

Cross Sectional and Longitudinal Studies in LOAD: AIBL Experience.



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The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing

Commenced 2006

PiB and MRI with follow-up in 288 of the 1100 participants
Imaging increased to 700 participants by 2012



AIBL cohort Dec2014: Total numbers (Inception and Enrichment)

Baseline	397 NMC	616 SMC	234 MCI	291 AD
18 month Enrichment visits in progress	348 NMC	465 SMC	123 MCI	233 AD
36 month	305 NMC	320 SMC	58 MCI	162 AD
54 month	261 NMC	299 SMC	51 MCI	102 AD
72 month	212 NMC	269 SMC	48 MCI	59 AD

90 month visits just started + tau imaging
in 240 commenced



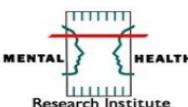
The Australian Imaging
Biomarkers and Lifestyle
Flagship Study of Ageing.

4.5 year data release

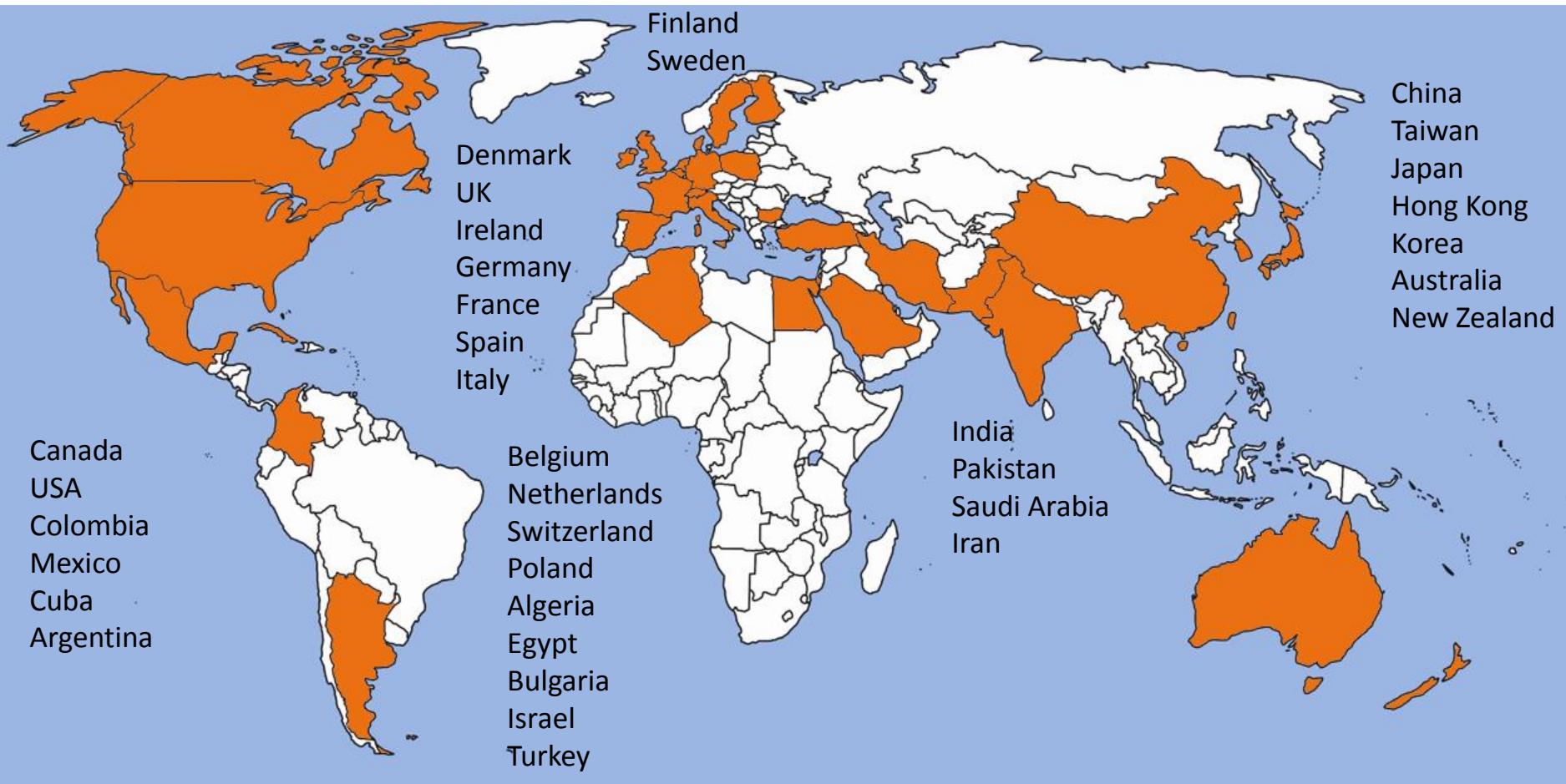
amyloid scan status known in 371 subjects with
4.5 yrs of follow-up and 250 new recruits

www.adni.loni.usc.edu

- *Data and Samples*
- *Access Data*



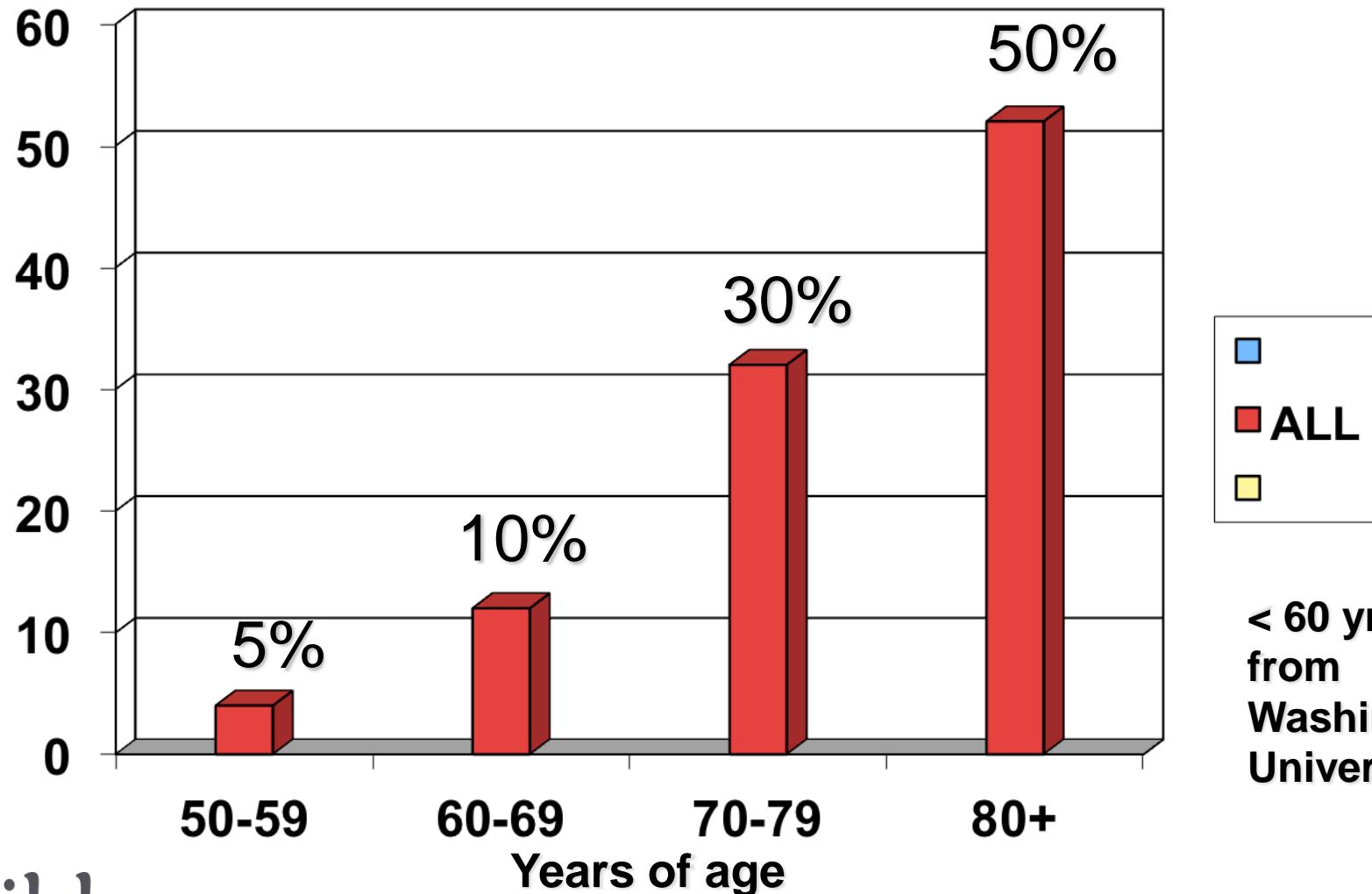
630 research groups granted access to AIBL@LONI through ADNI website



Includes access granted to the following companies:

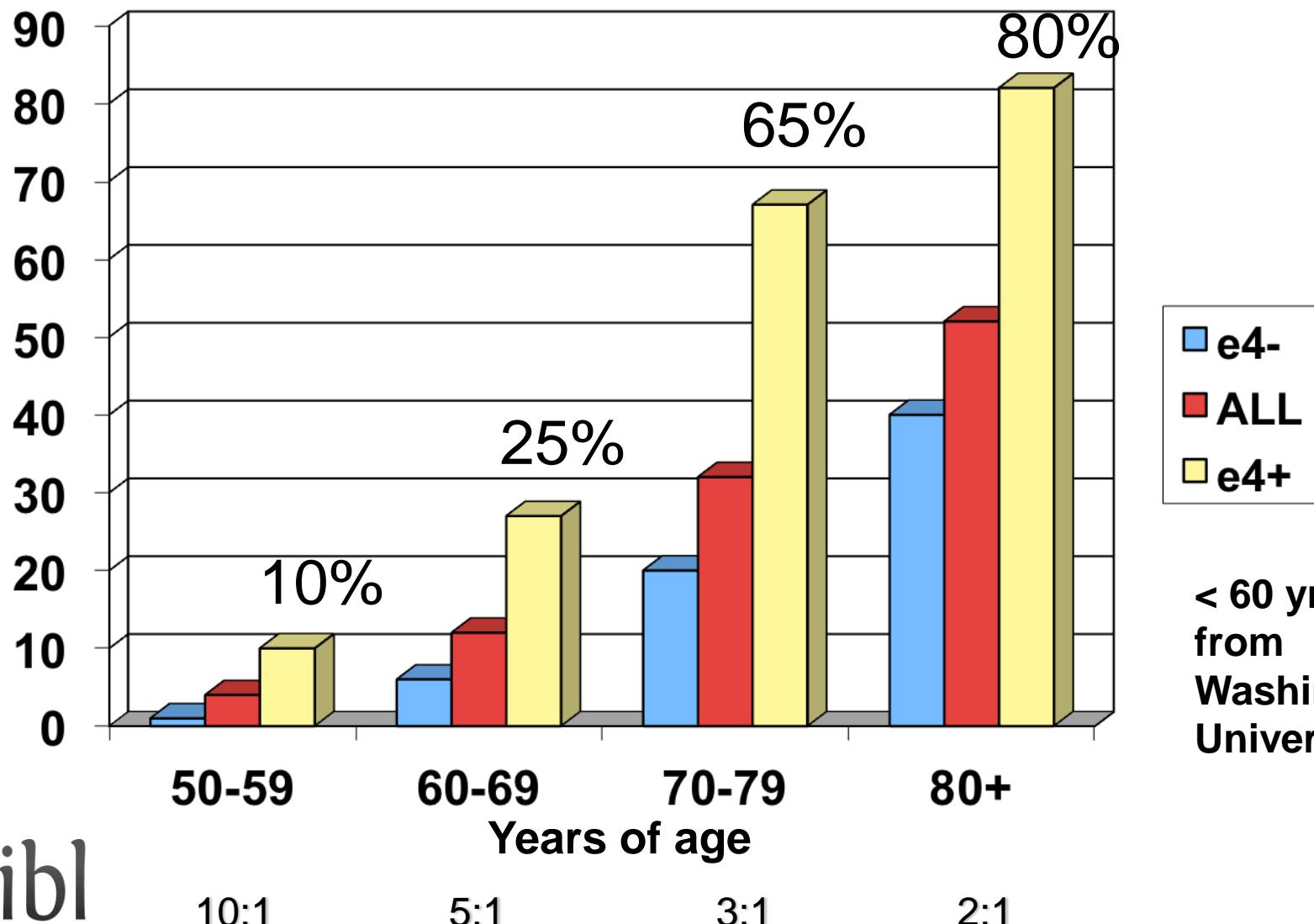
Abbott Labs, Abiant, ADM diagnostics, Astra Zeneca, Avid, BioClinica, Biogen Idec, Bristol-Myers Squibb, Cogstate Cytokinetics, Eisai, Elan, Eli Lilly, GE Health Care, General Resonance, Genetech, Imorphics, Iris Biotechnologies, Janssen, Johnson Johnson, M and M Scientific, Merck & Co, Mimvista, Pentara Corp, Pfizer, Philips, Predixion software, Rancho Biosciences, Servier, Siemens, Soft team solutions, UCB, United Biosource Corp.

% of healthy who are PiB+ve



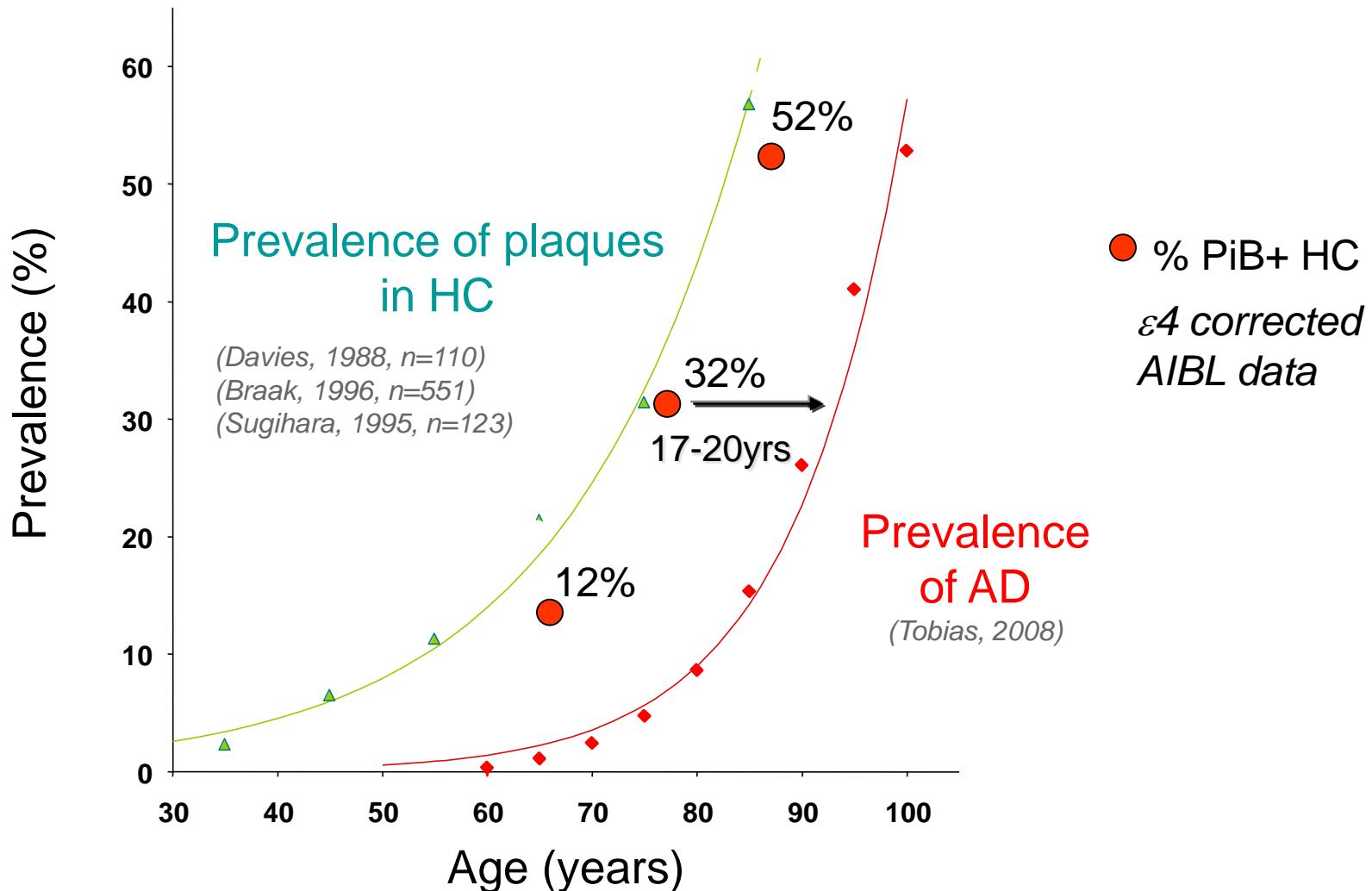
< 60 yrs data
from
Washington
University

ApoE- ϵ 4 and Risk of Amyloid in Healthy Older Persons

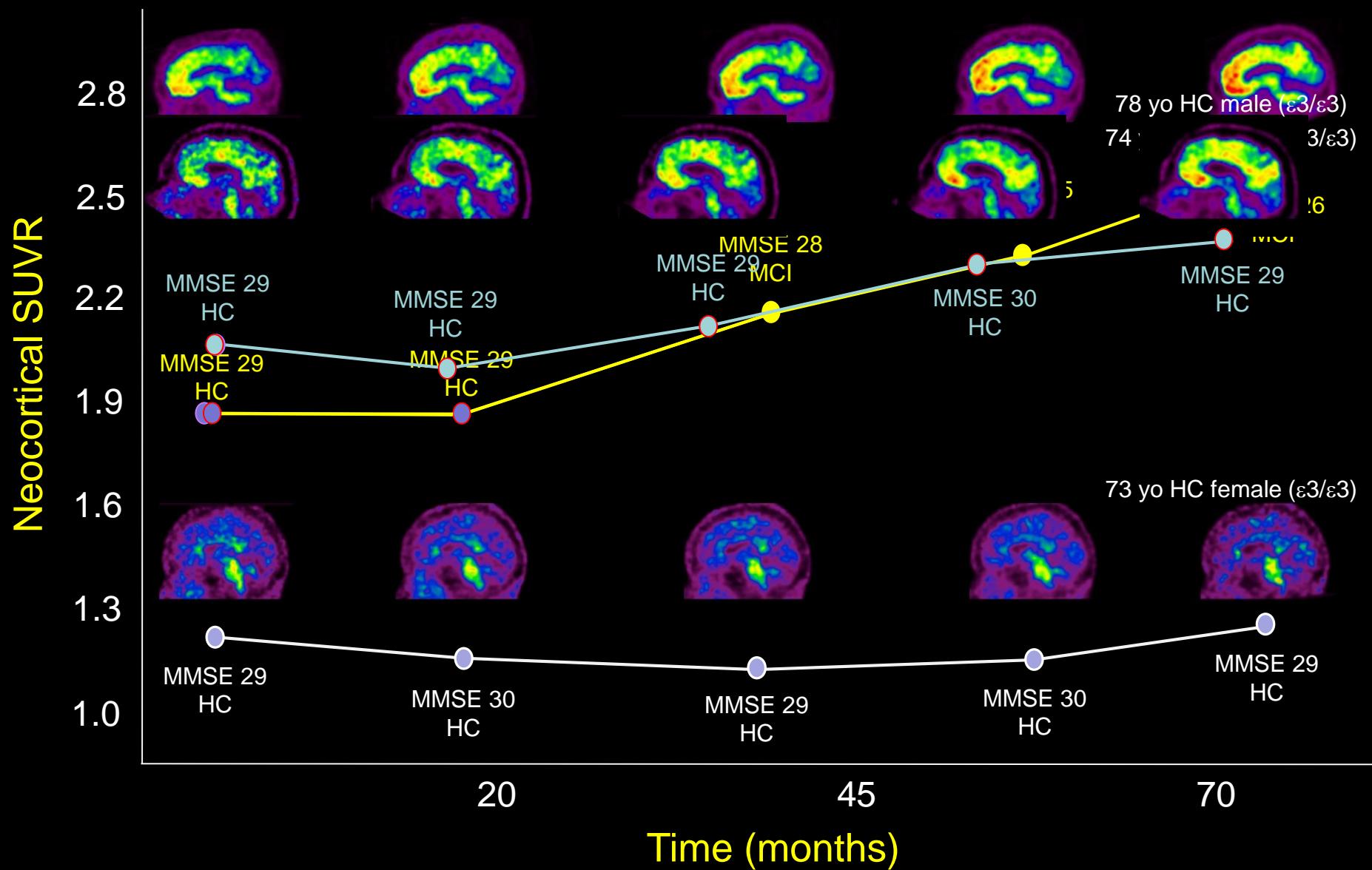


% PiB+ HC vs Age (by decade)

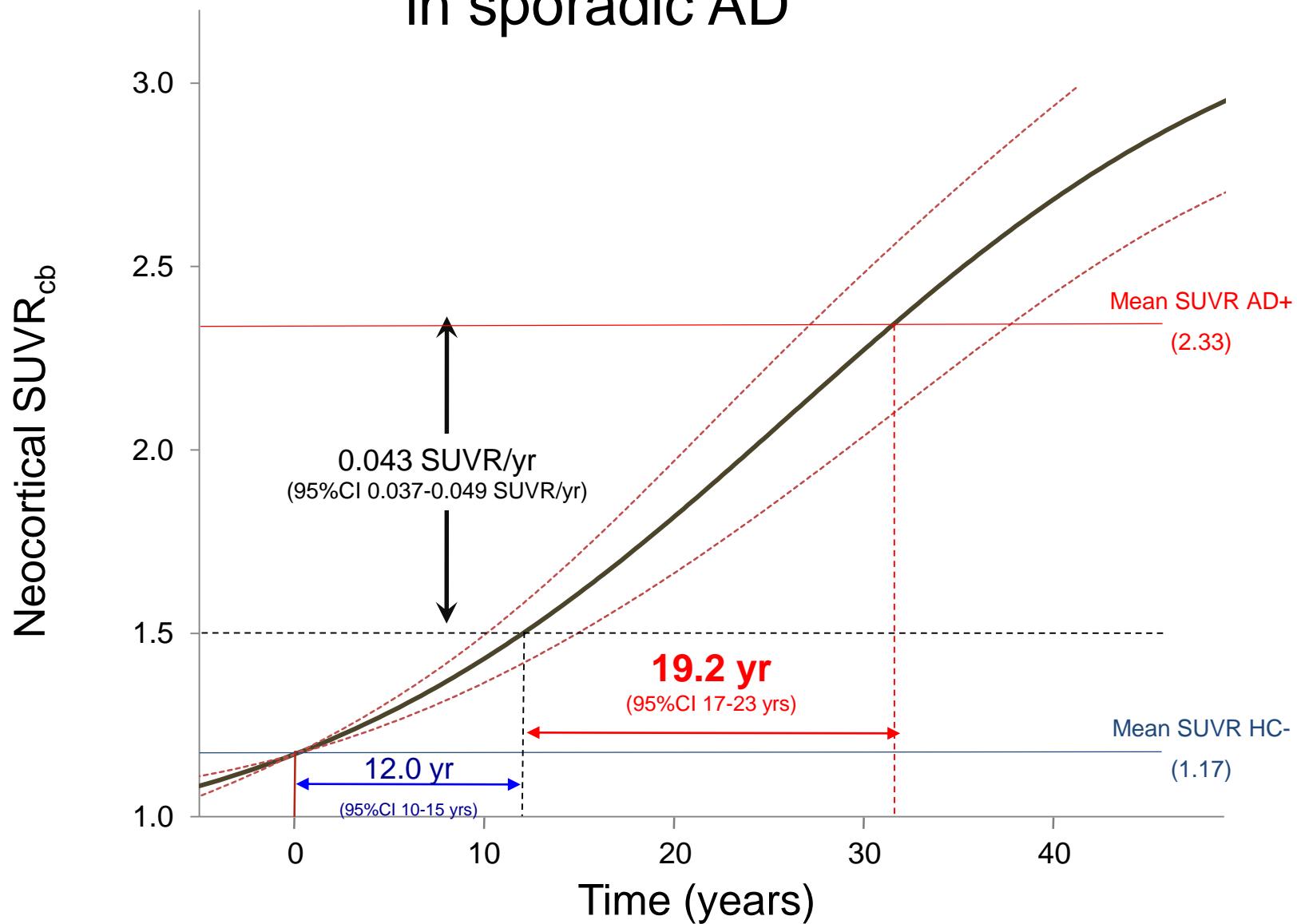
(PiB+ when SUVR >1.5)



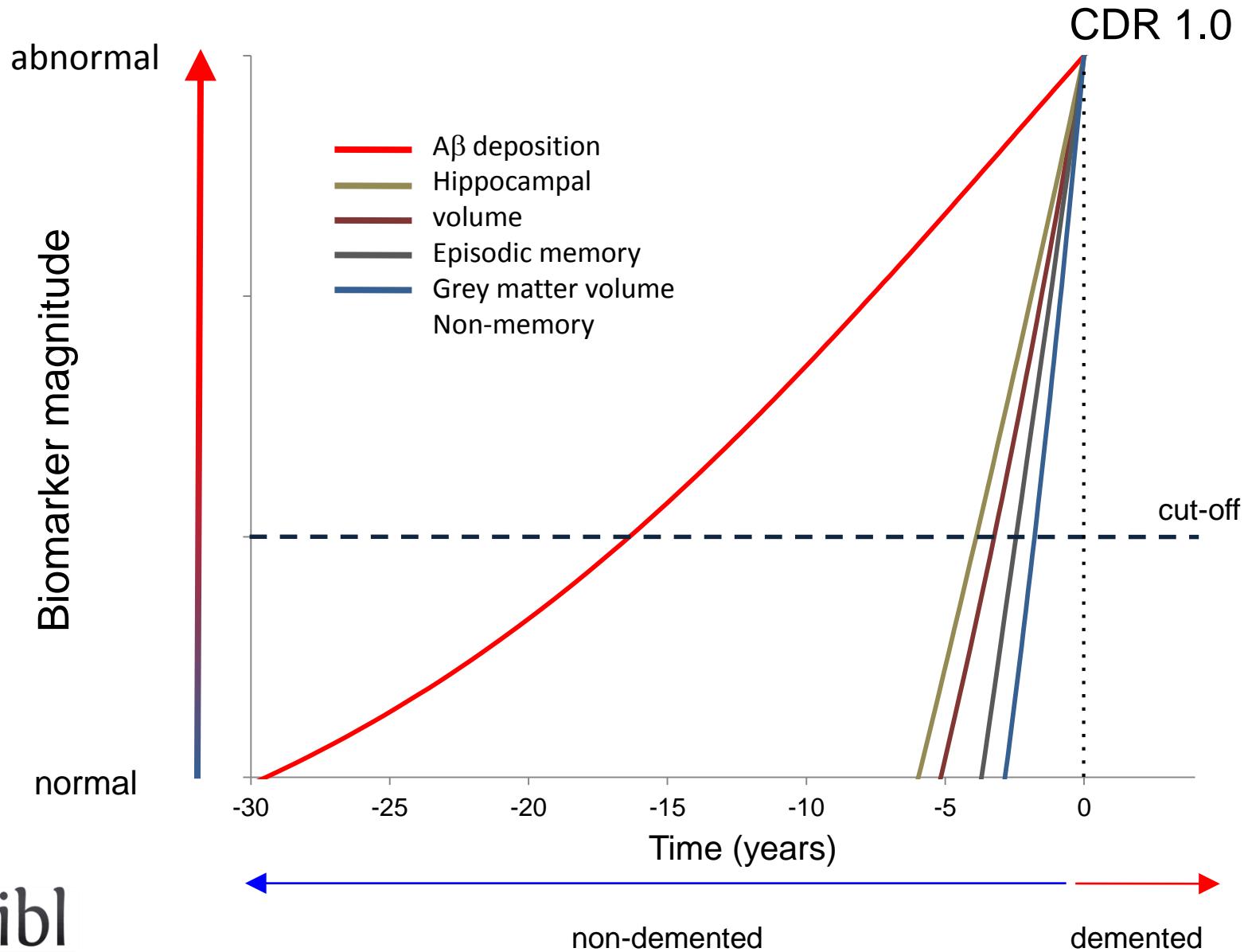
Longitudinal PiB PET 6-year follow-up



The natural history of A β deposition in sporadic AD



Relationship between “abnormality” and CDR of 1.0



MCI to AD over 3 years (n=87; 59% progressed)

	MCI positive for marker	Odds Ratio	PPV	NPV
HV	48	4	0.67	0.65
ApoE- ε 4	50	5	0.74	0.66
CVLT<-1.5	61	11	0.80	0.74
PiB	60	15	0.77	0.82
PiB+ ε 4	47	16	0.79	0.81
PiB+HV	35	44	0.83	0.90
PiB+CVLT	43	na	0.86	1.00

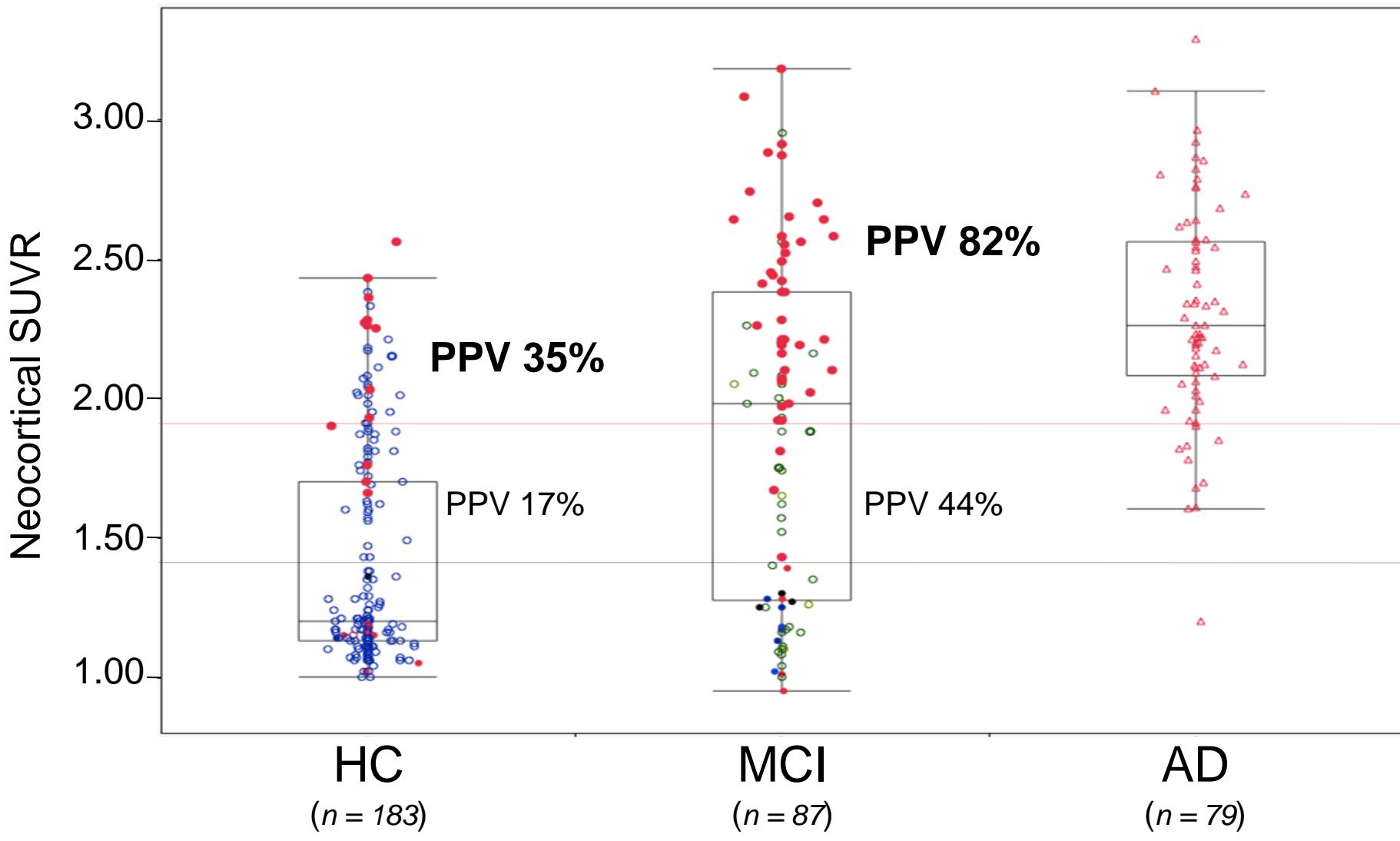
Prediction of Disease Progression MCI to AD (at 3 years follow-up)



	<i>PiB</i>	<i>MRI</i>	<i>Amnestic MCI</i>	<i>PiB+ve + aMCI</i>
Accuracy	0.78	0.66	0.77	0.90
PPV	0.77	0.67	0.80	0.86
NPV	0.82	0.65	0.74	1.00

Rowe CC et al. Annals of Neurology 2013

MCI who progressed to AD over 3 years – red circles



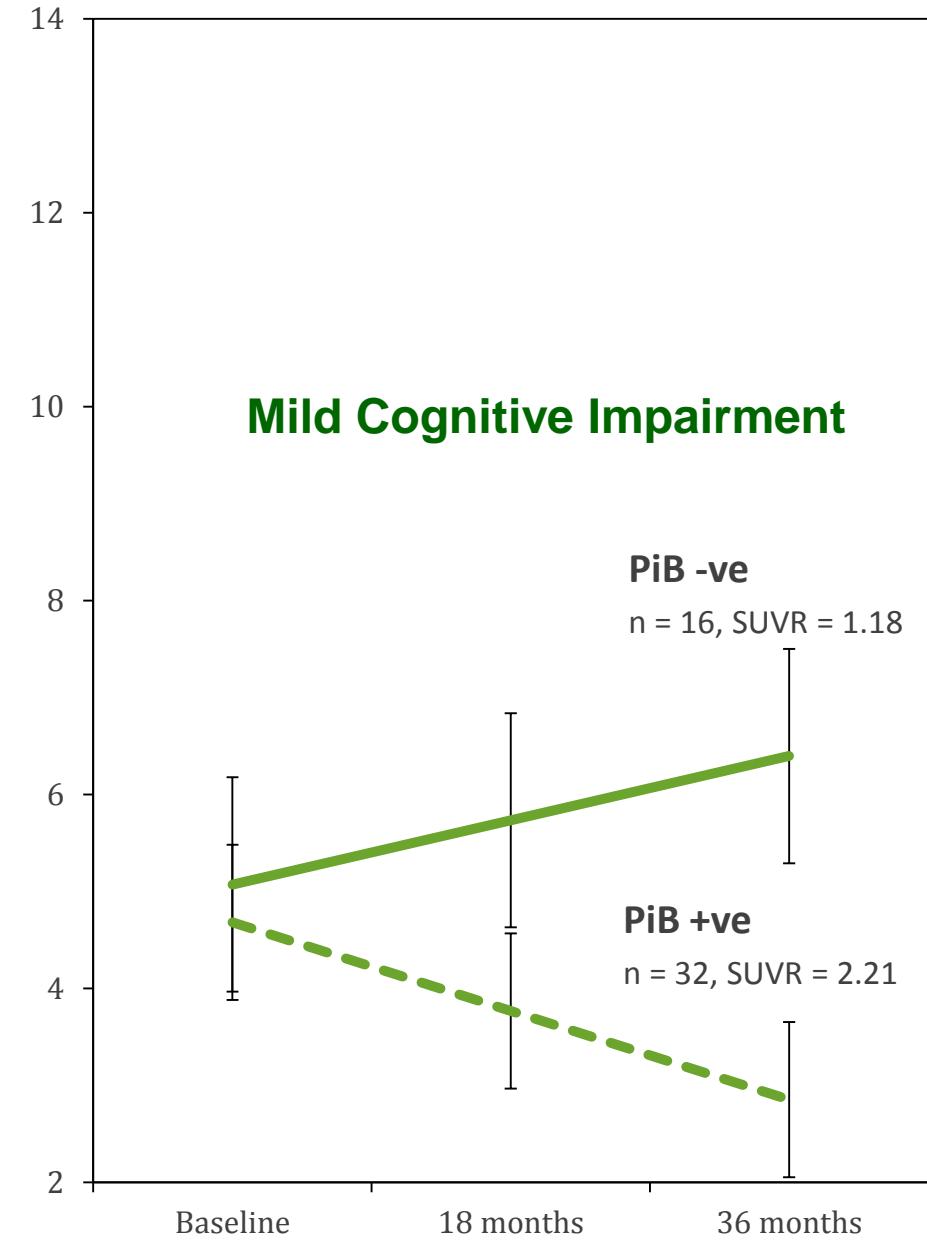
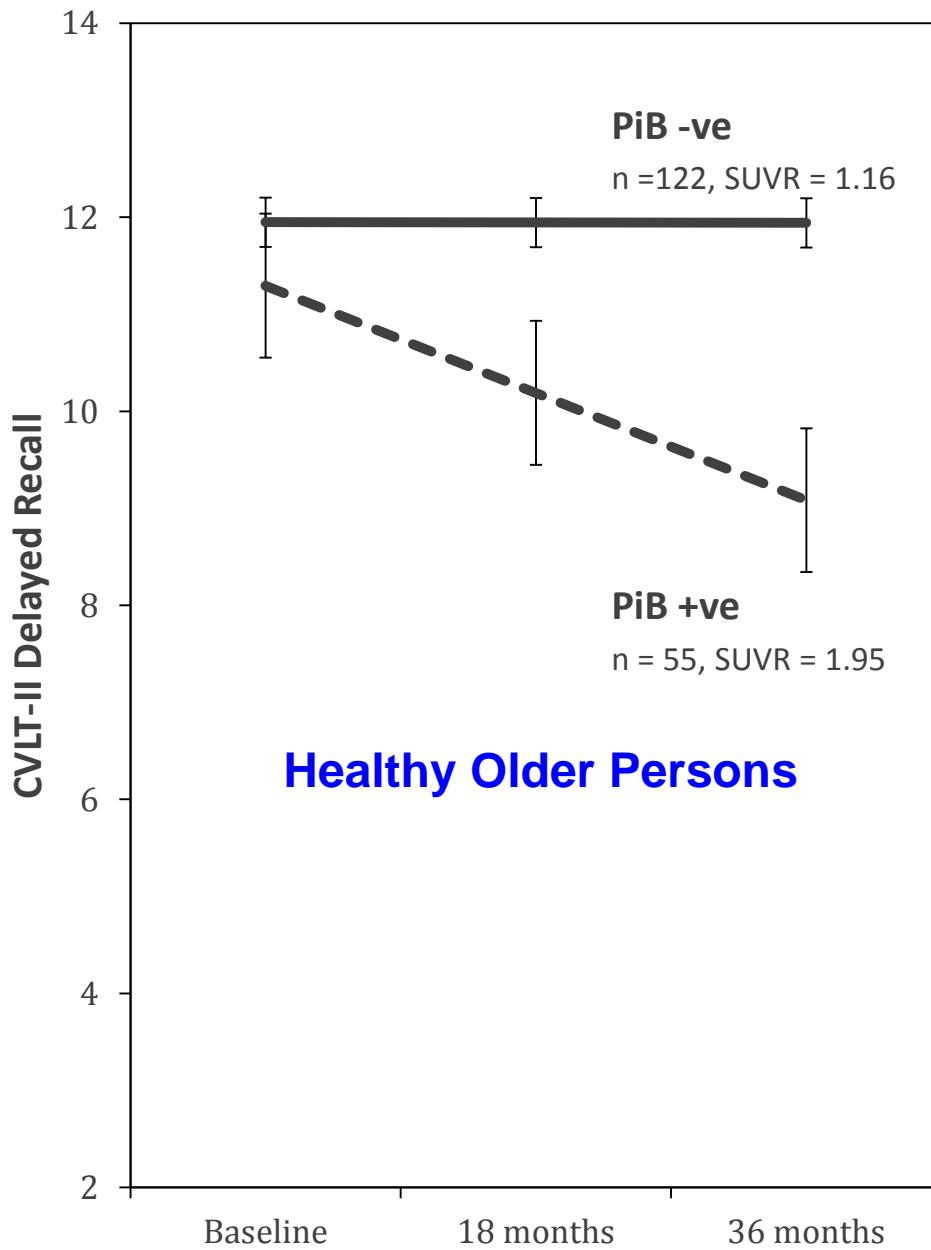
IWG-2 research diagnostic criteria for Alzheimer's disease

Dubois B, et al. Lancet Neurology 2014.

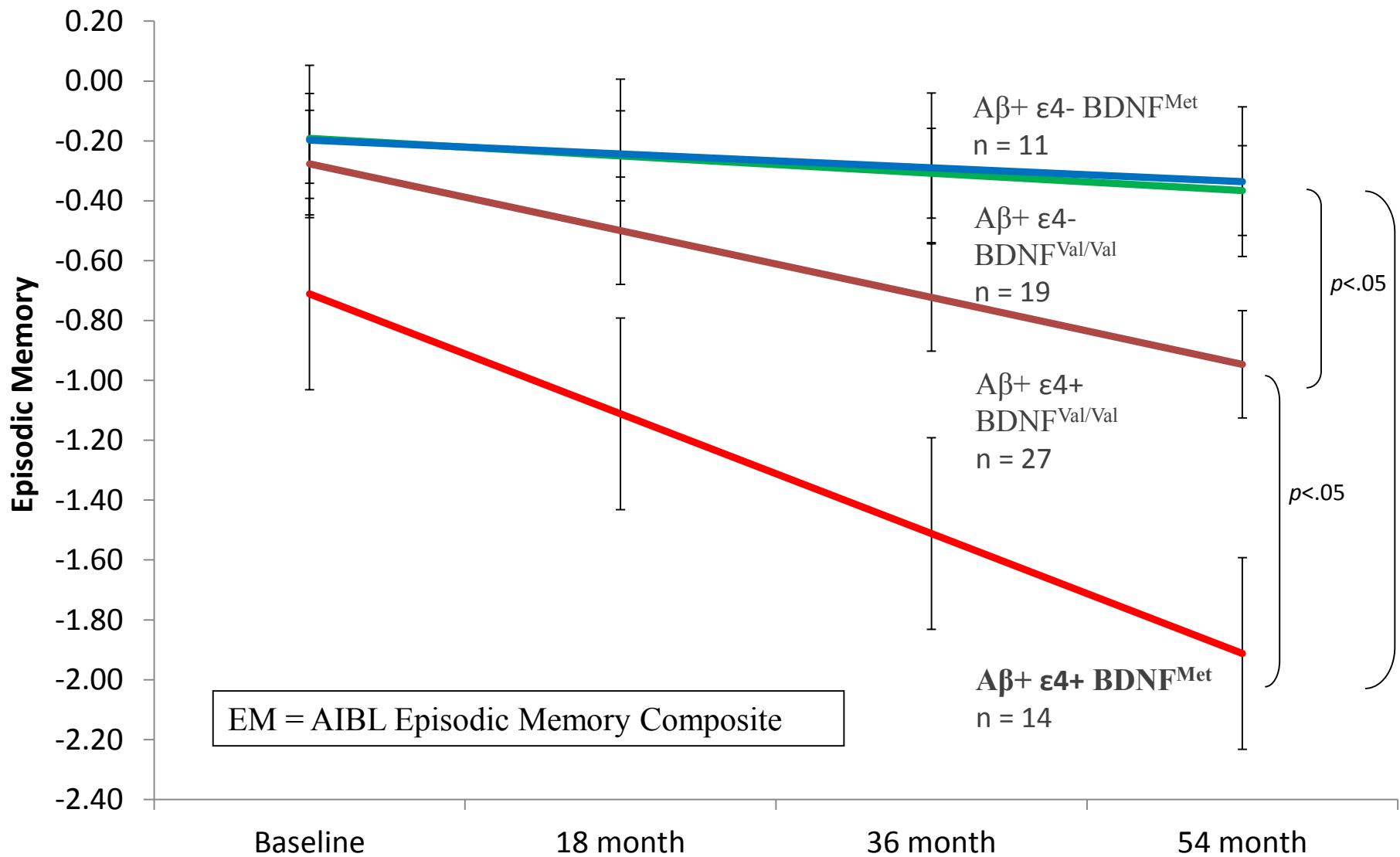
- Objective episodic memory impairment
plus
- Pathophysiological biomarker for AD
i.e. CSF (low A β ₄₂ with high tau) or **positive A β PET**

FDG and MRI for disease severity and progression

CVLT-II Delayed Recall over 36 mths

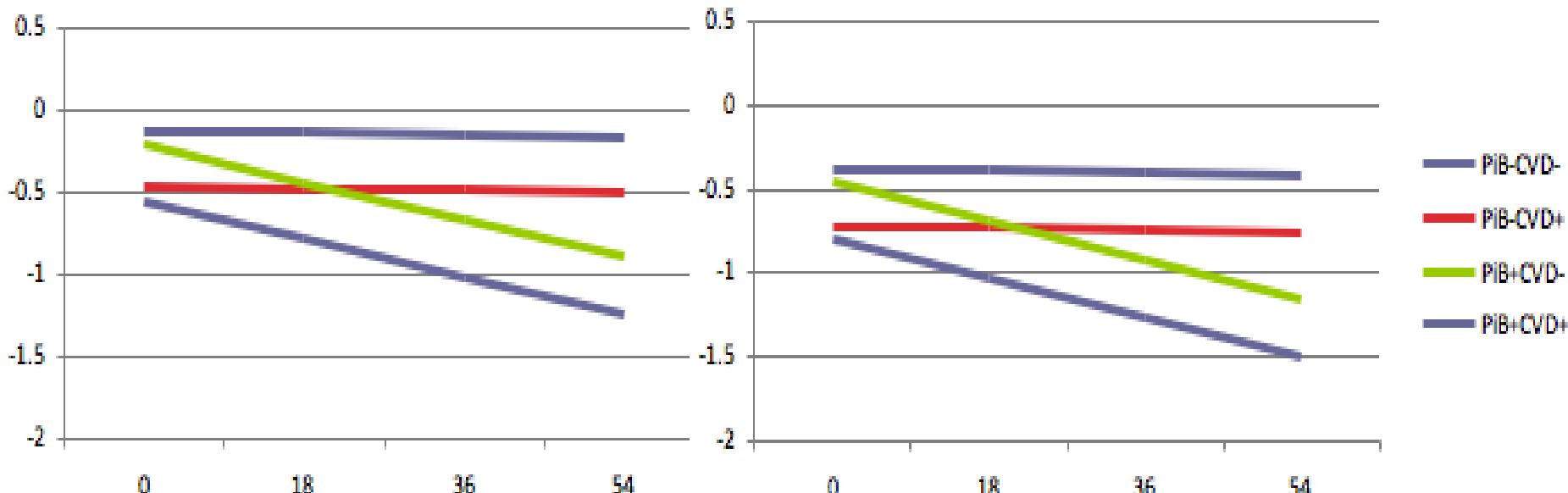


HA A β + 54 months: Effect of *APOE* & *BDNF*



PiB, Cerebrovascular Disease and Episodic Memory

Females



- Slope for PiB+ = -0.14 per year ($p<0.001$)
- Significant time x age interaction ($p=0.008$).
- Significant main effect but not time interaction for CVD ($p=0.01$), gender ($p=0.01$) and YOE ($p<0.001$)

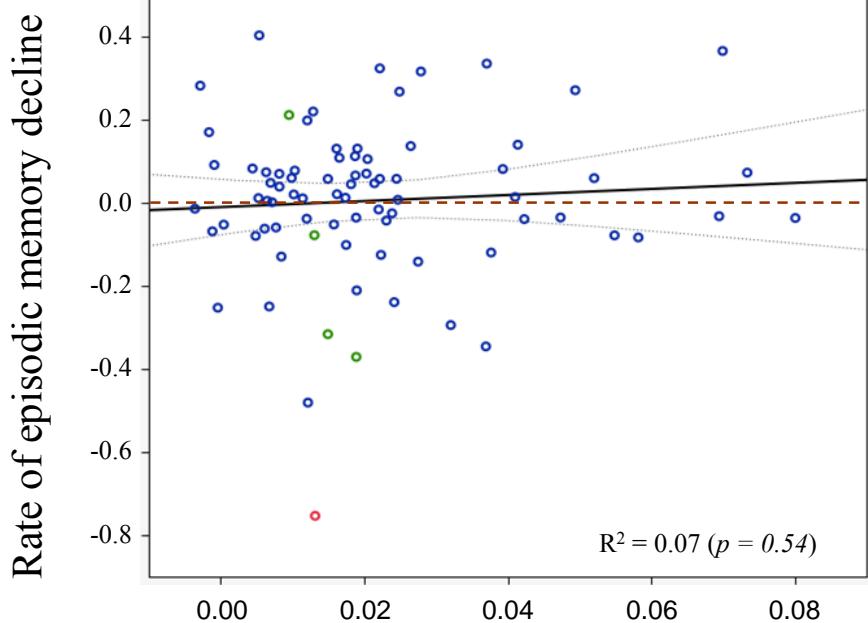
Relation between rate of A β deposition and rate of episodic memory decline in HC

4.5-year
follow-up

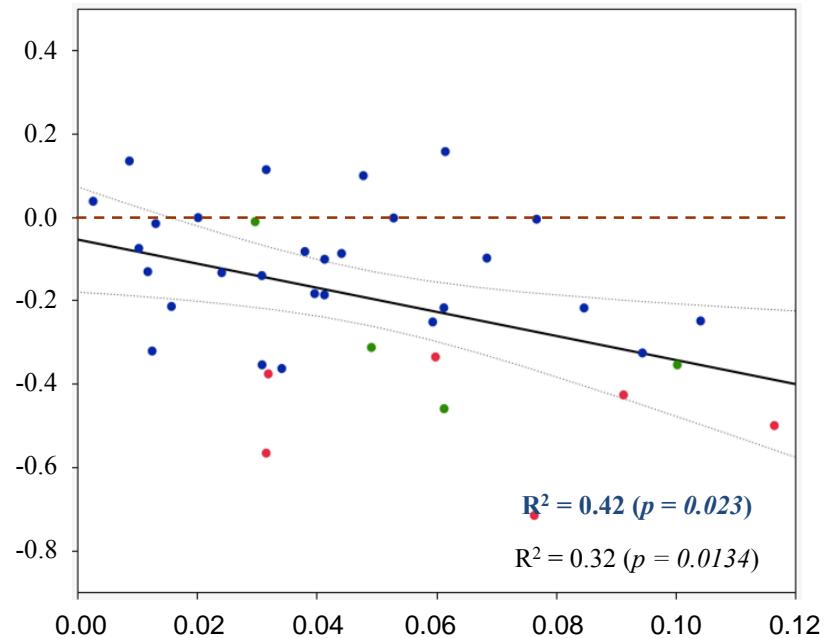
Accumulators

(n=120)

PiB-
(n=80)



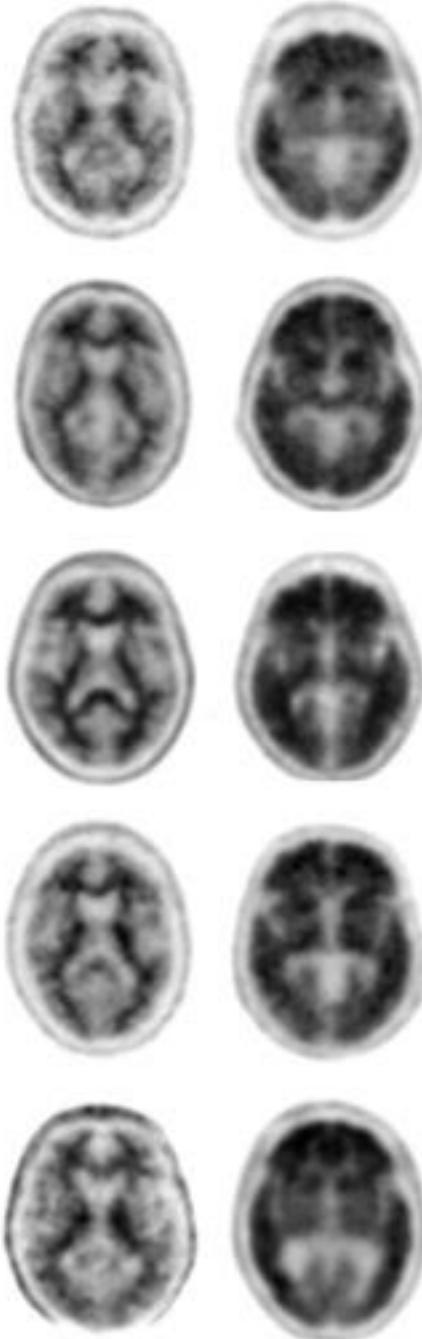
PiB+
(n=40)



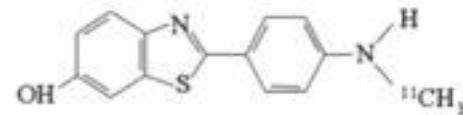
Rate of A β deposition (SUVR/yr)

adjusted for age, gender, education, ApoE

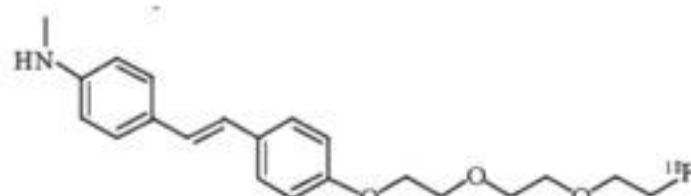
$\text{A}\beta$ ligands



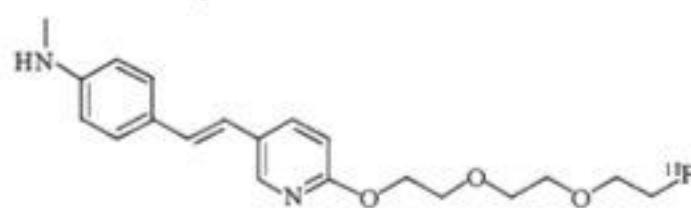
^{11}C -PiB



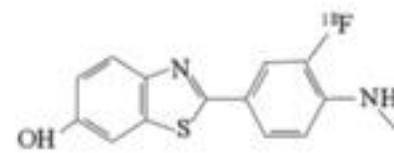
^{18}F -florbetaben



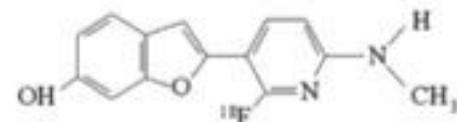
^{18}F -florbetapir



^{18}F -flutemetamol



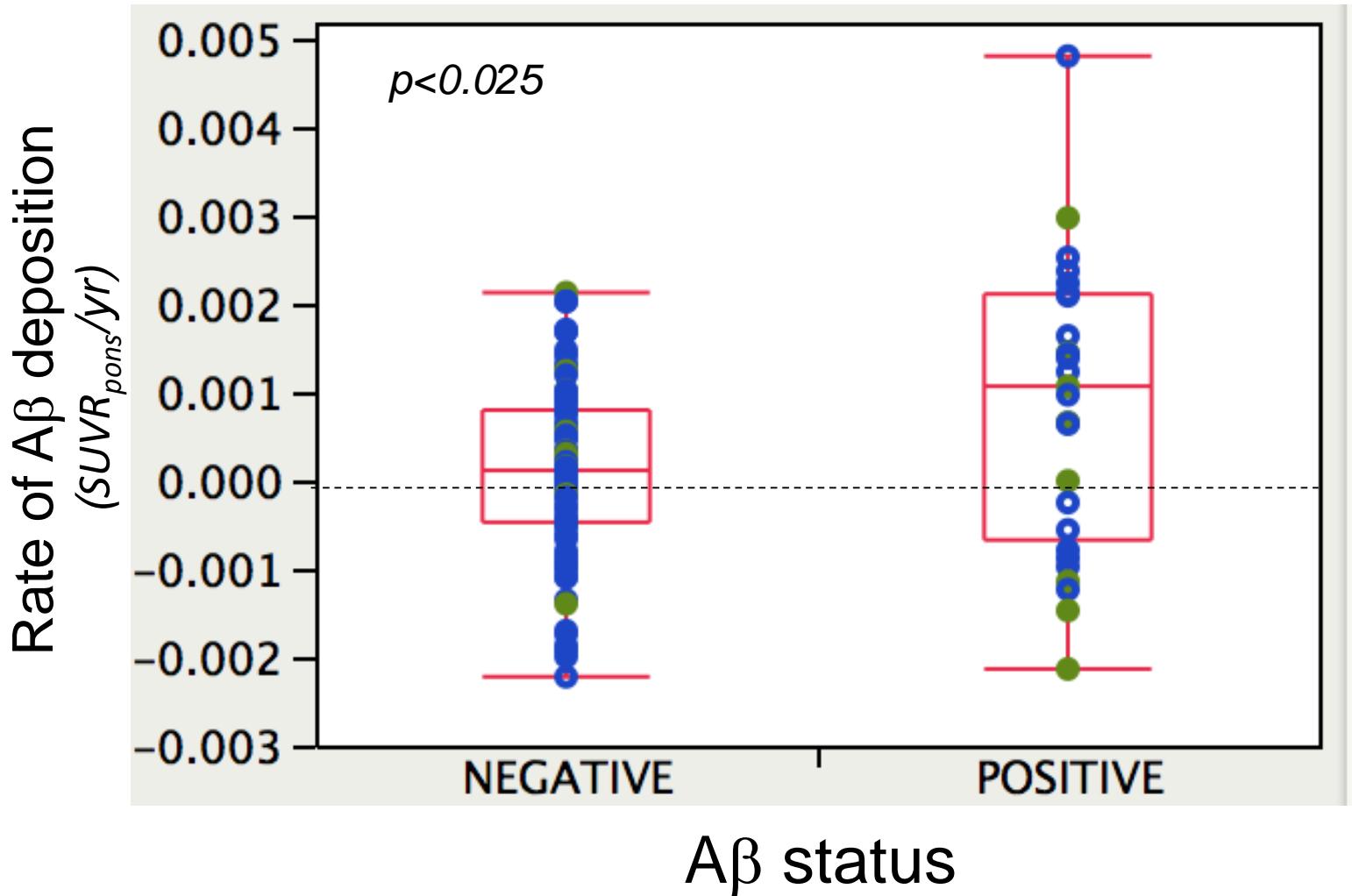
^{18}F -NAV4694



Rates of A β deposition

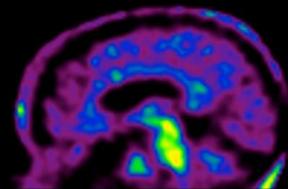
^{18}F -flutemetamol with 1.5 year follow-up

Significant increase of 3.3% per year in Flute +ve.

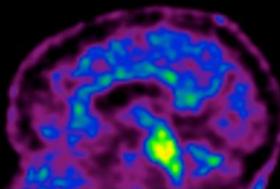


^{18}F -NAV4694 vs ^{11}C -PiB

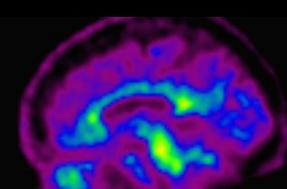
^{18}F -NAV4694



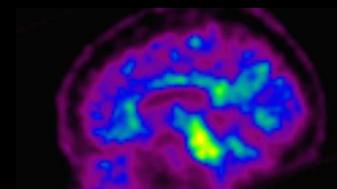
^{11}C -PiB



^{18}F -NAV4694

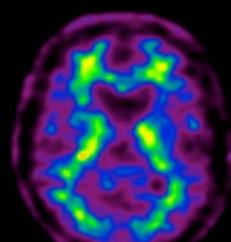
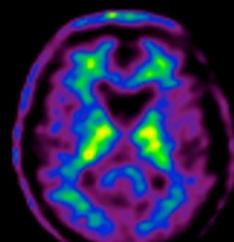


^{11}C -PiB

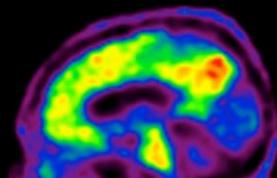


SUVR

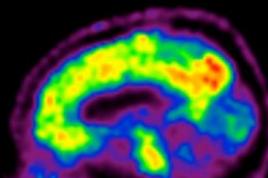
3.0



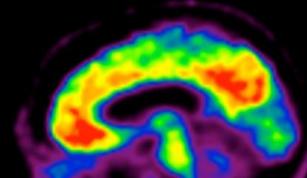
SUVR 1.28



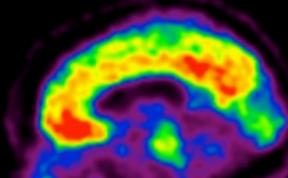
SUVR 1.32



SUVR 1.49

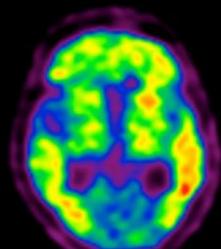
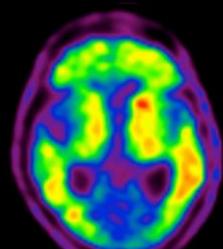


SUVR 1.54

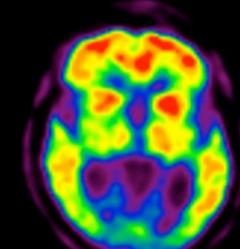


1.5

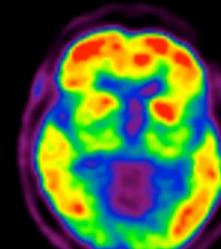
0.0



SUVR 2.17



SUVR 2.09



SUVR 2.46

SUVR 2.29

Rowe CC et al JNM 2013

A β & tau imaging in ageing and Alzheimer's disease

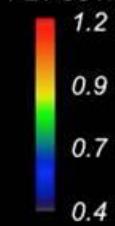
HC

^{18}F -FLUTEMETAMOL

L R

R L

$\text{PET-SUVR}_{\text{pons}}$



RT.LAT

LT.LAT

SUP

INF

RT.MED

LT.MED

POST

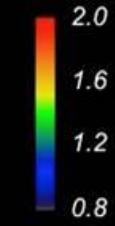
ANT

^{18}F -THK5117

L R

R L

$\text{PET-SUVR}_{\text{CbCtx}}$



RT.LAT

LT.LAT

SUP

INF

RT.MED

LT.MED

POST

ANT

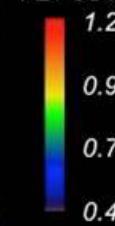
AD

^{18}F -FLUTEMETAMOL

L R

R L

$\text{PET-SUVR}_{\text{pons}}$



RT.LAT

LT.LAT

SUP

INF

RT.MED

LT.MED

POST

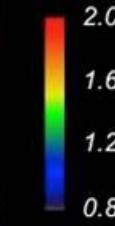
ANT

^{18}F -THK5117

L R

R L

$\text{PET-SUVR}_{\text{CbCtx}}$



RT.LAT

LT.LAT

SUP

INF

RT.MED

LT.MED

POST

ANT

Acknowledgements and thanks



SCIENCE AND
INDUSTRY
ENDOWMENT
FUND

AIBL is a large collaborative study and a complete list of contributors and the management committee can be found at www.aibl.csiro.au

This research was funded in part by the Science and Industry Endowment Fund and CSIRO.

We thank all who took part in the study.