Japanese ADNI
summary of J-ADNI1 data and current status on Apr 2016

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Atsushi Iwata, Clinical core PI of J-ADNI2/AMED preclinical

Japanese ADNI

The 1st nationwide observational early AD study in Japan

- **7-year study** (since 2007)
- **38 clinical sites**
- **Goal: 600 subjects**

537 finally enrolled by Apr 2013

- **1.5T MRI**
  (3D MPRAGE, ADNI phantom)
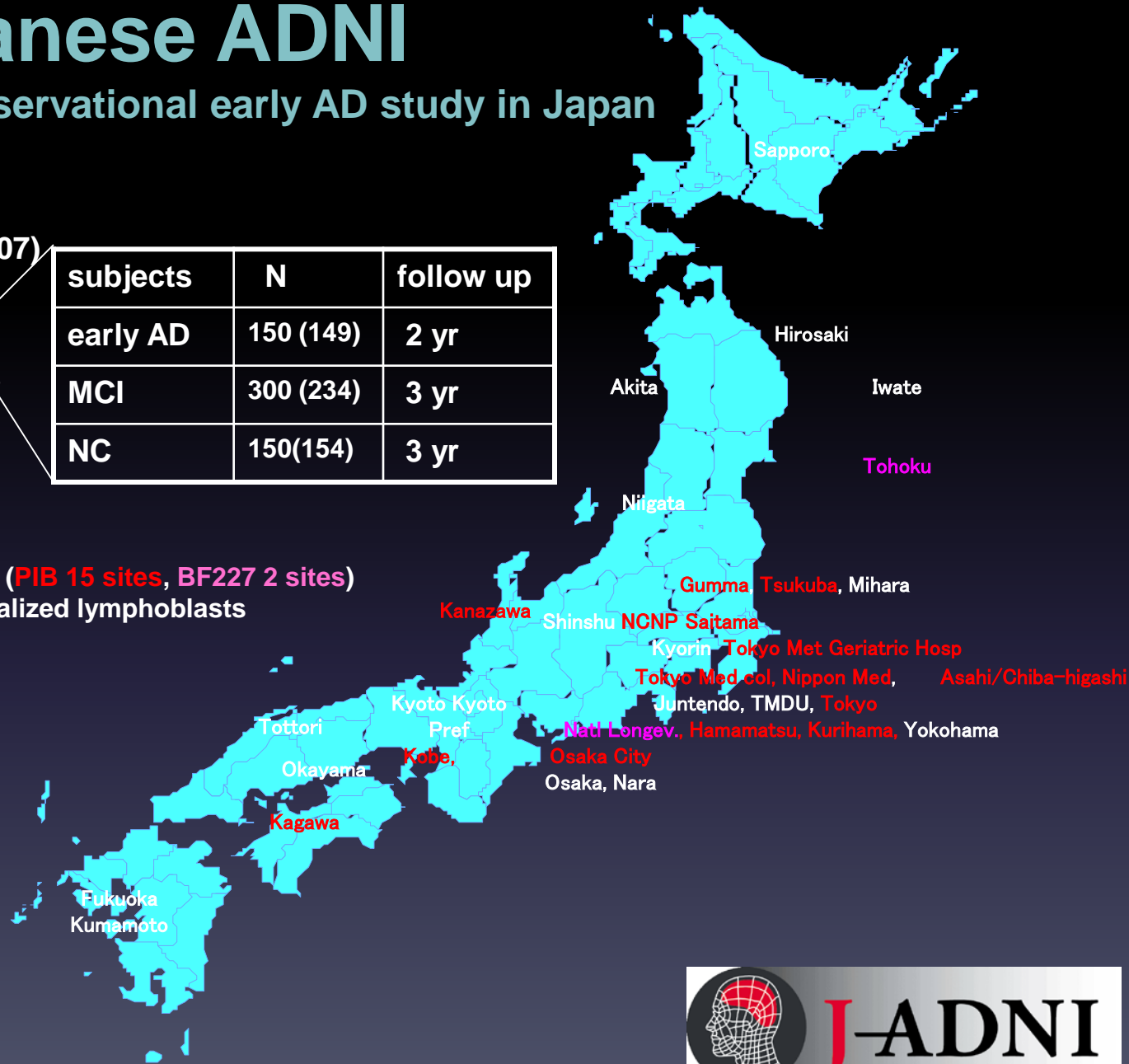- **PET**
  - ---FDG 67% (IC obtained)
  - ---amyloid 42% (IC obtained) (PIB 15 sites, BF227 2 sites)
- **Blood + apoE (100%), immortalized lymphoblasts**
- **CSF 40% (IC obtained)**
- **Clinical (14 test batteries)**

subjects	N	follow up
early AD	150 (149)	2 yr
MCI	300 (234)	3 yr
NC	150(154)	3 yr

Sapporo
Hirosaki
Akita
Iwate
Tohoku
Niigata
Gumma Tsukuba, Mihara
Kanazawa
Shinshu NCNP Saitama
Kyorin Tokyo Met Geriatric Hosp
Tokyo Med col, Nippon Med, Asahi/Chiba-higashi
Juntendo, TMDU, Tokyo
Kyoto Kyoto Pref
Natl Longev., Hamamatsu, Kurihama, Yokohama
Tottori
Kobe, Osaka City
Okayama Osaka, Nara
Kagawa
Fukuoka
Kumamoto

J-ADNI
Alzheimer's Disease Neuroimaging Initiative

J-ADNI database

- Released for research use from the National Bioscience Database Center (NBDC) of JST, Japan, on Jan 29, 2016.
- Please obtain approval from local ethics committee and apply to NBDC at
  http://humandbs.biosciencedbc.jp/en/data-use

- Total number of datasets
3691 Case Report Forms
3078 Cognitive Test Worksheets
2550 Clinical Dementia Rating
2459 1.5T MRI images, 256 3T MRI images
1387 FDG PET images
594 amyloid PET images
3067 blood tests
339 CSF Aβ and tau

J-ADNI Demographics

	Normal controls (n=154)	MCI (n=234)	AD (n=149)	P
Age, mean (SD)	68.3 (5.8) 76.4 (5.0)	72.8 (5.9) 75.3 (7.5)	73.6 (6.6) 75.8 (7.4)	<0.0001
Female (%)	51.9 48.0	50.4 35.4	57.0 47.4	
Years of education, mean (SD)	13.8 (2.8) 15.6 (3.1)	13.0 (2.8) 16.0 (2.9)	12.4 (3.1) 14.7 (3.1)	0.0002
Apolipoprotein E ε4: Positive (%)	24.0 26.6	52.1 53.5	59.6 65.6	<0.0001

Red: US-ADNI (WW-ADNI@Sendai, 2009)

Entry survival
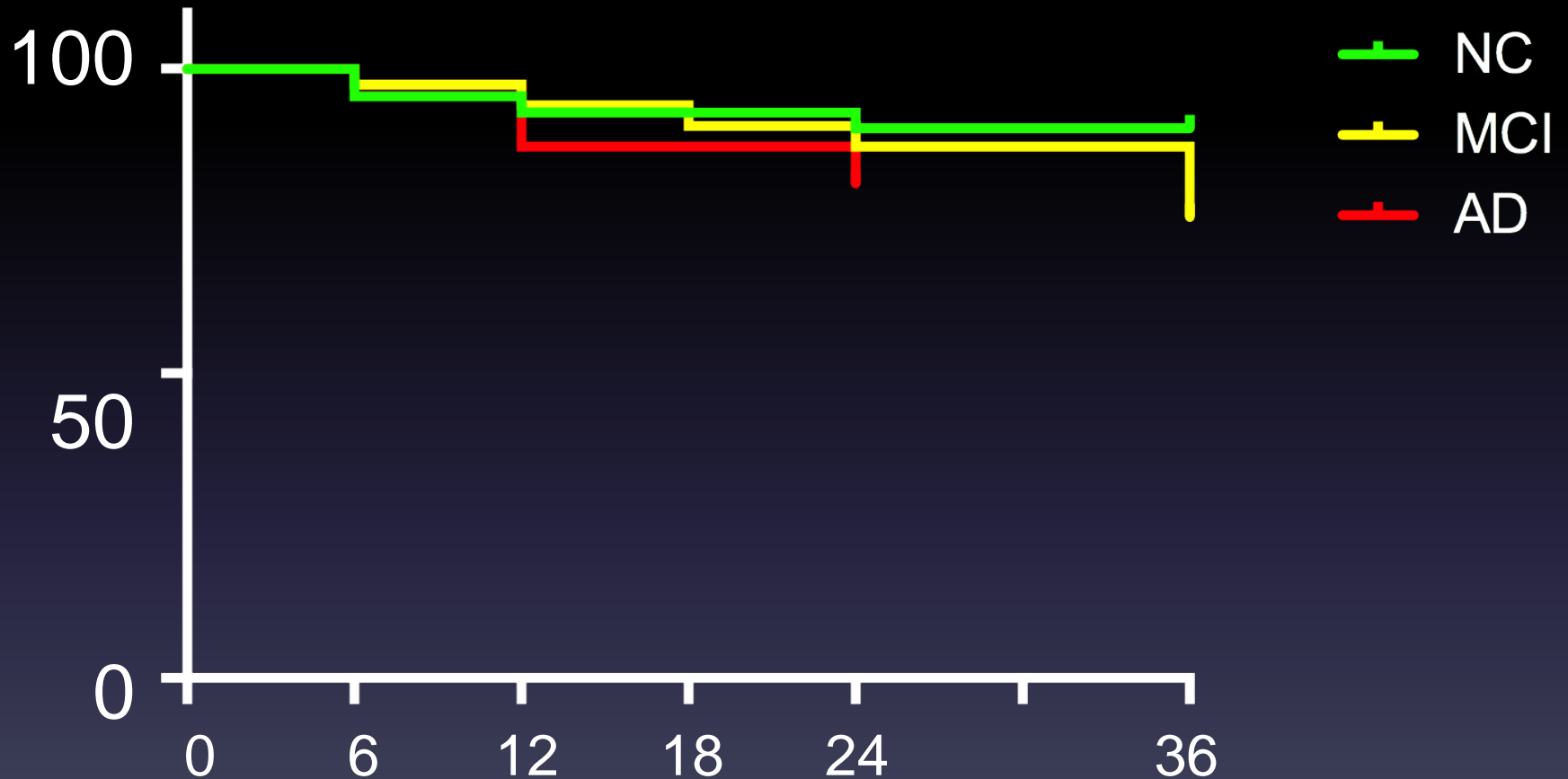
Completion NC 89.6% (3y), MCI 74.8% (3y), AD 81.2% (2y)

J-ADNI Cognitive Function baseline

|	Normal (n=154)	MCI (n=234)	AD (n=149)
MMSE	29.1(1.3)	26.4(1.7)	22.5(1.8)
memory			
Delayed recall (logical)	11.58 (3.52)	2.02 (2.09)	0.66 (1.15)
language			
Boston naming	28.6 (1.8) 27.9	25.6 (4.5) 25.5	24.4 (4.8) 22.3
Category fluency total	35.8 (7.4) 34.6	25.7 (6.7) 26.7	21.6 (6.3) 20.3
Executive function			
Trail A time	37.7 (12.6) 36.5	56.0 (25.7) 44.8	66.7 (32.7) 68.2
Trail B time	101.3 (45.5) 89.2	168.2 (78.2) 130.5	212.6 (79.3) 199.6
Digit symbol correct 120 sec (WAISIII)/90 sec (WAIS-R)	65.5 (14.7) 45.7	46.8 (15.4) 36.9	37.8 (14.3) 26.7
Visuospatial ability			
Clock draw: copy	4.97 (0.18) 4.86	4.81 (0.50) 4.65	4.60 (0.85) 4.31
Attention			
Digit span: Forward	9.28 (2.11) 8.78	9.25 (2.61) 8.22	8.17 (2.24) 7.54
Digit span: Backward	6.34 (2.03) 7.21	5.64 (1.63) 6.17	4.78 (1.64) 4.96

MMSE individual performances
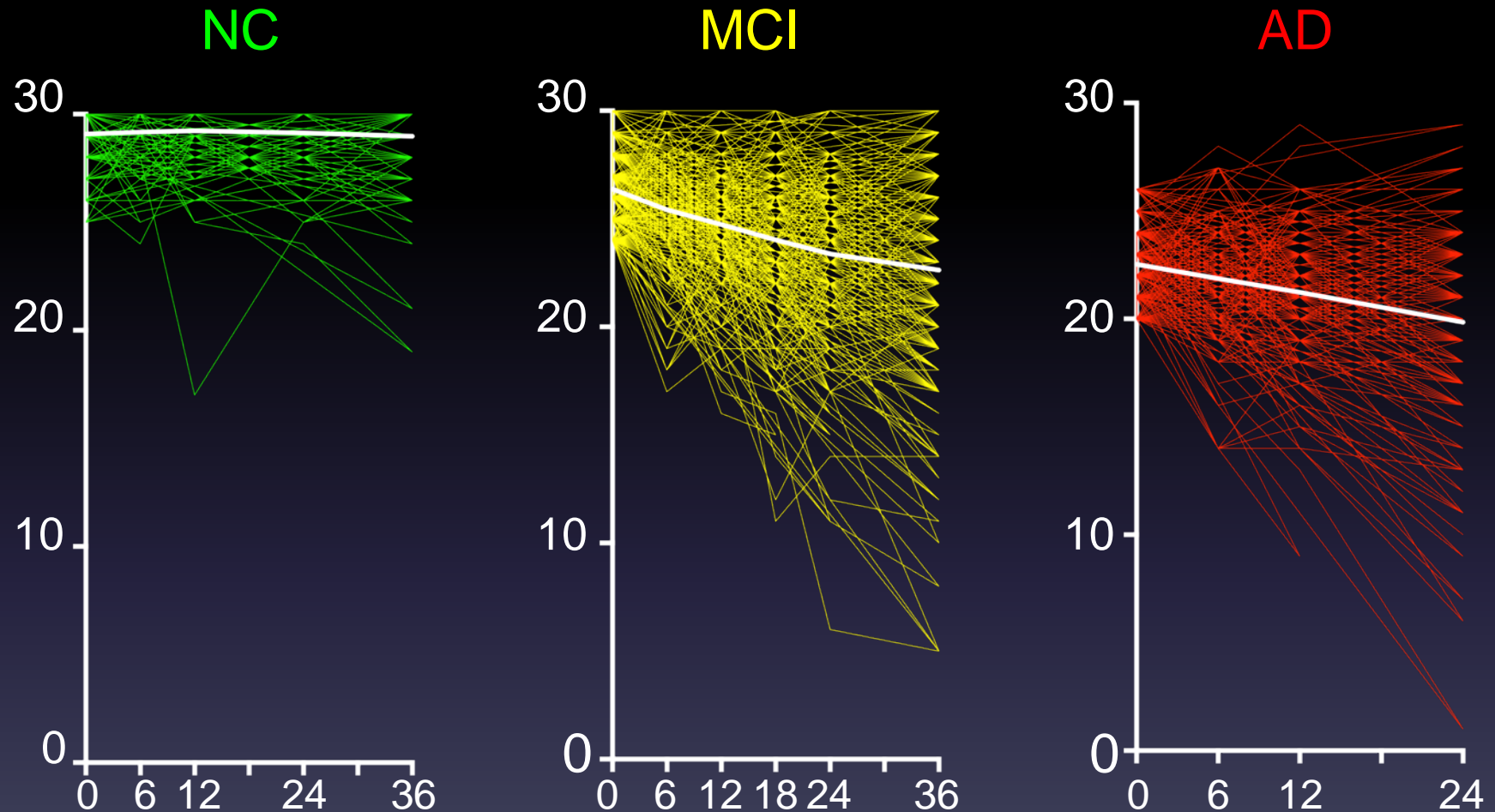
MMSE decline rate
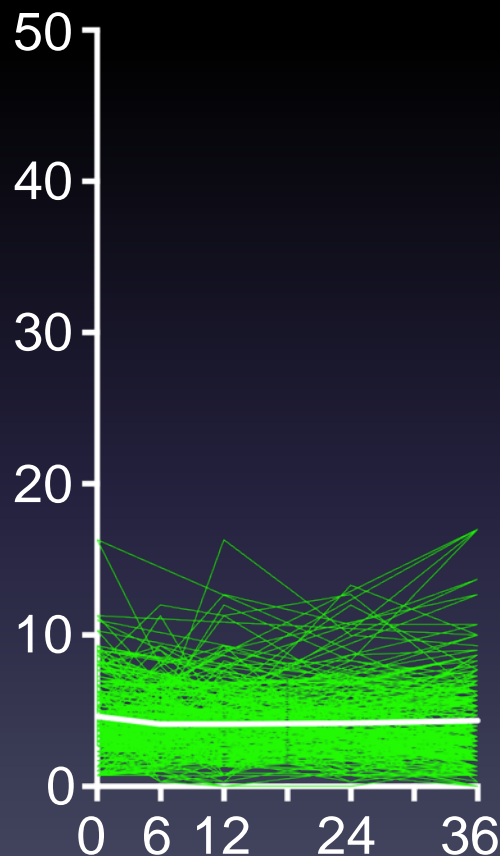NC -0.036/yr, MCI -1.25/yr, AD -1.34/yr
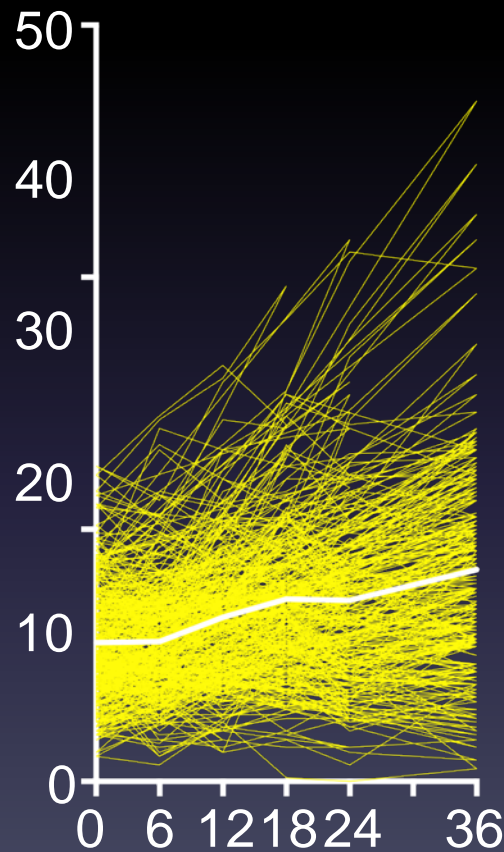
CDR sum of boxes individual performance in J-ADNI
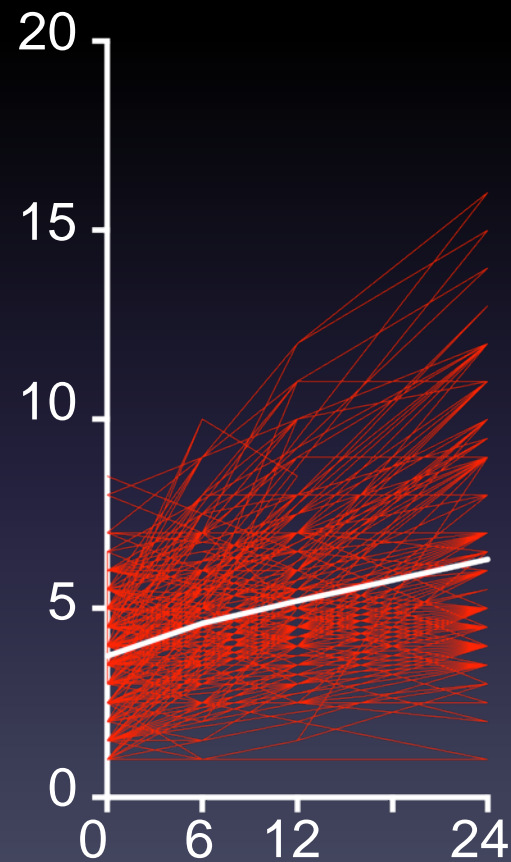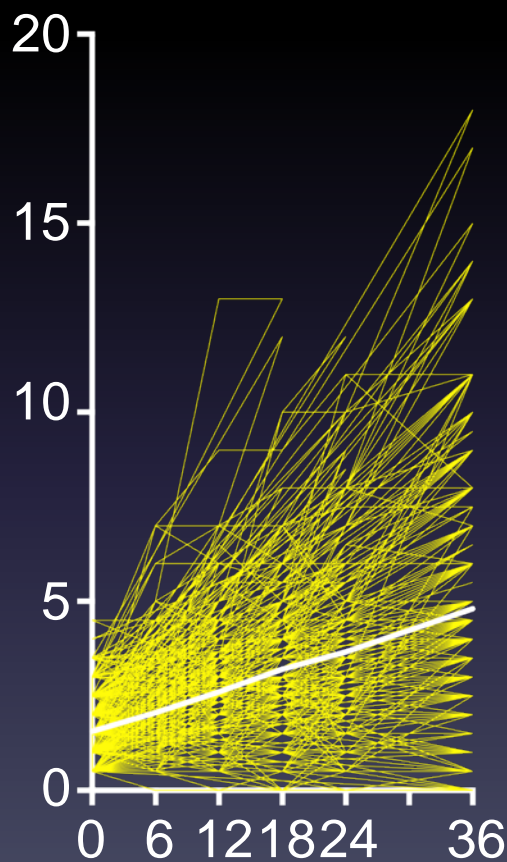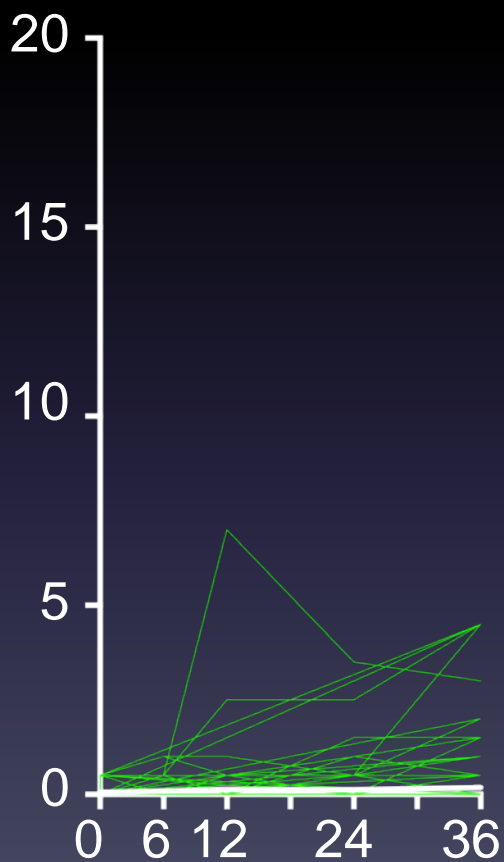
NC 0.04/yr, MCI 1.08/yr, AD 1.28/yr
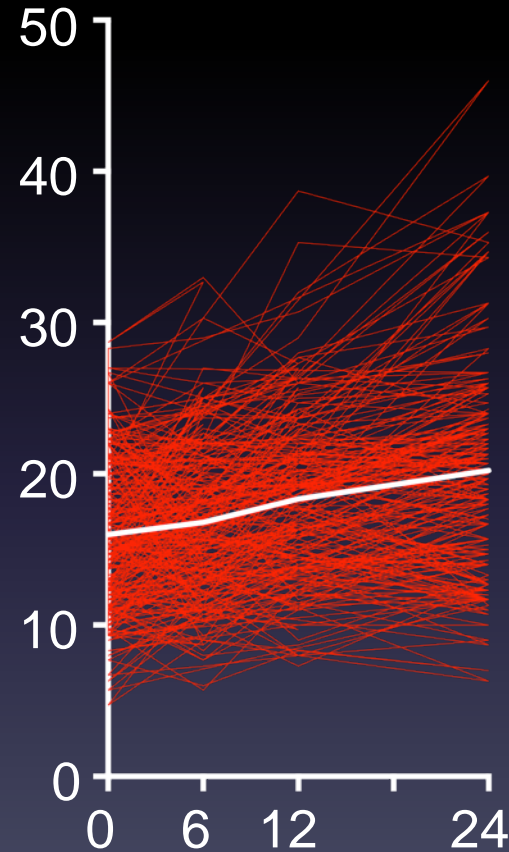
ADAS-cog11 trend in J-ADNI
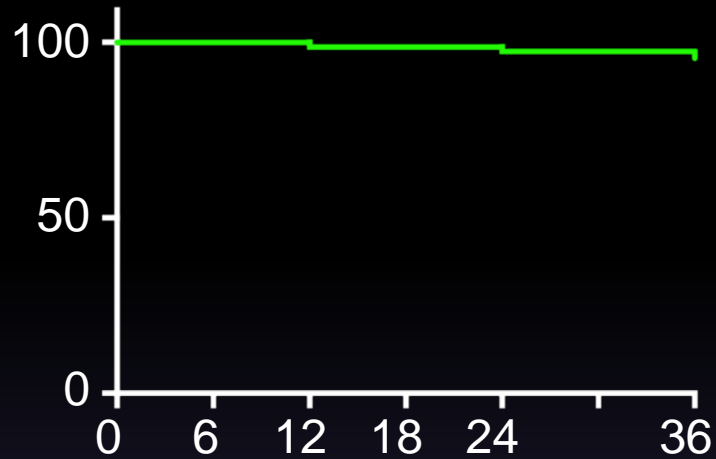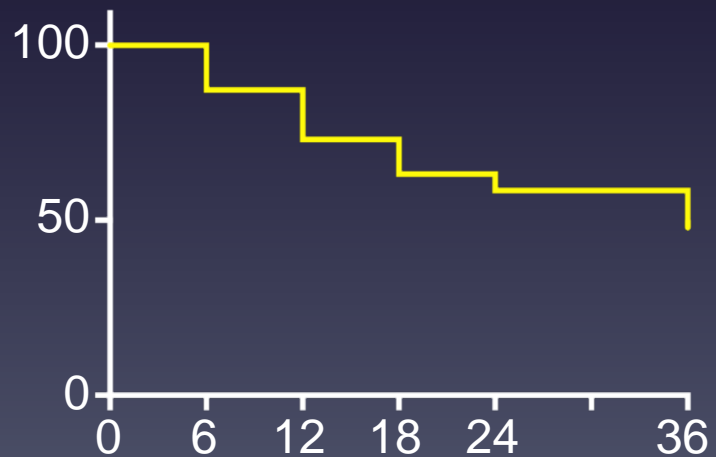
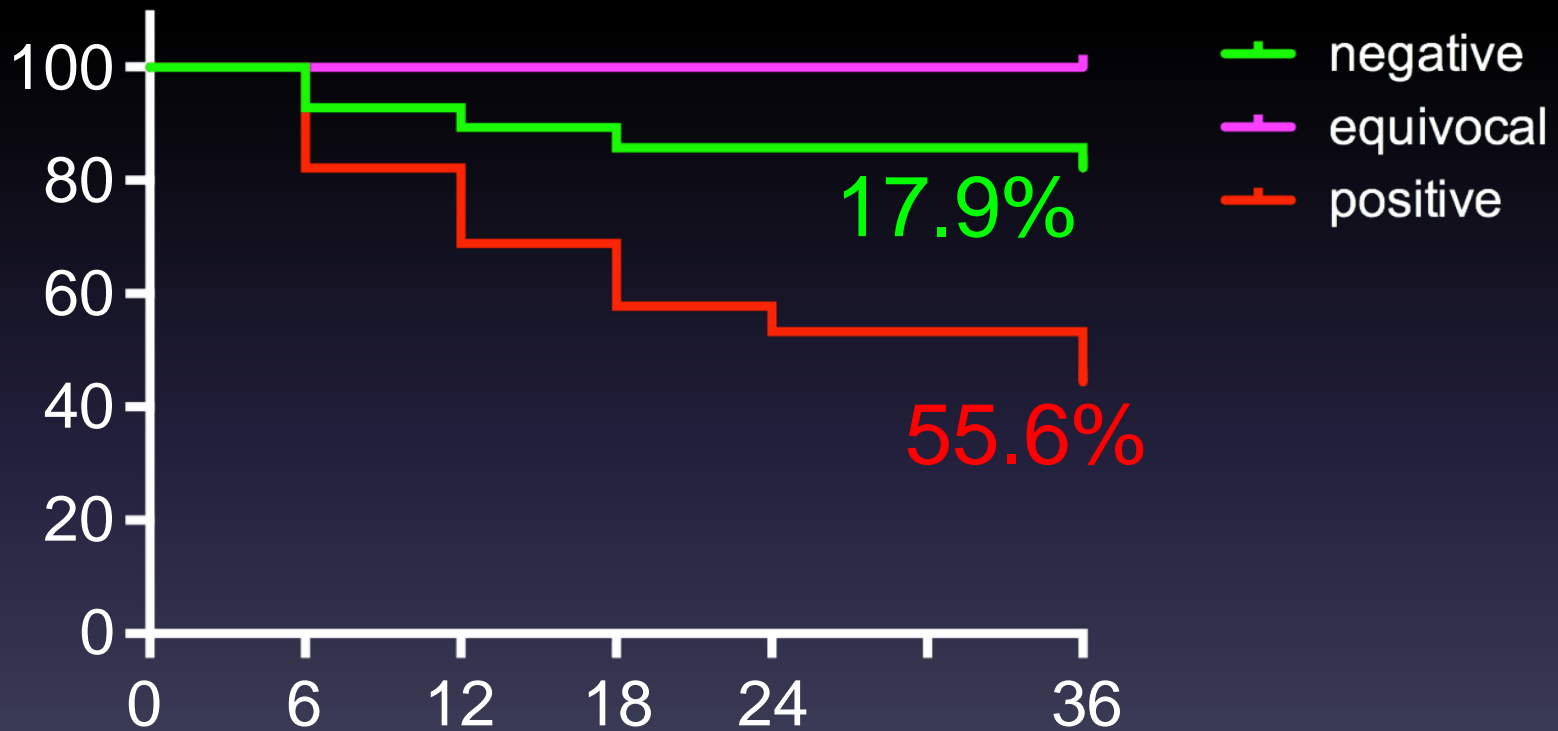NC: -0.09/yr, MCI +1.93/yr, AD: +2.11/yr

Conversion rate

NC to MCI

1 year conversion rate 1.3%
2 year conversion rate 2.6%
3 year conversion rate 4.5%

MCI to AD
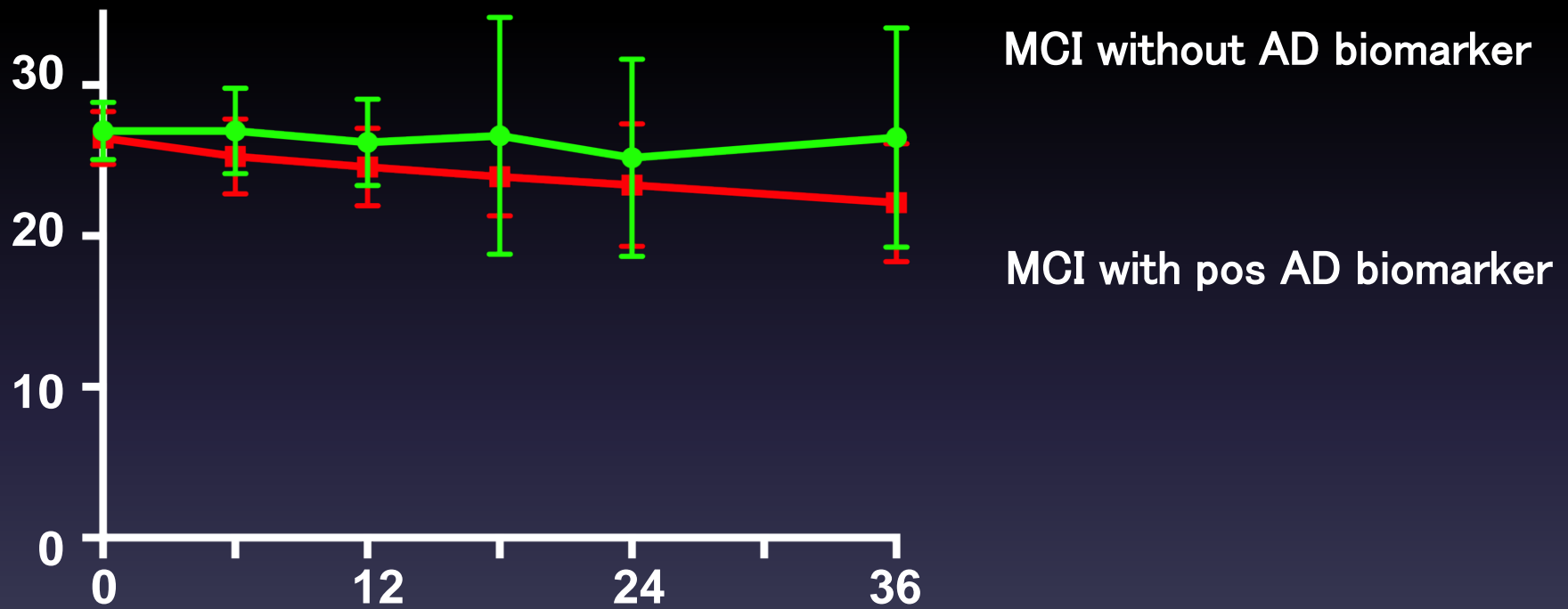
1 year conversion 26.2% (16.1% in US-ADNI1)
2 year conversion 41.5%
3 year conversion 52.1%

MCI to AD conversion by PET amyloid positivity
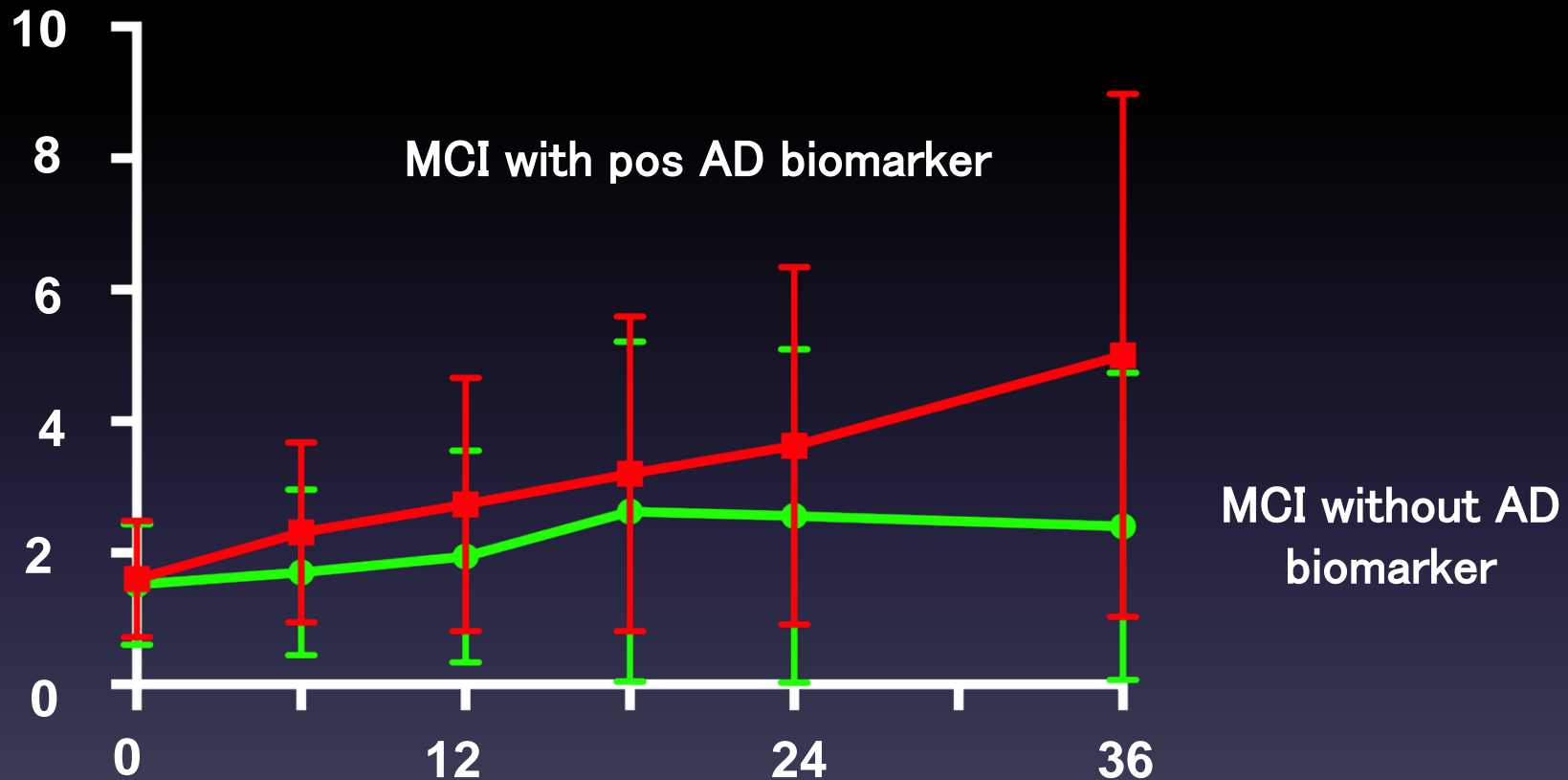
Conversion rate negative 6.0%/yr, positive 18.5%/yr

MCI MMSE by Aβ pathology

MCI without AD biomarker

MCI with pos AD biomarker

MCI with pos AD biomarker −1.43/yr
MCI with neg AD biomarker −0.14/yr

MCI CDR SOB by Aβ pathology

MCI with pos AD biomarker

MCI without AD biomarker

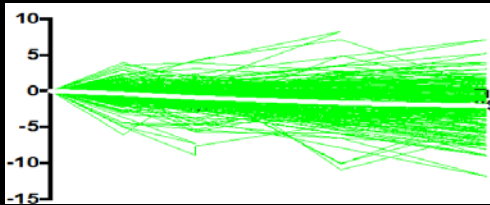MCI with pos AD biomarker 1.13/yrr

MCI without AD biomarker 0.29/yr

Hippocampal volume by Freesurfer (Matsuda, Iwata)

NC

MCI

AD

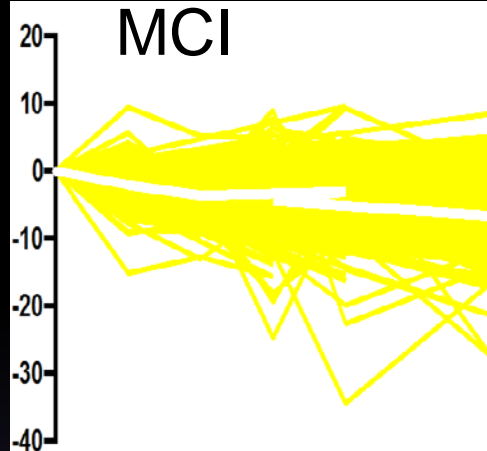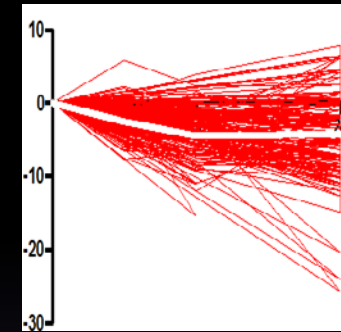Mean atrophy rate:
NC 2.25%/3y; 0.75%/y
MCI 6.63%/3y 2.21%/y
AD 4.26%/2y, 2.13%/y

Sample size estimation for MCI in one-year trial design using BSI

Measure	MCI			MCI controlling for normal aging		
	Total	ε4+	ε4−	Total	ε4+	ε4−
	235	121	112	235	121	112
Brain BSI	205	164	264	633	463	929
	[163 265]	[124 227]	[184 412]	[504 818]	[350 641]	[647 1447]
Hippo BSI	149	95	236	270	154	520
	[123 185]	[76 121]	[168 358]	[222 335]	[124 196]	[369 788]
CDR-SB	574	416	878	658	464	1058
	[400 893]	[273 713]	[478 2112]	[458 1024]	[304 795]	[576 2546]
ADAS-Cog	526	360	761	579	387	867
	[371 803]	[242 590]	[429 1705]	[408 883]	[260 636]	[489 1942]

Fujishima, Matsuda

MCI: hippocampal volume change in 12 months
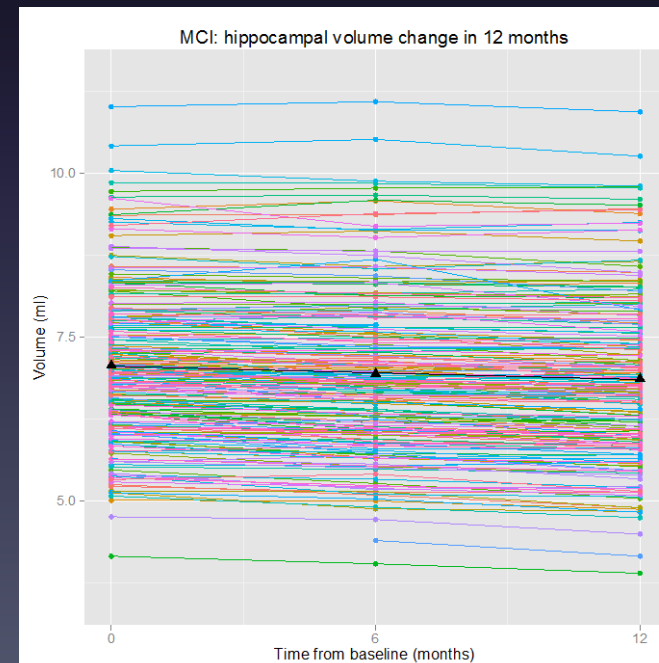
PiB-PET in J-ADNI

Kenji Ishii, amyloid PET core of J-ADNI
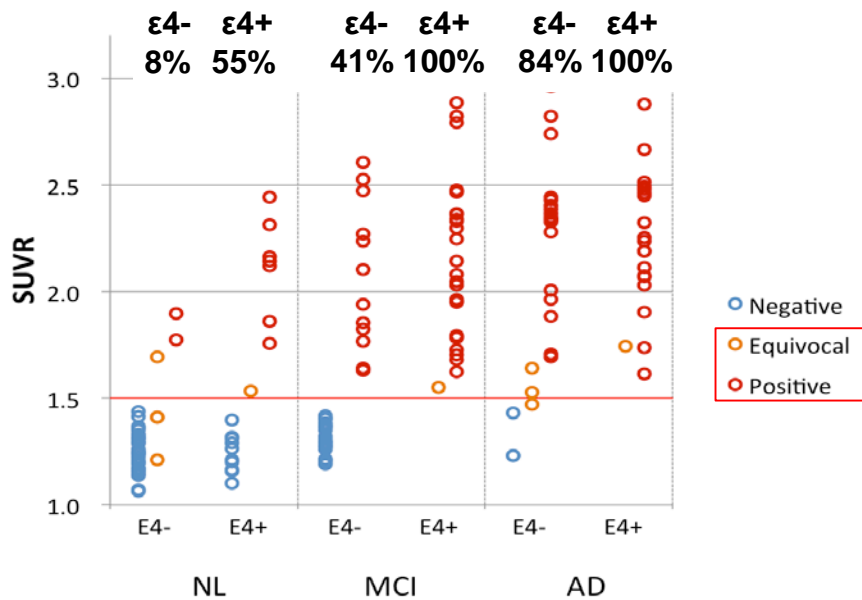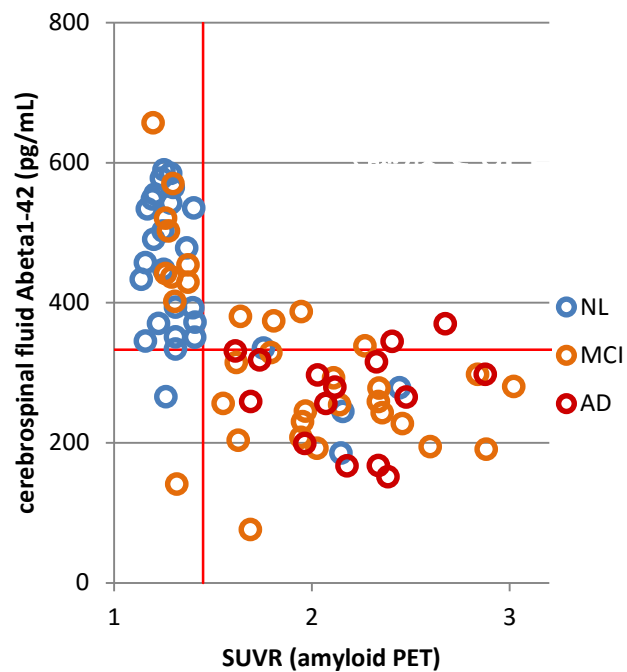
J-ADNI2/AMED preclinical AD Study

J-ADNI2/preclinical

Normal | Preclinical AD | early | MCI | late | AD

Failure of DMT trials in AD dementia
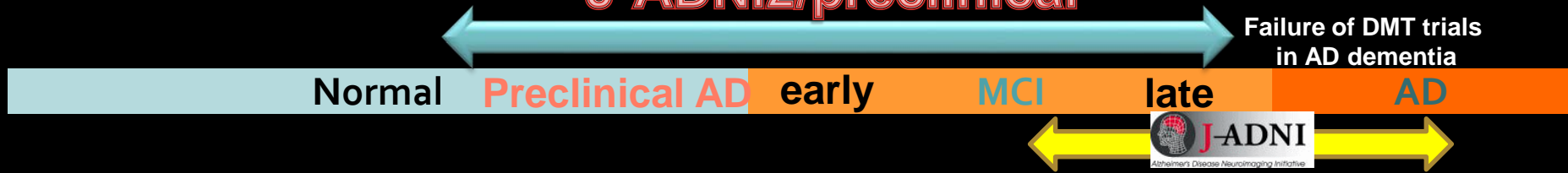
- Consists of two observational studies:(1)Preclinical AD (n=150) screened by amyloid PET, 3-y follow up (2) early (n=100) /late MCI (n=100) studies using protocols compatible to NA ADNI2/3; implementing FCSRT , E-Cog

- ~30 clinical sites, totally covered by ^{11}C-PiB, florbetapir or flutemetamol, at ~25 PET centers nationwide

- 3T MRI (including resting fMRI, ASL, DTI)

- CSF examination at baseline, 12M and 36M

- Towards successful clinical trials of DMTs in prodromal/preclinical AD; setting the basis for Trial Ready Cohort, providing data/mechanism for "funnel" to select at risk individuals for AD

J-DCS (Japanese Dementia Clinical study Support center)
toward trials for DMDs and establishing Trial Ready Cohort; funded by AMED 2016-2020

国立研究開発法人日本医療研究開発機構
Japan Agency for Medical Research and Development
AMED

Clinical Studies

DIAN-J observational
JADNI2/AMED preclinical
Osaka C Univ

A4 Japan
JADNI2/AMED preclinical
The Univ Tokyo

Data registration

Support analysis

J-DCS: providing support to clinical studies and trials on AD

Clinical study operation center

Study Management
Osaka City Univ

Project management
The Univ Tokyo

Data management
Cloud DB
The Univ Tokyo

QMS
The Univ Tokyo

Cognitive scales
The Univ Tokyo

Imaging
MRI: NCNP
PET: IBRI

Biomarkers
Niigata

Trial Ready Cohort

Risk evaluation funnel

Internet Registry of Orange Plan (NCNP)

certification

Network of clinical sites with experience in J-ADNI and J-ADNI2/preclinical