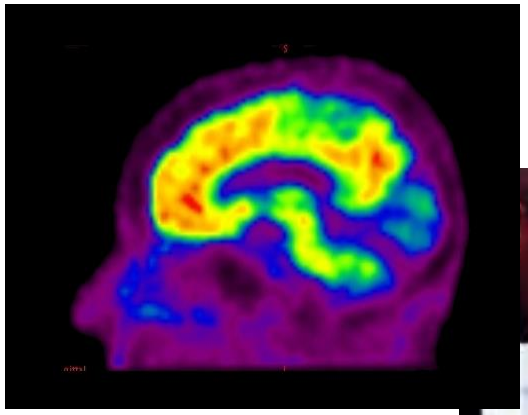
The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing – an example of Australian research on Alzheimer's disease



AIBL: Two site collaborative study

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

An Australian Government Initiative

The Cohort

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The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing

- A$3+ million study launched Nov 14th 2006 largest study of its kind in Australia
- Prospective longitudinal study

- Large scale cohort study: 1112 participants
- Patients with AD, MCI and healthy volunteers
- Multi-disciplinary approach, 4 research streams cognitive, imaging, biomarkers and lifestyle

Baseline

Clinical/cognitive data
80ml blood
Lifestyle information
PET & MRI scans (250 volunteers)

Follow-up (every 18 months)

Clinical/cognitive data
80ml blood
PET & MRI scans

Why AIBL?

Why would we want pre-symptomatic detection?

- To enable research into causes
- To identify at risk individuals for lifestyle research
- To identify at risk individuals for putative drug therapies
- Ultimately, to identify people who can have the onset of AD delayed by intervention
- Essential arm of a twin track strategy (early detection and effective intervention)

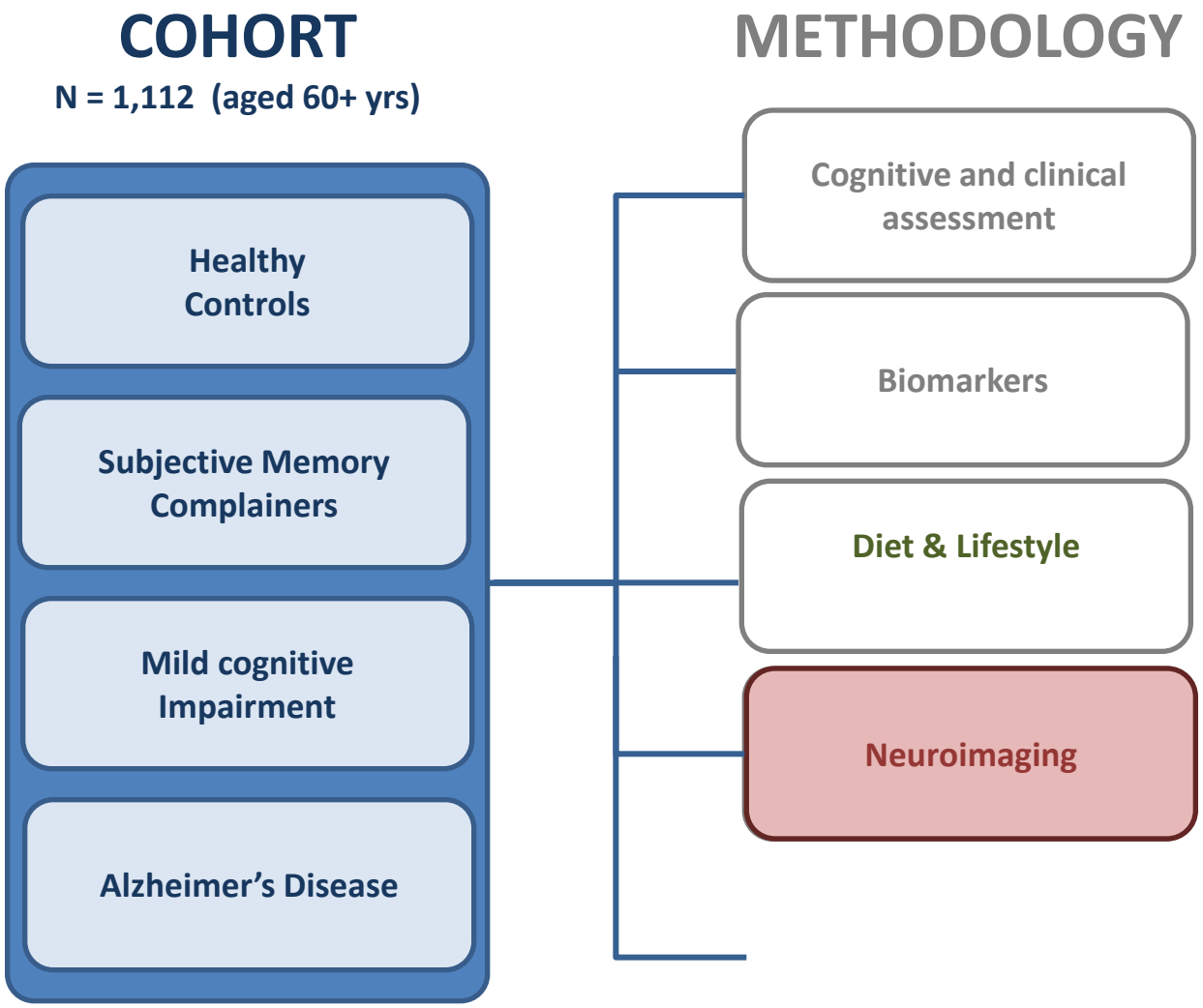
Study aims

1. To improve the understanding of the pathogenesis and diagnosis of Alzheimer's disease using neuropsychological, neuroimaging and biomarker techniques, with a focus on early diagnosis of AD

2. To examine lifestyle and diet factors that may be involved in the pathogenesis of AD, towards future lifestyle intervention

AIBL - overview

OVERVIEW: AIBL is the most comprehensive, longitudinal study of its kind in Australia, and aims to discover a way to develop biomarkers, diagnose patients earlier and prevent disease onset.



Methodology: Key outcomes

CLINICAL/COGNITIVE

Clinical and cognitive measures
• MMSE, CDR, Mood measures, Neuropsychological battery

Clinical classification information
• NINCDS-ADRDA (possible/probable) AD classifications
• ICD-10 AD classifications
• MCI classifications
• Memory complaint status (in HC)

Medical History, Medications and demography

LIFESTYLE

Lifestyle information

Detailed dietary information
Detailed exercise information
Objective activity measures (actigraph – 100 volunteers)
Body composition scans (DEXA)

BIOMARKERS

Comprehensive clinical blood pathology

Genotype
• Apolipoprotein E, WGA in subgroup

Stored fractions (stored in LN within 2.5 hrs of collection)
• Serum
• Plasma
• Platelets
• red blood cell,
• white blood cell (in dH20)
• white blood cell (in RNAlater, Ambion).

NEUROIMAGING

Neuroimaging scans (initially in 287 volunteers)

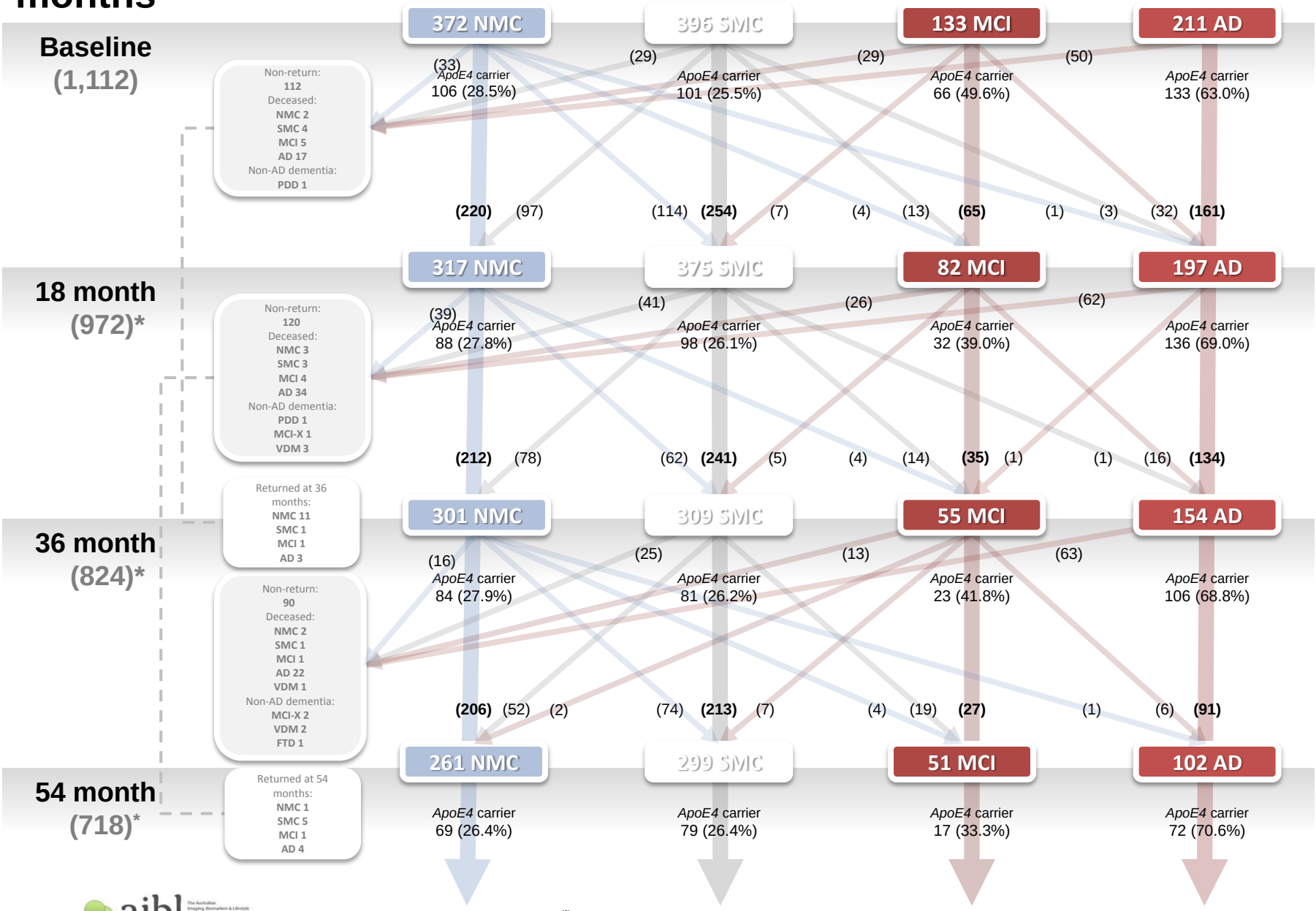
PET Pittsburgh Compound B (PiB)

Magnetic Resonance Imaging
• 3D T1 MPRAGE
•T2 turbospin echo
•FLAIR sequence

Assessments

- BP, HR, weight, height, abdominal girth
- 80 ml blood
- 2 hours neuropsychological testing
- HADS and GDS
- Medication list
- Diet and lifestyle questionnaires
- PiB PET scan and MRI for ¼
- Diagnostic panel evaluation
- DA file review
- Repeat every 18 months

AIBL: Longitudinal cohort: Baseline to 54 months



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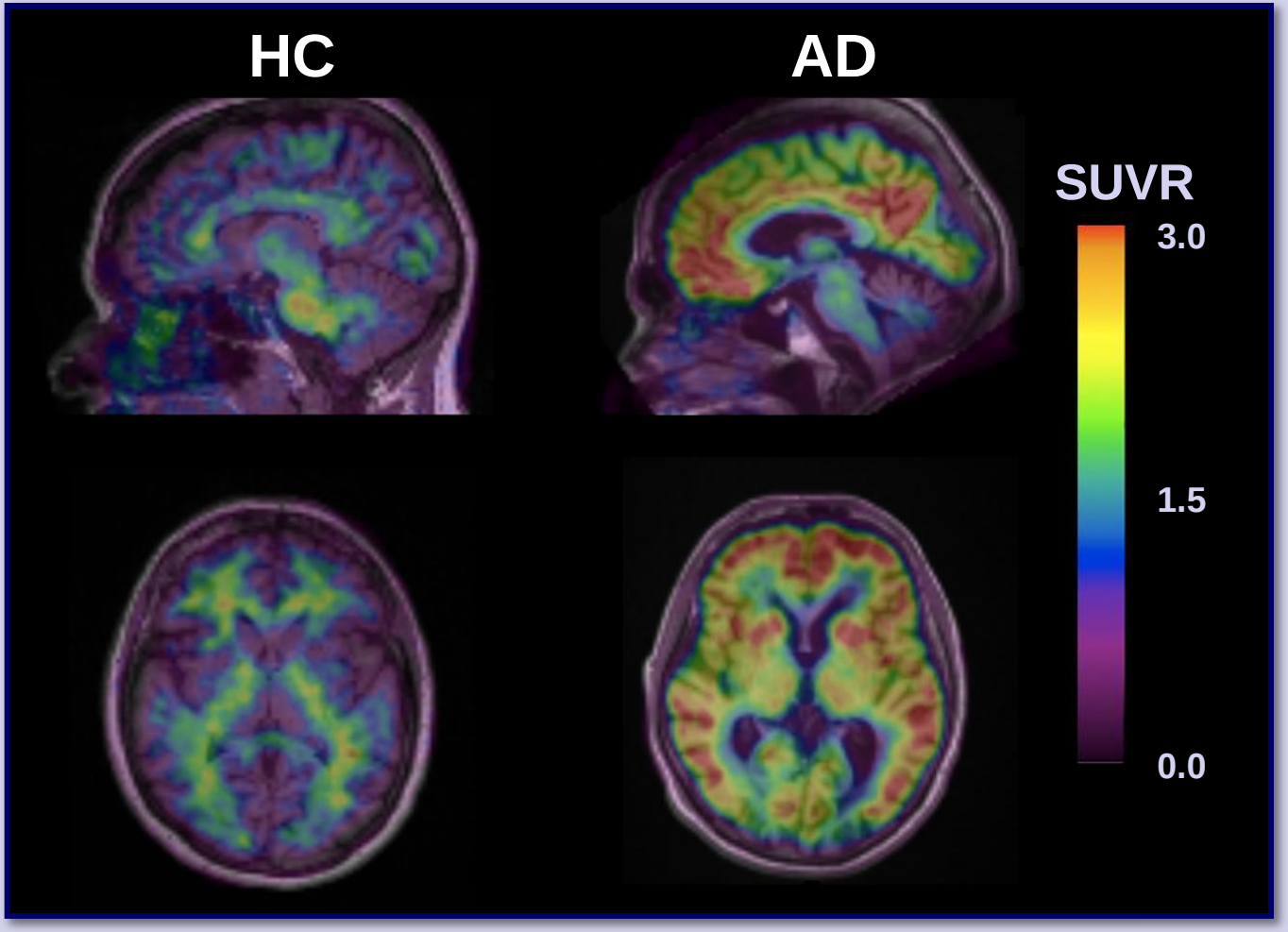
*Total active participants at each time point including non-AD dementia.

(NMC) Non-Memory Complainer, (SMC) Subjective-Memory Complainer, (MCI) Mild Cognitive Impairment, (AD) Alzheimer's disease, PDD (Parkinson's Disease Dementia), FTD (Frontotemporal Dementia), VDM (Vascular Dementia), MCI-X (Mild Cognitive Impairment non-AD related).

Imaging results

- Imaging collaboration led by Chris Rowe and Victor Villemagne at Austin Health and by Nat Lenzo, Roger Price and Peter Robins in WA with strong input from CSIRO via Olivier Salvado et al.

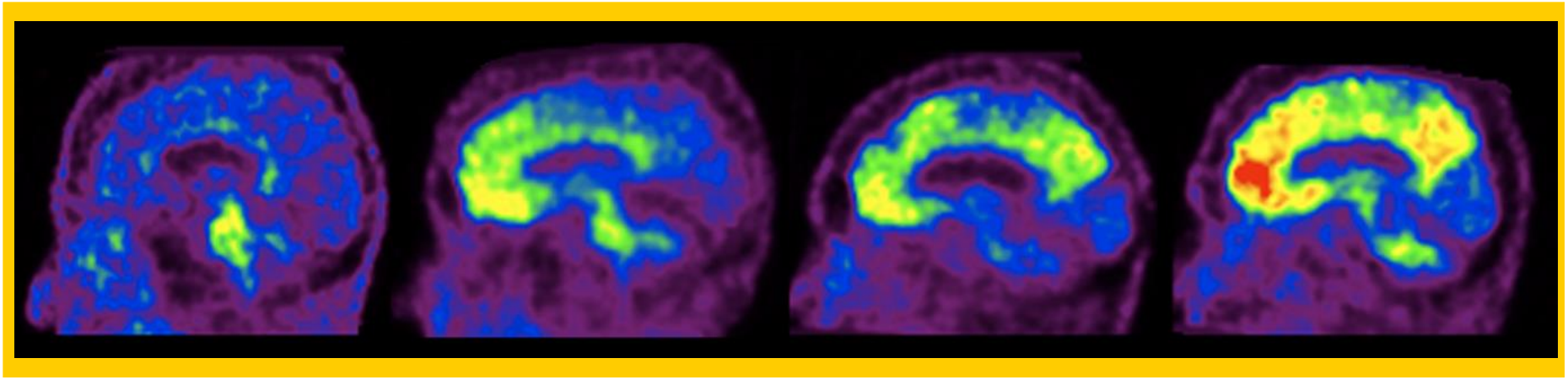
^{11}C-PiB for Aβ Imaging

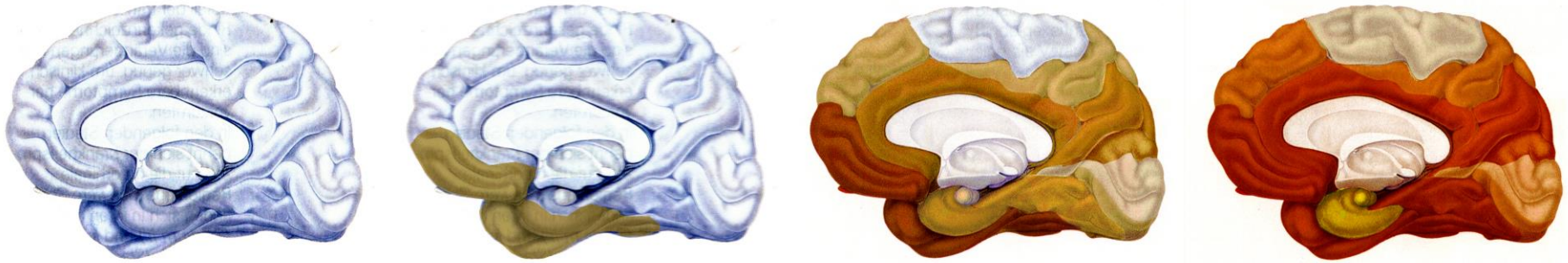


SUVR, standardized uptake value ratio.

Villemagne VL, Rowe CC. *Int Psychogeriatr.* 2011;23(suppl 2):S41-S49.

The binding of PIB matches the histopathology of Abeta





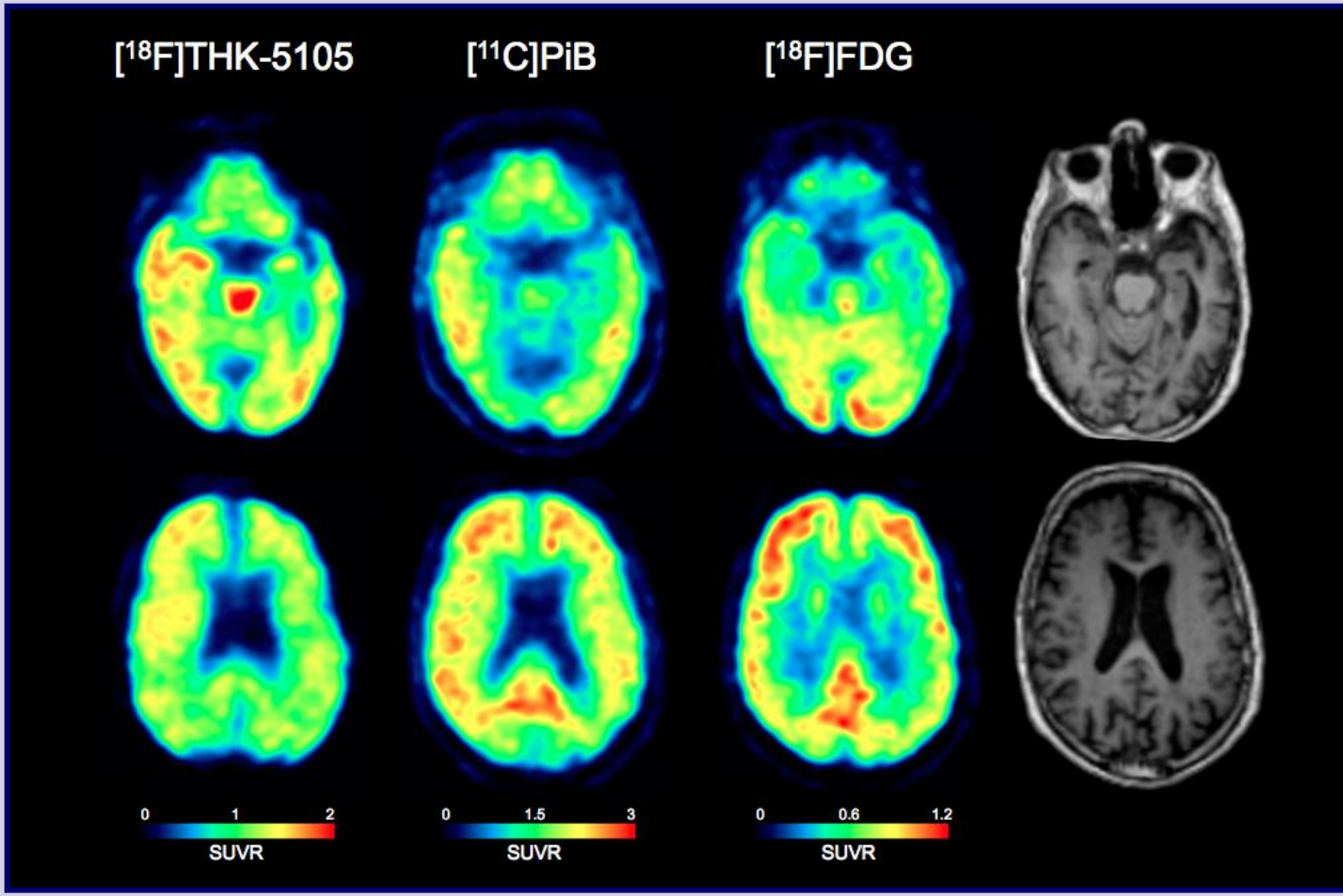
Braak Stages (1997)

A

B

C

Tau, Aβ, and Glucose Metabolism in Alzheimer's Disease



FDG, fluorodeoxyglucose.
Villemagne and Rowe; used with permission (unpublished).

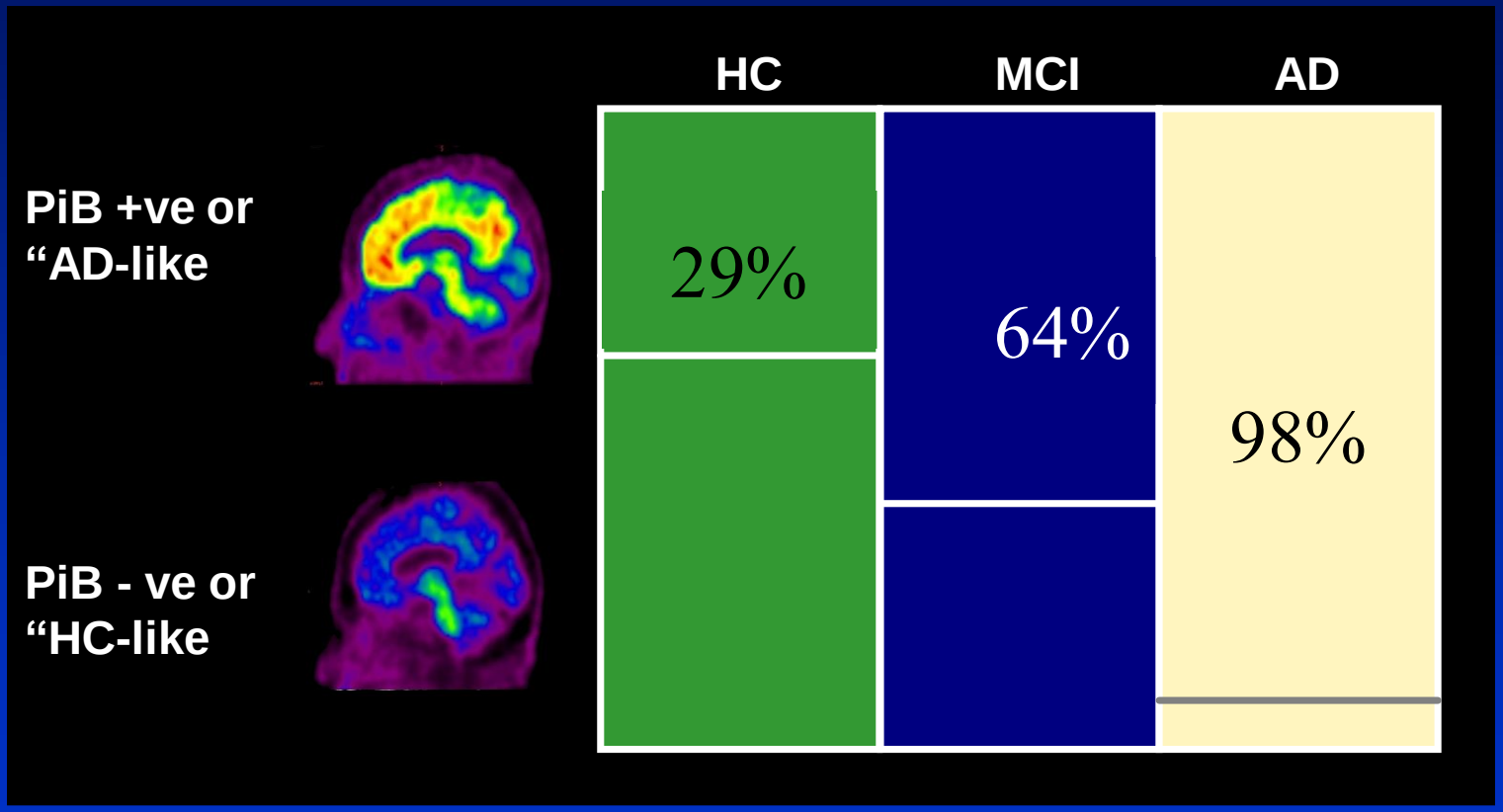
Imaging Cohort Baseline demographics (*n=288*)

	HC*	MCI	AD
	178	57	53
Age	73.6 ± 7.6	77.4 ± 7.5*	74.0 ± 8.7
MMSE	28.8 ± 1.2	27.1 ± 2.3*	20.5 ± 4.9*
%ApoE ε4	43%	54%	71%*

*enriched with ApoE ε4

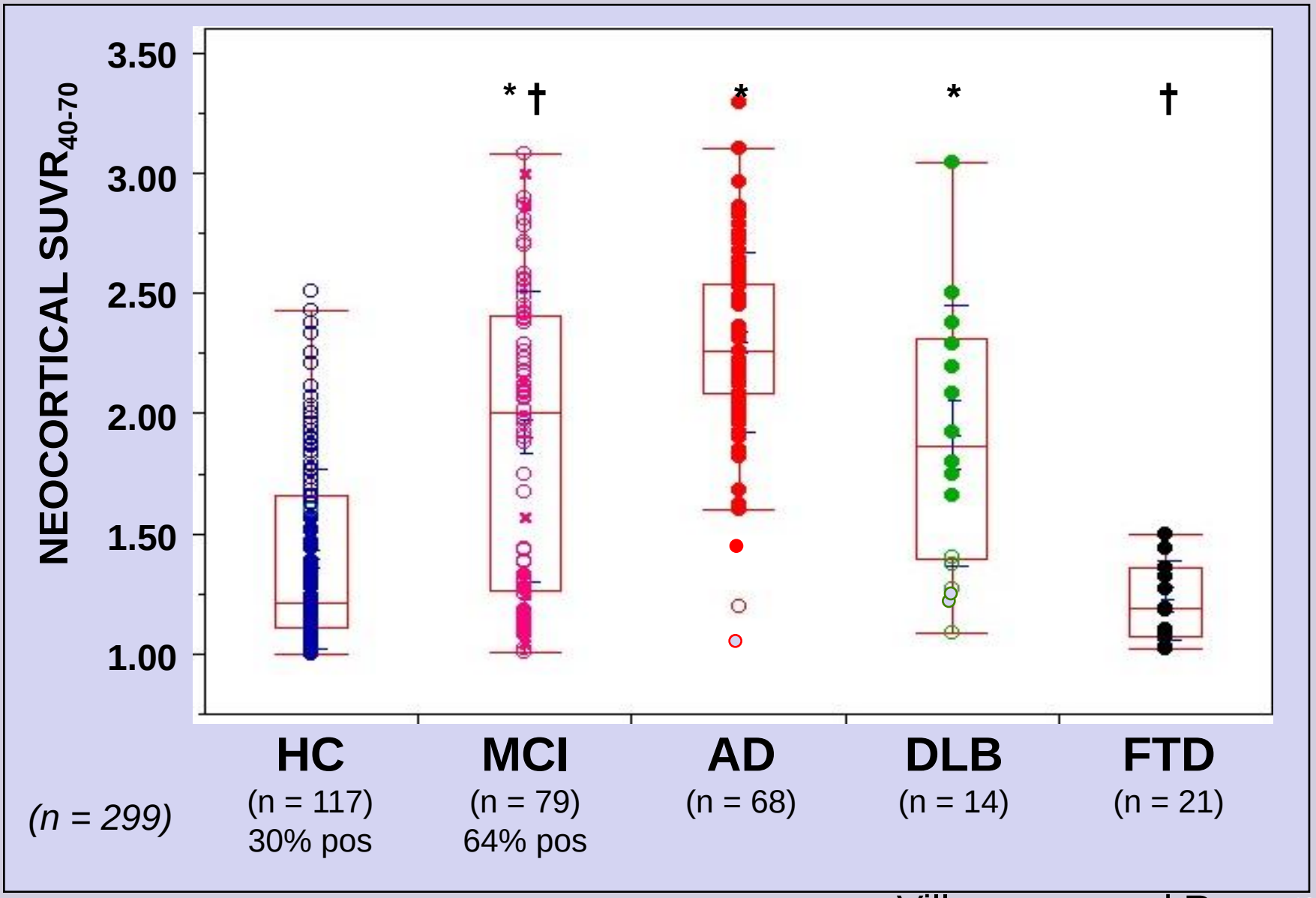
**Significantly different from HC, p <0.05*

Percentage of PiB + volunteers



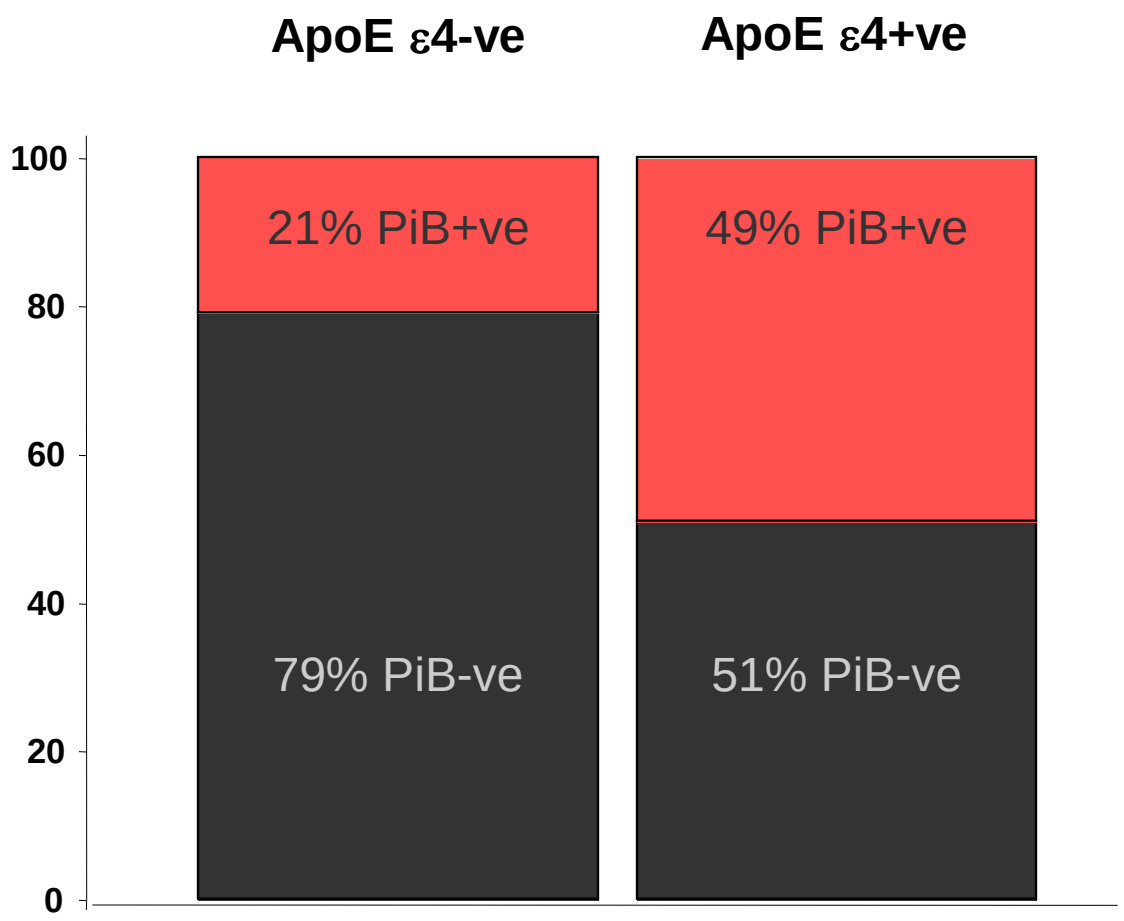
Significant differences between the three groups ($p<0.001$)

Aβ burden quantification



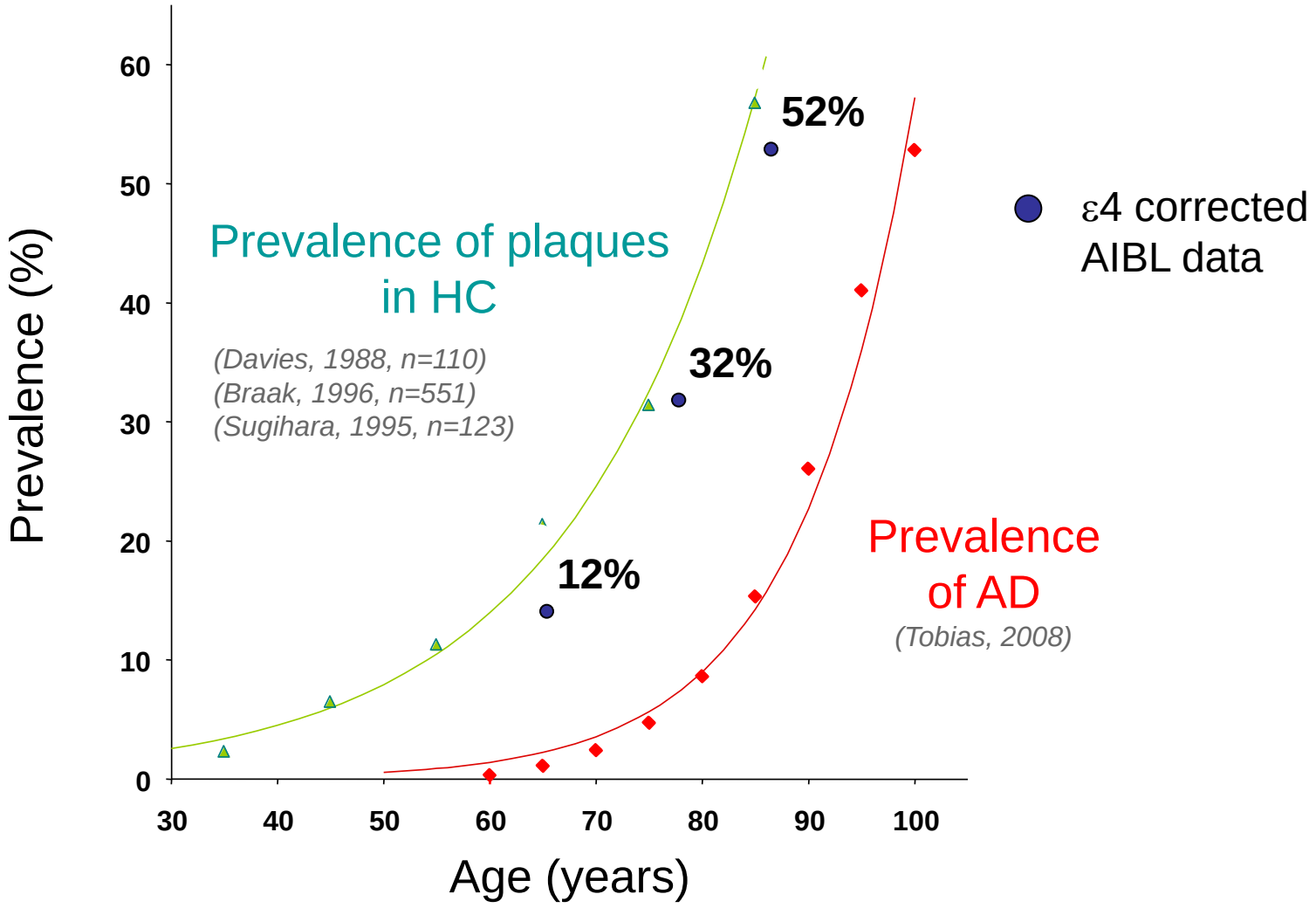
Villemagne and Rowe

Influence of ApoE ε4 status on PiB+ in Healthy Controls

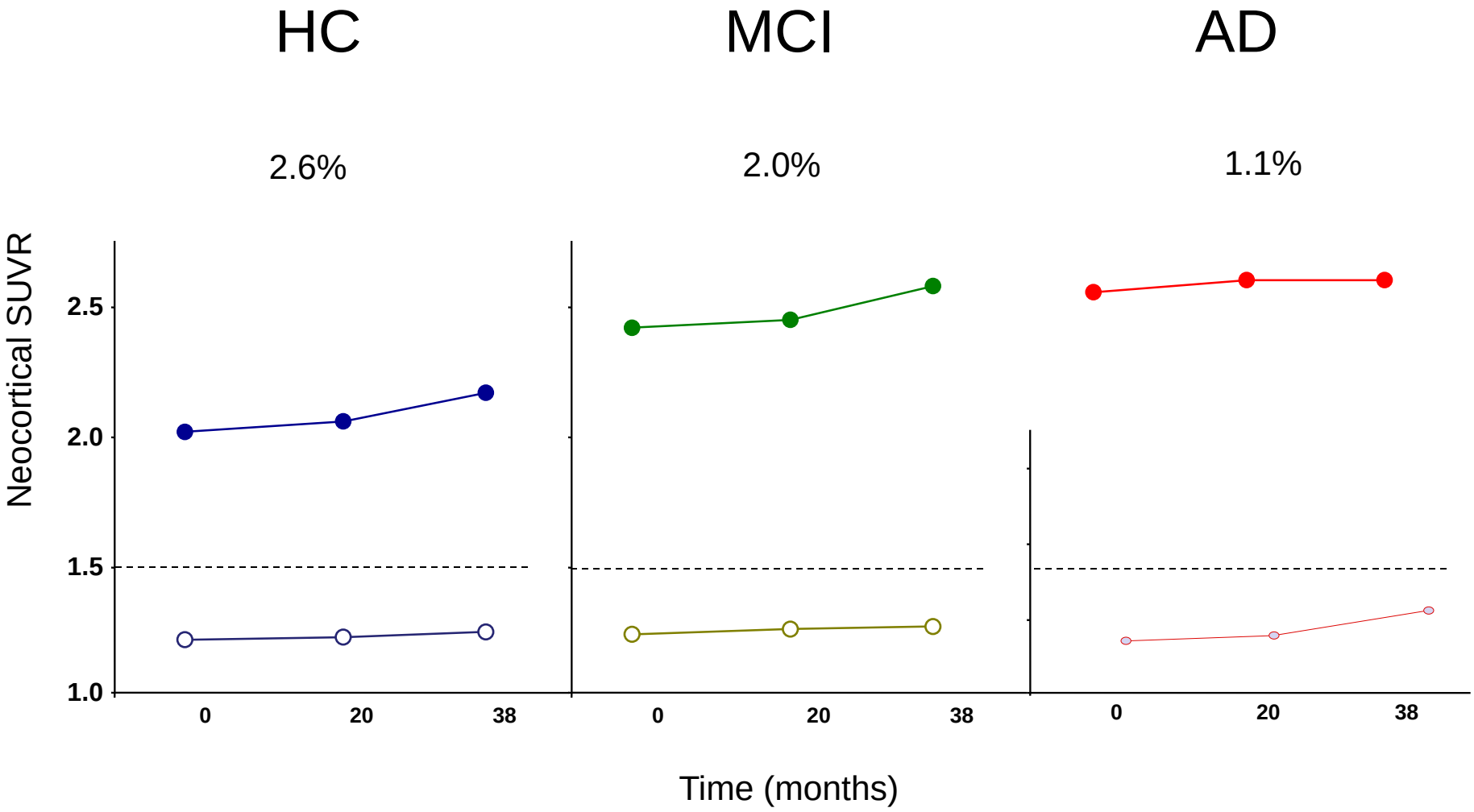


PiB+ vs Age in Healthy Controls

(AIBL ApoE ε4 prevalence corrected data)



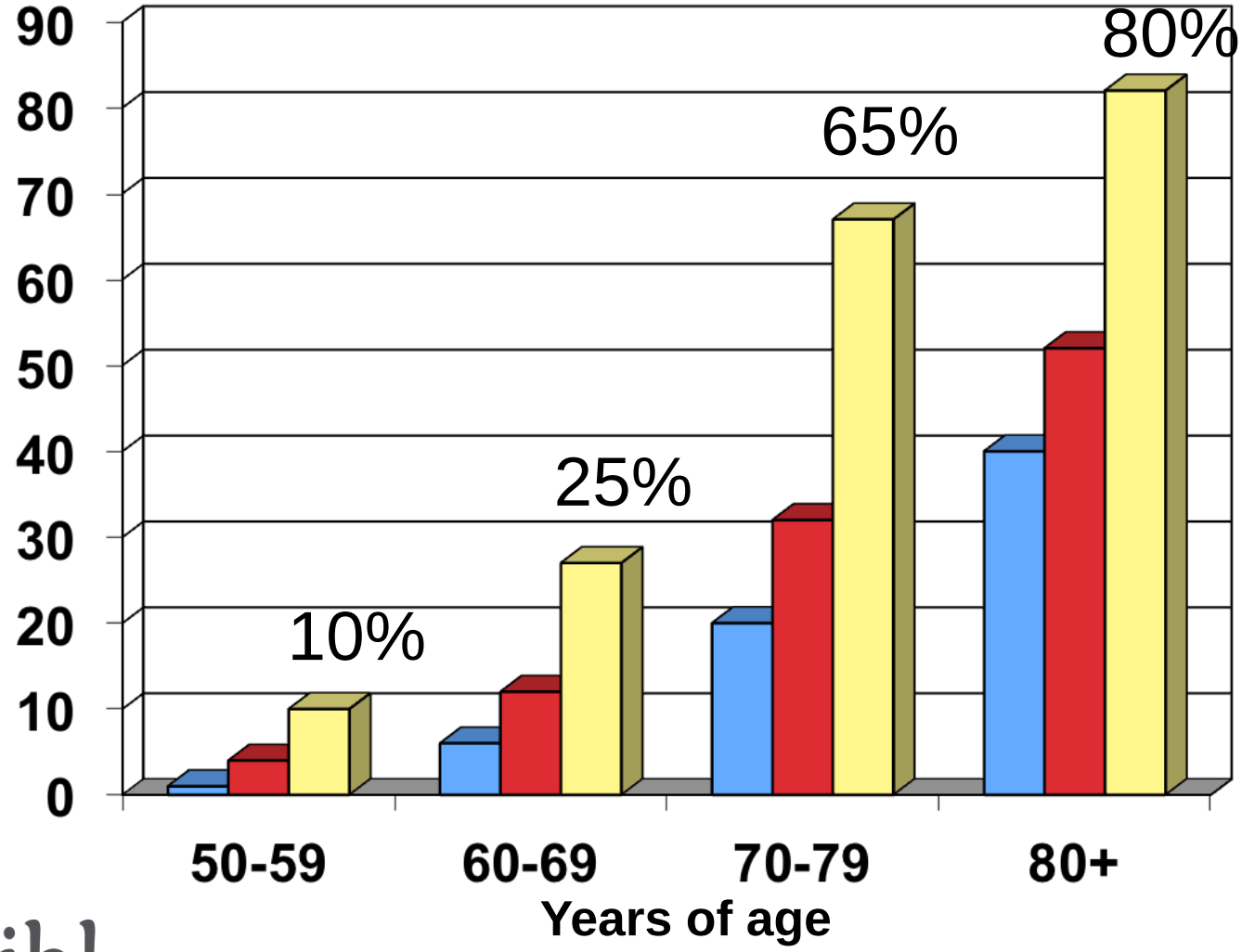
Longitudinal PiB PET follow-up



* *PiB+/PiB- SUVR cut-off = 1.5*

Villemagne / Rowe

ApoE-ε4 and Risk of Amyloid in Healthy Older Persons



< 60 yrs data from Washington University

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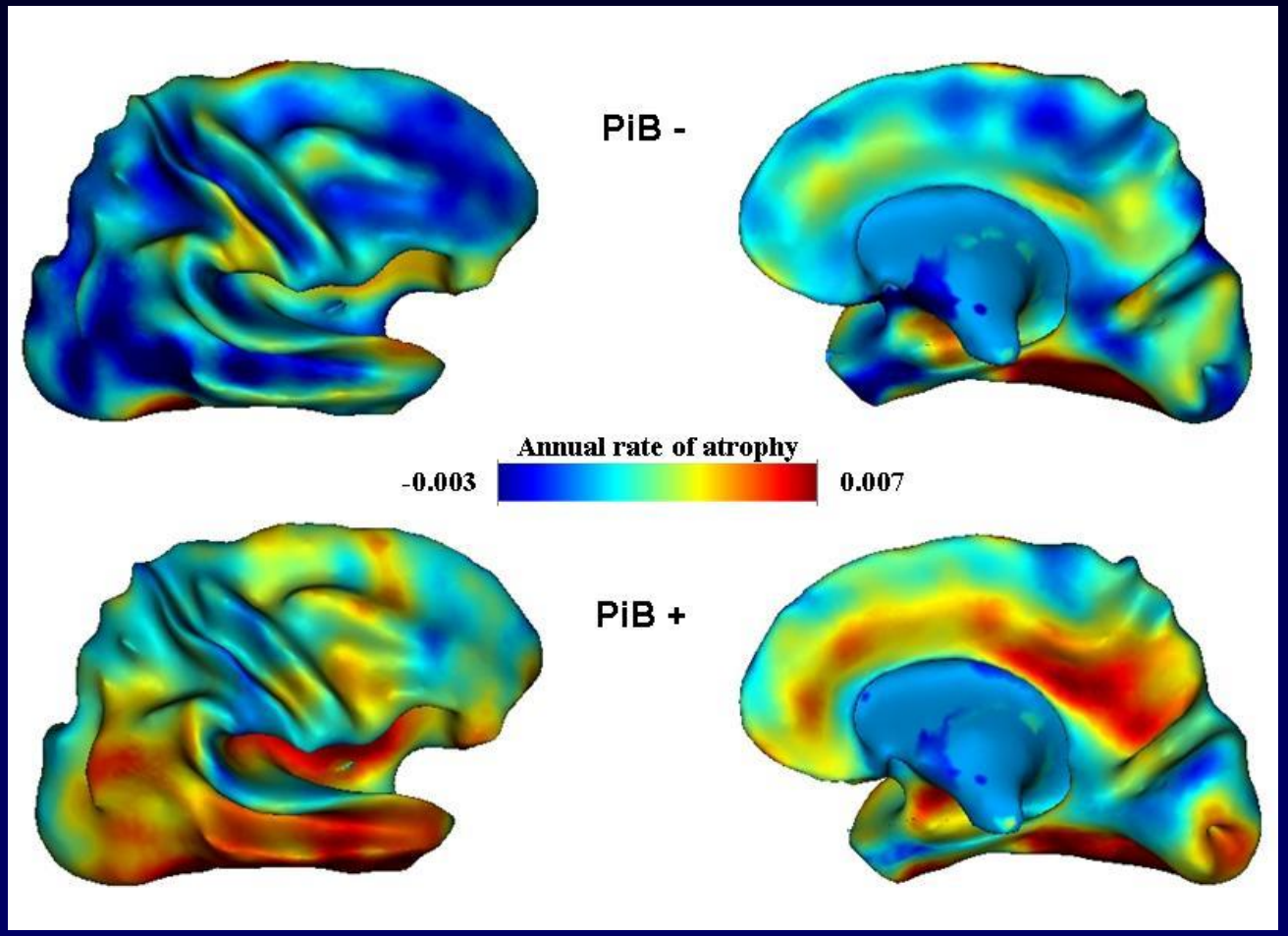
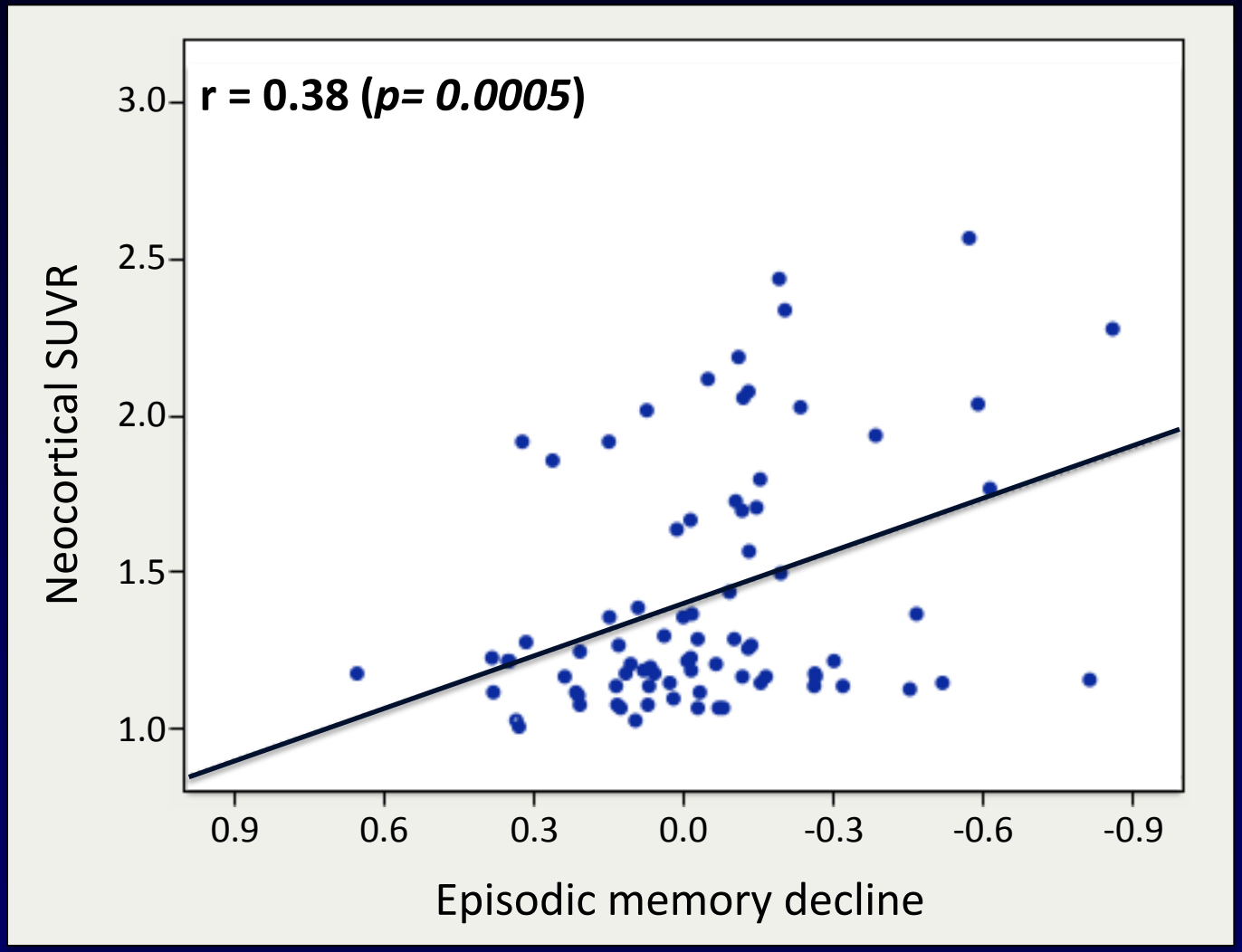
Average rate of atrophy over one year in HC PiB- vs PiB+.



BASELINE Aβ burden correlates with memory decline over 3 years in HC



AIBL+
Prediction of Progression: HC to MCI/AD

36 months
n=195

PiB-ve Subjects:	129
Converters to MCI/AD	**7%**

PiB+ve Subjects:	66
Converters to MCI/AD	**19%**

AIBL+
Prediction of Progression: MCI to Dementia

36 Months
n=92

PiB -ve :	34
Converters to AD	**10%**
Other dementia	**17%**
No dementia	**73%**

PiB +ve :	58
Converters to AD	**56%**
No dementia	**44%**