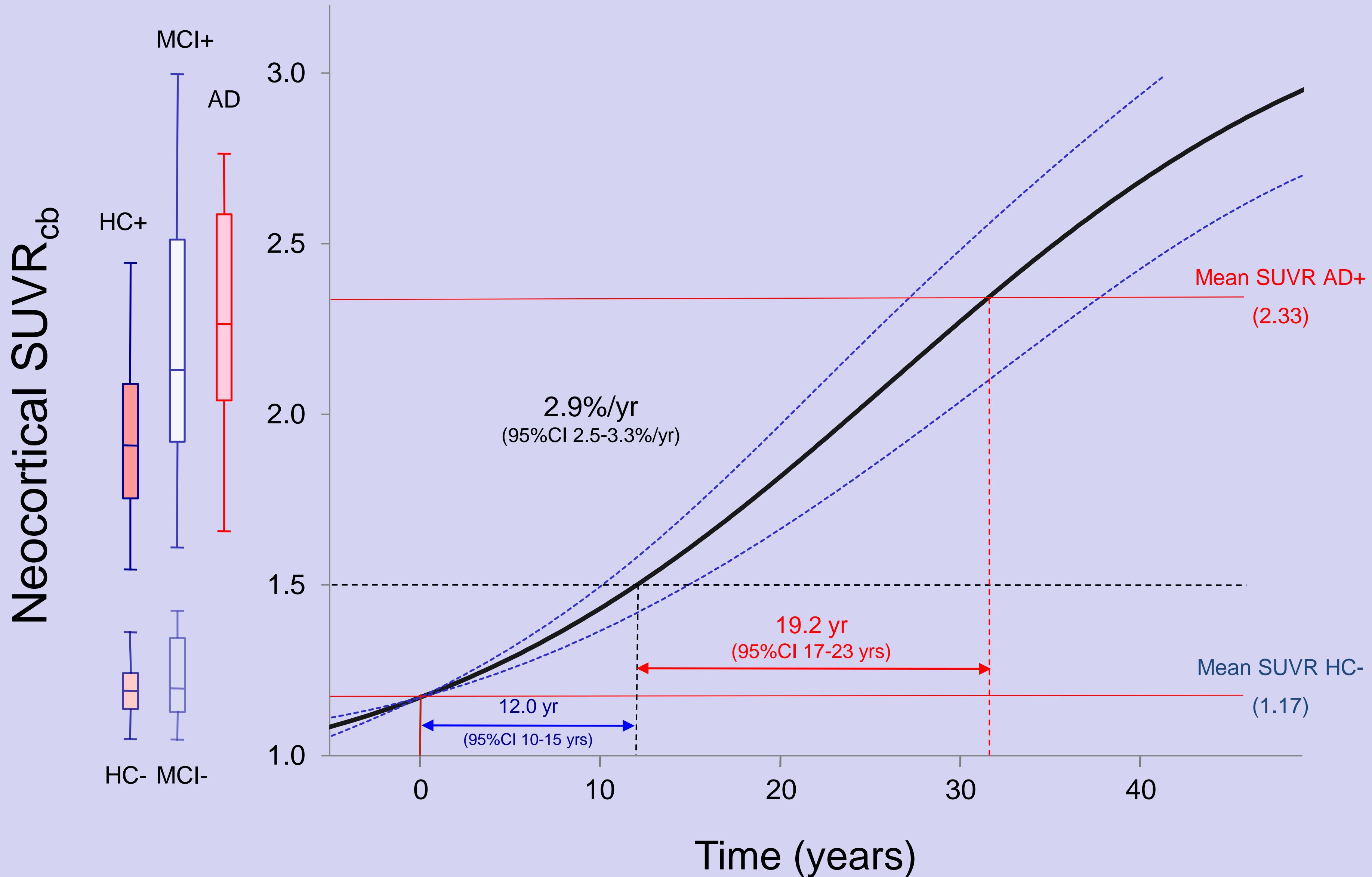
Achievements of Aβ PET imaging

- Improved diagnosis of AD vs FTD
- Earlier diagnosis of AD in MCI phase (“Prodromal” AD)
- Opened a broad window (15 years) for preclinical intervention
- Improved subject selection for therapeutic trials
- Measures effectiveness of anti-Aβ agents
- Permits the study of AD related pathology in non-demented persons and its relationship to genetic and potentially modifiable environmental factors.

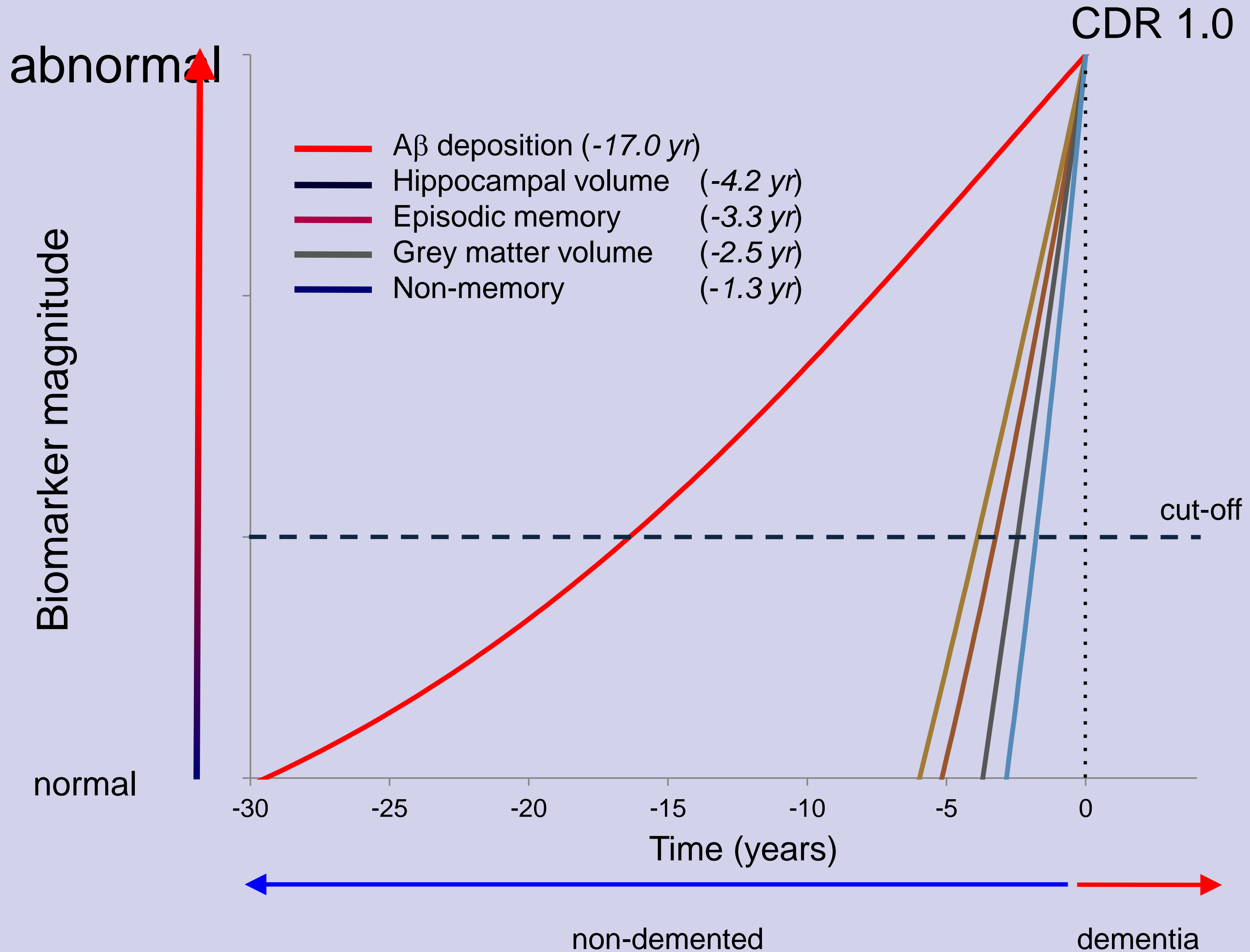
Prediction of Progression: MCI to AD
(at 36 months follow-up)

	ACCURACY	*Odds Ratio*	*NPV*
PiB+ve (SUVR >1.5)	0.80	25	0.93
ApoE ε4+	0.76	10	0.80
Composite Memory (<2.0)	0.70	6	0.81
Hippocampal atrophy	0.68	5	0.75
PiB+ve plus Hippo atrophy	0.89	>100	1.00

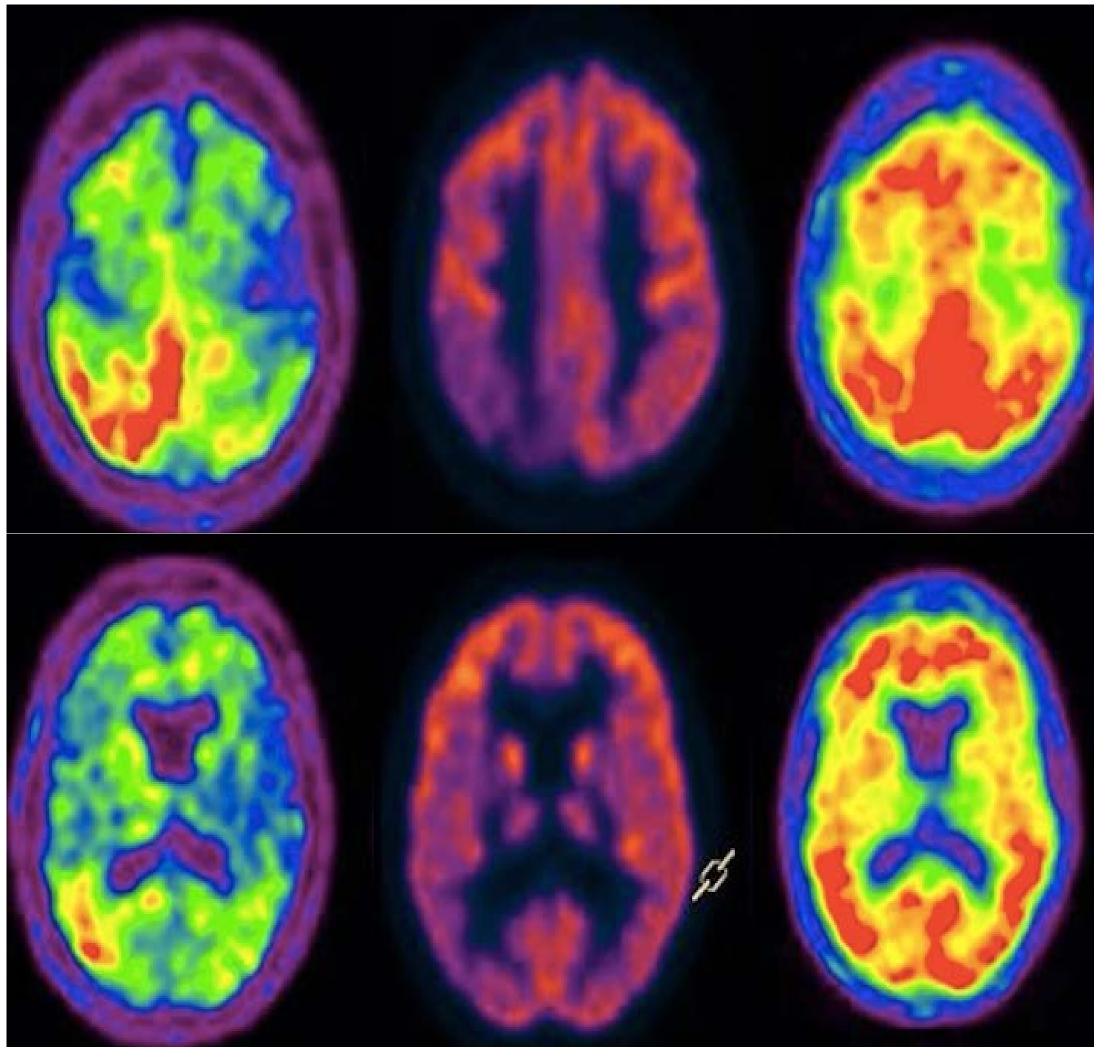
AIBL: Aβ deposition over time



Relationship between “abnormality” and CDR of 1.0



Tau deposition corresponds to reduced regional perfusion and metabolism while amyloid is diffuse



Tau PET rCBF PET Amyloid PET

AIBL Publications in peer-reviewed journals to November 2017

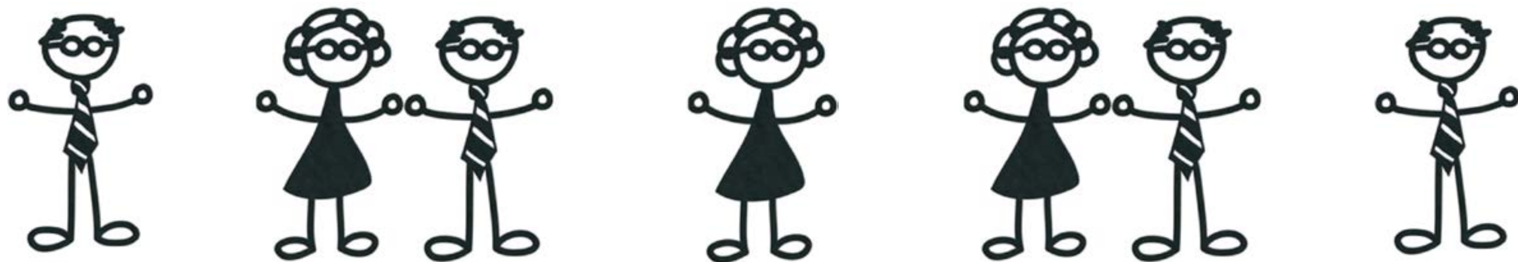
- 2007 – 4
- 2008 – 1
- 2009 – 8
- 2010 – 8
- 2011 – 16
- 2012 – 21
- 2013 – 37
- 2014 - 31
- 2015 - 31
- 2016 – 25
- 2017 - 30
- 2018 - 10 to date
- Total – at least 206

Key Publications

- ELLIS K *et al.*(2009) The AIBL flagship study of ageing: methodology and characteristics of 1112 individuals recruited for a longitudinal study of AD. Int Psychogeriatrics, 21: 672-687, doi:10.1017/S1041610209009405.
- BOURGEAT P *et al.* (2010) β amyloid burden in the temporal neocortex is related to hippocampal atrophy in elderly subjects without dementia. Neurology, 74: 121-127. doi: 10.1212/WNL.0b013e3181c918b5.
- ROWE C *et al.* (2010) Amyloid imaging results from the Australian Imaging Biomarkers and Lifestyle (AIBL) study of aging. Neurobiology of Aging, 31: 1275-1283. doi: 10.1016/j.neurobiolaging.2010.04.007.
- CHÉTELAT G *et al.* (2012) Accelerated cortical atrophy in cognitively normal elderly with high β-amyloid deposition. Neurology, 78:477-484. doi: 10.1212/WNL.0b013e318246d67a. ***This paper was awarded Best Paper 2012 de Leon Prize in Neuroimaging from the International Society to Advance Alzheimer's Research and Treatment (ISTAART)***
- BROWN BM *et al.* (2013) Physical activity and amyloid-β plasma and brain levels: results from the Australian Imaging, Biomarkers and Lifestyle study of ageing. Molecular Psychiatry, 18: 875-881. doi: 10.1038/mp.2012.107.
- VILLEMAGNE V *et al.* (2013) Amyloid β deposition, neurodegeneration and cognitive decline in sporadic Alzheimer's disease: a prospective cohort study. Lancet Neurology, 12: 357-367. doi: 10.1016/S1474-4422(13)70044-9. ***This paper was awarded Best Paper 2013 de Leon Prize in Neuroimaging from the International Society to Advance Alzheimer's Research and Treatment (ISTAART), the second year in a row that research from the AIBL project won this prize.***
- LIM YY *et al. (*2013) BDNF Val66Met A-beta amyloid and cognitive decline in preclinical Alzheimer's disease. Neurobiology of Aging, 34: 2457-2464. doi: 10.1016/j.neurobiolaging.2013.05.006.
- ROWE C *et al.* (2013) Predicting Alzheimer's disease with β amyloid imaging: results from AIBL. Annals of Neurology, 74: 905-913.
- LIM YY *et al.* (2014) Effect of amyloid on memory and non-memory decline from pre-clinical to clinical Alzheimer's disease. Brain, 137: 221-231. doi: 10.1093/brain/awt.286.
- LIM YY *et al.* (2014) Effect of *BDNF* Val66Met on memory decline and hippocampal atrophy in prodromal Alzheimer's disease. PLoS One, 9: e86498.
- LIM YY *et al.* (2015) Relationships between performance on the Cogstate brief battery, neurodegeneration and Aβ accumulation in cognitively normal older adults with MCI. Archives of Clinical Neuropsychology, 30: 49-58. doi: 10.1093/arclin/acu068. ***This paper won the 2016 Nelson Butters Award for Research Contributions to Clinical Neuropsychology, presented by the National Academy of Neuropsychology for the best paper of the year in the journal Archives of Clinical Neuropsychology.***
- BROWN B, *et al.* (2016) The relationship between sleep quality and brain amyloid burden. Sleep, 39: 1063-1068. doi: 10.5665/sleep.5756.
- HARRINGTON K *et al. (*2017) Using robust normative data to investigate the neuropsychology of cognitive aging. Archives of Clinical Neuropsychology, 32: 142-154. doi: 10.1093/arclin/acw106. ***This paper won the 2017 Nelson Butters Award for Research Contributions to Clinical Neuropsychology, presented by the National Academy of Neuropsychology for the best paper of the year in the journal Archives of Clinical Neuropsychology. This was the second year in a row that these authors won the award.***
- PEDRINI S *et al.* (2017). A blood-based biomarker panel indicates IL-10 and IL-12/23040 are jointly associated as predictors of β-amyloid load in an AD cohort. Scientific Report, in press, accepted 26/9/17.

AIBL Collective Remembering Project

Prof Amanda Barnier, Macquarie University



Memory and collaboration

- We believe that through relationships with other people we develop expert "remembering systems" that have cognitive payoffs, such as the ability to recall more information with another person than if we recalled alone
- However, most attempts to demonstrate this in the lab have actually shown the opposite. That is, people typically recall less with another person than if they did this individually. We call this "collaborative inhibition"

Memory and collaboration over a lifetime

- One explanation for collaborative inhibition is that the groups tested (typically young university students) have not had the time, nor the intimacy, to develop the specific knowledge and strategies that *facilitate* the memory of their partner
- One group we believe this would not apply to is long-married couples. With the help of **AIBL** we sought to investigate whether such couples did help each other recall more information

Real example of how hearing difficulty influences performance

Husband: Scotland. Ireland. England. France. Germany. Luxembourg. Norway. Holland. Um. Sweden.

Wife: *I'm having terrible trouble hearing you.*

…

Husband: Greenland.

Wife: *Hmm?*

Husband: Greenland I said.

Wife: *Speak up!*

Husband: Greenland! Turkey. No Turkey. That's not part of Europe. Belgium.

Wife: *Norway. Sweden. Finland.*

Husband: Scotland.

Wife: *I don't think we said Wales. Jutland.*

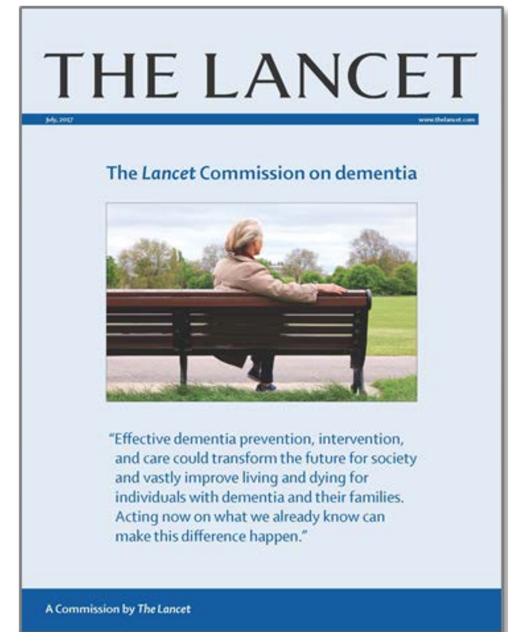
Husband: Hmm? Did you say Denmark?

Diet and Lifestyle

- Nicola Lautenschlager et al.
- FABS 2008 MCI & SCD - exercise helps cognition (a bit)
- FABS 2 AD - subjects' health benefited but cognition did not
- AIBL Active - Changes in body mass, composition & distribution resulting from increased PA are positive health benefits for this target group
- Imaging results to come
- Physical Activity Guidelines for SCD and MCI www.unimelb.edu.au go to medicine and select psychiatry then to AUPOA
- Belinda Brown et al.
- Mediterranean diet – associated with better cognition – cause or effect?

Lancet commission

Dementia prevention, intervention, and care



Gill Livingston

Andrew Sommerlad, Vasiliki Orgeta, Sergi G Costafreda, Jonathan Huntley, David Ames, Clive Ballard, Sube Banerjee, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Eric Larson, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

Partners **UCL, AS, ESRC, ARUK**

Key areas

- Prevention
- Intervention
- Care

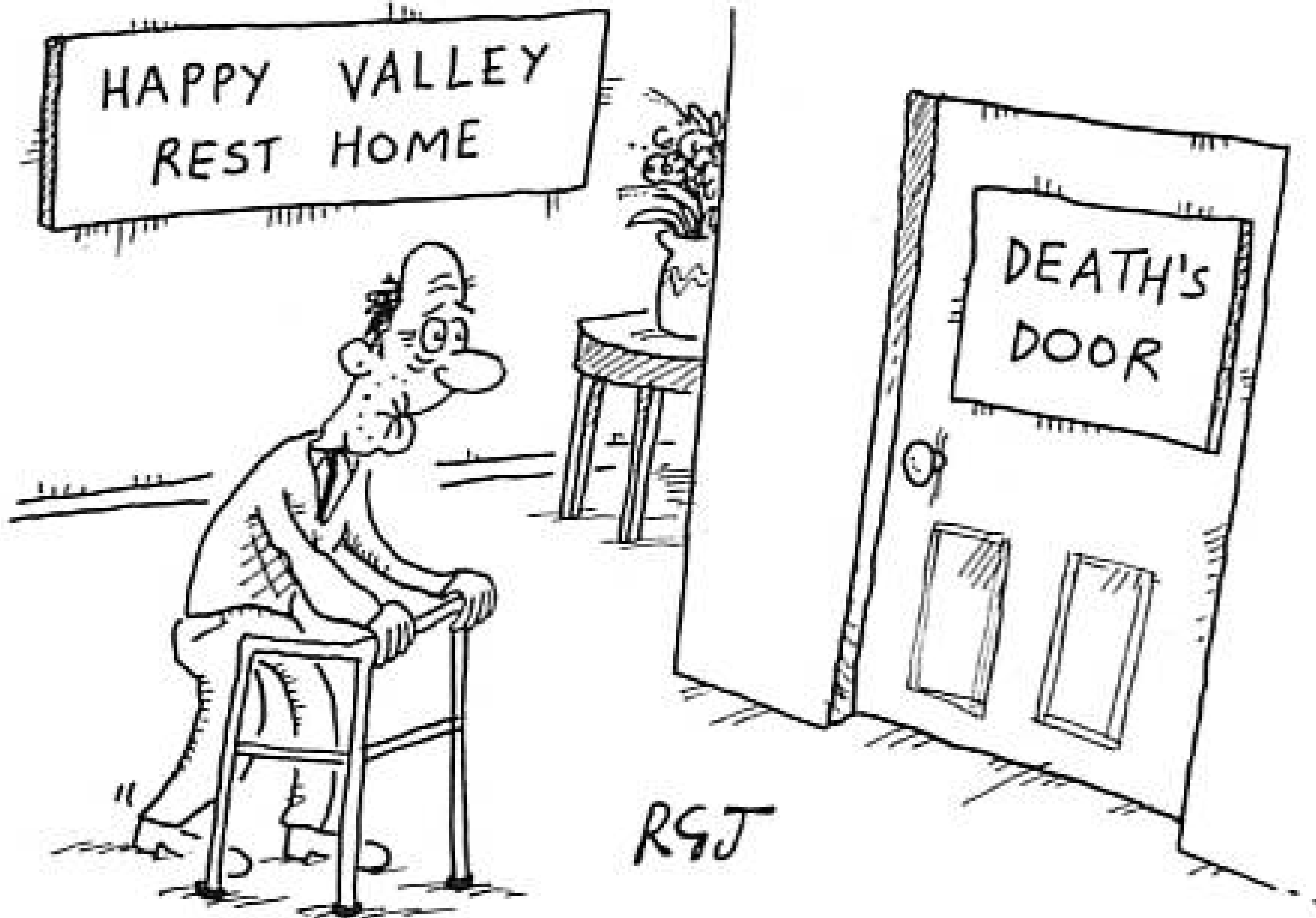
10 Key headline messages

- **The number of PWD is increasing globally**
- **Be ambitious about prevention**
- **Treat cognitive symptoms**
- **Individualise dementia care**
- **Care for family carers**
- **Plan for the future**
- **Protect PWD**
- **Manage neuropsychiatric symptoms**
- **Consider end of life**
- **Technology**

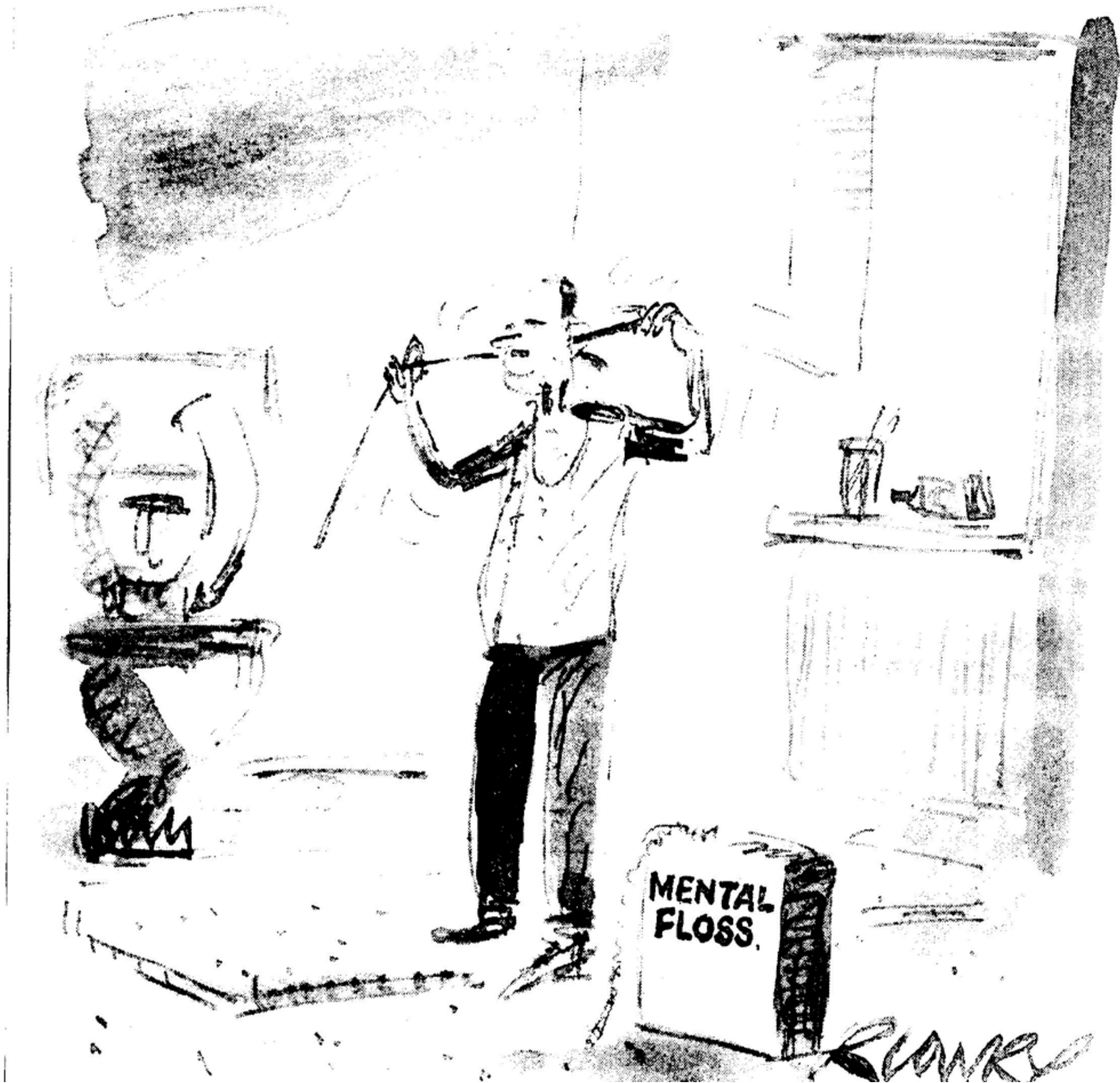
Teaching

- Nursing and allied health
- Medical students
- Psychiatry trainees
- PhD supervision
- Other postgraduate and public education

The Future


HAPPY VALLEY
REST HOME
DEATH'S
DOOR
RGJ

ONE WAY
ONE WAY
STOP
NO RIGHT TURN
STOP
SOUTH
906
NORTH
906
MONESSEN 3


MENTAL FLOSS.

Current Trials For Alzheimer's Disease:

- Symptomatic Treatment
- Anti-amyloid (antibodies, BACE-1 inhibitors)
- Anti-tau

Across the preclinical, prodromal and AD dementia spectrum

Are we already winning?

- Age-specific prevalence of dementia reported to be falling in some populations
  - 2005 Duke, USA – prevalence of severe cognitive impairment fell between 1982 and 1999
  - 2013 Cognitive Function and Ageing Study (CFAS, UK)
    - 2 cohorts of >65 year-olds assessed 20 years apart (1990-93, 2008-11)
    - 24% decrease in prevalence of dementia (Odds Ratio 0.7 [95% C.I. 0.6-0.9, p=0.003) in the later cohort
  - 2013 Christensen et al (Denmark)
    - Compared individuals born in 1905 (at age 93, n=2262), to those born in 1915 (at age 95, n=1584).
    - More recent (1915) cohort scored higher on cognitive tasks and ADL scores (plus more lived longer)
  - 2015 PAQUID Cohort, Bordeaux, France
    - 2 cohorts aged >65y, 1988-89 (n = 1,469) and 1999-2000 (n = 2,104)
    - 40% decline in dementia incidence between two cohorts
  - 2016 Framingham cohort
    - 5,205 persons aged >60y assessed each decade from 1975 to present
      - Reduction in dementia incidence by 22%, 28%, 44% respectively
      - Despite increases in BMI, Diabetes, and population ageing
      - Findings not completely explained by trends to better VRF management
      - Risk reduction only observed in those with at least High School Diploma

Manton 2005, Matthews 2013, Christensen 2013

UNITED STATES OF AMERICA
MARINE ONE
December 15, 2014
Aboard
M1_3896

Thank you

- Schoolteachers
- Amelia Greenfield

- Mervyn Callaghan
- Ian Collier
- Michael Collins Persse
- Tommy Garnett
- Dick Johnson

- University Teacher
- Herbert Bower

- Mentors
- Ed Chiu
- Brian Davies
- Nori Graham
- Anthony Mann
- Bruce Singh

- Collaborators
- Nick Allen
- Deborah Ashby
- Kerryn Bennetts
- Nick Bradfield
- Henry Brodaty
- Rachel Buckley
- Sam Burnham
- Alistair Burns
- Ashley Bush
- Esther Cerin
- Gael Chételat
- Terry Chong
- Michael Connors
- Liz Cyarto
- David Darby
- Patricia Desmond
- Briony Dow
- Colleen Doyle
- Kathryn Ellis
- Leon Flicker
- Chris Fowler
- Steve Gibson
- Anita Goh
- Suzy Harrigan
- Karra Harrington
- Anne Hassett
- Rob Helme
- Di Kirby
- Glynda Kinsella
- Nicola Lautenschlager
- Simon Laws
- Tim Layton
- Raymond Levy
- Yen Ying Lim
- Dina LoGiudice
- Samantha Loi
- Lance Macaulay
- Ralph Martins
- Paul Maruff
- Colin Masters
- Maree Mastwyk
- Eileen Moore
- Kirsten Moore
- John O'Brien
- Daniel O'Connor
- Debra O'Connor
- Kerryn Pike
- Margaret Pozzebon
- Stephanie Rainey-Smith
- Alan Rembach
- Craig Ritchie
- Jo Robertson
- Chris Rowe
- Perminder Sachdev
- Olivier Salvado
- Greg Savage
- Issy Schweitzer
- David Scott
- Ajit Shah
- John Snowdon
- Cassandra Szoeke
- Brian Tress
- Julian Trollor
- Virginia Tuckwell
- Victor Villemagne
- Alissa Westphal
- Siegfried Weyerer
- Michael Woodward

- Clinical Colleagues
- Francine Moss
- Anne Unkenstein

- Secretaries
- Yvonne Liddicoat
- Marilyn Kemp
- Roz Seath
- Lynette Bon

- Patients and Research Participants

- Family
- Gordon Ames
- Joan Ames
- Eleanor Flynn
- Elizabeth Ames
- Jennifer Ames
- Phil Ames
- Paul Rogers