The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing

aibl

(AUSTRALIAN ADNI)

July 2013 UPDATE – Biomarkers

Samantha Burnham

CSIRO

THE UNIVERSITY OF MELBOURNE

NNF NATIONAL NEUROSCIENCE FACILITY

NARI

MENTAL HEALTH Research Institute

ECU EDITH COWAN UNIVERSITY

Alzheimer's Australia Living with dementia

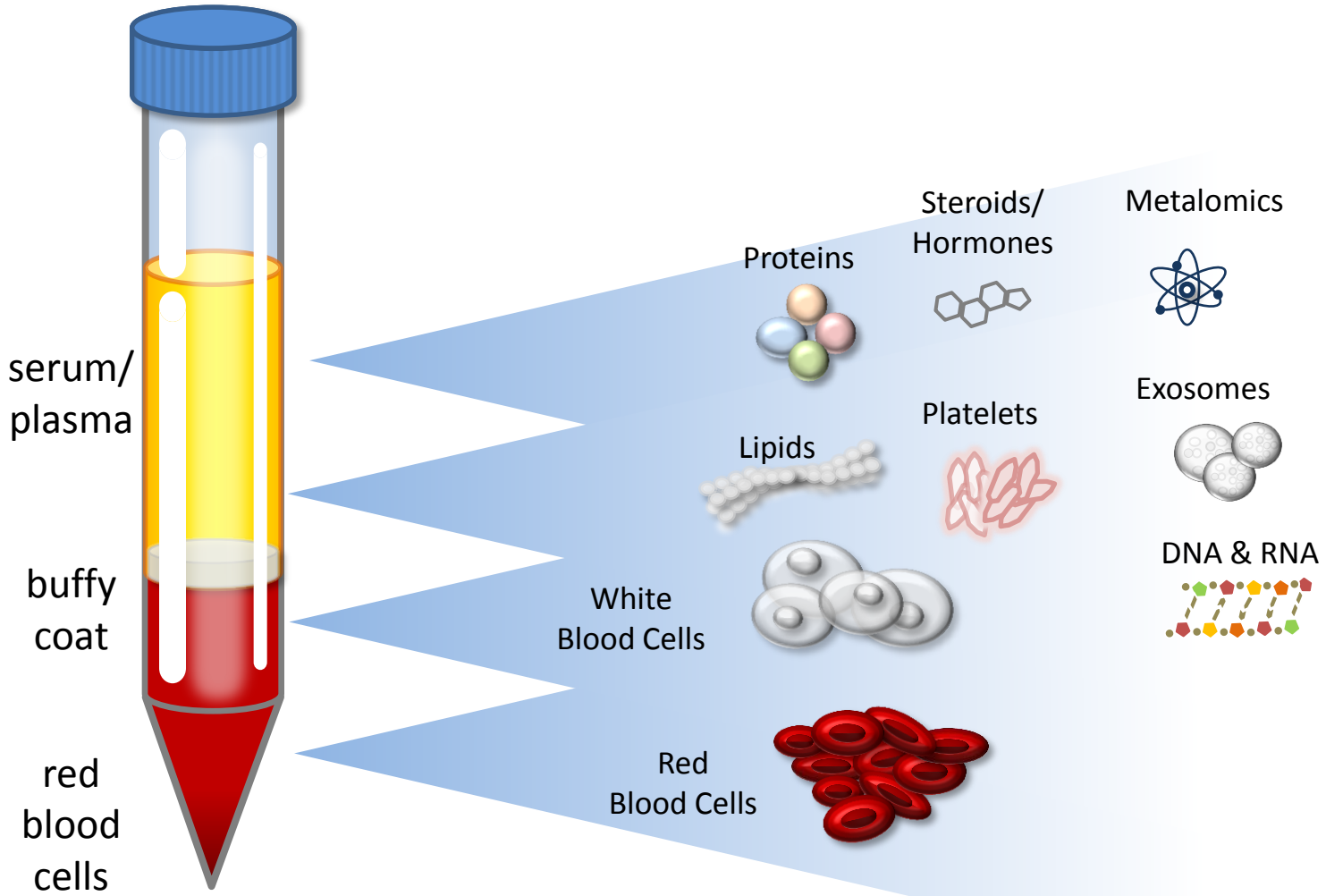
THE UNIVERSITY OF WESTERN AUSTRALIA

CogState

Austin Health

MACQUARIE UNIVERSITY SYDNEY ~ AUSTRALIA

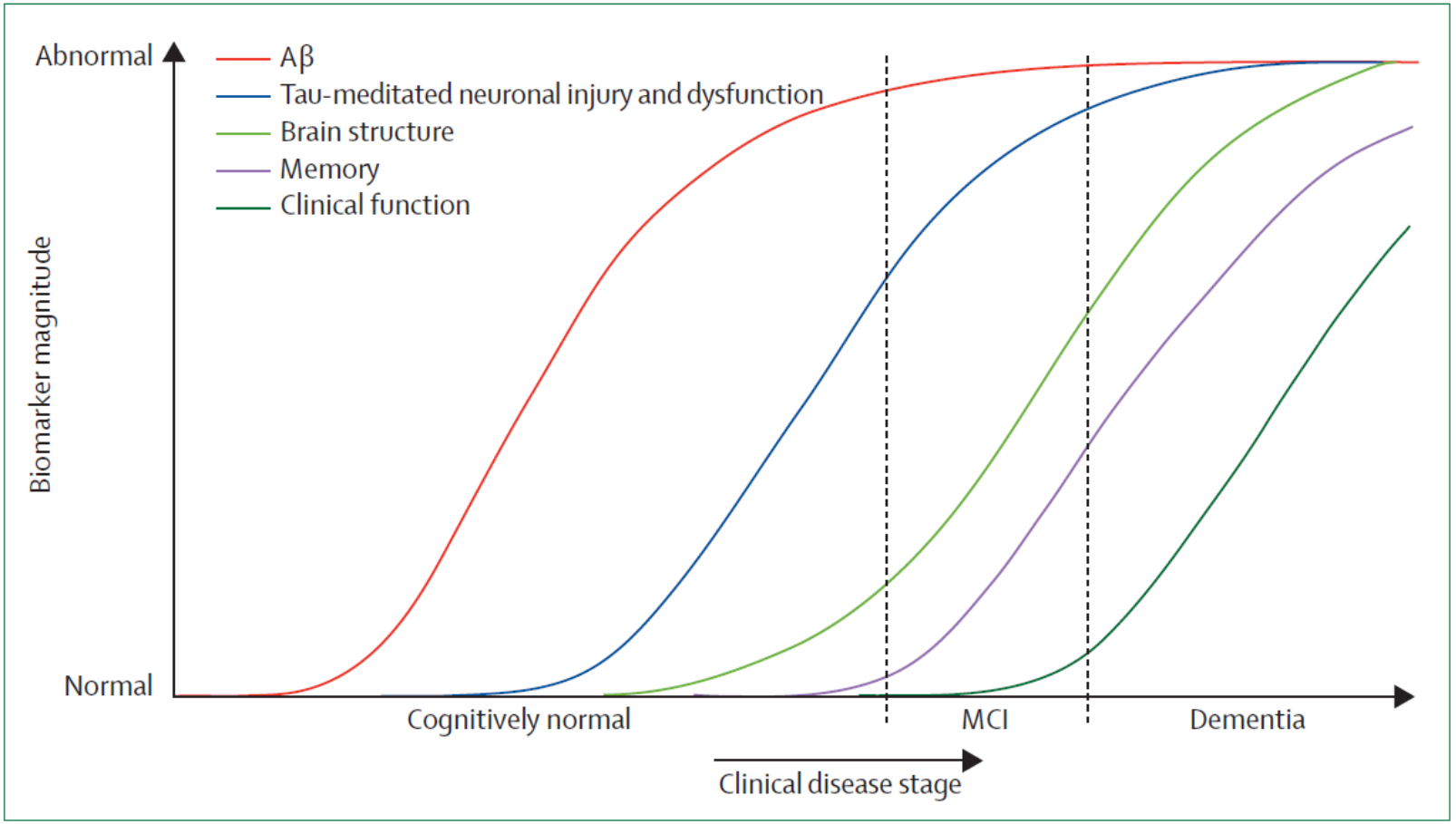
Fractions and Analytes



Fractions and Analytes

Blood tube type	Fraction
1. Serum	Serum
2. Whole EDTA Blood	WB
3. EDTA (PGE1)	Plasma
4. Li/Hep	Plasma
5. EDTA (PGE1)	Platelet
6. Li/Hep	Platelet
7. EDTA (PGE1)	WBC
8. Li/Hep	WBC
9. EDTA (PGE1)	RBC
10. Li/Hep	RBC
11. PaxGene tube	RNA

Aims and Objectives



Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade, Clifford R Jack Jr, David S Knopman, *et al. Lancet Neurol 2010; 9: 119–28*

Diagnostic & NAB Estimate

ORIGINAL CONTRIBUTION

ONLINE FIRST

Blood-Based Protein Biomarkers for Diagnosis of Alzheimer Disease

James D. Doecke, PhD; Simon M. Laws, PhD; Noel G. Faux, PhD; William Wilson, PhD; Samantha C. Burnham, PhD; Chiou-Peng Lam, PhD; Alinda Mondal, MSc; Justin Bedo, PhD; Ashley I. Bush, MD; Belinda Brown, BSc; Karl De Ruyck, BSc; Kathryn A. Ellis, PhD; Christopher Fowler, BSc; Veer B. Gupta, PhD; Richard Head, PhD; S. Lance Macaulay, PhD; Kelly Pertile, BSc; Christopher C. Rowe, MD; Alan Rembach, PhD; Mark Rodrigues, MSc; Rebecca Rumble, BSc; Cassandra Szoeke, MD; Kevin Taddei, BSc; Tania Taddei, BSc; Brett Trounson, BSc; David Ames, MD; Colin L. Masters, MD; Ralph N. Martins, PhD; for the Alzheimer's Disease Neuroimaging Initiative and Australian Imaging Biomarker and Lifestyle Research Group

ARCH NEUROL PUBLISHED ONLINE JULY 16, 2012 WWW.ARCHNEUROL.COM
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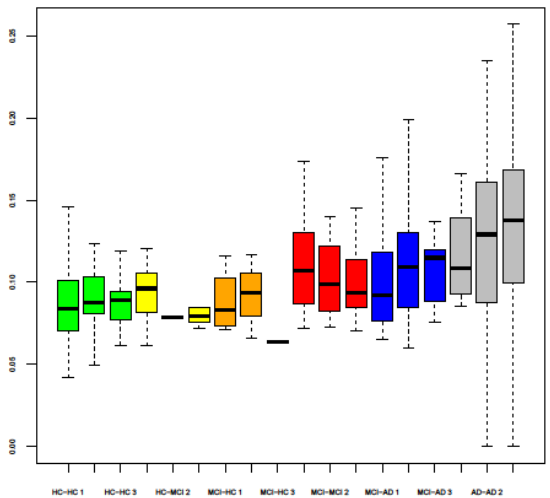
Original Article

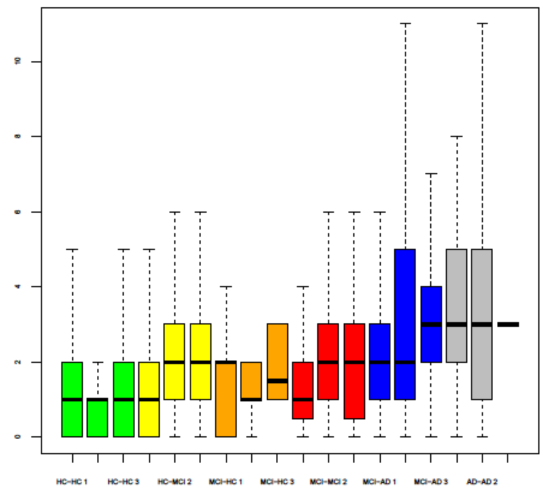
Molecular Psychiatry , (30 April 2013) | doi:10.1038/mp.2013.40

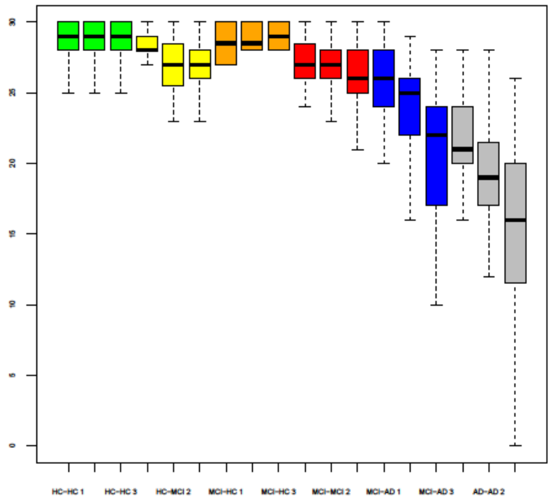
A blood-based predictor for neocortical Aβ burden in Alzheimer's disease: results from the AIBL study

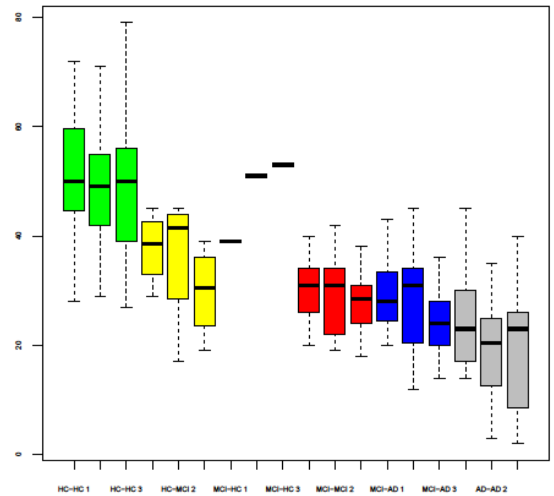
S C Burnham, N G Faux, W Wilson, S M Laws, D Ames, J Bedo, A I Bush, J D Doecke, K A Ellis, R Head, G Jones, H Kiiveri, R N Martins, A Rembach, C C Rowe, O Salvado, S L Macaulay, C L Masters, V L Villemagne, Alzheimer's Disease Neuroimaging Initiative1617 and Australian Imaging, Biomarkers and Lifestyle Study Research Group18

Transition Trajectories

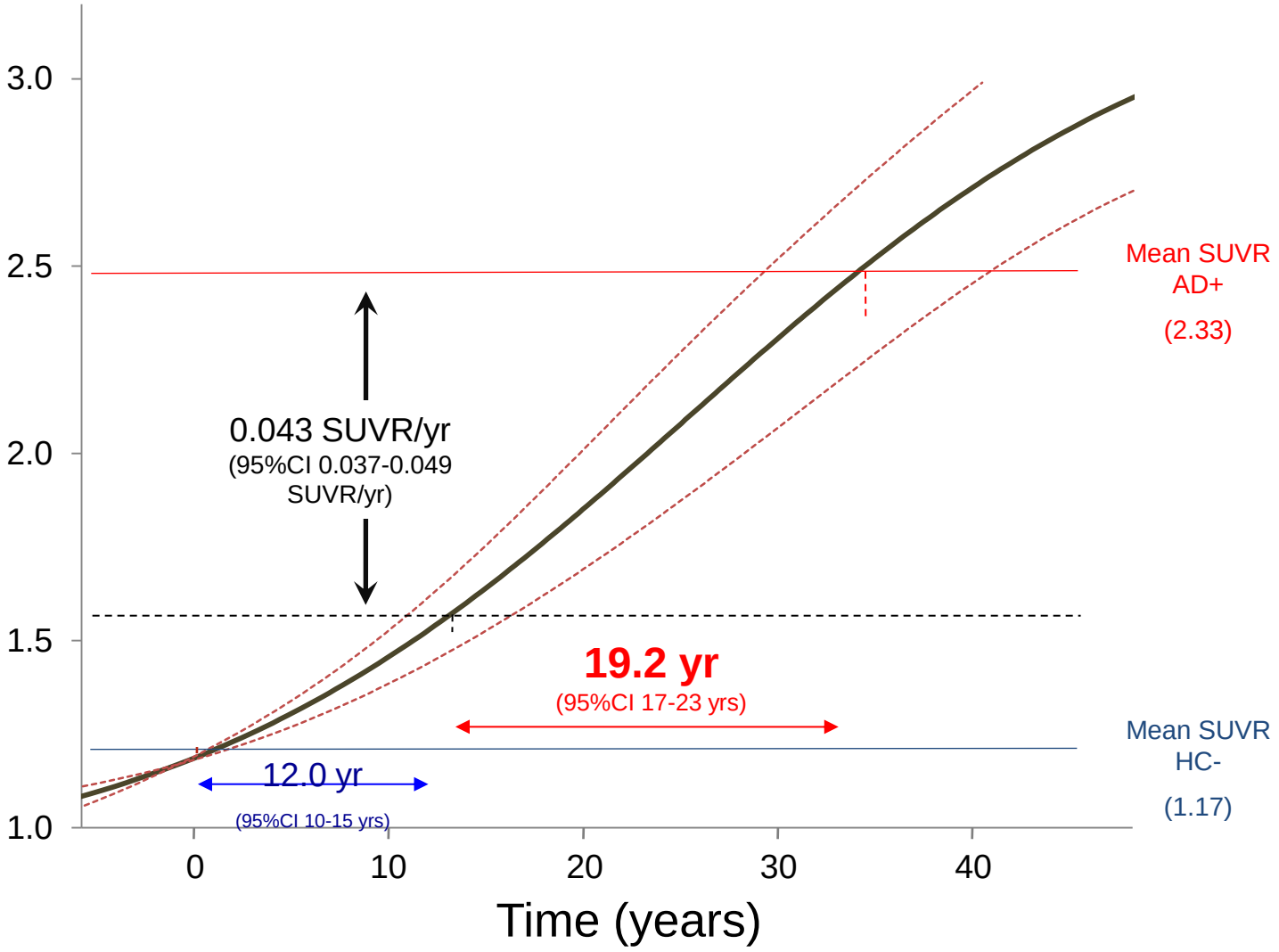






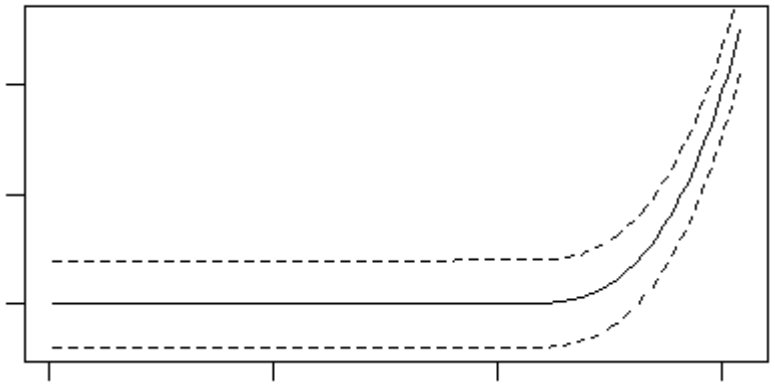


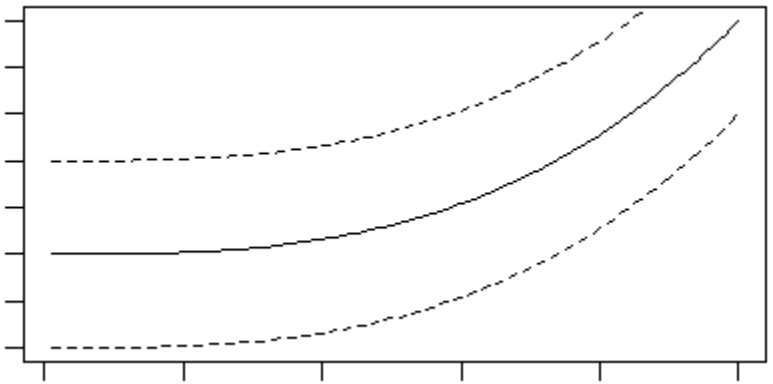
Longitudinal Models



www.thelancet.com/neurology Published online March 8, 2013 http://dx.doi.org/10.1016/S1474-4422(13)70044-9

Longitudinal Models





Summary

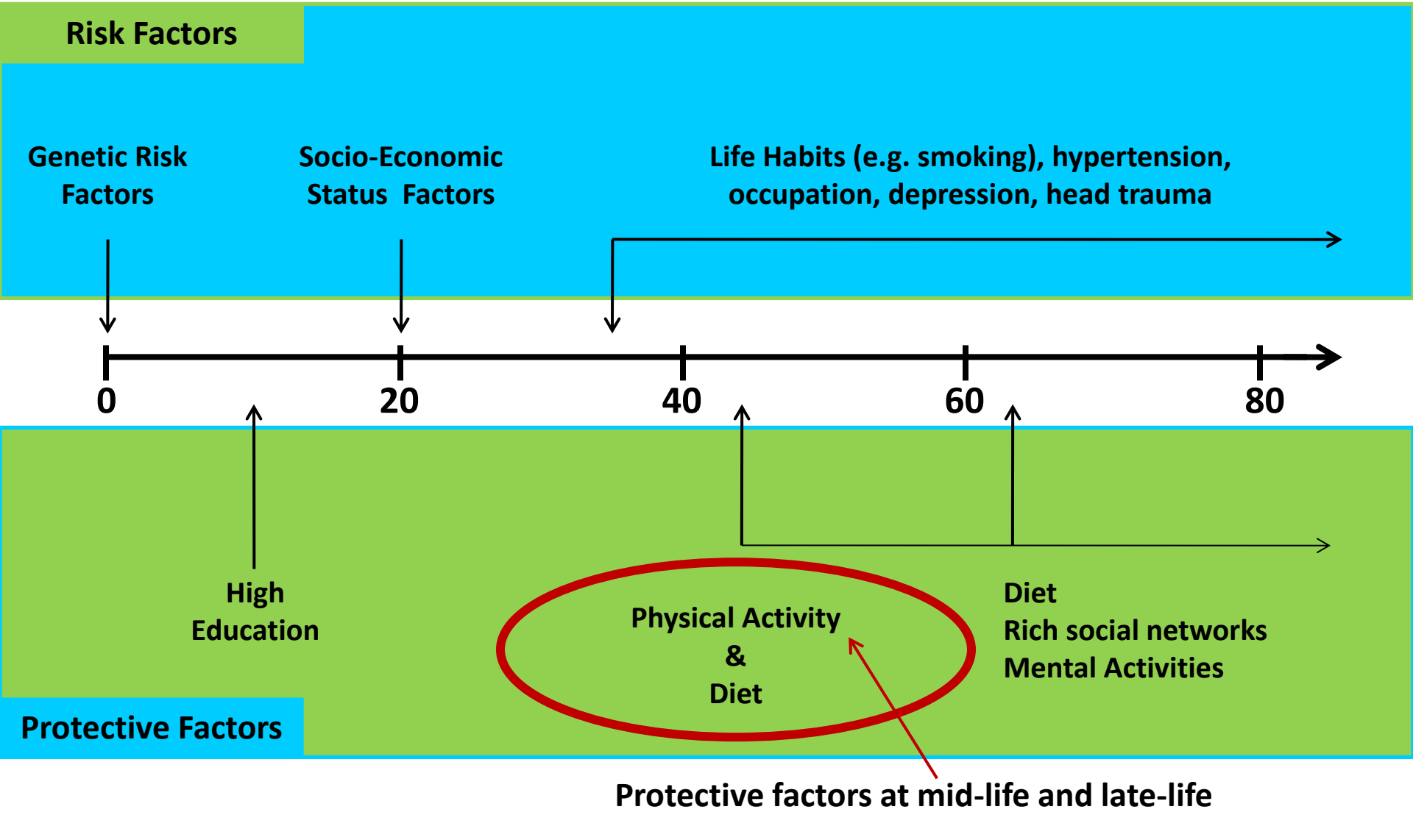
Validation is imperative

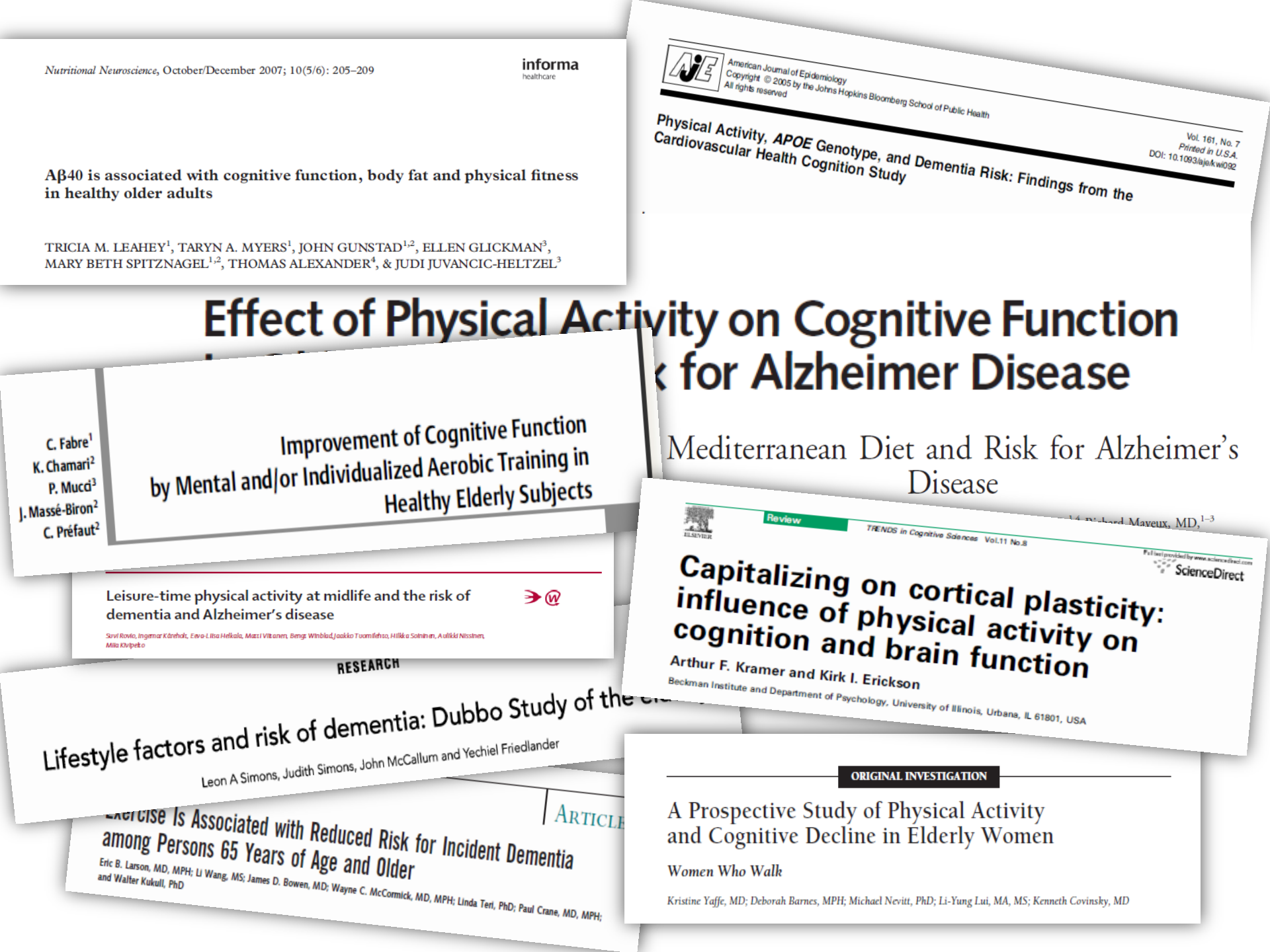
THE AUSTRALIAN IMAGING, BIOMARKERS AND LIFESTYLE STUDY OF AGEING (AIBL): LIFESTYLE PROGRAMME

Stephanie Rainey-Smith, PhD
Edith Cowan University, Western Australia

Lifestyle factors in Alzheimer's Disease

A healthy lifestyle is associated with reduced cognitive decline and AD risk





Nutritional Neuroscience, October/December 2007; 10(5/6): 205–209

informa
healthcare

Aβ40 is associated with cognitive function, body fat and physical fitness in healthy older adults

TRICIA M. LEAHEY[1], TARYN A. MYERS[1], JOHN GUNSTAD[1,2], ELLEN GLICKMAN[3], MARY BETH SPITZNAGEL[1,2], THOMAS ALEXANDER[4], & JUDI JUVANCIC-HELTZEL[3]

American Journal of Epidemiology
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Vol. 161, No. 7
Printed in U.S.A.
DOI: 10.1093/aje/kwi092

Physical Activity, *APOE* Genotype, and Dementia Risk: Findings from the Cardiovascular Health Cognition Study

Effect of Physical Activity on Cognitive Function

for Alzheimer Disease

C. Fabre[1]
K. Chamari[2]
P. Mucci[3]
J. Massé-Biron[2]
C. Préfaut[2]

Improvement of Cognitive Function by Mental and/or Individualized Aerobic Training in Healthy Elderly Subjects

Mediterranean Diet and Risk for Alzheimer's Disease

Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease

Review

TRENDS in Cognitive Sciences Vol.11 No.8

ScienceDirect

Capitalizing on cortical plasticity: influence of physical activity on cognition and brain function

Arthur F. Kramer and Kirk I. Erickson

Beckman Institute and Department of Psychology, University of Illinois, Urbana, IL 61801, USA

RESEARCH

Lifestyle factors and risk of dementia: Dubbo Study of the

Leon A Simons, Judith Simons, John McCallum and Yechiel Friedlander

ARTICLE

Exercise Is Associated with Reduced Risk for Incident Dementia among Persons 65 Years of Age and Older

Eric B. Larson, MD, MPH; Li Wang, MS; James D. Bowen, MD; Wayne C. McCormick, MD, MPH; Linda Teri, PhD; Paul Crane, MD, MPH; and Walter Kukull, PhD

ORIGINAL INVESTIGATION

A Prospective Study of Physical Activity and Cognitive Decline in Elderly Women

Women Who Walk

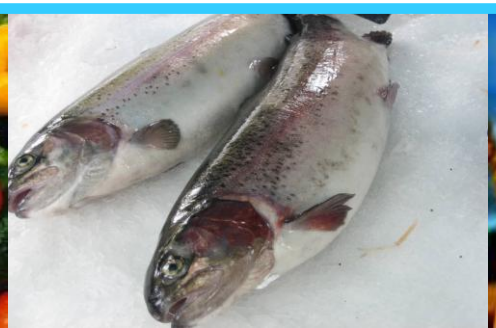
Kristine Yaffe, MD; Deborah Barnes, MPH; Michael Nevitt, PhD; Li-Yung Lui, MA, MS; Kenneth Covinsky, MD

AIBL Lifestyle Programme

Led by Professor Ralph Martins

Aim: Identification of lifestyle and dietary modifications which prevent or delay onset of AD

Dietary data

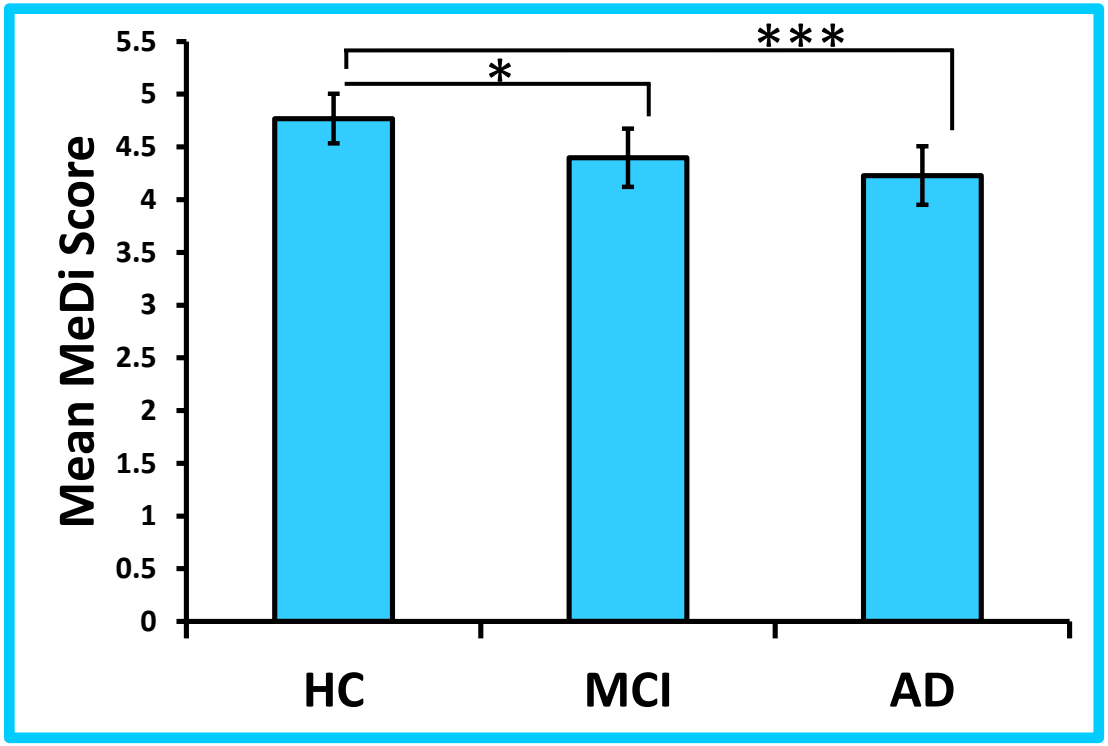
Methods

- CSIRO FFQ (online)
- Cancer Council of Victoria (CCV) FFQ
  - Previously validated in multiple epidemiological studies *(Keogh et al., 2010)*
  - Quantifies intake of 74 foods and beverages
  - Data can also be used to examine dietary patterns

Dietary Pattern Analysis

- **Mediterranean diet (MeDi)** - 'a priori' method
  - Includes high intake of fruit and vegetables, fish, legumes, cereals and unsaturated fatty acids
  - Low intake of dairy, meat and poultry and saturated fatty acids
  - Regular but moderate alcohol intake
- **Prudent diet** - 'a posteriori' (factor analysis)
  - Heavily loaded with vegetables, fruits and nuts
- **Western diet** - 'a posteriori' (factor analysis)
  - Heavily loaded with red and processed meats, high fat dairy products, chips, refined grains, potatoes, sweets and condiments.

Higher Adherence to MeDi in Healthy Controls compared to MCI and AD Groups



Mean ± SEM. *p<0.05; ***p<0.001; multinomial logistic regression models. Controlling for age, gender, education, APOE genotype, country of birth, BMI, total caloric intake, smoking status, history of hypertension, angina, stroke, diabetes and heart attack.

From: Gardener, Rainey-Smith et al 2012, Translational Psychiatry.

Higher MeDi and prudent diet adherence is associated with improved cognitive performance at baseline

Composite Cognitive Scores	MeDi Score		Prudent score	
Cognitive Domain	**Unadjusted**	**Adjusted**	**Unadjusted**	**Adjusted**
Verbal Memory	**0.143****	**0.138***	0.108	0.105
Visual Memory	0.077	0.081	**0.117***	**0.119***
Executive Function	**0.135***	**0.127***	0.051	0.047
Language	**0.139***	**0.128***	**0.217****	**0.220****
Visuospatial Function	**0.131***	**0.135***	**0.138***	**0.138***

Linear regression analysis; standardised β values shown. $p < 0.01$ = statistical significance. Fully adjusted model includes age, gender, YOE, APOE ε4 allele carriage, country of birth, BMI, energy intake, past/current smoking status, and history of hypertension, angina, stroke, heart attack and diabetes as covariates.

From: Gardener, Rainey-Smith et al 2013, Neurology (under review).

Higher western diet adherence at baseline is associated with greater cognitive decline at 36 months

- Global cognitive function (MMSE score)
- Visuospatial functioning and memory (RCFT, 3 min delay)
- Language, attention, fluent productivity and executive function (Fruit and furniture total and switching)

Linear regression analysis; standardised β values; $p < 0.01$ = statistical significance. Fully adjusted model includes age, gender, YOE, APOE ε4 allele carriage, country of birth, BMI, energy intake, past/current smoking status, and history of hypertension, angina, stroke, heart attack and diabetes as covariates.

From: Gardener, Rainey-Smith et al 2013, Neurology (under review).

Linear models show association between western dietary pattern and change in clinical classification

- Higher western diet adherence at baseline $\rightarrow \uparrow$ number of transitions from HC to MCI or AD at 36 months ($p < 0.001$).

- When analysis was stratified by APOE ε4 allele carriage, association was seen only in non APOE ε4 allele carriers.

From: Gardener, Rainey-Smith et al 2013, Neurology (under review).

Physical activity data



Physical Activity and AD

- **Physical activity has previously been associated with:**
  - Reduced cognitive decline and AD risk
  - Enhanced cognitive functioning
- **Most mechanistic studies have been animal studies**
- **AIBL array of biomarkers and comprehensive neuropsychological battery**
  - Potential to investigate association of physical activity with a number of AD-related factors in one cohort.

Methods

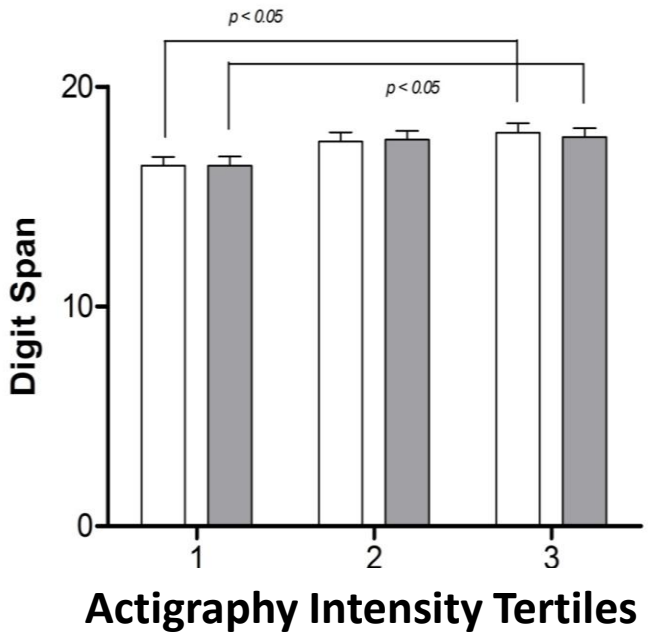
- **International physical activity questionnaire**
  - Answers used to calculated metabolic equivalent score (METs·min/wk^{-1})

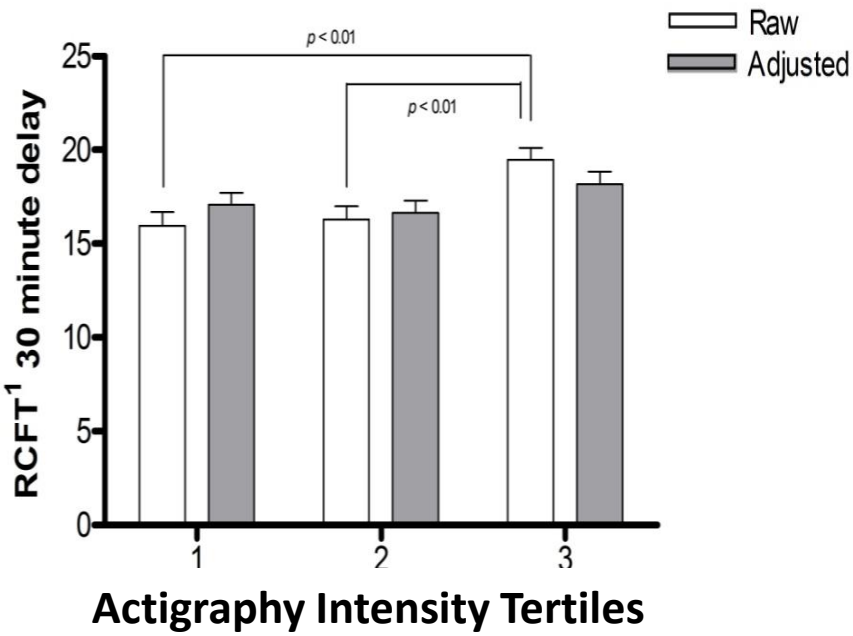
- **Actigraph**
  - Total counts (volume of activity)
  - Peak counts (intensity of activity)

- **To date all analyses have been on cognitively healthy controls only**

Cross-sectional analyses

Peak counts and cognitive function



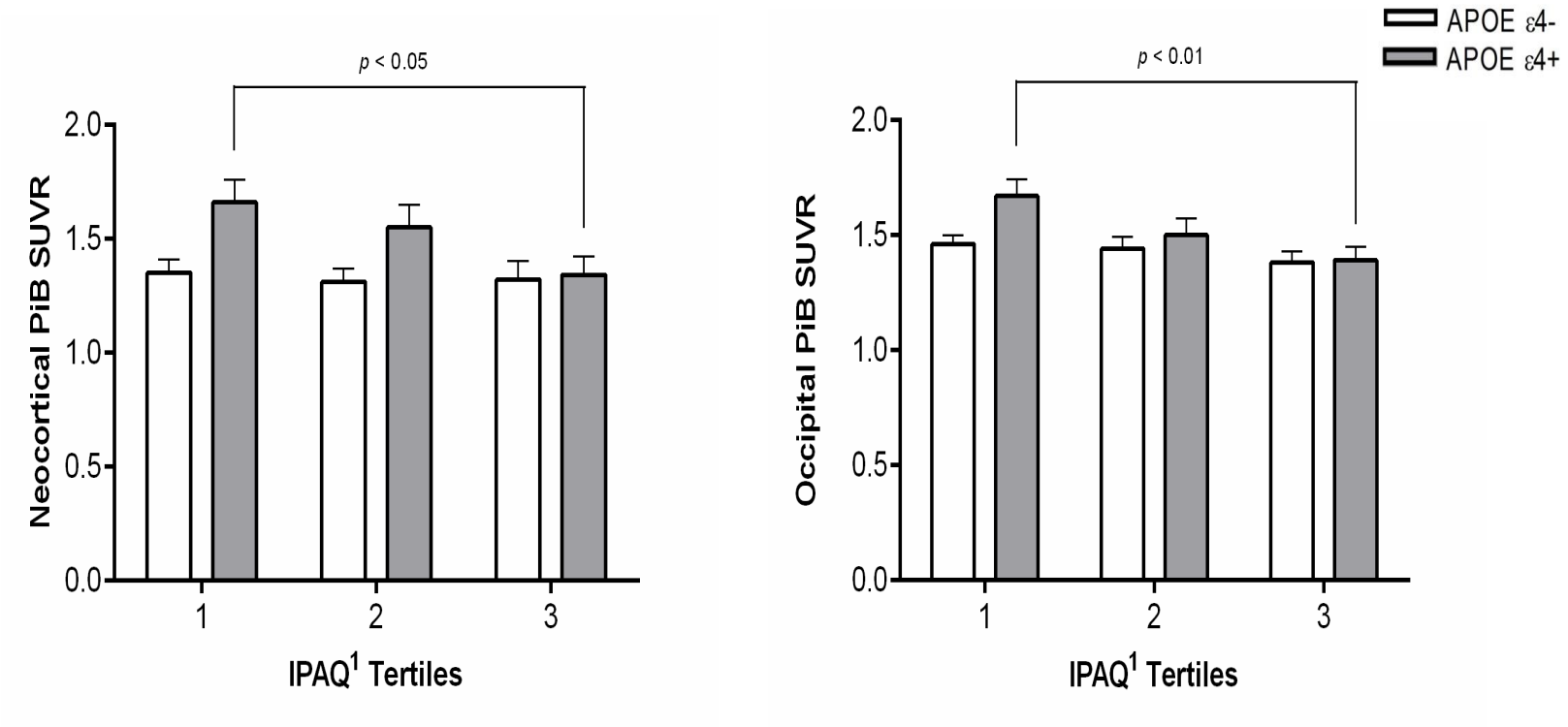


Raw and adjusted (for age, gender and YOE) of cognitive test score means (+ standard error) for each actigraphy intensity (peak count) tertile. [1]RCFT, Rey figure complex test.

Brown et al (2012), Translational Psychiatry, .

Cross-sectional analyses

Physical activity (IPAQ) and PiB SUVR

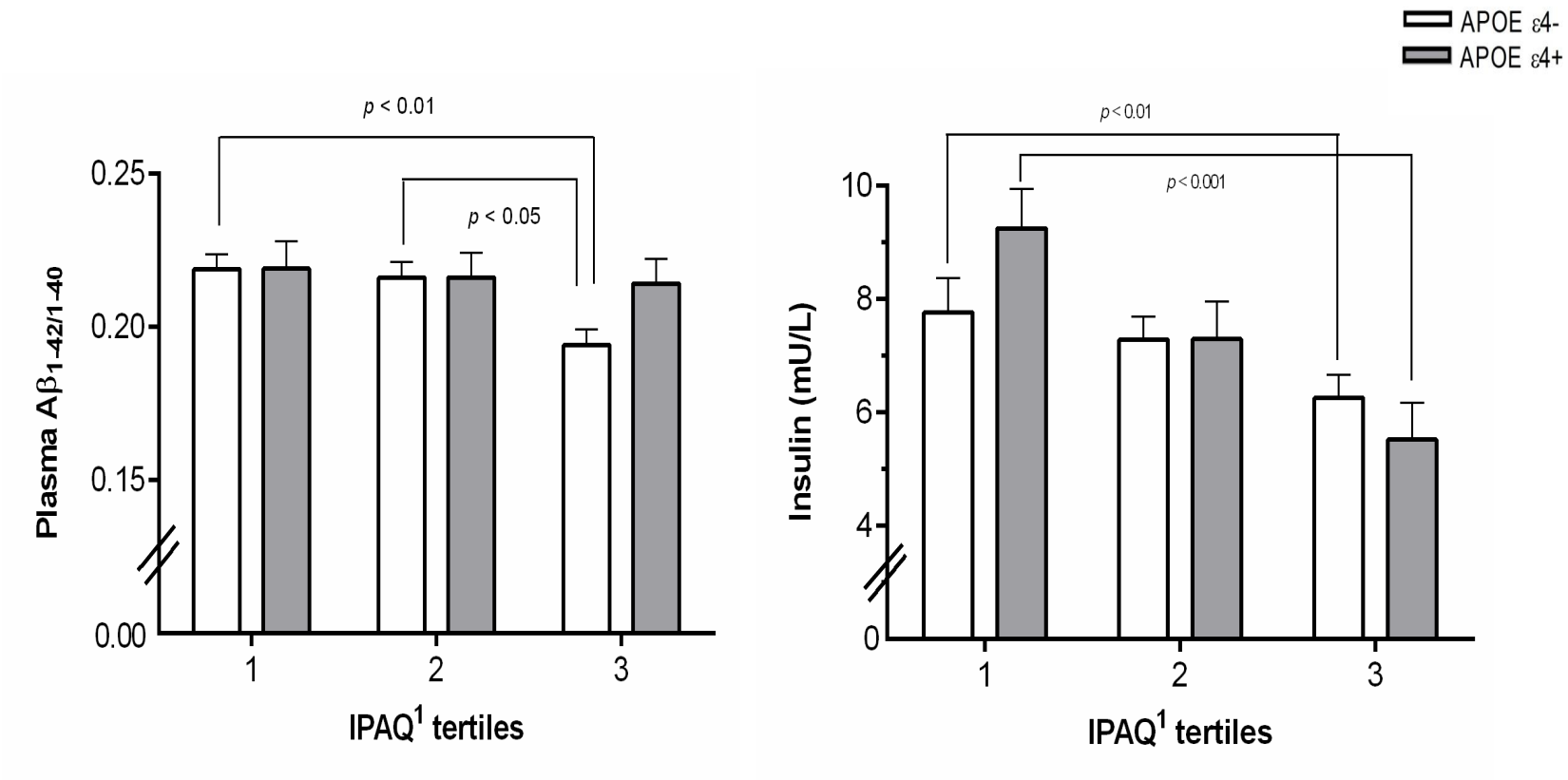


Adjusted means ± standard error (corrected for age, gender and years of education) of PiB SUVR for each self-report IPAQ tertile; after stratification by APOE ε4 allele carriage.

From: Brown et al 2012, Molecular Psychiatry.

Cross-sectional analyses

Physical activity (IPAQ) and blood biomarkers



Adjusted means ± standard error (corrected for age and gender) of blood biomarkers across each self-report IPAQ tertile

From: Brown et al 2012, Molecular Psychiatry.

Acknowledgements and Thanks

AIBL study participants, their families, and the AIBL study team

Osca Acosta
David Ames
Jennifer Ames
Manoj Agarwal
David Baxendale
Justin Bedo
Carlita Bevage
Lindsay Bevege
Pierrick Bourgeat
Belinda Brown
Rachel Buckley
Samantha Burnham
Ashley Bush
Tiffany Cowie
Kathleen Crowley
Andrew Currie
David Darby
Daniela De Fazio
Kim Lucy Do
James Doecke
Harriet Downing
Denise El- Sheikh
Kathryn Ellis
Kerryn Dickinson
Noel Faux
Jonathan Foster
Jurgen Fripp
Christopher Fowler
Samantha Gardener
Veer Gupta
Gareth Jones
Adrian Kamer
Jane Khoo
Asawari Killedar
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Tae Wan Kim
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Eleftheria Kotsopoulos
Gobhathai Kunarak
Rebecca Lachovitski
Simon Laws
Nat Lenzo
Qiao-Xin Li
Xiao Liang
Kathleen Lucas
James Lui
Georgia Martins
Ralph Martins
Paul Maruff
Colin Masters
Yumiko Matsumoto
Sabine Matthaes
Simon McBride
Andrew Milner
Claire Montague
Lynette Moore
Audrey Muir
Christopher O' Halloran
Graeme O'Keefe
Anita Panayiotou
Athena Paton
Jacqui Paton
Jeremiah Peiffer
Svetlana Pejoska
Kelly Pertile
Kerryn Pike
Lorien Porter
Roger Price
Parnesh Raniga
Alan Rembach
Carolina Restrepo
Miroslava Rimajova
Jo Robertson
Elizabeth Ronsisvalle
Rebecca Rumble
Mark Rodrigues
Christopher Rowe
Stephanie Rainey-Smith
Olivier Salvado
Jack Sach
Greg Savage
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Kevin Taddei
Tania Taddei
Brett Trounson
Marinos Tsikkos
Victor Villemagne
Stacey Walker
Vanessa Ward
Michael Weinborn
Andrea Wilson
Bill Wilson
Michael Woodward
Olga Yastrubetskaya
Ping Zhang

AIBL is a large collaborative study and a complete list of contributors can be found at www.aibl.csiro.au AIBL is funded in part by a grant from the Science and Industry Endowment Fund. We thank all who took part in the study.

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