The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing

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(AUSTRALIAN ADNI)

July 2012 UPDATE – Imaging

Christopher Rowe MD – *Neuroimaging stream leader*

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

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The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing.

October 2011

100 Vietnam veterans
AIBL-DOD
MRI, CSF, F-18 PET

Replacement MCI and sMC

100 new participants
MRI + F-18 Flutemetamol
Funded by GE

Women's Healthy Aging Program

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200 new participants
MRI + F-18 Florbetaben
Funded by Bayer/Piramal

October 2006

823 not imaged → 738 not imaged → 632 not imaged

- 100 participants
  MRI + Flutemetamol
  Funded by GE
- 213 participants
  MRI + AV-45
  Funded anon ?
- 250 participants
  MRI and 11C-PiB
  Funded by WA Govt ?

288 imaged
MRI + 11C-PiB
Funded by CSIRO → 230 imaged
MRI + 11C-PiB
Funded by CSIRO → 192 imaged
MRI and 11C-PiB
Funded by SIEF → 130 participants
MRI and 11C-PiB
Funded by SIEF ?

0 yrs

1112 participants recruited to AIBL

1.5 yrs

968 participants remain in AIBL

3 yrs

824 remain

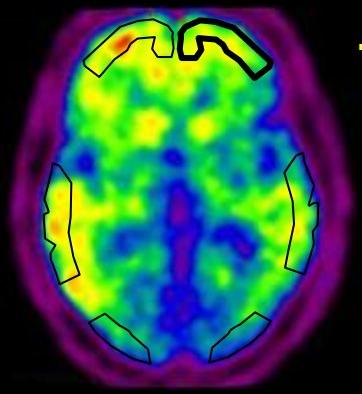
4.5 yrs

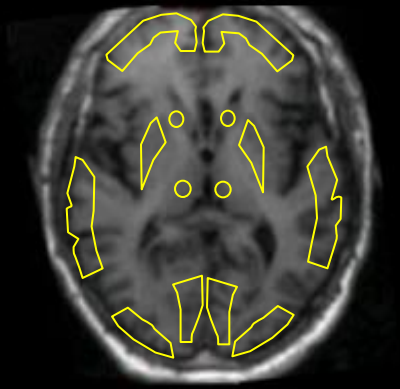
All to have MRI & amyloid PET

6 yrs

^{11}C-PIB – Image Quantification

Regions





Neocortical $SUVR_{40\text{-}70}$

= cortical activity / cerebellar grey matter activity from 40 to 70 minutes post injection

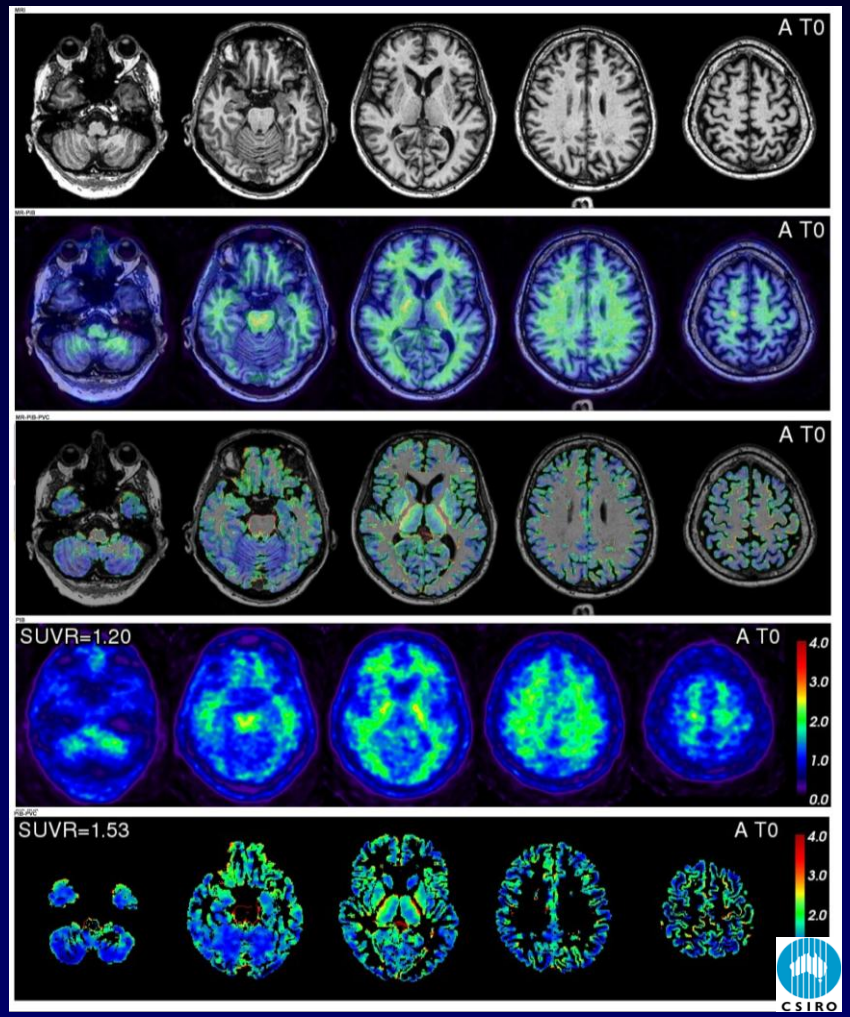
Negative is <1.5

Follow-up PiB co-registered to baseline and saved prior ROI set used.

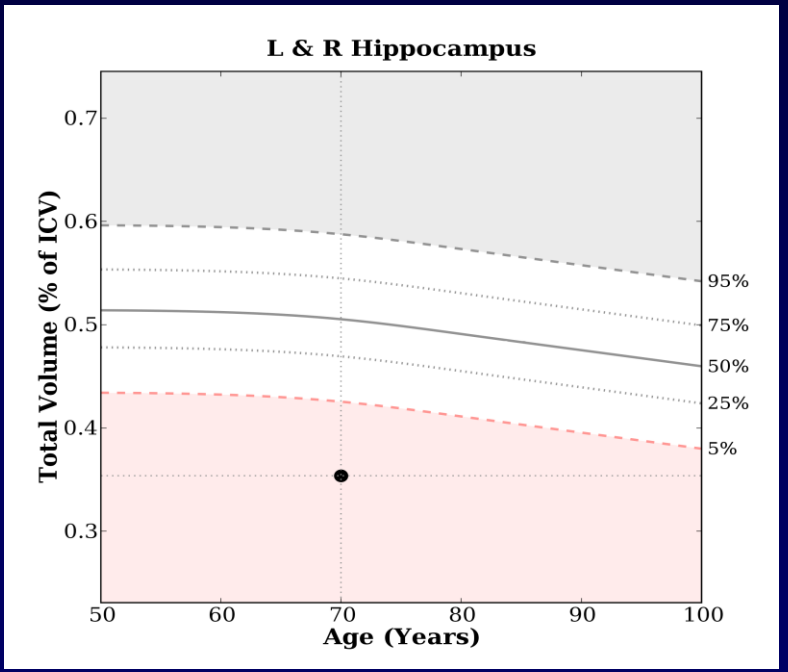
Single operator for all PiB scans.

Image Analysis

2. Automatic: co-registration + MRI segmentation
(GM, WM, CSF) + AAL template + PVC



NeuroQuant

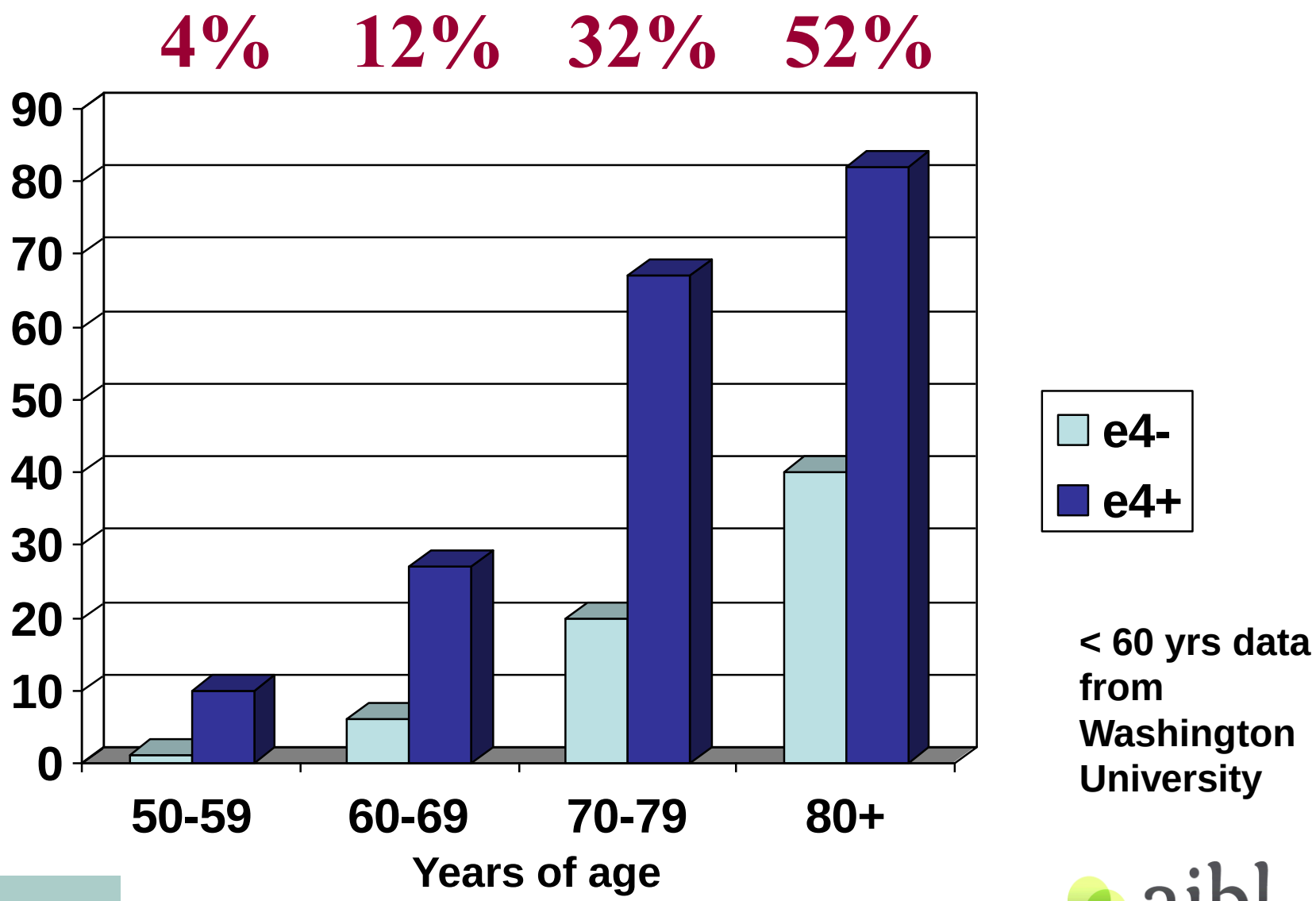


Imaging Cohort Demographics

	HC (n=195)	MCI (n=92)	AD (n=79)
Age	72	74	73
Gender (M:F)	47%	50%	50%
MMSE	29	27	21
CDR	0.0	0.5 ± 0.2	1.0 ± 0.5
CDR SOB	0.06 ± 0.2	1.25 ± 0.9	4.36 ± 1.7
% ApoE ε4	41%	61%	65%
Years of Education	13.4	12.5	12.4

Baseline Imaging Findings

% of Healthy who are PiB+ve



< 60 yrs data from Washington University

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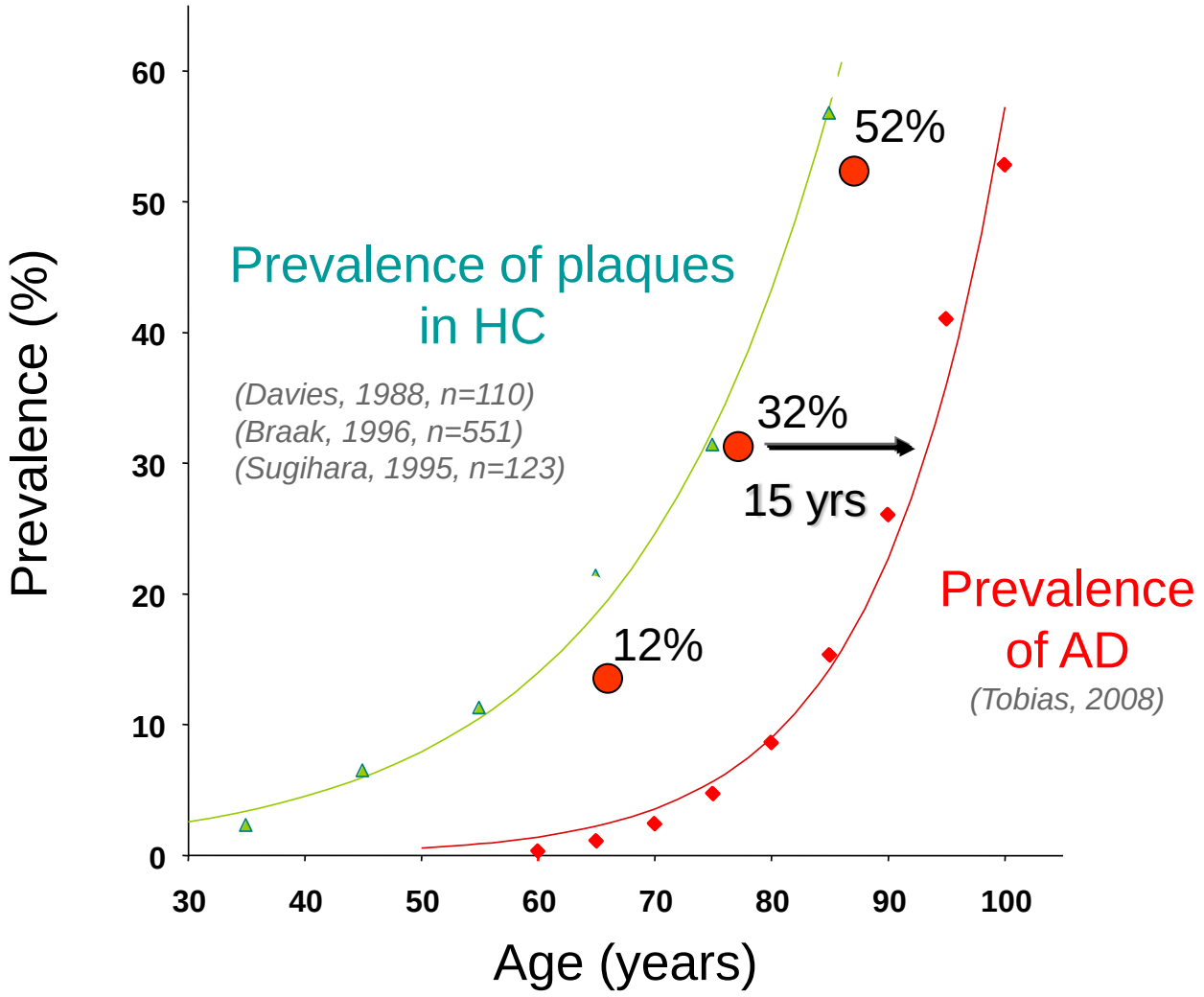
% PiB+ HC vs Age (by decade)

(PiB+ when SUVR >1.5)



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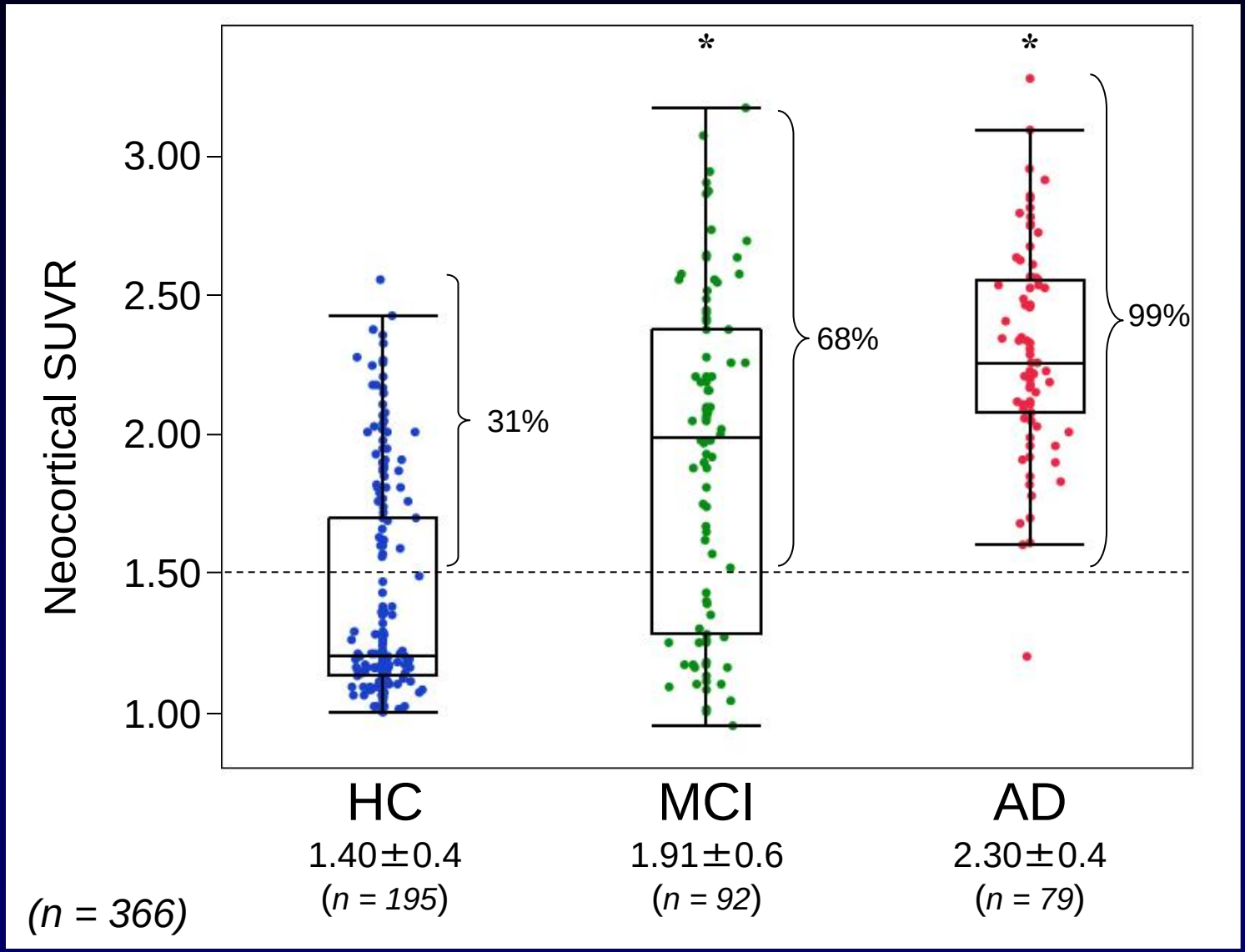
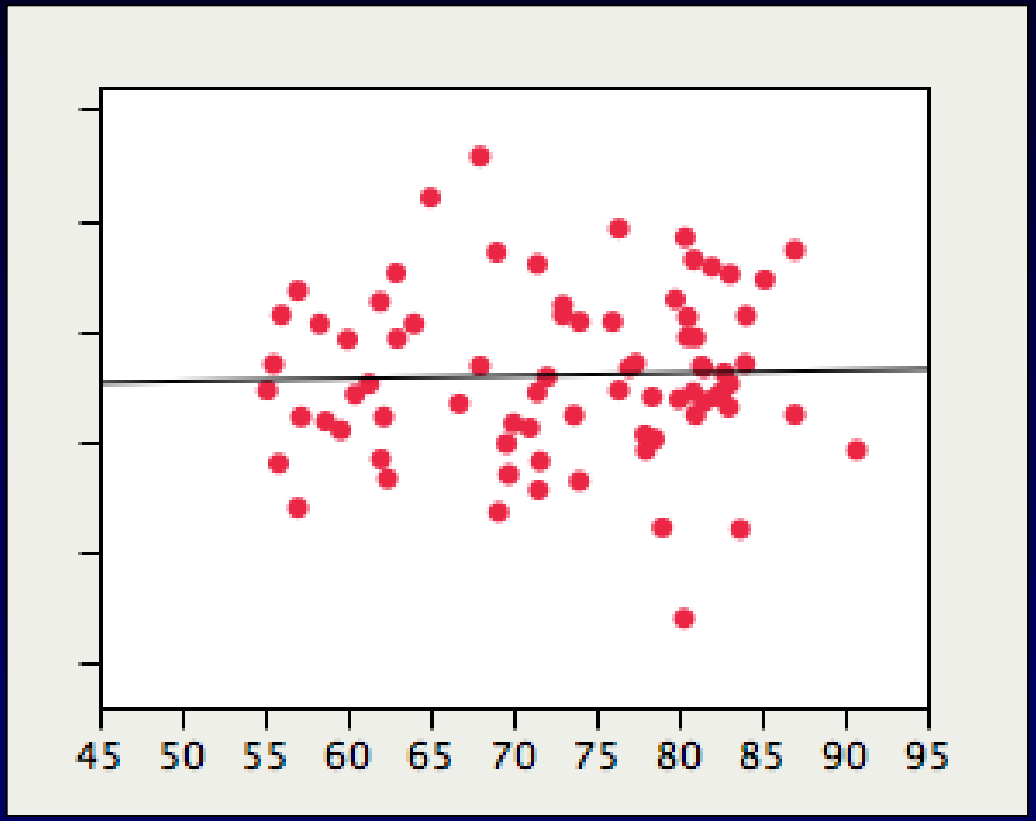
PiB neocortical SUVR in AIBL+



*Statistically significant results compared to controls (p< 0.0001)

Aβ burden vs Age

Older AD do not have less PiB binding



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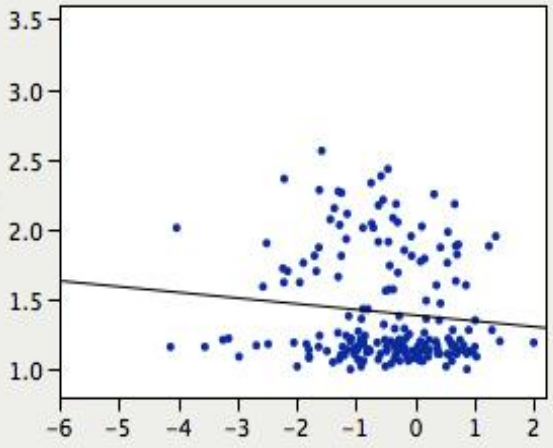
Aβ vs Memory

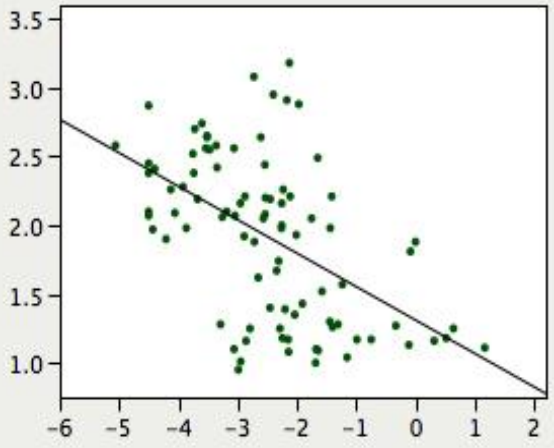
HC

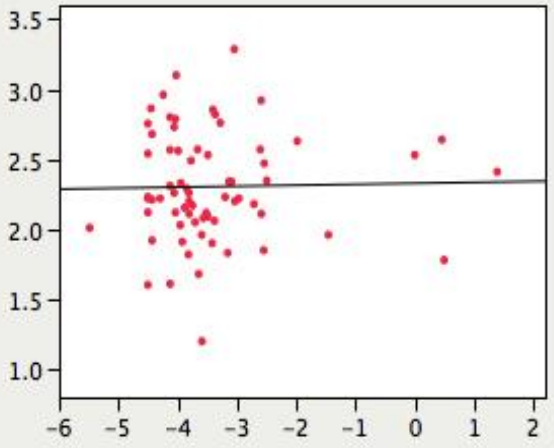
MCI

AD

Neocortical SUVR







r= -0.20 (p = 0.13)

r= -0.53 (p < 0.0001)

Episodic Memory

Follow-up Data

LONGITUDINAL DATA
Progression over 3 years

	HC-	HC+
• PiB rise (SUVR/yr)	0.01	0.05 (2.5%)
• Memory Decline (SD/yr)	-0.02	-0.17

	MCI-	MCI+
• PiB rise (SUVR/yr)	0.01	0.05
• Memory Decline (SD/yr)	-0.04	-0.21

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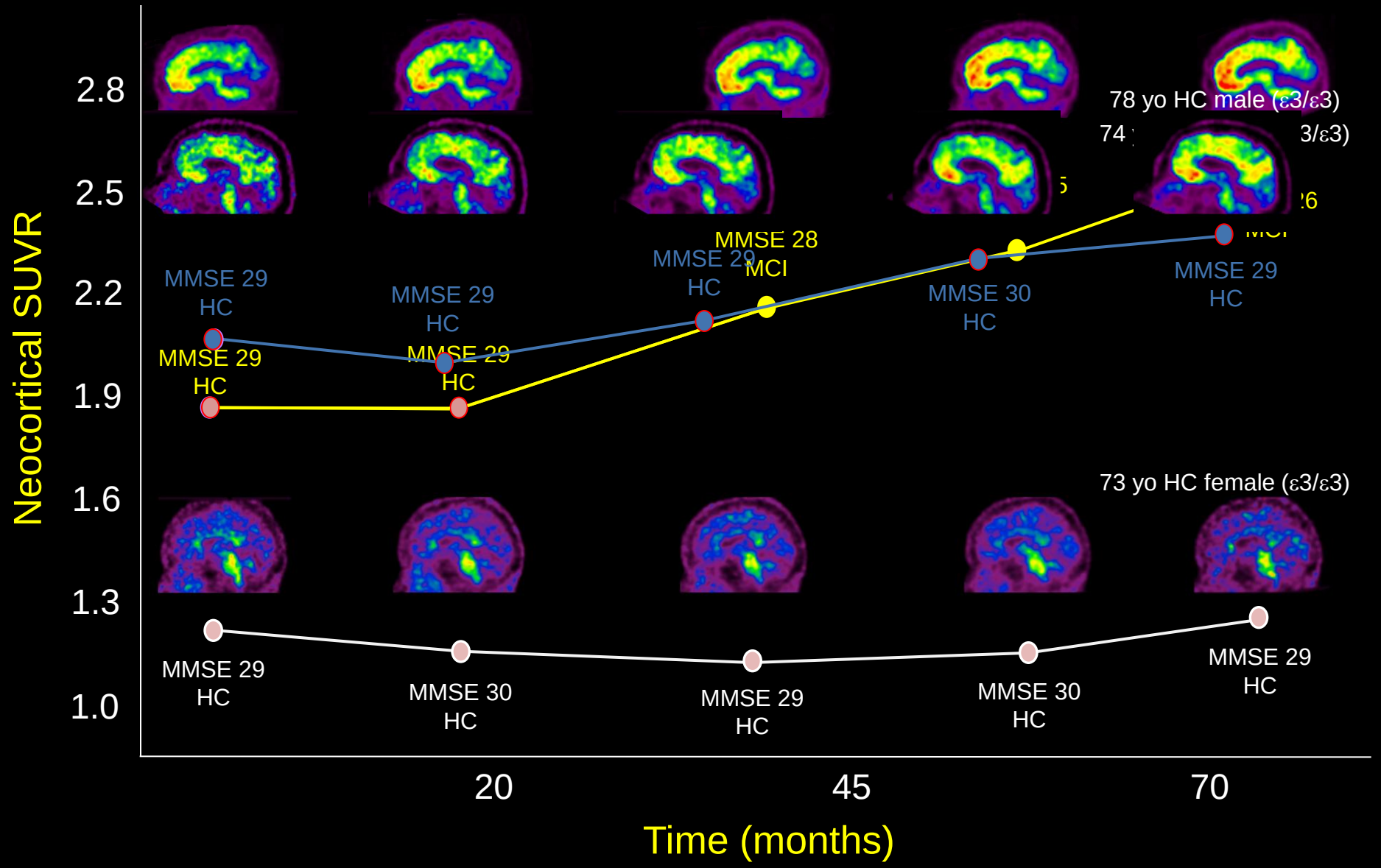
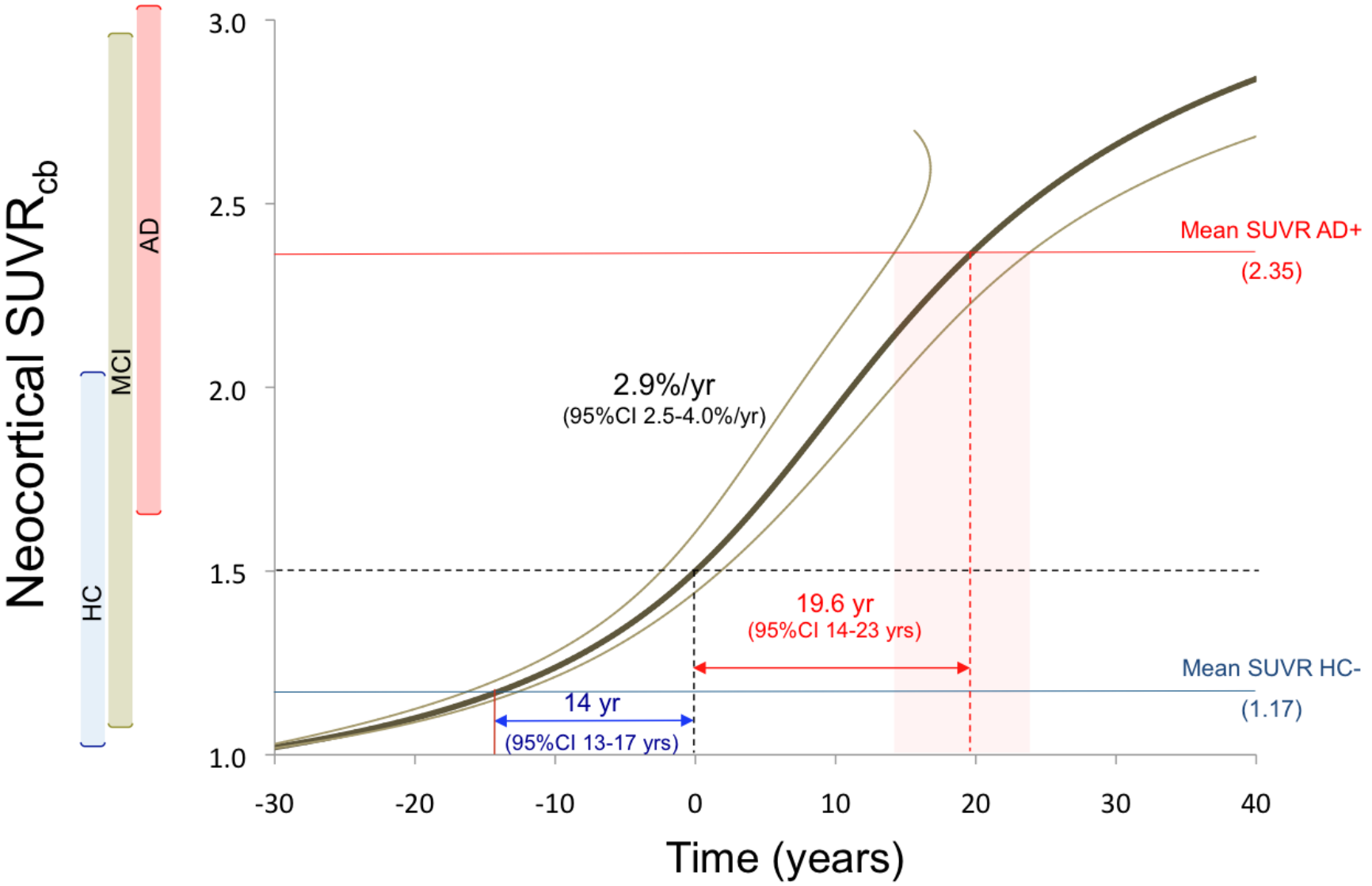
Longitudinal PiB PET
6-year follow-up



Aβ deposition over time

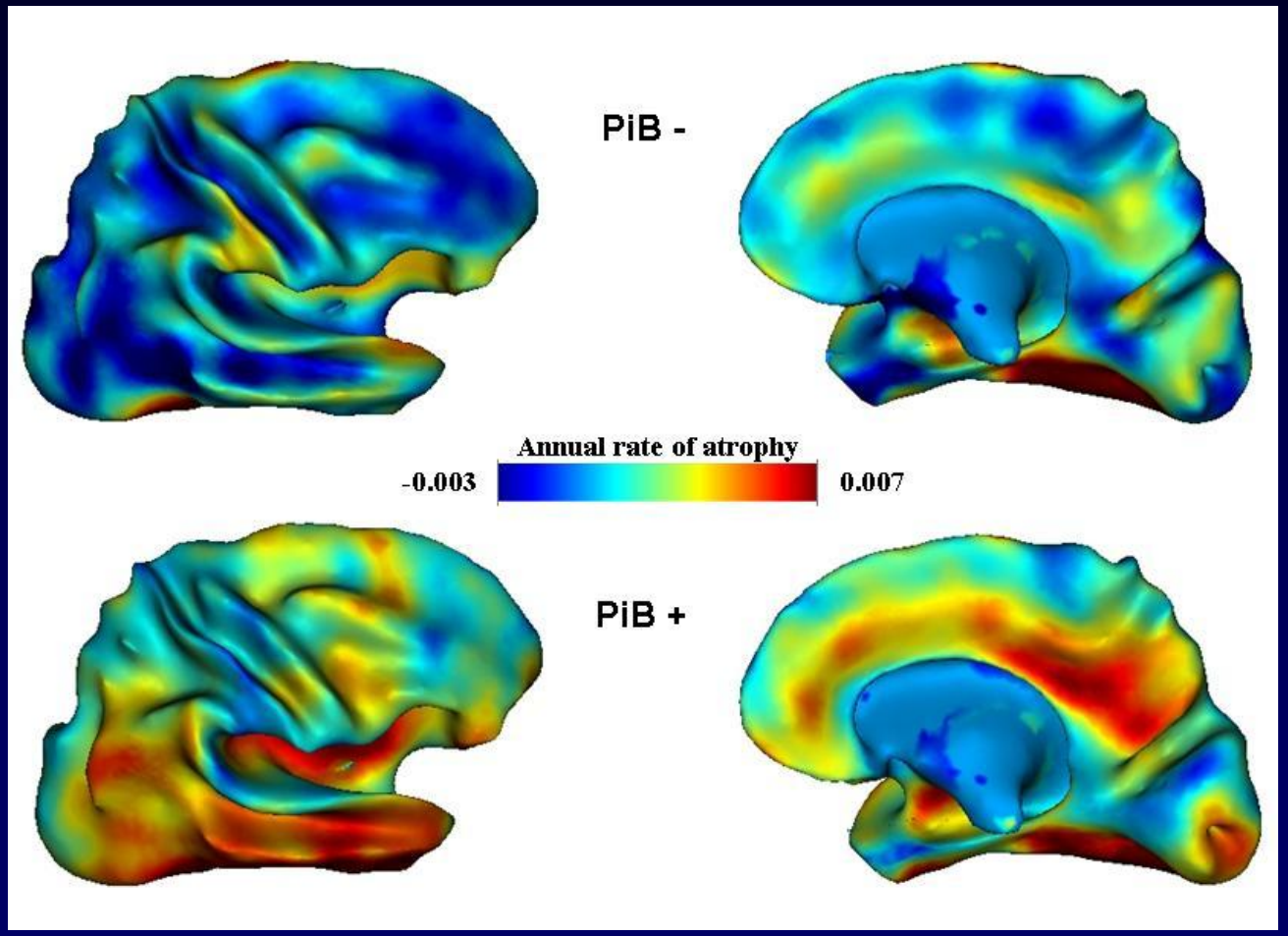
3-5 year follow-up

(*n=158*)



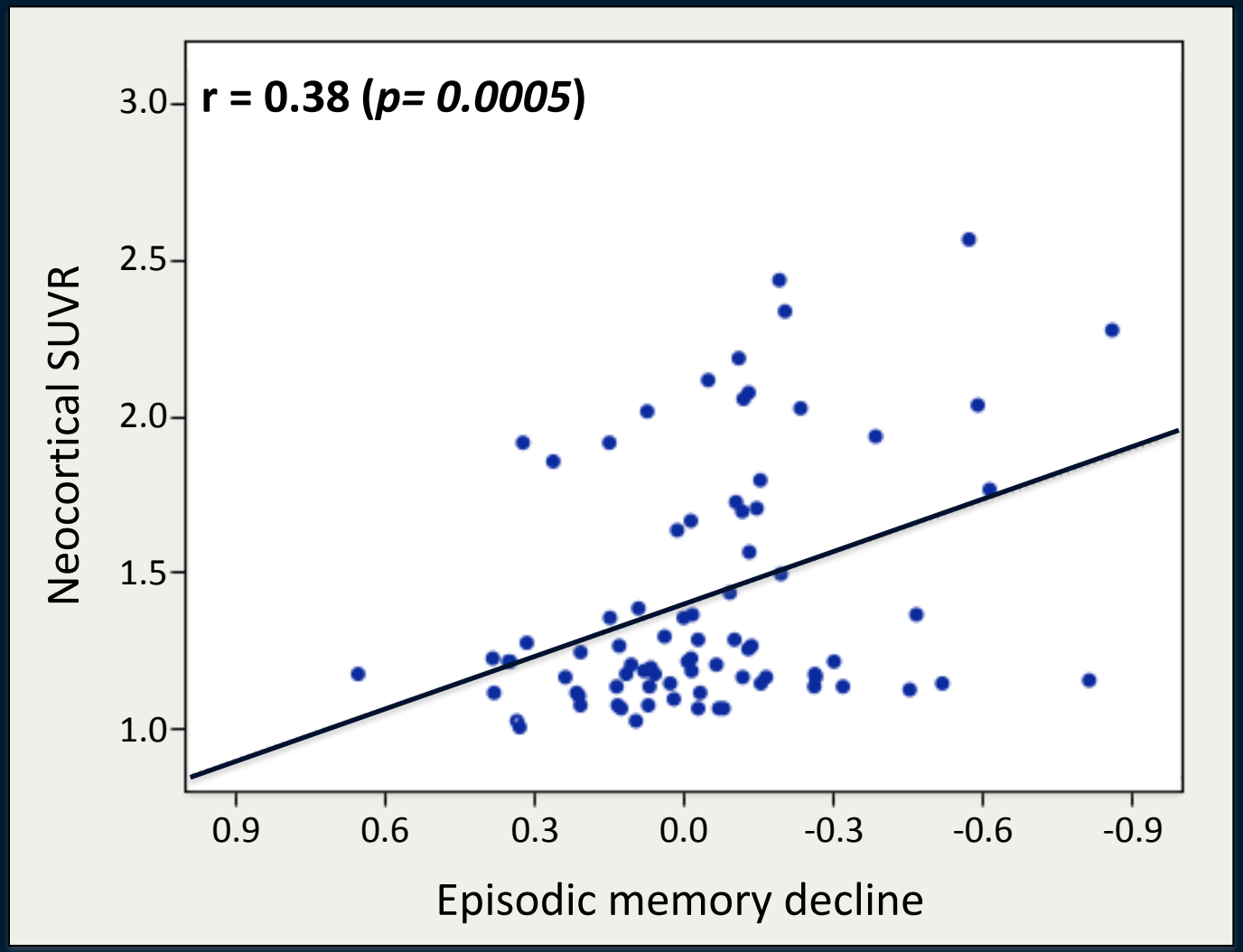
Villemagne et al, Kinetics of Aβ deposition, AAIC, 2012

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



Relation between baseline Aβ burden and memory decline in healthy controls

(36 months follow-up)



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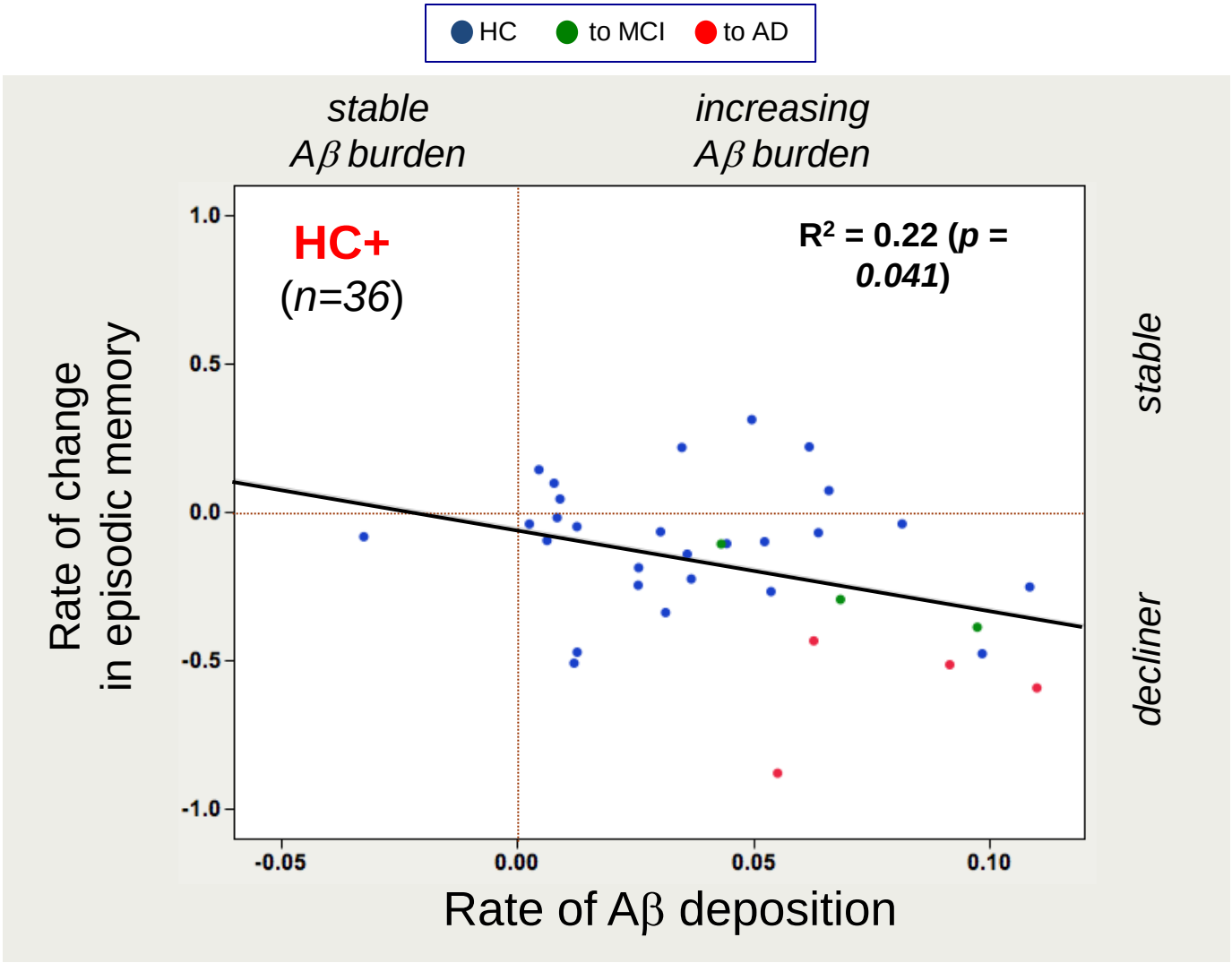
Relation between rate of Aβ deposition and rate of memory decline

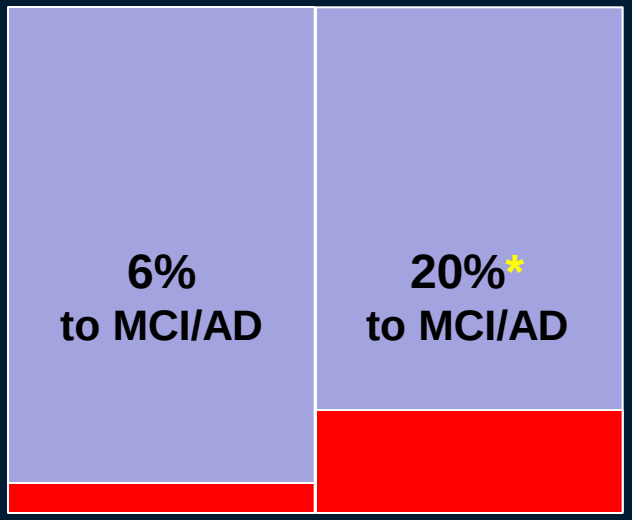
3-5 year follow-up



PiB SUVR cut-point 1.5

3 year clinical progression

HC
(*n=194*)

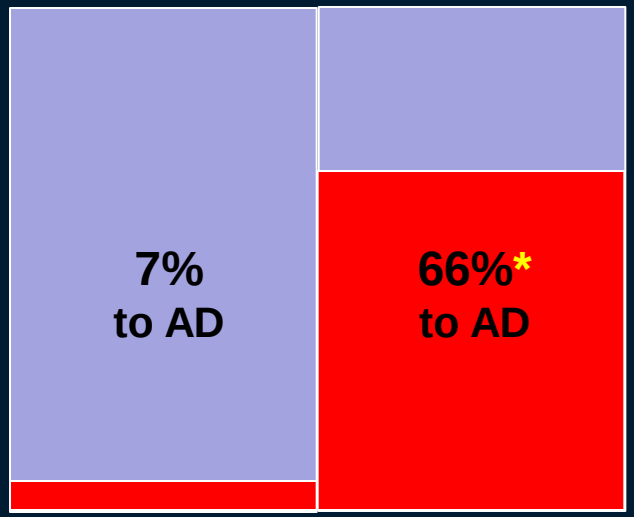


Hazard Ratio 3.6 (OR 4)

**(p= 0.016)*

Corrected for age, gender, education

MCI
(*n=92*)



Hazard Ratio 11 (OR 25)

**(p< 0.0001)*

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Prediction of Progression: HC to MCI/AD
(at 36 months follow-up)
n=194

	ACCURACY	*PPV*	*NPV*	*Odds Ratio*	*CI*
Hippocampal atrophy	0.54	0.16	0.92	2	0.8-6
PiB+ve (SUVR >1.5)	0.57	0.2	0.94	4	4-10
PiB + Hipp Vol (n=118, ++ vs --)	0.63	0.32	0.94	7	2-26
Composite Memory (< -1.0 SD)	0.64	0.3	0.97	14	4-43
Memory + Hipp Vol (n=123, ++ vs --)	0.65	0.32	0.98	23	4-129
PiB + Memory (n=126, ++ vs --)	0.73	0.48	0.97	31	7-125

Prediction of Progression: MCI to AD
(at 36 months follow-up)
n=92

	ACCURACY	*PPV*	*NPV*	*Odds Ratio*	*CI*
Hippocampal atrophy	0.68	0.61	0.75	5	2-14
Composite Memory (<-2.0 SD)	0.70	0.59	0.81	6	2-18
ApoE ε4+	0.76	0.71	0.80	10	
PiB+ve (SUVR >1.5)	0.80	0.66	**0.93**	25	5-114
PiB+ve MRI-ve (n=6/13+- vs 0/11--)	0.75	0.46	**1.00**	>100	n/a
PiB-ve MRI+ve (n=1/12-+ vs 0/11--)	0.54	0.08	**1.00**	<1	
PiB + Hipp Vol (n=29/37++ vs 0/11--)	0.89	0.78	**1.00**	>100	n/a

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Summary

- Aβ deposition is slow and of similar rate in PiB+ HC and MCI (3% SUVR per year).
- A plateau occurs with advancing dementia.
- Aβ is common in older HC

  11% if 60-69
  32% if 70-79
  51% if 80+ years

  and strongly related to genetics i.e. ApoE-ε4 status (risk 2-3X)

Over 3 Years

- Aβ in HC is associated with faster cognitive decline and grey matter atrophy.
- 20% of PiB+ HC develop MCI/AD *(c.f. 6% of PiB-)*
- 74% PiB+ MCI develop AD *c.f. 16% of PiB- Odds Ratio = 25 (but 20% PiB- develop other dementias)*
- Combination of biomarkers provides better prediction *(e.g. if PiB+ and hippocampal atrophy = 86% accuracy, PPV 78%).*

Baseline and 18 mth MRI, PiB scans and corresponding clinical data are available from ***www.loni.ucla.edu/ADNI/Data/***

(look for the AIBL button in the ADNI data site)

36 month data coming soon!