ADNI Clinical Core

Paul Aisen

Ron Petersen

Michael Donohue

Jennifer Salazar

ADNI Steering Committee Meeting

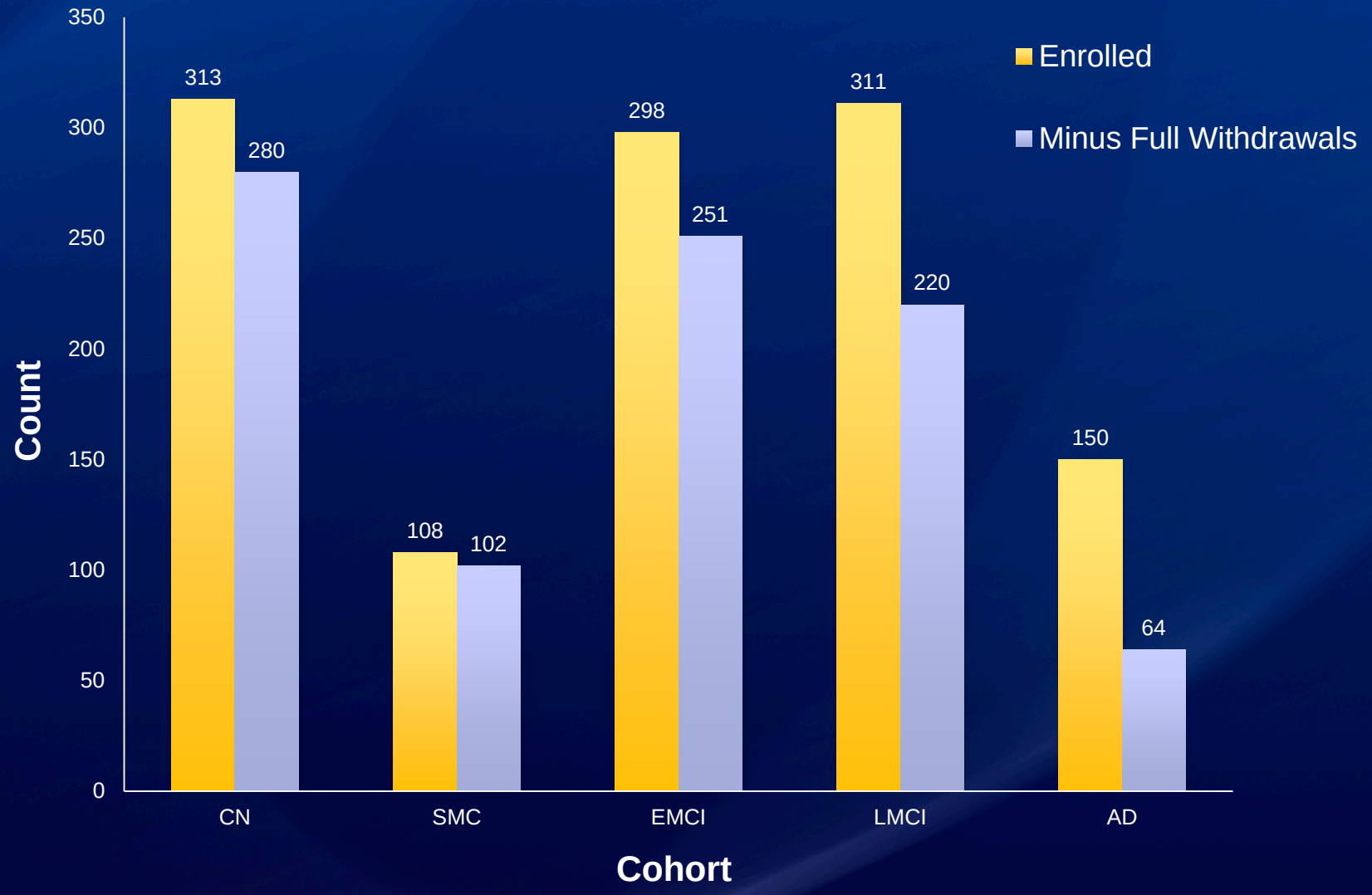
Washington, DC

April 20, 2015

MAYO CLINIC

ADNI 2 Enrollment by Cohort

Total at initial entry (includes 276 ADNI 1 + 120 ADNI GO rollovers): ***1180***
Current total (minus reported withdrawals): ***917***



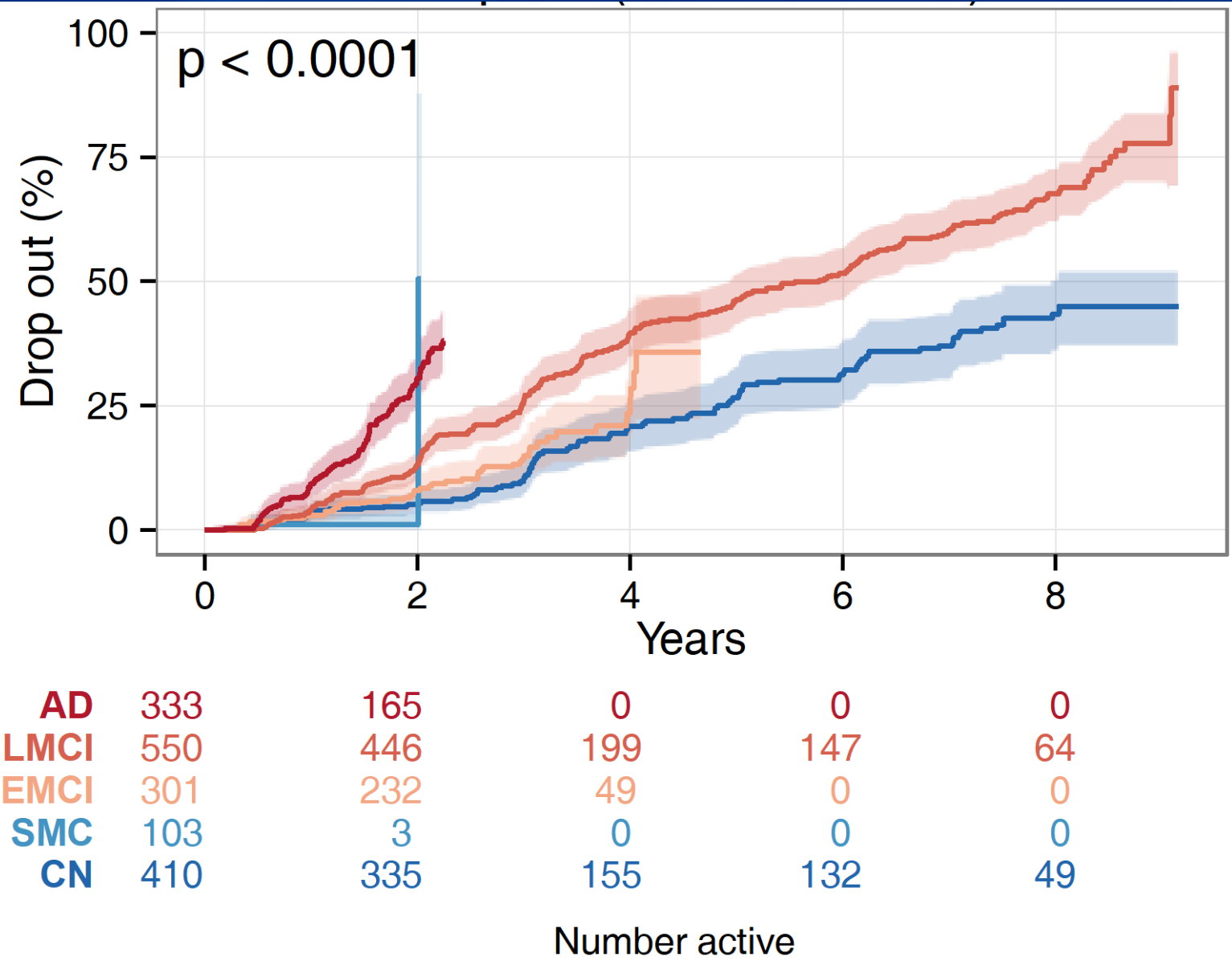
MAYO CLINIC

ADNI GO + 2 Baseline

	CN n=184	SMC n=103	EMCI n=301	LMCI n=160	AD n=145	Combined n=893	P
Age (yrs)	73.4 (6.3)	72.2 (5.6)	71.3 (7.4)	72.2 (7.5)	74.6 (8.1)	72.5 (7.3)	<0.001
Female	94 (51%)	61 (59%)	132 (44%)	74 (46%)	59 (41%)	420 (47%)	0.027
Education	16.5 (2.5)	16.7 (2.6)	16.0 (2.7)	16.5 (2.6)	15.8 (2.7)	16.3 (2.6)	0.009
CDR-SB	0.0 (0.1)	0.01 (0.2)	1.3 (0.8)	1.7 (1.0)	4.5 (1.7)	1.5 (1.7)	<0.001
ADAS 13	9.2 (4.5)	8.9 (4.3)	12.7 (5.4)	18.7 (7.1)	31.0 (8.4)	15.5 (9.6)	<0.001
MMSE	29.0 (1.3)	29.0 (1.2)	28.3 (1.6)	27.6 (1.8)	23.1 (2.1)	27.6 (2.6)	<0.001
Part. ECog	1.3 (0.3)	1.6 (0.3)	1.8 (0.5)	1.8 (0.5)	1.9 (0.6)	1.7 (0.5)	<0.001
Study Part. Ecog	1.2 (0.3)	1.3 (0.3)	1.6 (0.5)	1.9 (0.7)	2.7 (0.7)	1.7 (0.7)	<0.001

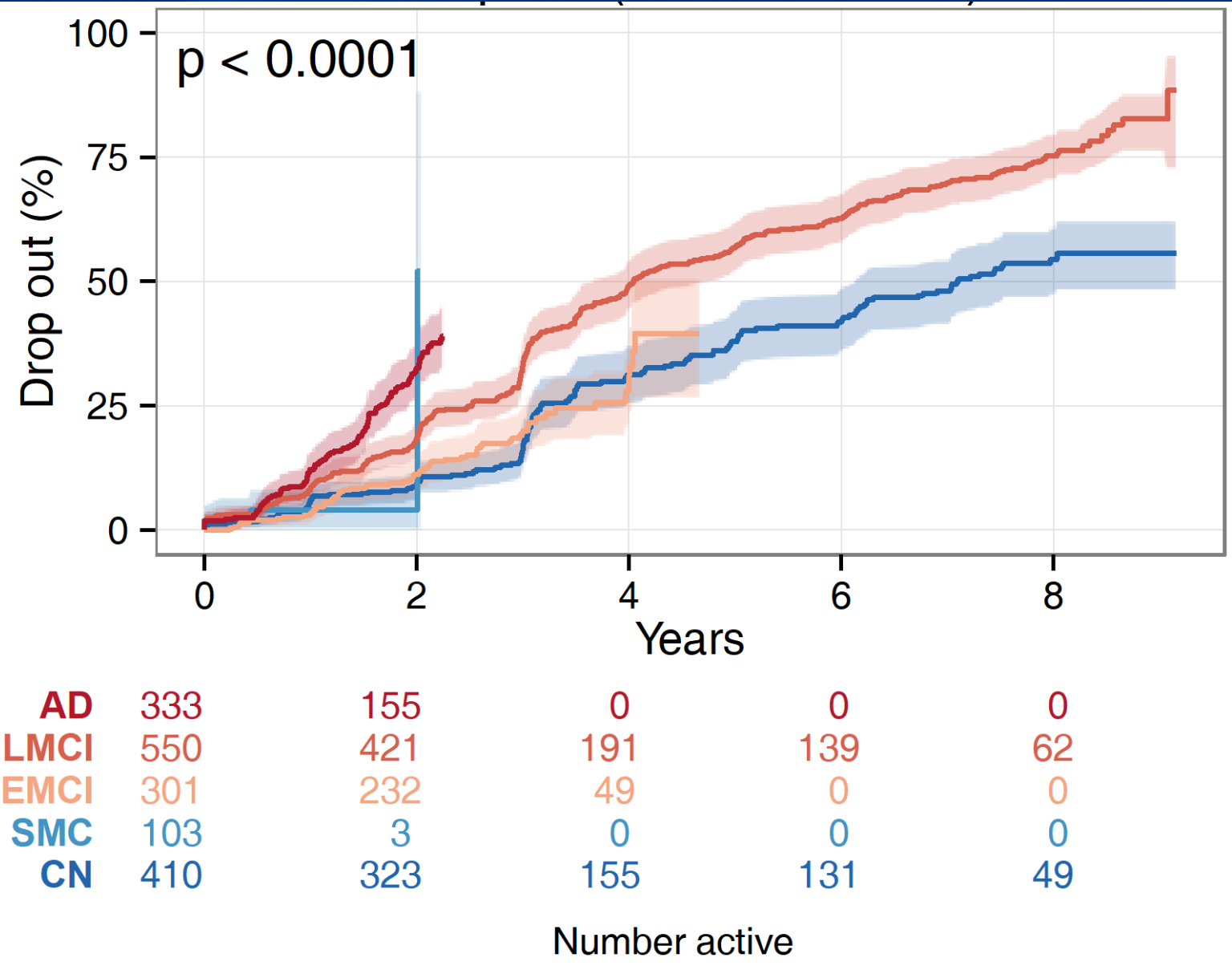
MAYO CLINIC

Dropout Rate



dropout = reported withdrawals

Dropout Rate

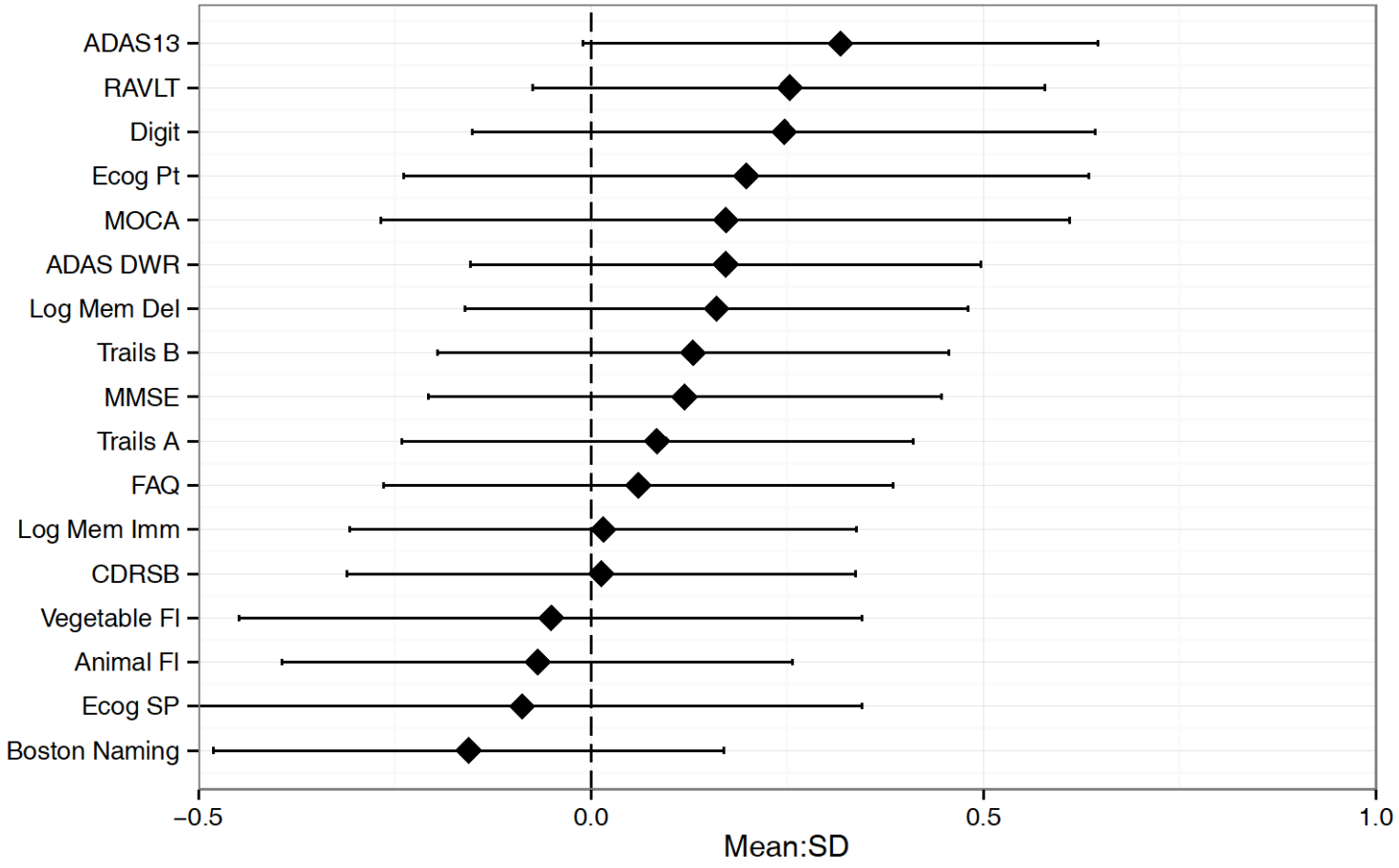


dropout = reported withdrawals or no new data in last 18 months

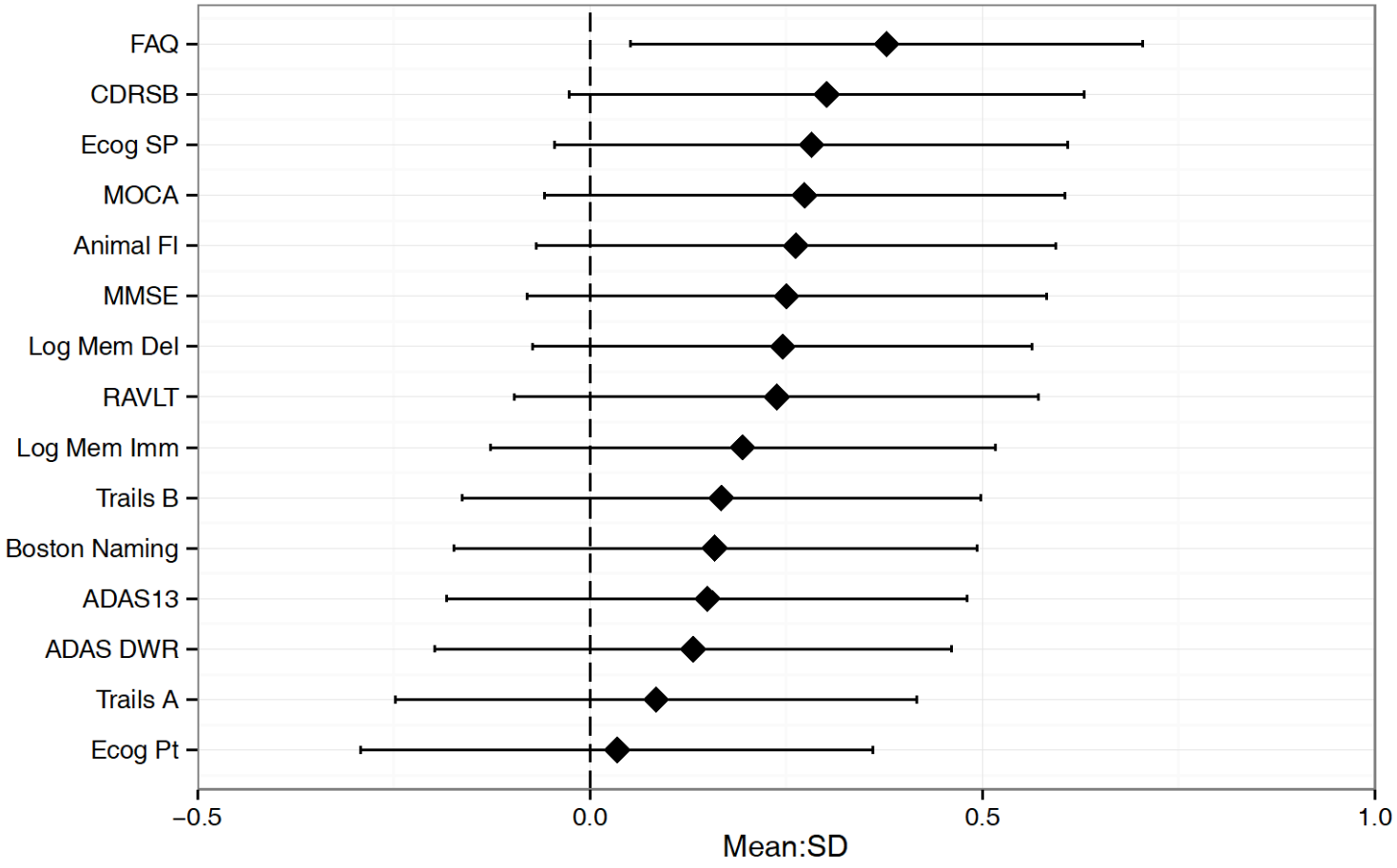
Instrument sensitivity to *APOE* related change

- The following slides summarize MMRM estimates of the *APOE*-ε4 group difference in change from baseline at 24 months.
- Estimated differences are reported on a common scale (mean:SD).
- CN, EMCI, LMCI, and AD are modeled separately.

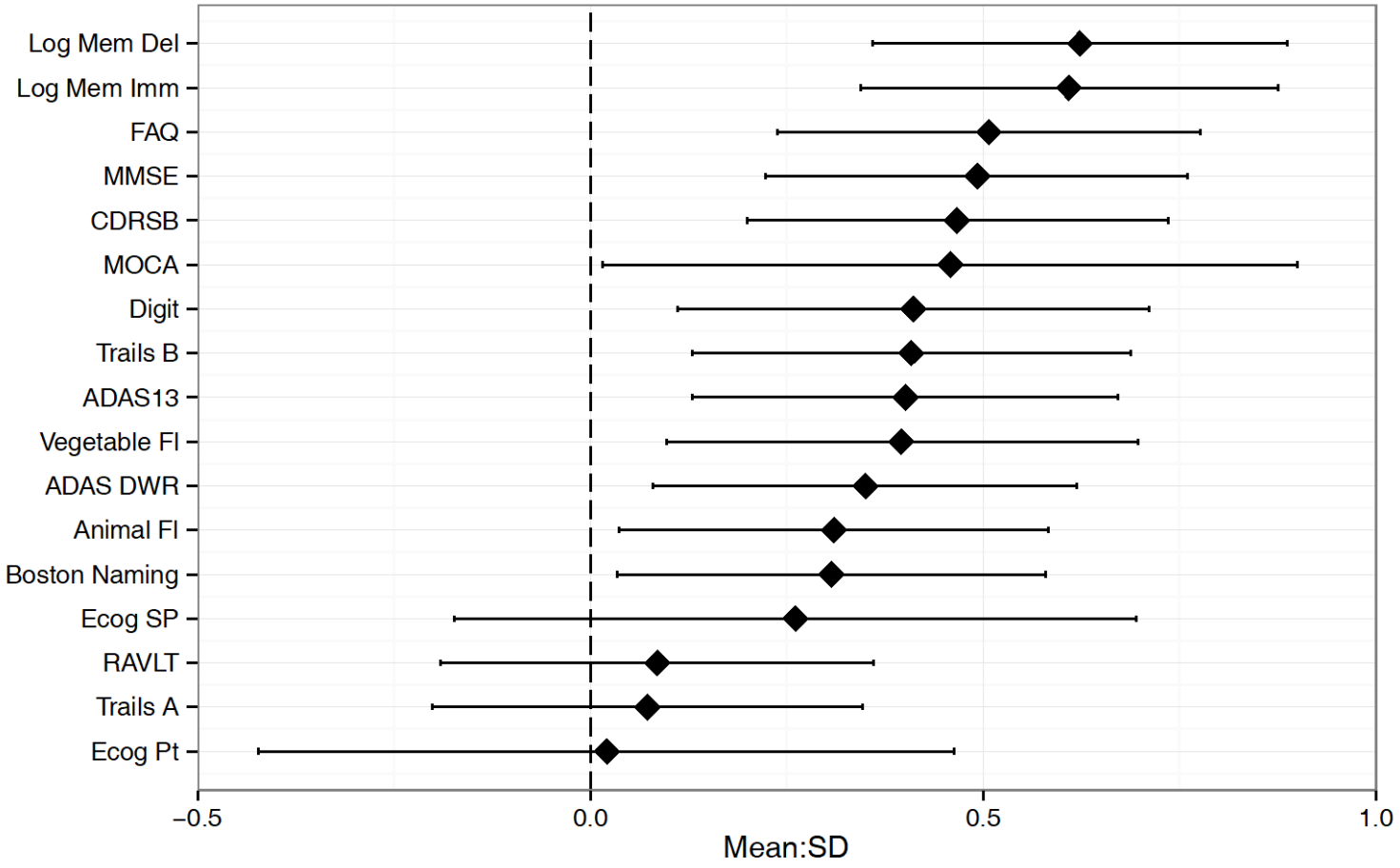
NC *APOE* group diff. in 2-yr change



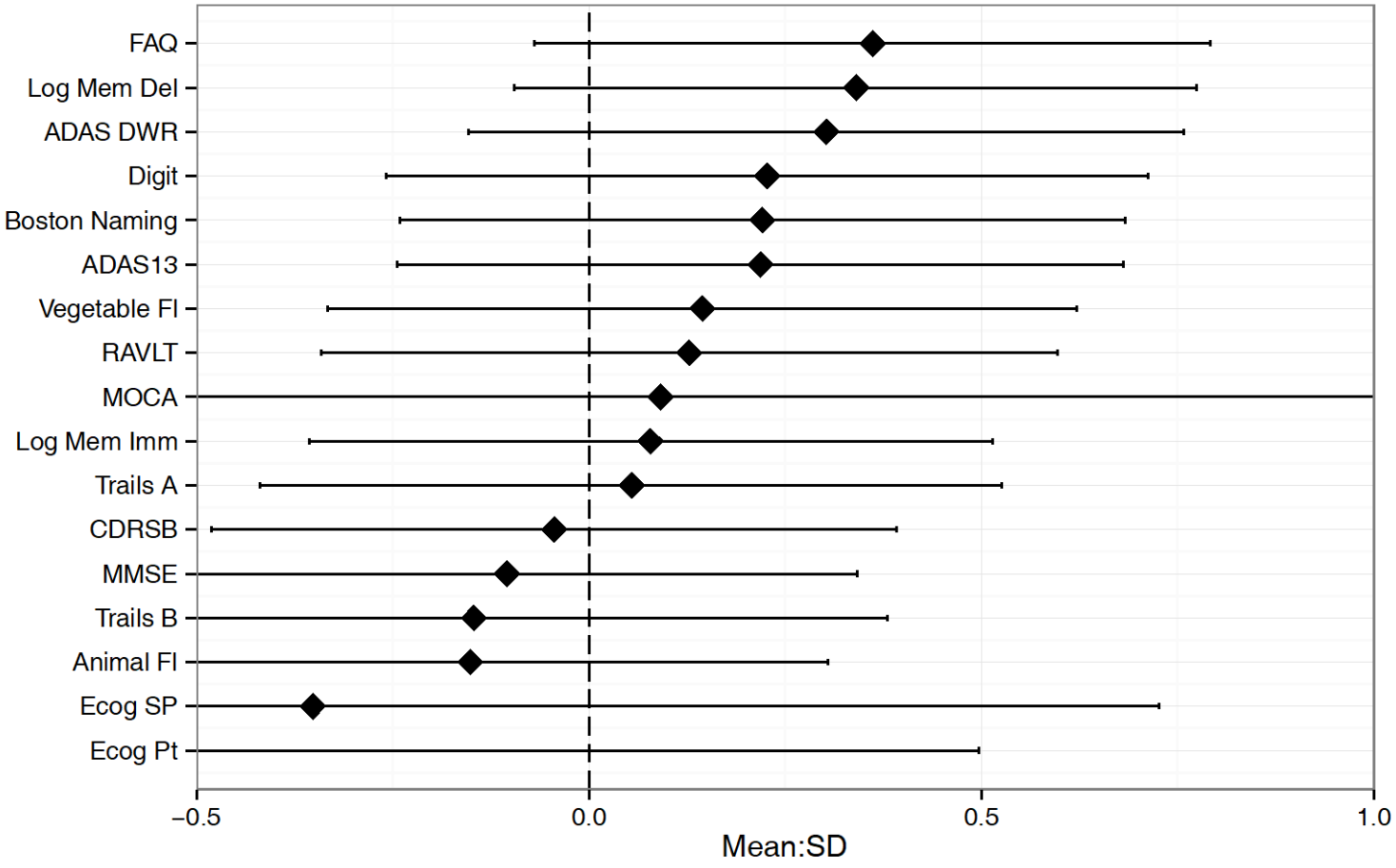
EMCI *APOE* group diff. in 2-yr change



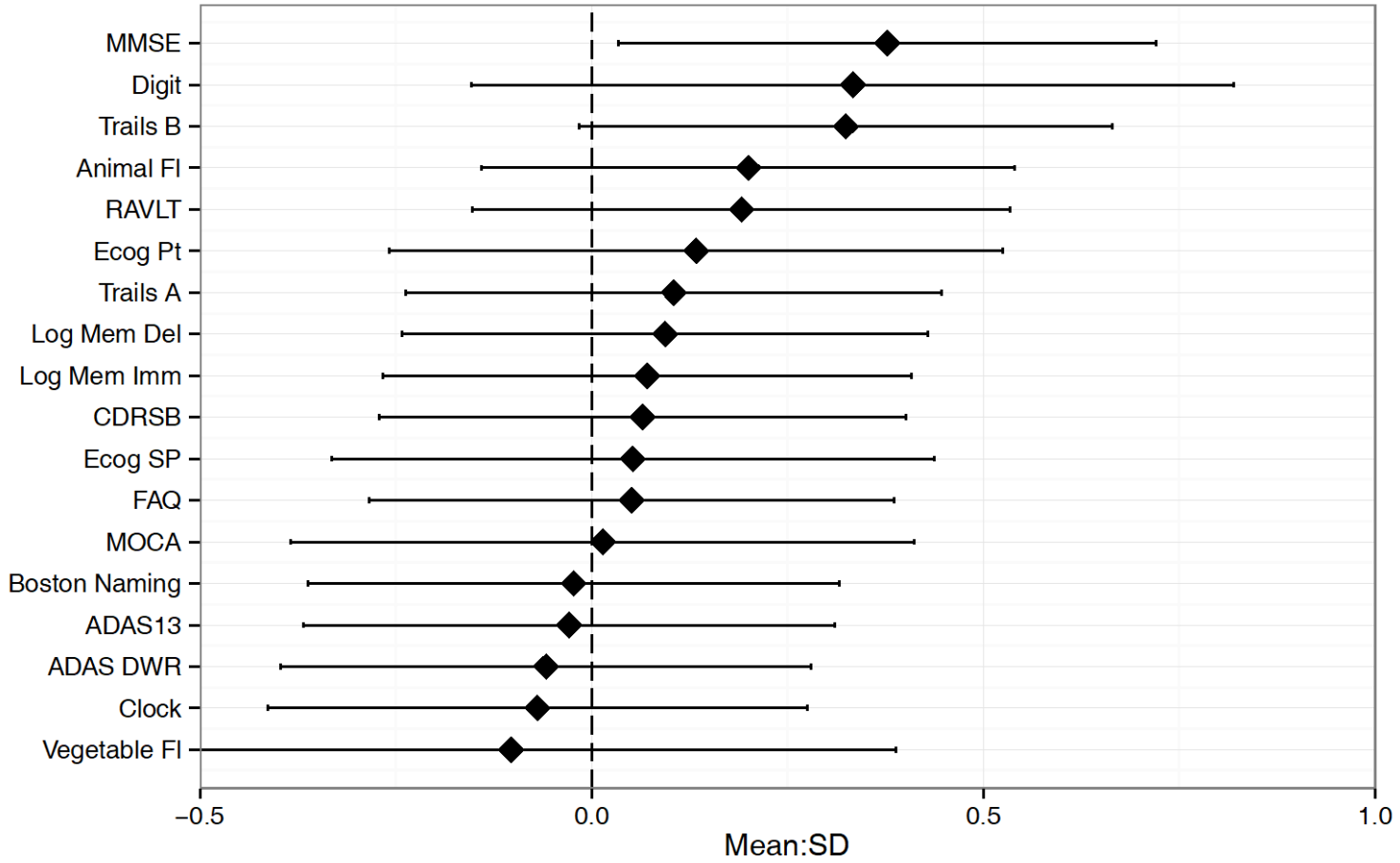
LMCI *APOE* group diff. in 2-yr change



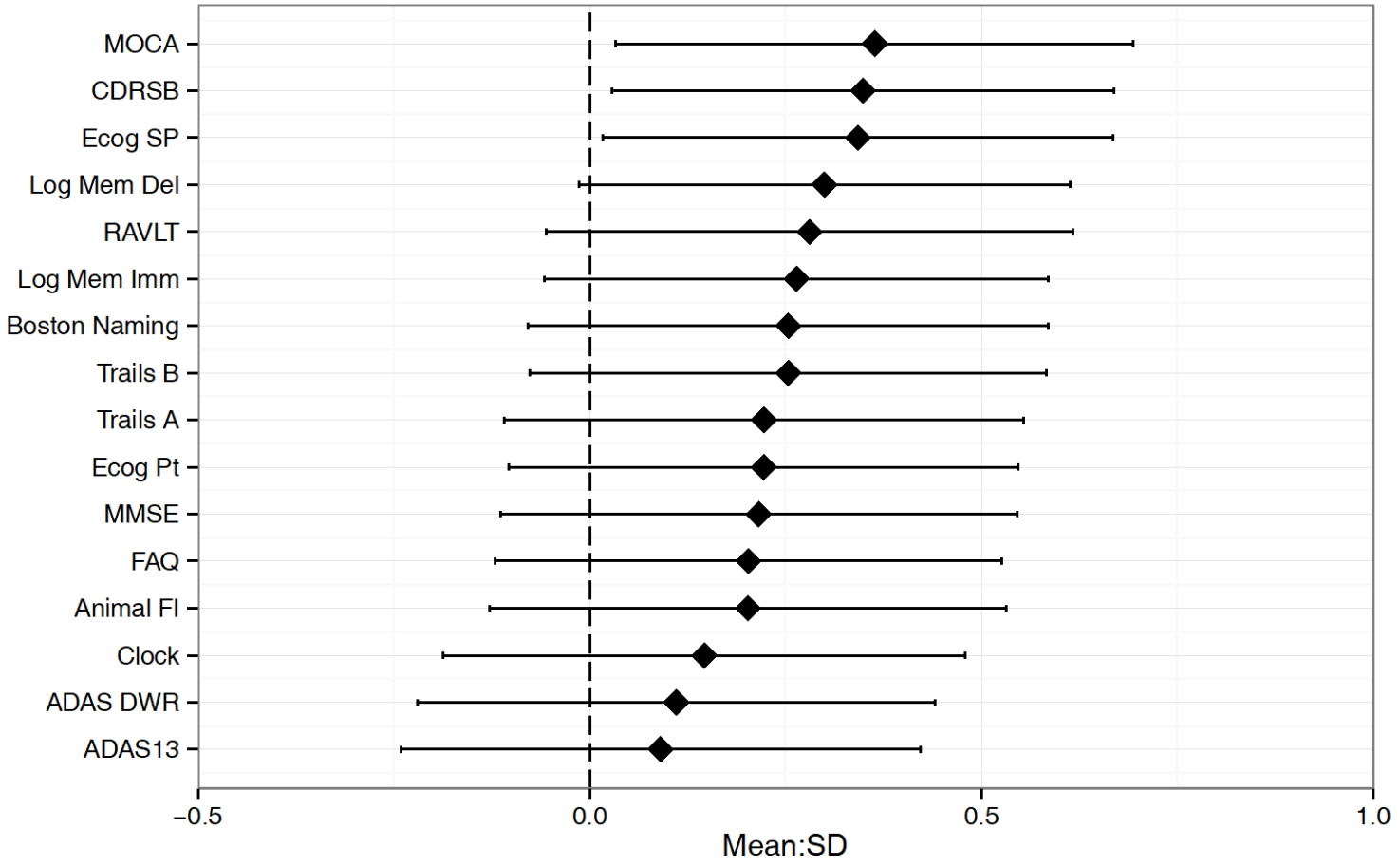
AD *APOE* group diff. in 2-yr change



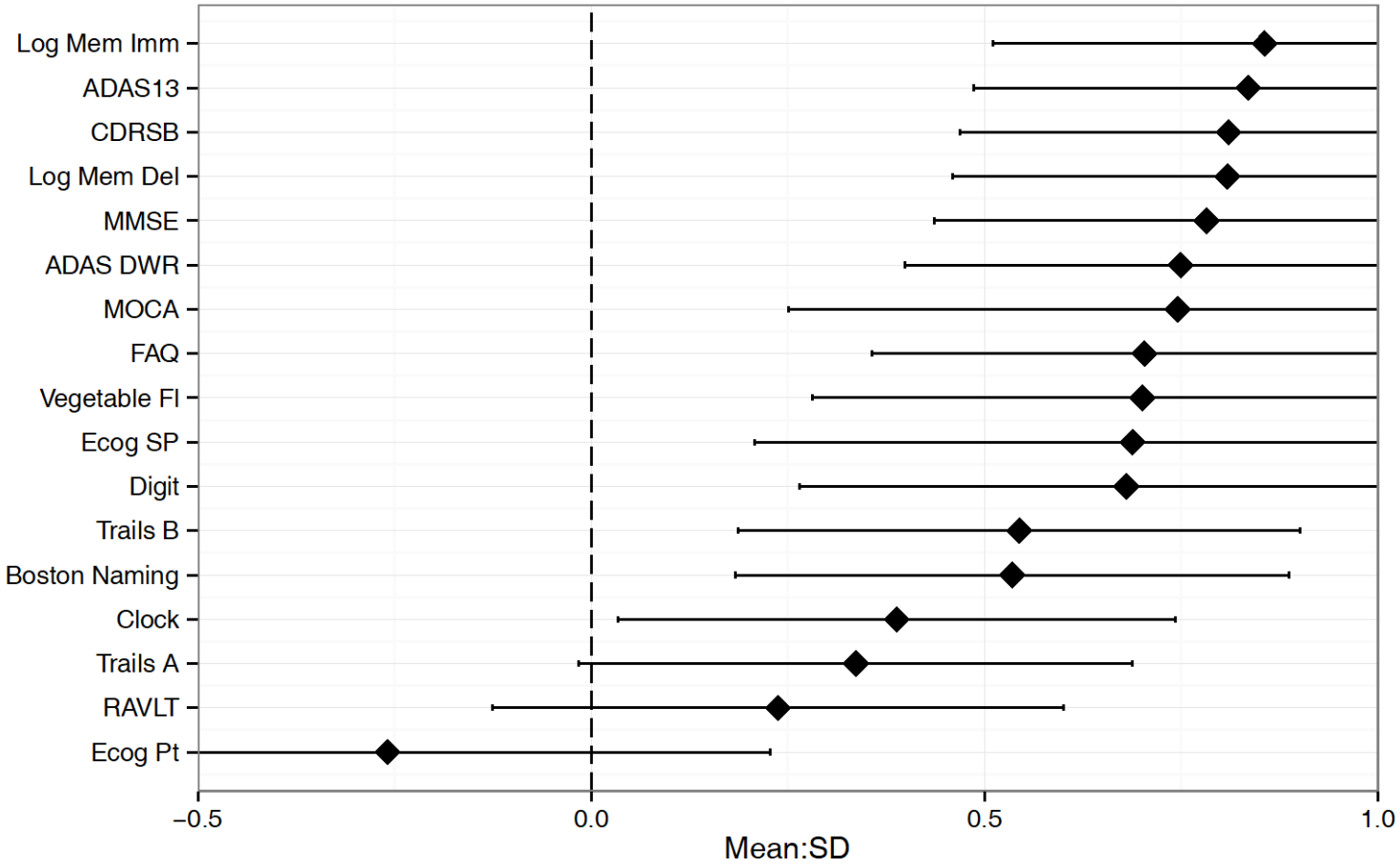
NC Amyloid group diff. in 2-yr change



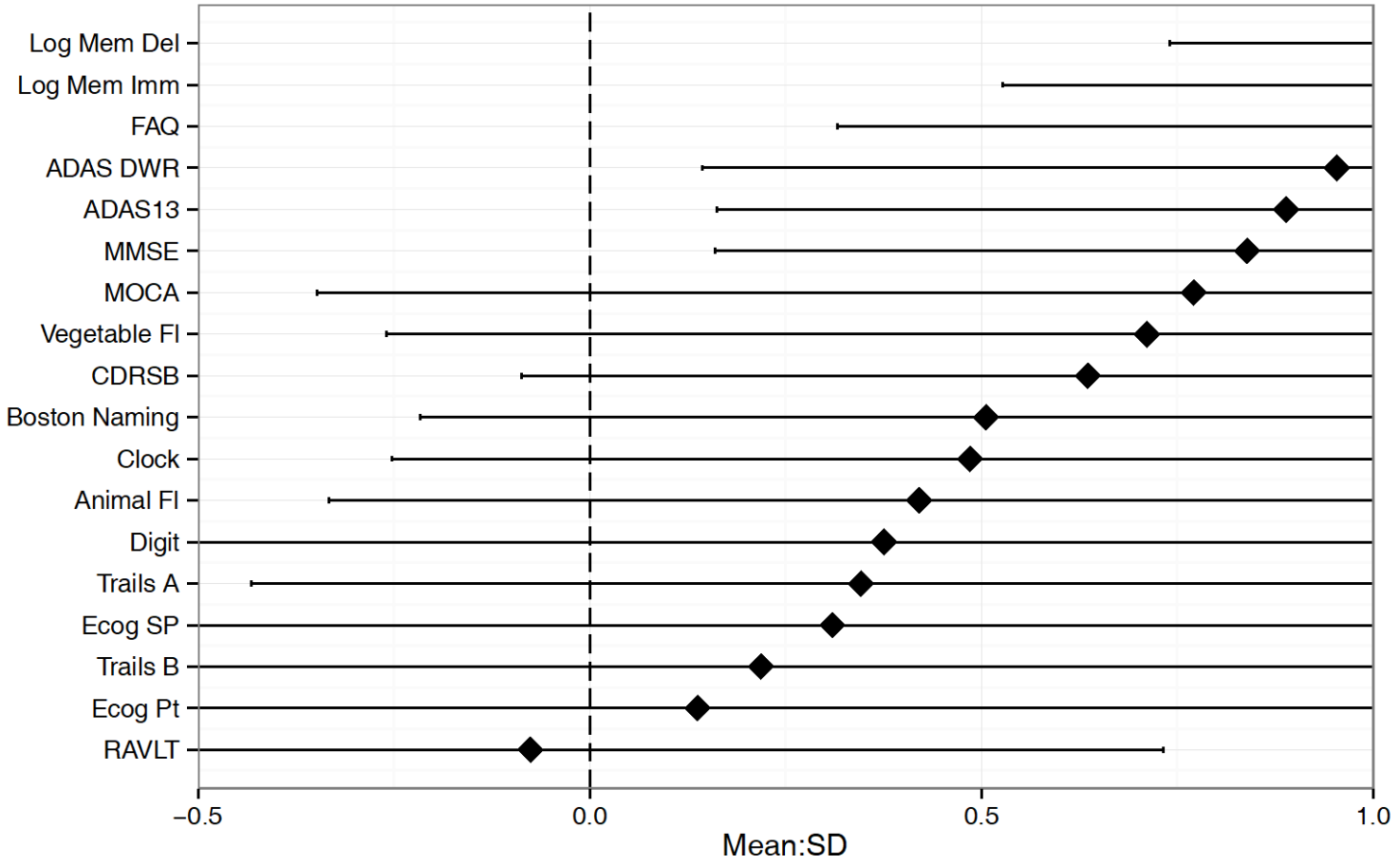
EMCI Amyloid group diff. in 2-yr change



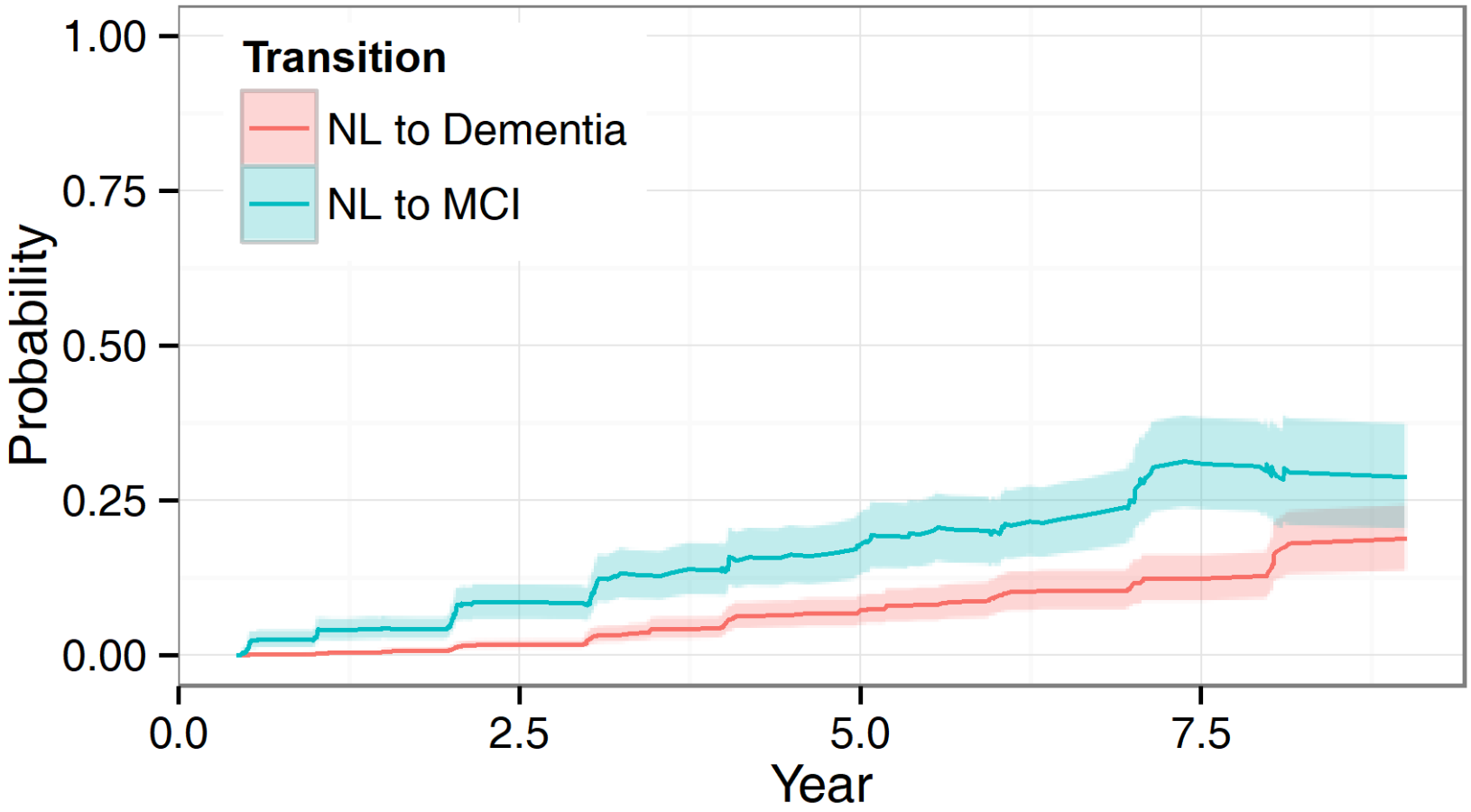
LMCI Amyloid group diff. in 2-yr change



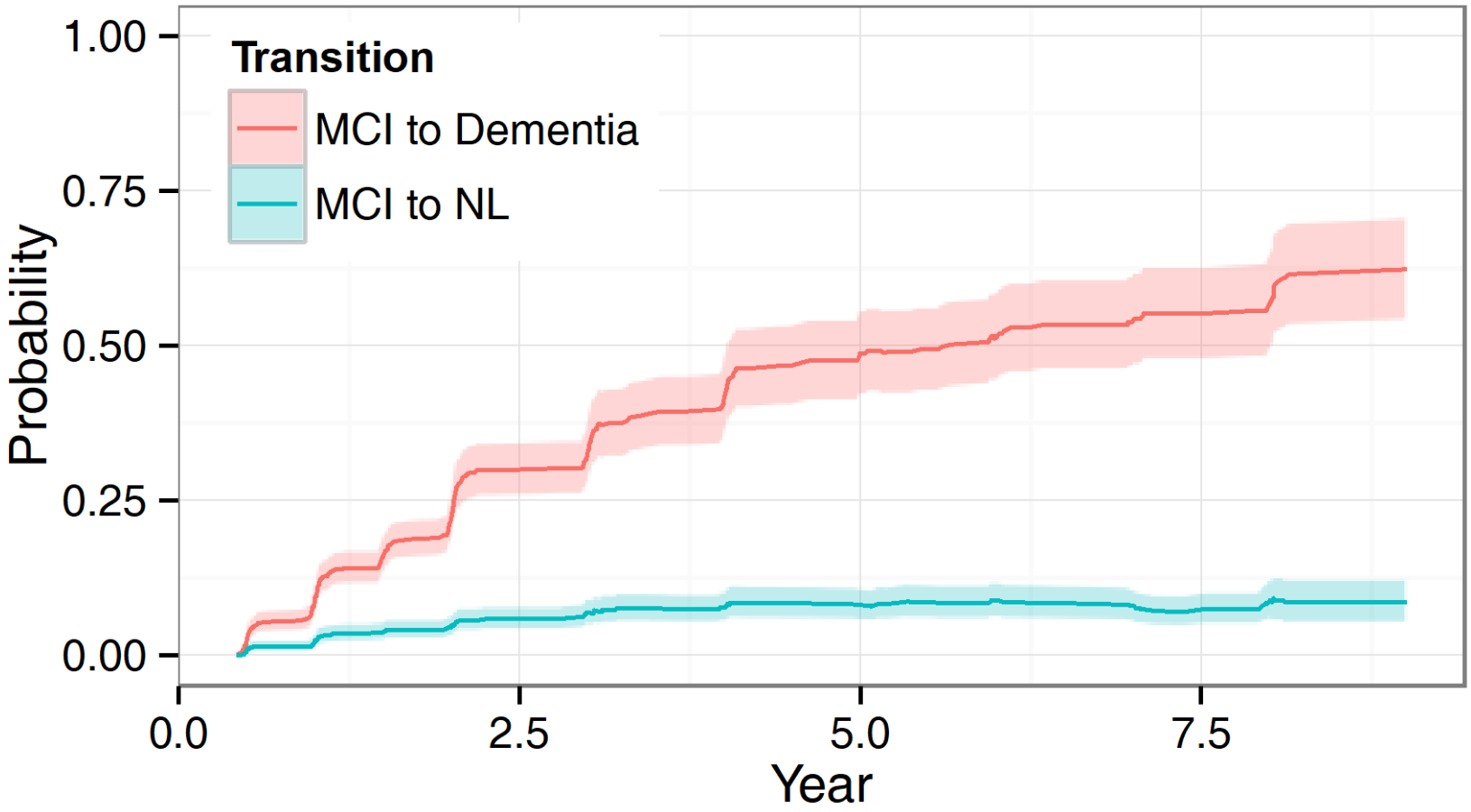
AD Amyloid group diff. in 2-yr change



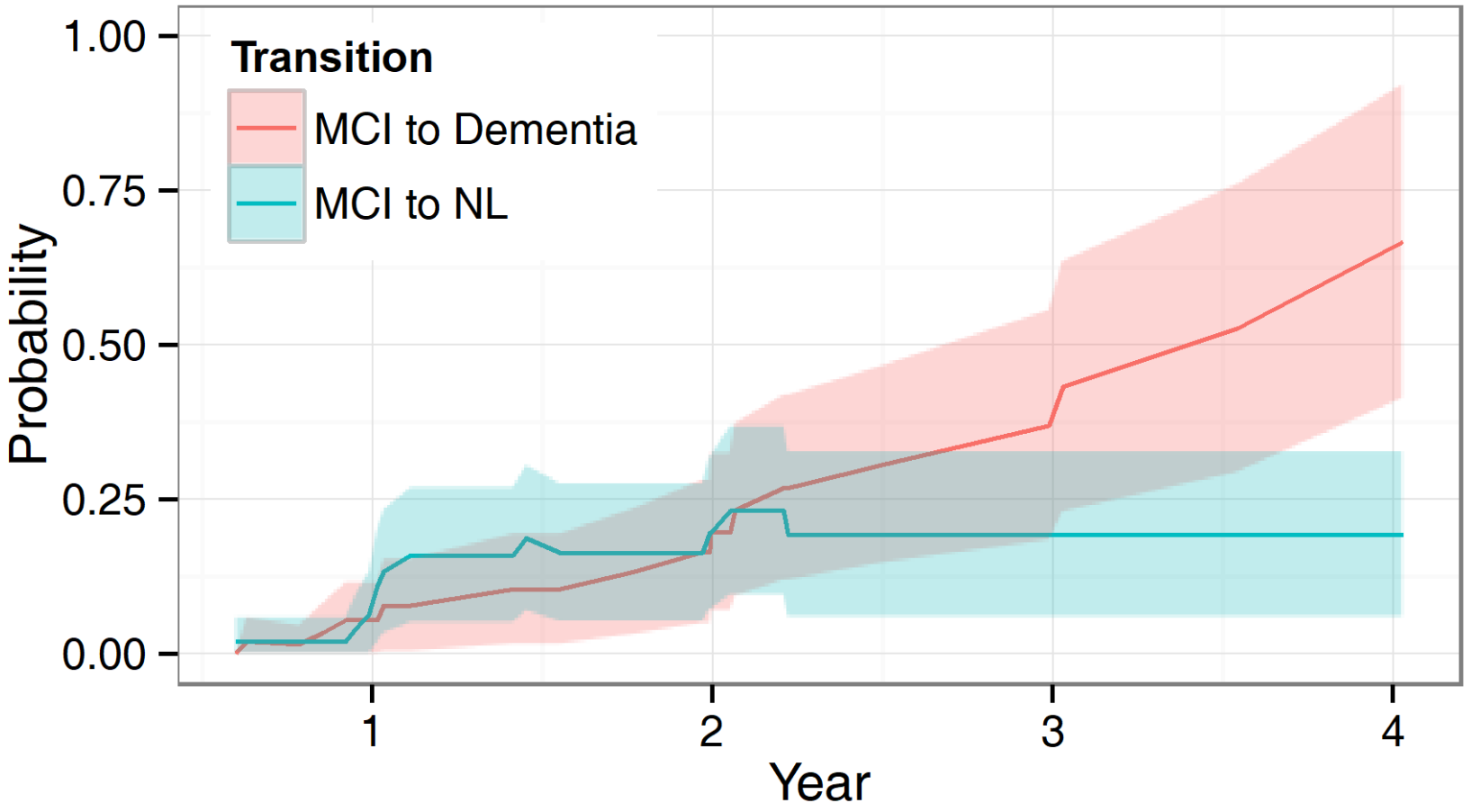
Transitions from NL



Transitions from MCI



Transitions from “de novo” MCI



ADNI 3 CLINICAL CORE PLANS

Paul Aisen
Ron Petersen
Mike Donohue
Mike Weiner

The aims of the ADNI3 Clinical Core will include:

- Oversight of ADNI3 clinical activities, data management, tracking and quality control, recruitment and retention of participants, regulatory oversight and financial management.
- Characterization of the cross-sectional features and longitudinal trajectories of cognitively normal older individuals and mild cognitive impairment.
- Study of the relationships among clinical/demographic, cognitive, genetic, biochemical and neuroimaging features of AD from the preclinical through dementia stages.
- Assessment of genetic, biomarker and clinical predictors of decline.
- Refinement of clinical trial designs, including secondary prevention, slowing of progression in symptomatic disease, and cognitive/behavioral management.

Key hypotheses of ADNI3 Clinical Core

- All or almost all normal participants with brain amyloidosis will show cognitive decline compared to those without amyloidosis, and will progress to MCI.
- Confirmation of this hypothesis is critical to early stage trial design and regulatory support.
- MCI participants who are biomarker positive (amyloid and tau) will progress more rapidly than those who are negative

Other hypotheses

- Amyloid-related cognitive decline involves episodic memory, executive function and orientation across the spectrum of AD
- AD-related cognitive decline can be captured by unsupervised web-based testing
- Early stage AD cognitive decline predicts later functional and clinical decline
- Web-based registries will facilitate recruitment for ADNI (and therapeutic trials)

ADNI3 cohorts

- ADNI3 will carry forward roughly 300 normals (w/wo subjective concerns) and 300 MCI (EMCI+LMCI)
- ADNI3 will enroll modest numbers of new normal and MCI participants
- ADNI3 will follow MCI participants who progress to AD dementia

Possible adjustments to assessments

- Drop RAVLT, add FCSRT.
- Drop Boston Naming.
- Drop Clock Drawing.
- Add web-based cognitive testing.
- CFI instead of eCOG?
- Other subjective concerns measures?

- Reaching a consensus will be challenging, but we need to begin the discussion even as we work on additional analyses.