The Women's Healthy Ageing Project

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Consultant Neurologist

THE WOMEN'S HEALTHY AGEING PROJECT
WHAP

THE UNIVERSITY OF MELBOURNE

Disclosures

- may accrue revenue from patent; diagnostic assay for seizure prediction,
- has been a paid clinical consultant and speaker for the Australian Commonwealth, Pfizer, Sanofi, other relationships subject to confidentiality clauses
- has been a chief investigator on research projects receiving funds from Bayer, Merck, Piramal and GE Healthcare.
- on the Board of Executive Directors for the Western Health Service, Victoria

Evolution

- Early Detection
- Need to study people >65 to ascertain disease
- Prodrome of AD is several decades
- Midlife vascular risk factors strongest impact on late life disease (MCI, AD) diagnosis.
- Strongest thearapeutic window in midlife?
- Need 20 years longit., prospect. with RF, confound. and cognitive trajectory measures

WHAP Measures n=438 - 252

- COGNITION: 4 times over 15 yrs

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
NeuroCognitive Testing									X			X		X								X

- CLINICAL, PSYCH: 12 times over 22 yrs

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Clinical, Psychological	X	X	X	X	X	X	X	X	X			X		X								X

- LIFESTYLE, PHYSICAL: 11 times over 22yrs

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Lifestyle and Examination	X	X	X	X	X	X	X	X	X			X		X								X

- BIOMARKER, STORED SPEC: 11 x over 22yrs

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Biomarker Analysis and Biobank Storage -70 Nit		X	X	X	X	X	X	X	X			X		X								X

- NUTRITION and DENSIT.: 3 times over 22 years

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Fat, bone Density Scans			X		X		X															
Nutritional Assessment				X					X													X

- BRAIN IMAGING MRI, FMRI, 18F Florbetaban

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Cerebral MRI and FMRI												X										X
Cerebral Amyloid Scans																						X

15 Years

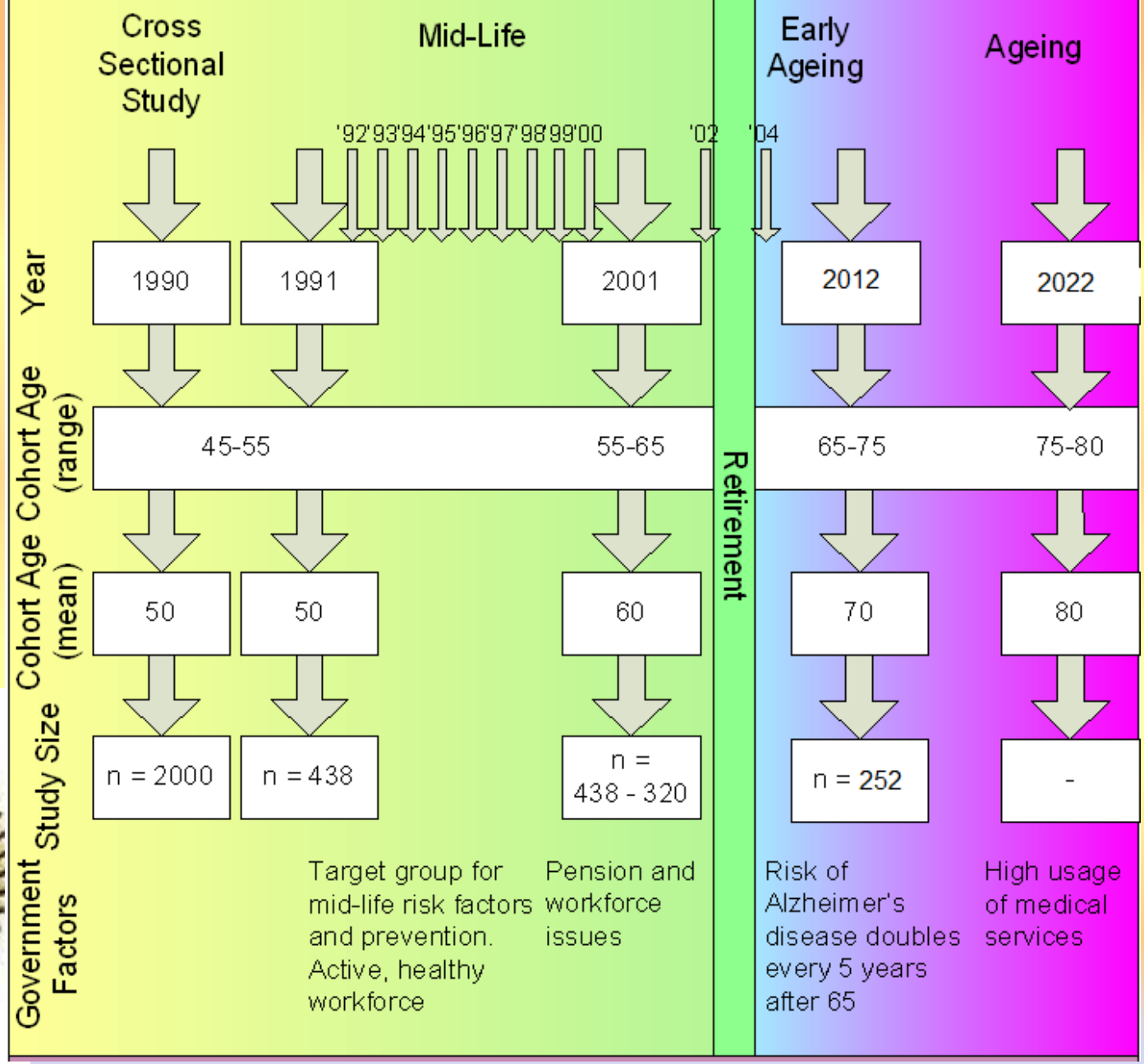
Cognitive change

67% ret^{n}

22 Years

Lifespan change

58% ret^{n}



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How do WHAP survivors compare?

- A two-cohort study. AIBL BL;WHAP FU
- Not statistically significant mean age, vascular risk factors (PROCAM), education (both higher than ave pop.)
- Statistically significant difference in the proportion of APOE 4 positive participants AIBL >WHAP

Appannah, A., Szoeke, C., Ellis, K., Rowe, C., Martins, R., Masters, C., Ames, A., Bush, A. & The AIBL research group (2012). Investigating cardiovascular risk factors on cognition: A two-cohort study. Alzheimer's & Dementia 8 (4): P318-319.

Data lock 2014: Research Questions

- Lifespan risk on late life
  - Cognitive Trajectories (submitted)
  - Amyloid (O3-10-01 vascular)
- Cognitive Trajectories and amyloid accrual over 65
  - Can we see subtle decline prior to amyloid accrual (O2-10-04)
- Cognitive Trajectories and functional decline (SF 36; wellbeing; self report)

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Study on Texture Features of Cingulum in Different Gender Patients with Alzheimer's disease and Mild Cognitive Impairment based on MR Images

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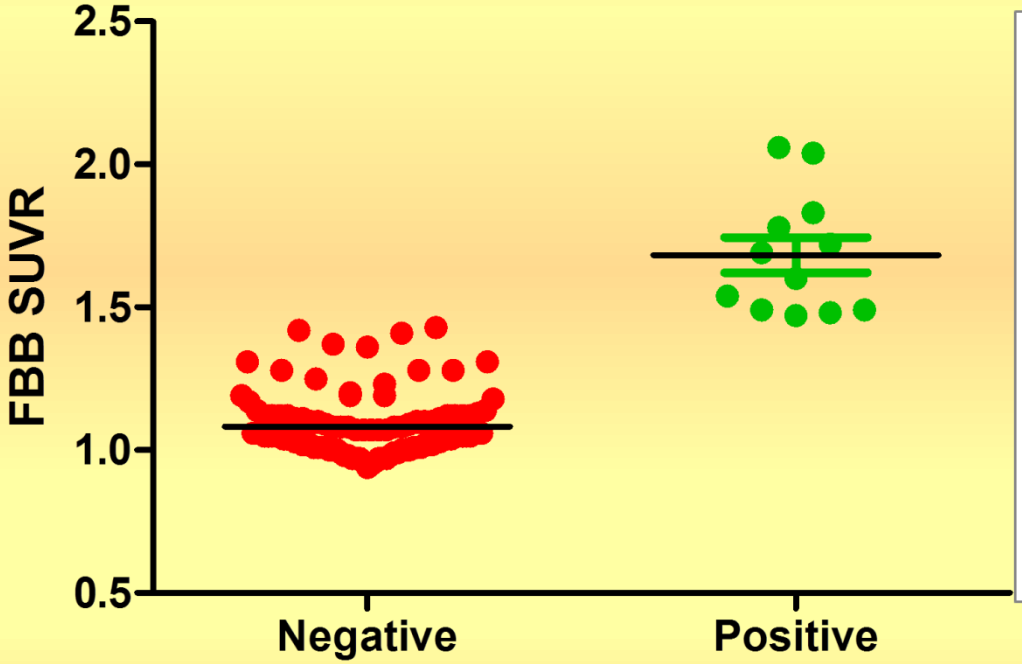
Keywords: Alzheimer's disease; Mild cognitive impairment; Magnetic resonance image; Cingulum; Gender; Texture features

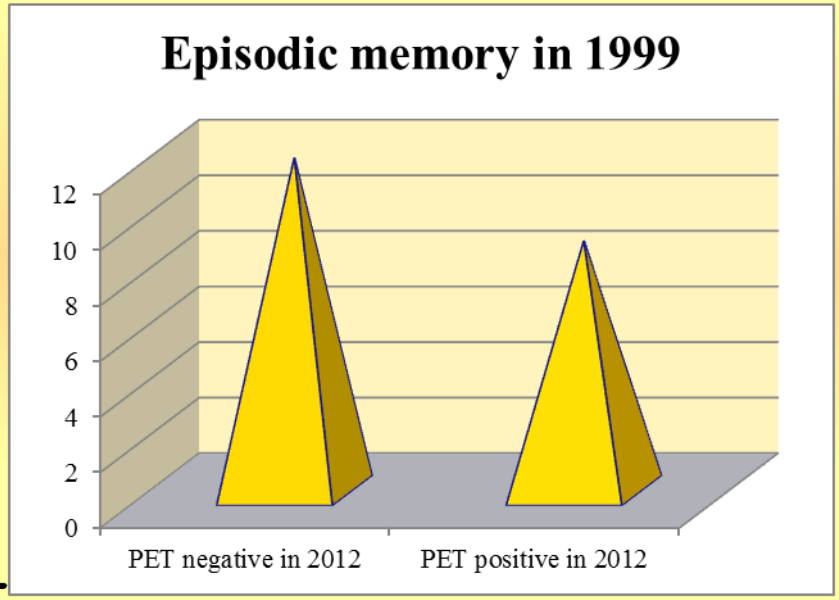
Abstract. The aim of this article is to study the texture features of cingulum in patients with Alzheimer's disease (AD) and mild cognitive impairment (MCI) based on magnetic resonance images, and explore the texture differences derived from different gender among each group. Texture analysis was performed on 7 AD patients, 14 MCI patients and 11 normal controls (NC). Texture features extracted from gray level co-occurrence matrix and run-length matrix were analyzed between each two groups. The results showed that texture features of the anterior cingulum had significant differences in the multiple comparisons and features of the posterior cingulum had significant differences between AD and MCI group as well as AD and NC group. There were significant differences between AD and MCI group as well as AD and NC group in male's cingulum. While in female's cingulaum, the differences were founded between AD and NC group. The results indicated that the pathological changes in cingulum could be reflected by texture features and the pathological changes may be different in the two genders.

Introduction

Alzheimer's disease (AD) is a neurodegenerative disease, which is the most common form of dementia. Recent memory disorder, impairment on language, emotion and cognitive are showed on the patients with AD. With the decline of brain function, the patients can not live independently[1].

125 with 18F Florbeteban amyloid imaging





<u>July 16, WEDNESDAY:</u>
POSTER Presentation (P4-082)
1145 – 1415hrs
4:00pm - 5:30pm

Piramal
knowledge action care

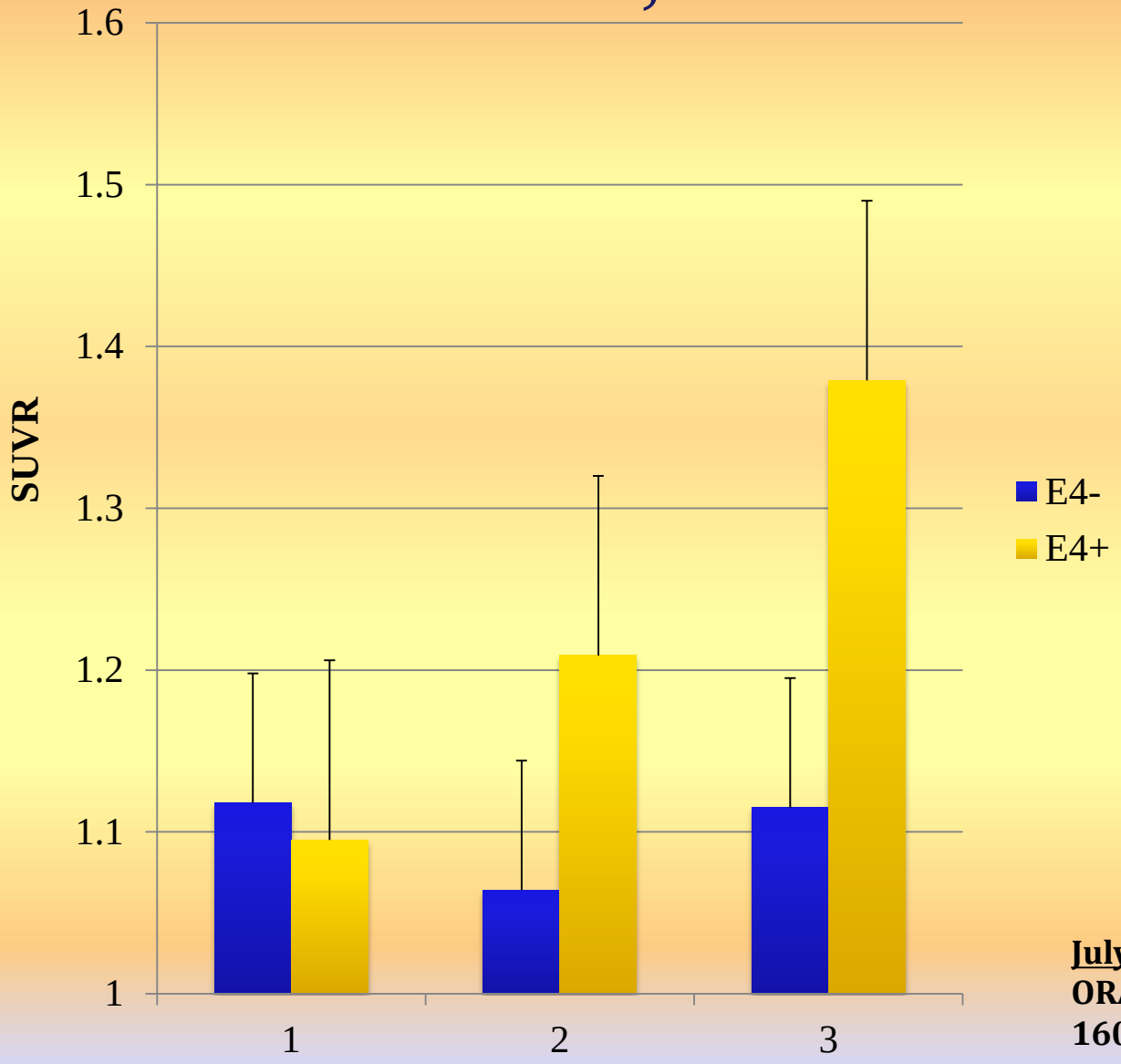
The Women's Healthy Ageing Project
WHAP

The University of Melbourne

Who refused PET scan

- no significant differences for distance lived from assessment centre, age or education.
- Recalled fewer words on CVLT word recall
- 10 vs 11.4, p=0.008, adjusted for age and education

Midlife PROCAM, E4 and Late-life FBB SUVR



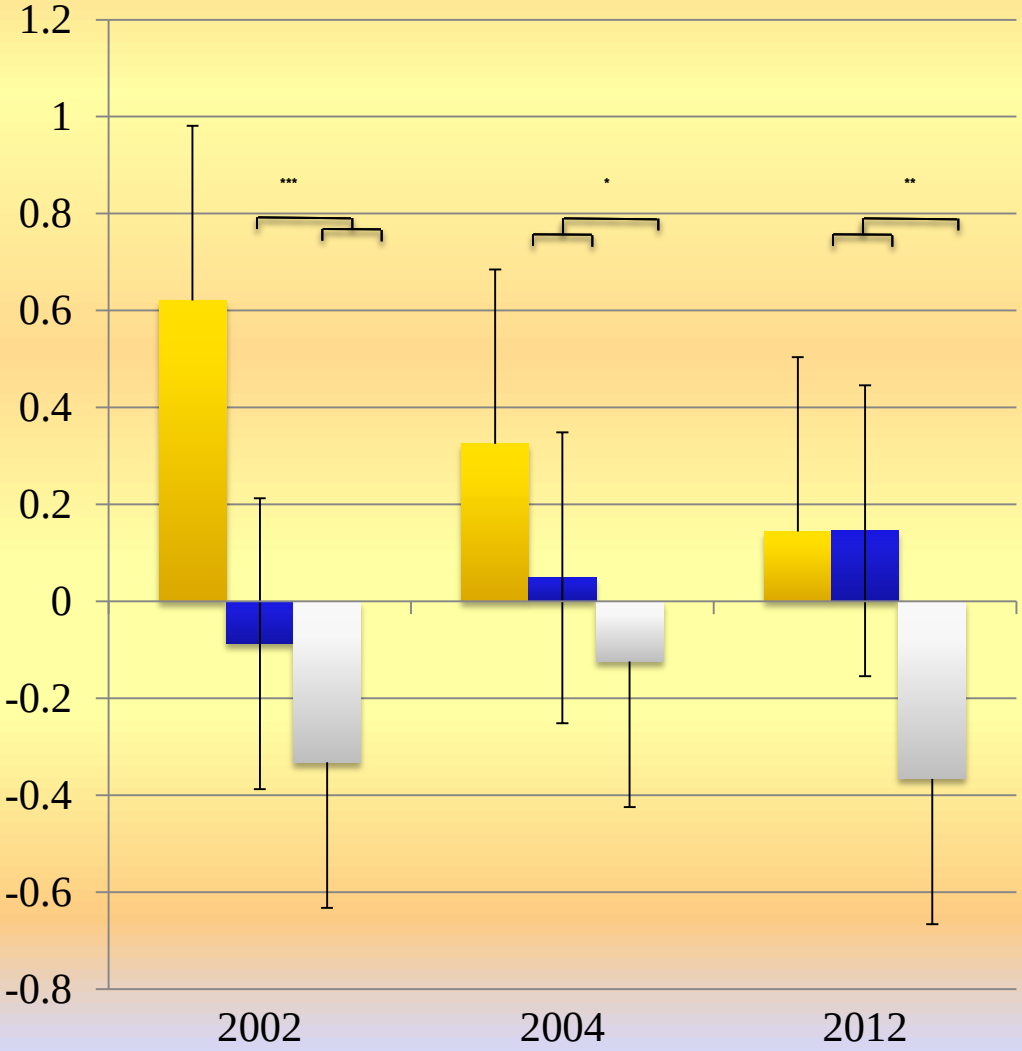
- Interaction of Midlife PROCAM tertile x APOE ε4 status significantly associated with late-life FBB SUVR (p=0.04).

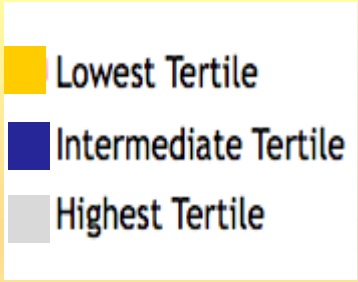
- ie. the association of high vascular risk tertile with Aβ was greatest in ε4+

- age and years of education.

<u>July 15, TUESDAY:</u>
ORAL Presentation (O3-10-01)
1600 – 1730hrs

Results – CVLT-long delay





- Adjusted mean (95% confidence interval) for CVLT-delay z-score by FBB Tertile
- Adjusted for age, education and E4 status
- * p<0.1, ** p<0.05, ***p<0.001

<u>July 14, MONDAY:</u>

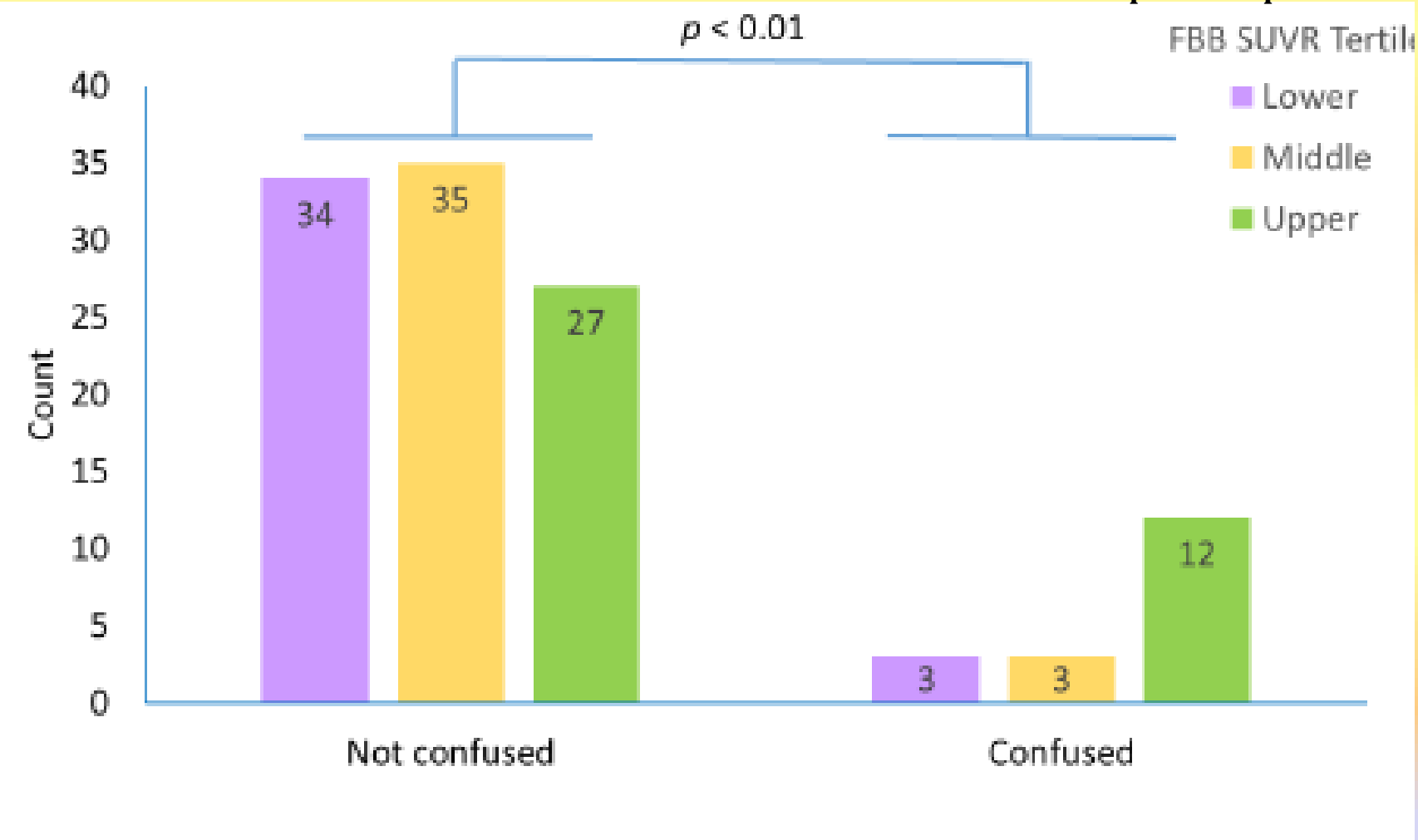
ORAL Presentation (O2-10-04)

4:00pm - 5:30pm

Reported SCI and amyloid accrual

SMC not associated with amyloid accrual

July 13, SUNDAY:
ORAL Presentation (**P1-181**)
4:00pm - 5:30pm



Work Plan

- Earlier detection for those at risk for cognitive decline
  - From 45
  - Hormones and hormone therapy
- Lifespan approach to risk of cognitive decline
  - Cummulative risk
  - Critical windows, Timing
  - Impact on QOL and Functional measures
- Lifespan biobank
  - ? Biomarker at 45 which can determine risk of cognitive decline
  - ? Biomarker at 45 which can determine risk of amyloid accrual
- Imaging biomarkers
  - Change in MRI 2002 to 2012, amyloid accrual 2012

Participants and their families

WHAP
A/Prof Cassandra Szoeke
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Dr Alan Rembach
Brett Trounsen

Australian Government
National Health and Medical Research Council

The Royal Melbourne Hospital Neuroscience Foundation
BIOGRID AUSTRALIA
Alzheimer's Australia Living with dementia
alz.org® | alzheimer's association
CogState
Bayer
Austin Health

National Health and Medical Research Council (NHMRC), Ramaciotti Foundation, Bayer Healthcare, Piramal Life-Science, *Brain Foundation, Alzheimer's Association of Australia, Australian Menopausal Society, Brain Foundation, Shepherd Foundation, Scobie and Claire McKinnon Foundation, Alzheimer's Association, Collier Trust Fund, J.O. & J.R. Wicking Trust, Mason Foundation.*

THE FLOREY INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH
Piramal knowledge action care

THE WOMEN'S HEALTHY AGEING PROJECT

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July 12, SATURDAY:

POSTER Presentation (IC-P-020)

"Evidence of amyloid on Florbetaben-PET is associated with reduced episodic memory 10 years prior: results from the Women's Healthy Ageing Project"

POSTER Presentation (IC-P-021)

"Midlife Vascular Risk, Apolipoprotein E-4 and Amyloid status 20 years later: Results from the Women's Healthy Ageing Project

POSTER Presentation (IC-P-023)

"Subjective memory complaints ten years prior have no relationship with brain amyloid - data from the Women's Healthy Ageing Project"

July 13, SUNDAY:

POSTER Presentation (P1-181)

"Subjective memory complaints ten years prior have no relationship with brain amyloid - data from the Women's Healthy Ageing Project"

POSTER Presentation (P1-335)

" A simple test of episodic memory predicts conversion to disease (MCI/AD) A DECADE later – data from the Women's Healthy Ageing Project (WHAP)"

July 14, MONDAY:

ORAL Presentation (O2-10-04)

"Evidence of amyloid on Florbetaben-PET is associated with reduced episodic memory 10 years prior: results from the Women's Healthy Ageing Project"

July 14, MONDAY:

POSTER Presentation (P2-381)

"Grandparenting is associated with cognitive functioning in older women: results from the Women's Healthy Ageing Project"

July 15, TUESDAY:

ORAL Presentation

1600 – 1730hrs

Location: HALL A1 (BCCC)

"Midlife Vascular Risk, Apolipoprotein E-e4 and Amyloid status 20 years later: Results from the Women's Healthy Ageing Project."

POSTER Presentation (P3-090)

"Apolipoprotein E4 gene predicts changes in episodic memory from midlife to late-life: data from the Women's Healthy Ageing Project (WHAP)"

July 16, WEDNESDAY:

POSTER Presentation (P4-082)

"Participants who refuse PET scan had significantly lower episodic memory than those who consented to scan – data from the Women's Healthy Ageing Project"

POSTER Presentation (P4-056)

"Participants with a positive amyloid scan in the Women's Healthy Ageing Project had significantly worse episodic memory than those with a negative scan"