Validating Alzheimer's Pathological Cascade by Merging ADNI With PAQUID

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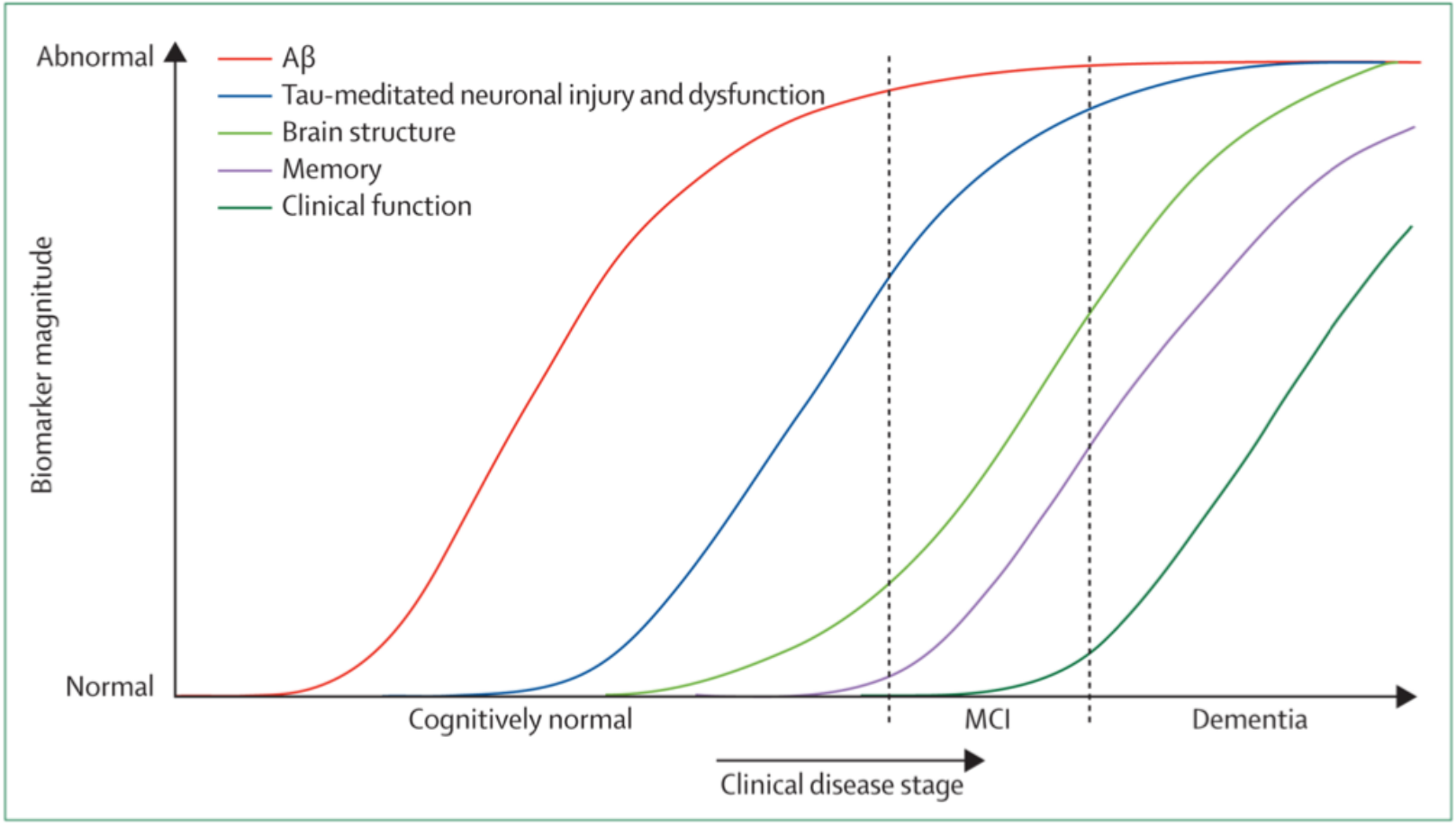
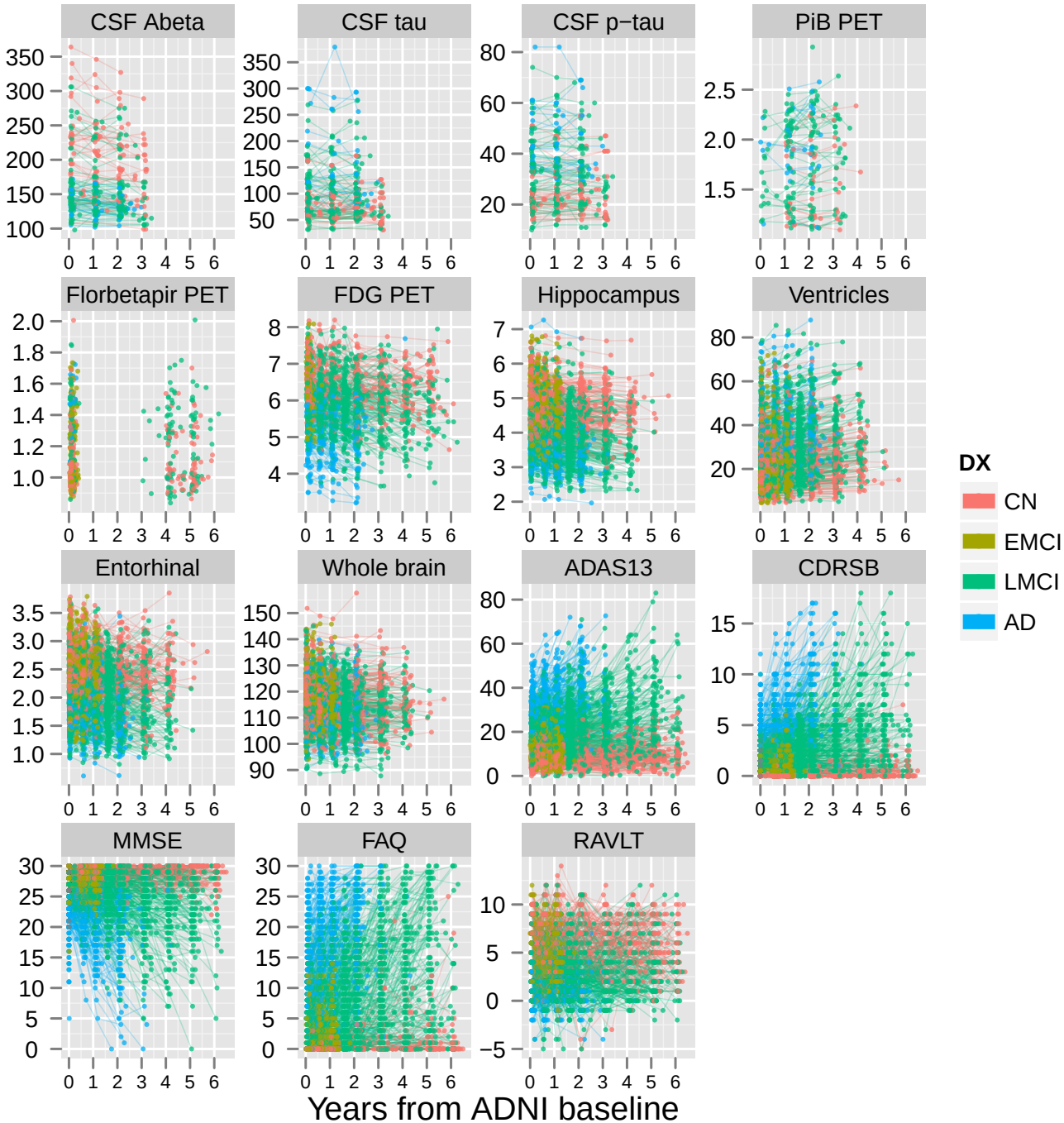
Disclosures

- NIA, AD Cooperative Study (ADCS)
- CTSA, UC San Diego CTRI KL2 Award
- Consultant to Bristol-Myers Squibb

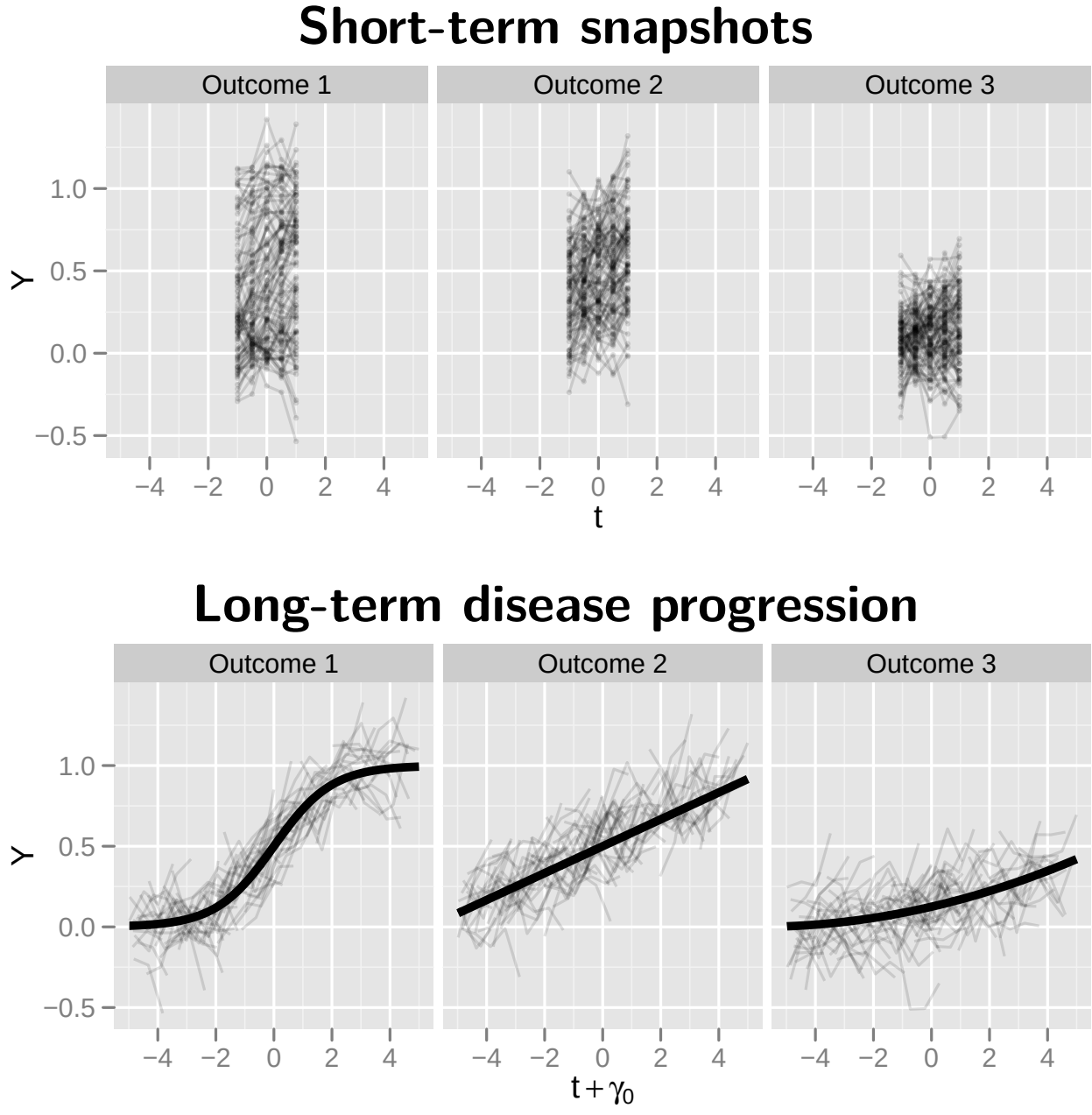
Motivation: Jack et al 2010 *The Lancet Neurology*



Raw ADNI data



Artificial data



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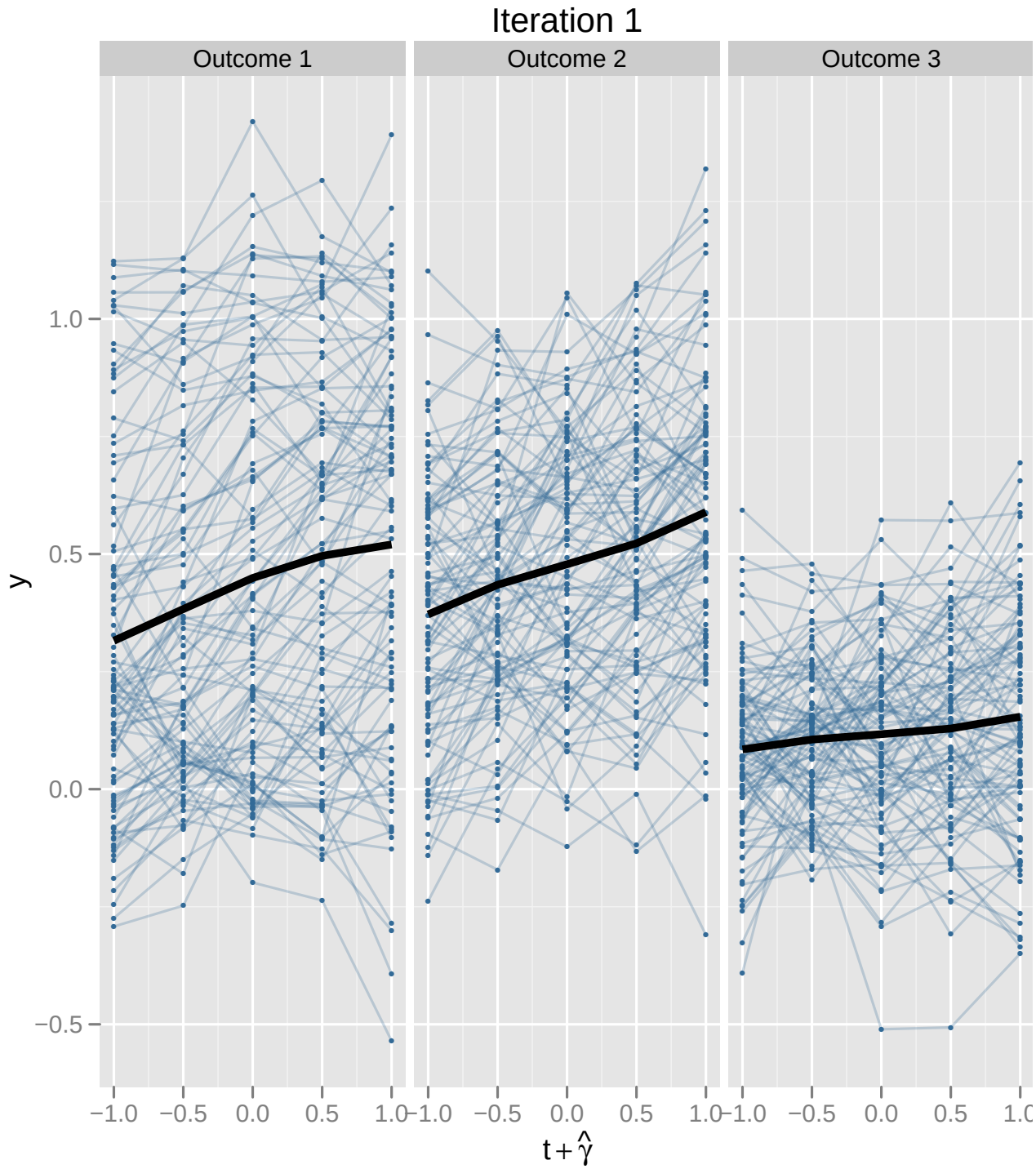
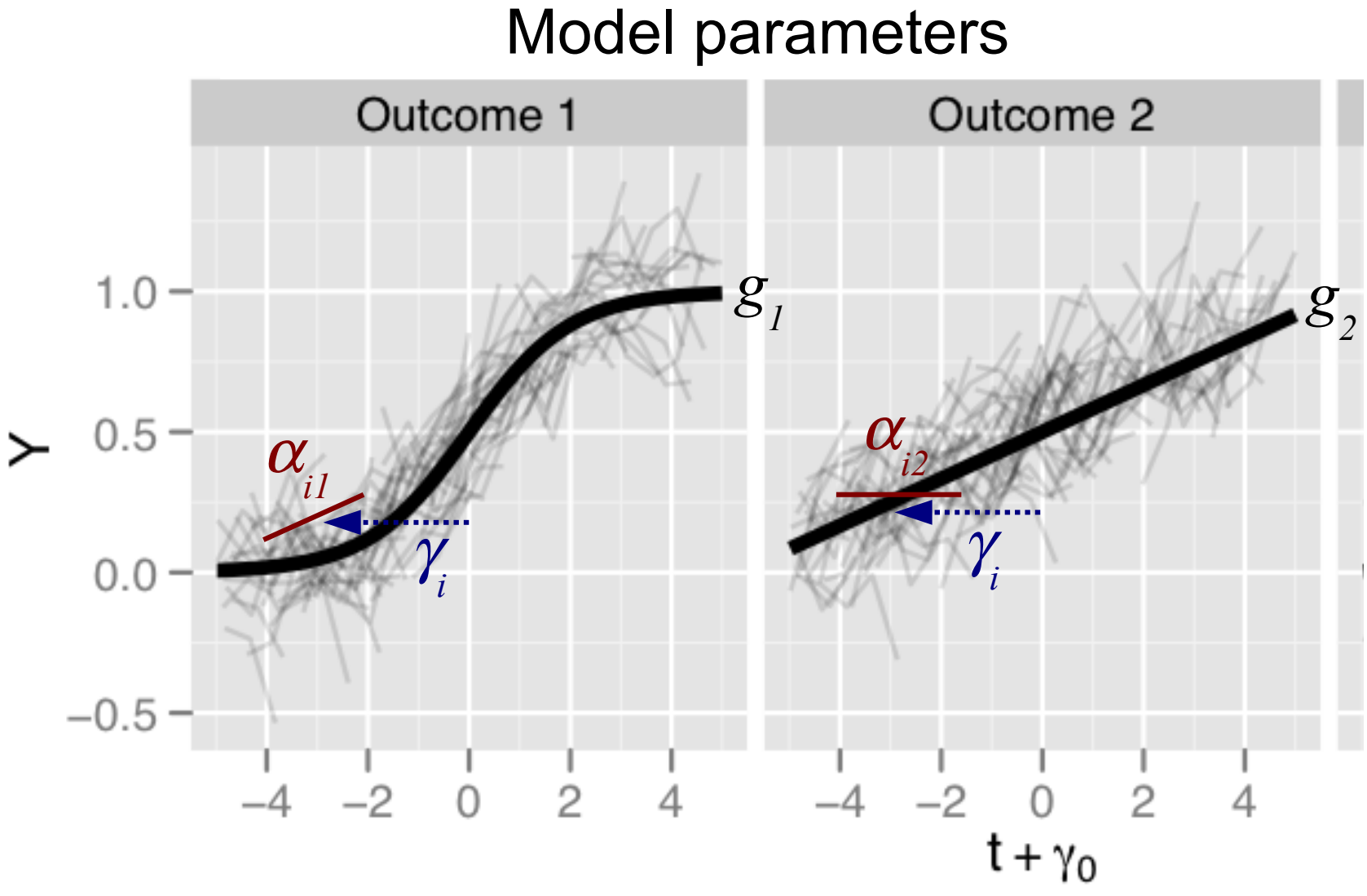
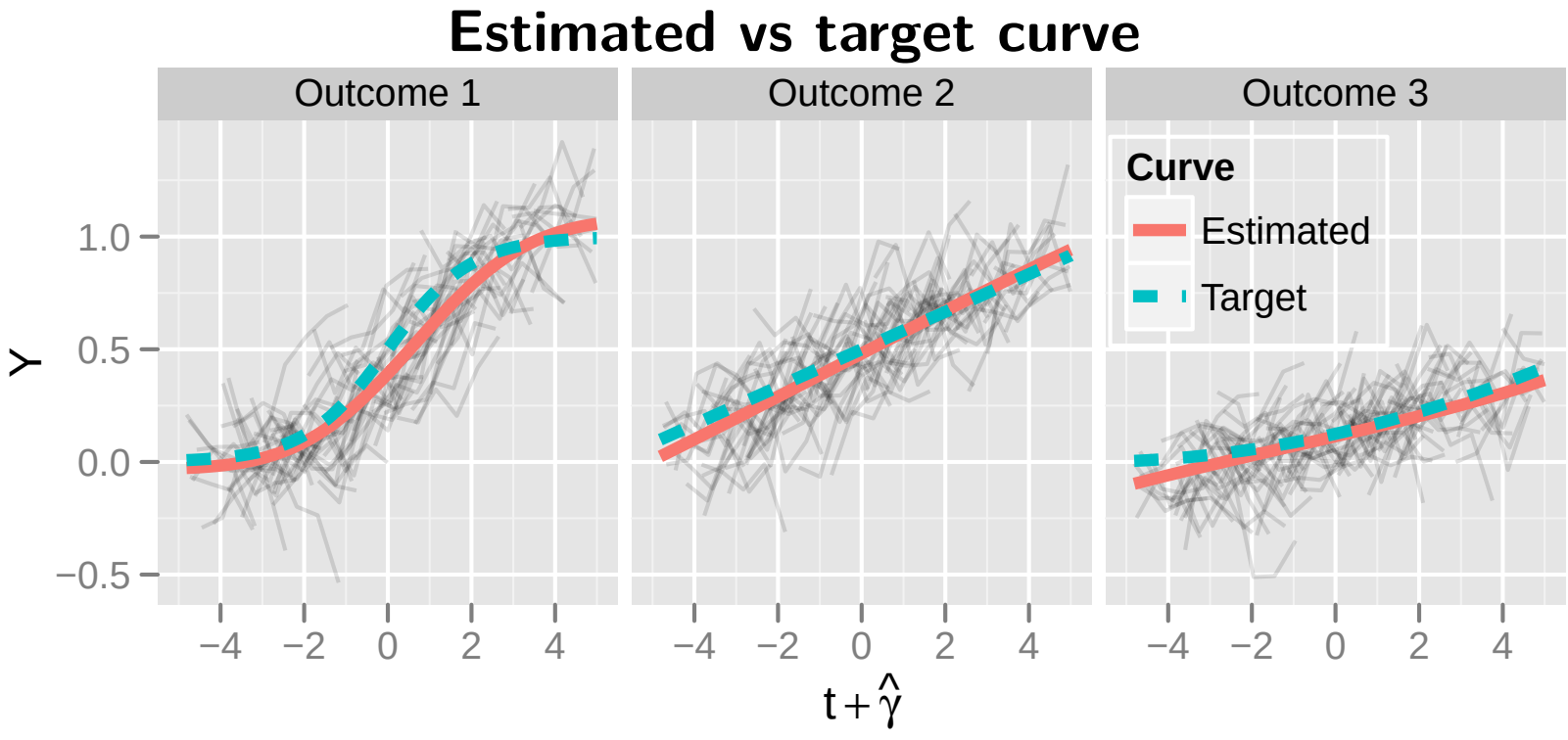


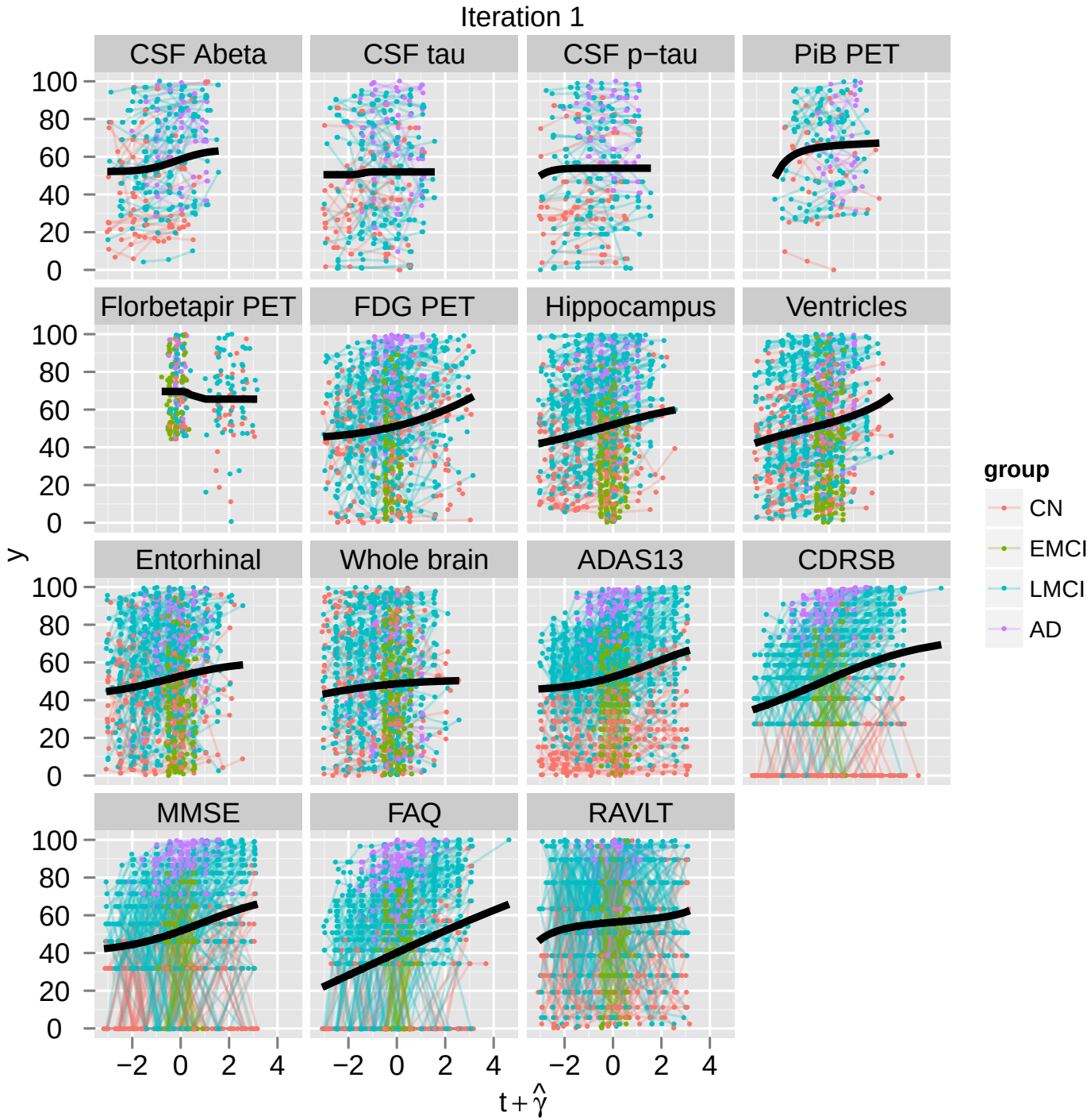
Model: $Y_{ij}(t) = g_j(t + \gamma_i) + \alpha_{0ij} + \alpha_{1ij}t + \varepsilon_{ij}(t)$



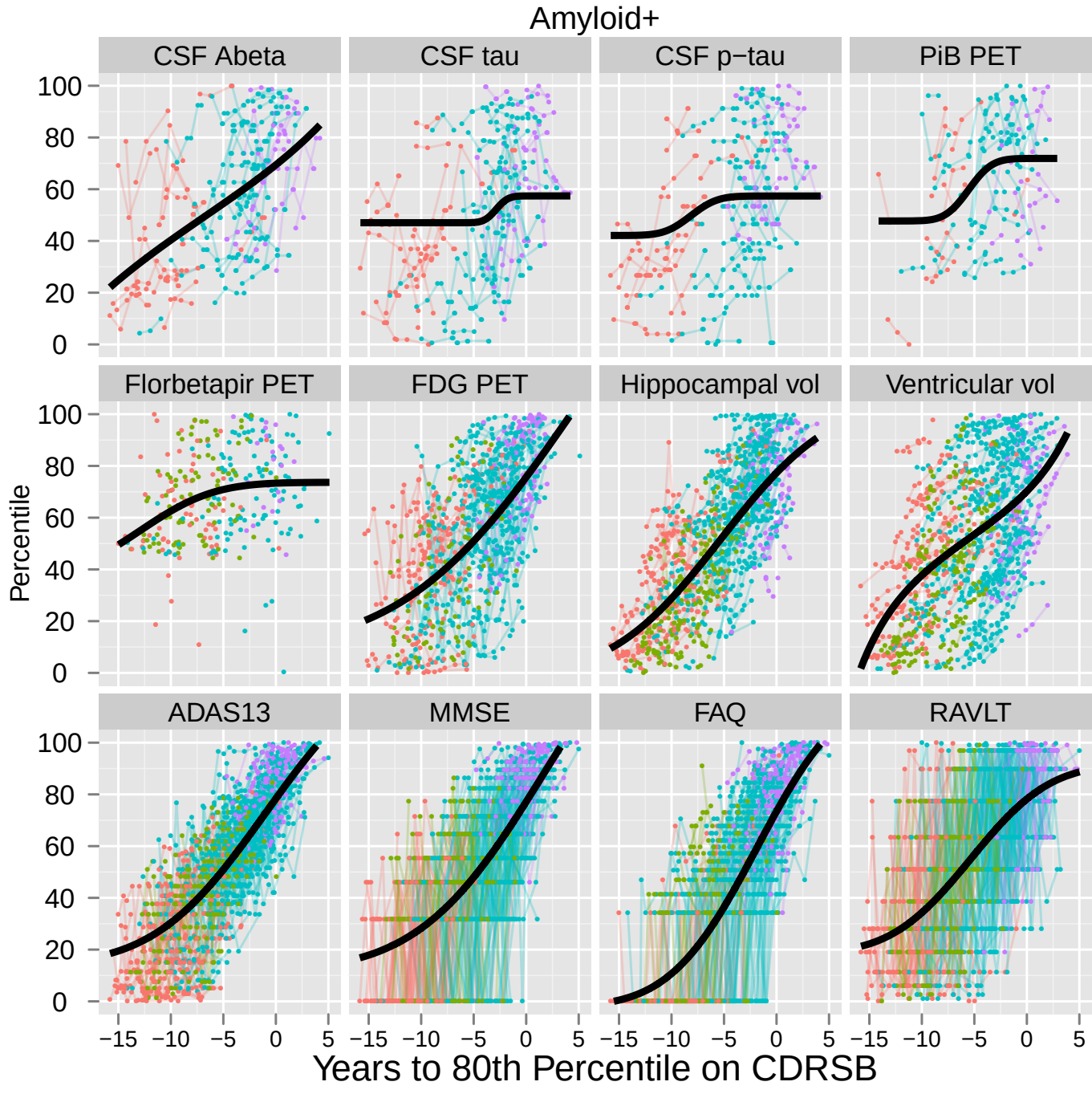
Artificial data

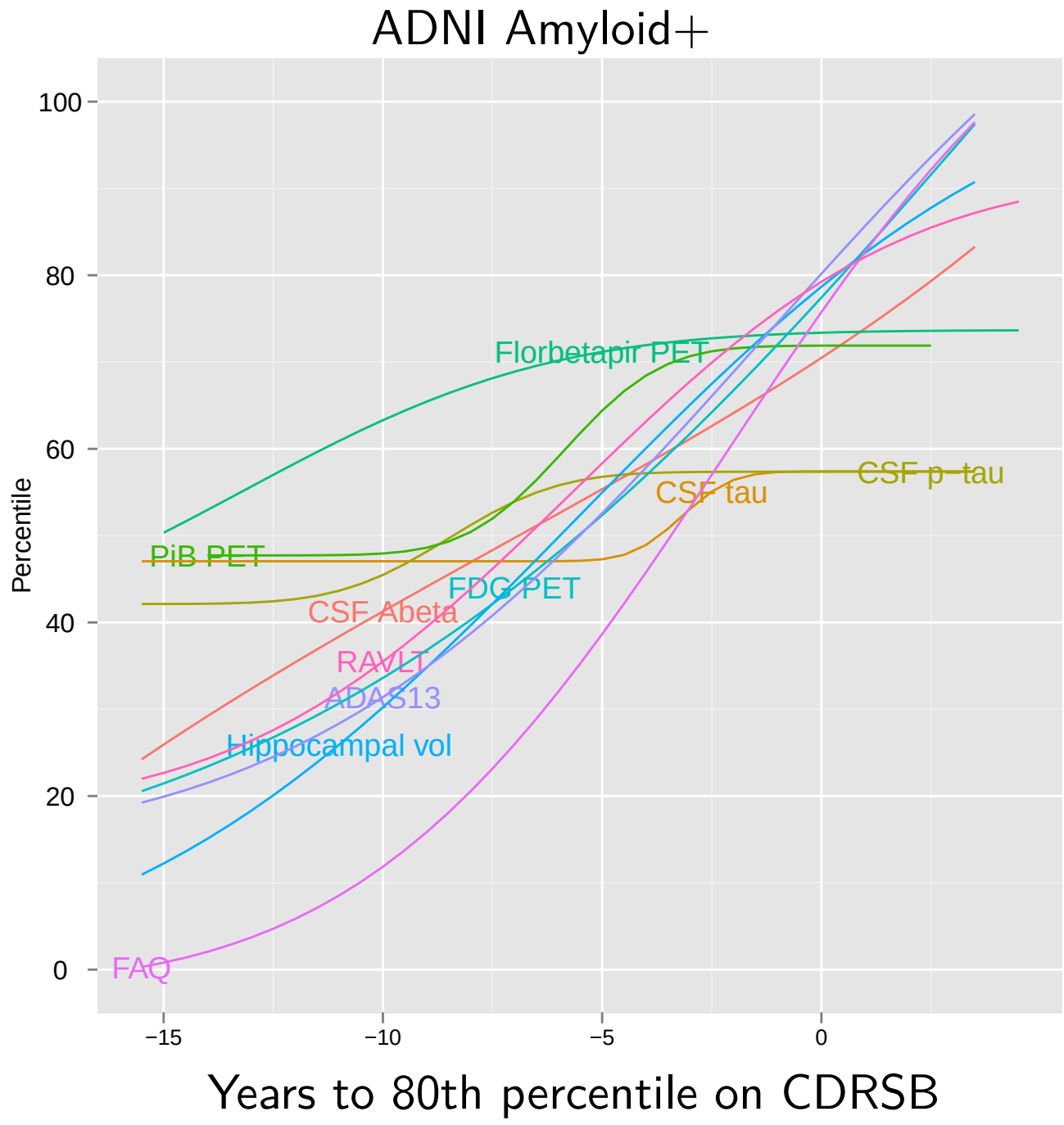


Real ADNI Amyloid+ data



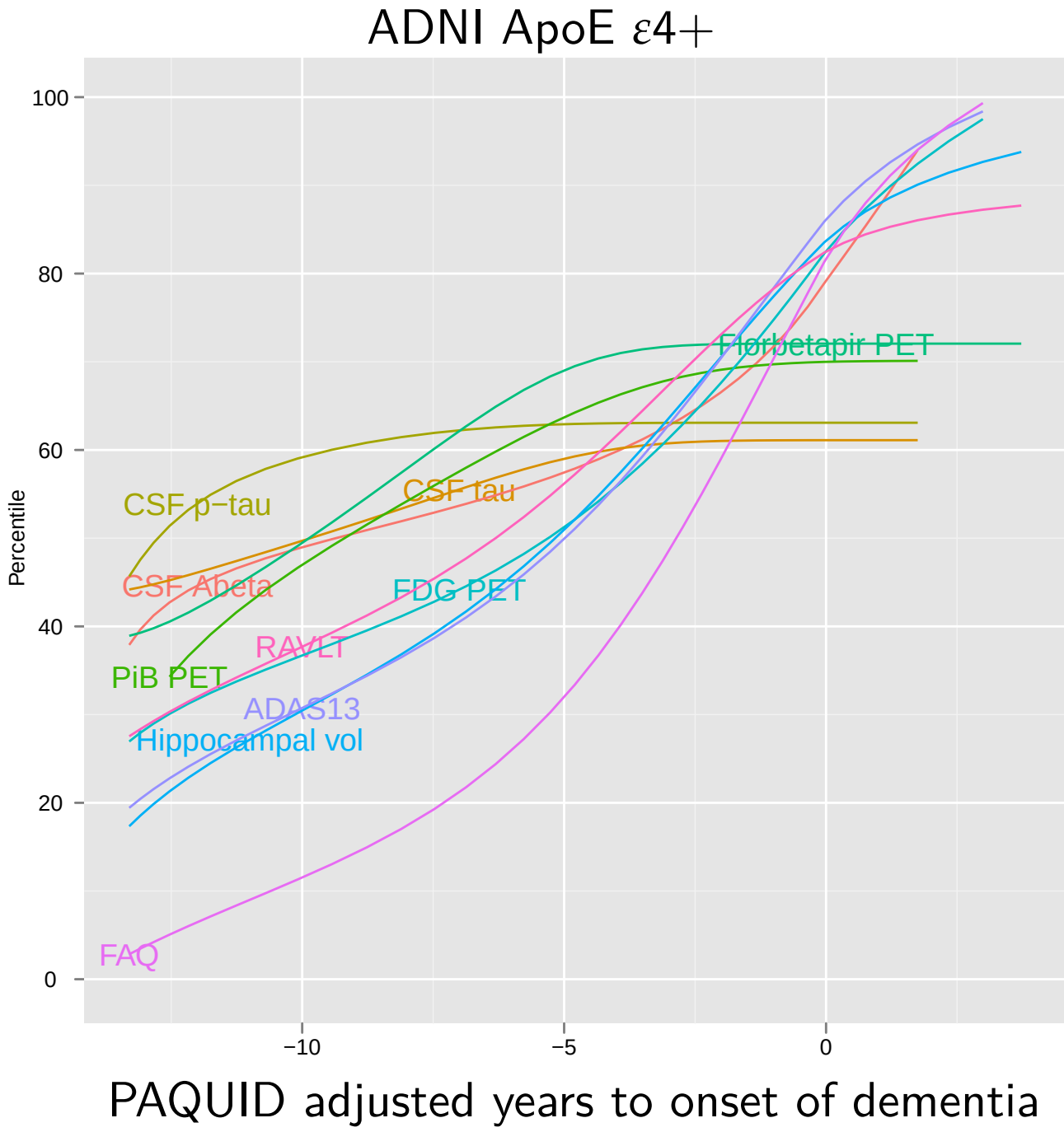
Real ADNI Amyloid+ data




ADNI Amyloid+
Percentile
100
80
60
40
20
0
−15
−10
−5
0
Florbetapir PET
PiB PET
FDG PET
CSF Abeta
CSF tau
CSF p−tau
RAVLT
ADAS13
Hippocampal vol
FAQ
Years to 80th percentile on CDRSB

Post-processing with "Personnes Agées QUID" (PAQUID)

- French study of n =3,777 individuals aged 65 years or older followed from 1988 until present.
- Amieva et al (2008) provide **long-term** estimates of MMSE progression derived from **long-term** data.
- 15 year MMSE trajectory estimated from $n = 43$ ApoE e4+ AD progressors used to calibrate our time-scale to approximate "time-to-onset".


ADNI ApoE ε4+
Percentile
100
80
60
40
20
0
−10
−5
0
CSF p−tau
CSF tau
CSF Abeta
FDG PET
RAVLT
PiB PET
ADAS13
Hippocampal vol
Florbetapir PET
FAQ
PAQUID adjusted years to onset of dementia

Thank you!

- NIH, CTSA
- NIA, AD Cooperative Study (ADCS)
- ADNI & PAQUID collaborators, volunteers and their families