ADNI-2 Accomplishments: Highlights of Biostatistics Accomplishments

Laurel Beckett, Danielle Harvey, Michael Donohue
with help from Daniel Tancredi, Naomi Saito, Teresa Filshtein, and Cathy Wang

University of California, Davis and University of California, San Diego (MD)

labeckett@ucdavis.edu

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Outline

Highlights of Biostatistics Core accomplishments in ADNI-2

ADNI-2 has continued the work of ADNI-1 and ADNI-GO), but also has expanded the data collected. This wealth of data presents corresponding challenges.

We will highlight contributions of the Biostatistics Core that provide new insights drawn from the ever-richer ADNI data.

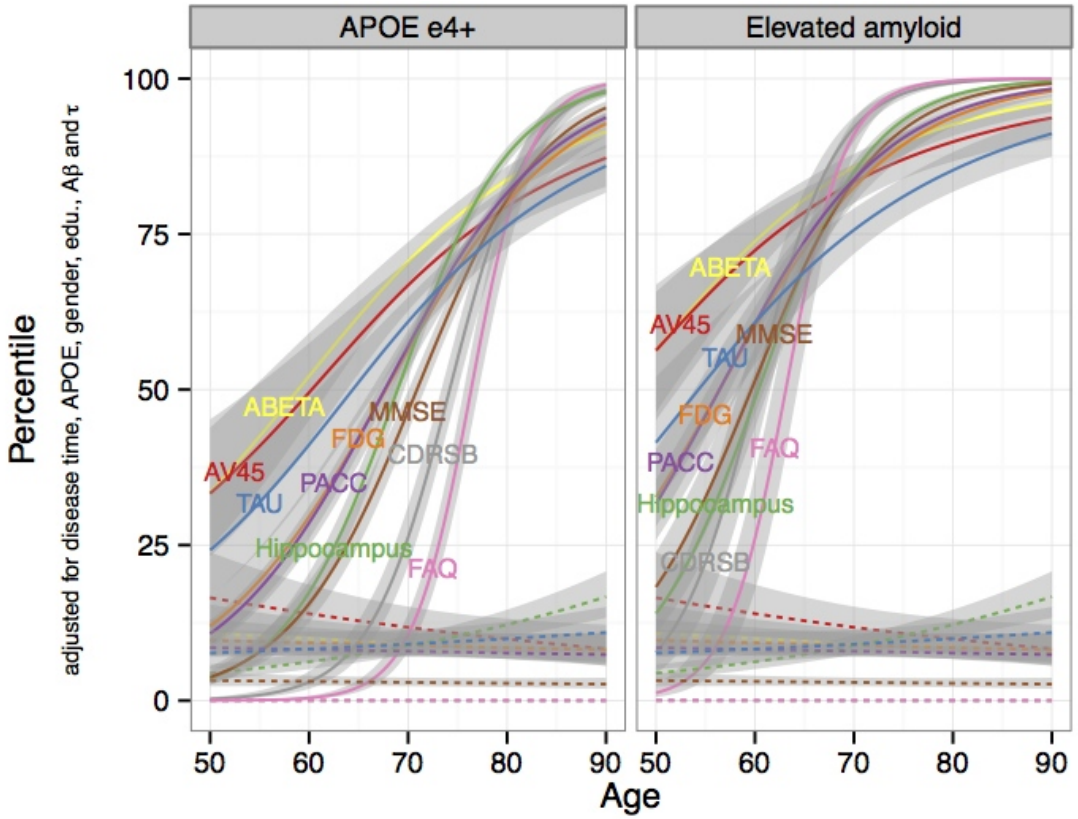
- Richer longitudinal data allows modeling trajectories and sequences.
- New groups (eMCI, SMC) increase breadth of data across disease process and fill in gaps.
- New measures increase depth of data on participants.

Extended longitudinal follow-up: rich but challenging

- Some participants (from ADNI-1) followed almost 10 years.
- Not everyone has every measurement, and some changed, so we've had to work out ways to reconcile.
- For example, is "amyloid positive" the same if based on CSF, PiB, or AV45?
- We cover a wide range from NC to MCI to AD, but rarely in same person!
- Sophisticated statistical methods help us to align people against age or study time.

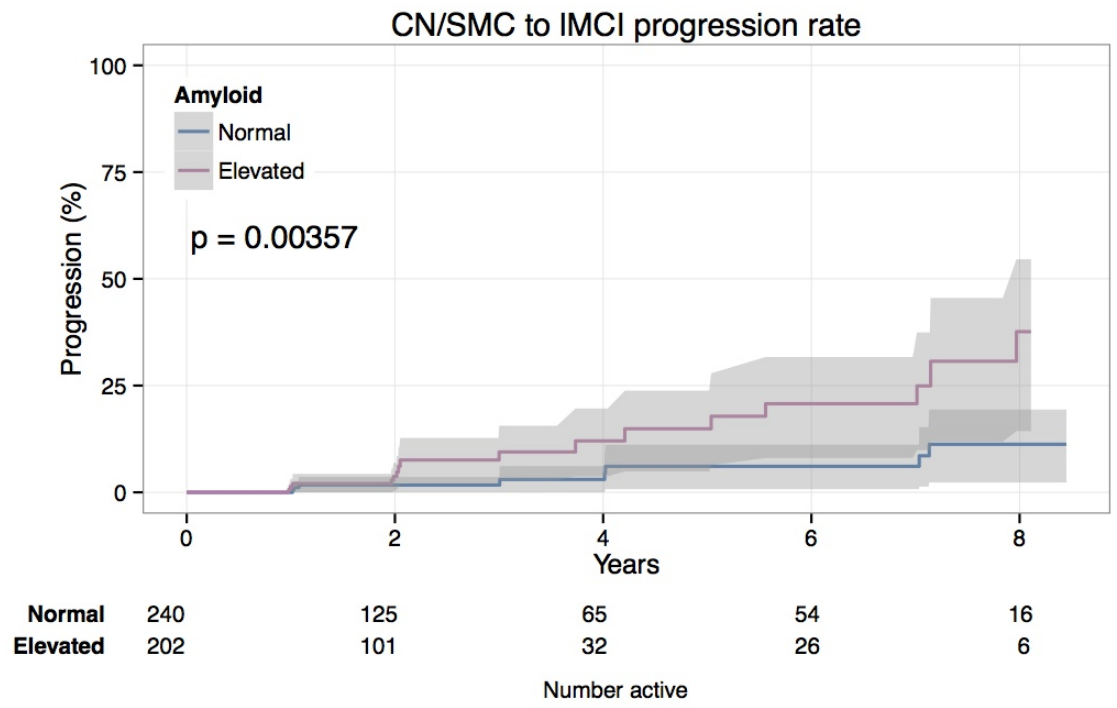
Rich longitudinal panel data allow sophisticated modeling

Figure : Solid lines show impact of E4+, amyloid+ on trajectories (Donohue *et al*, *JAMA Neur* 2014)



Extended follow-up picks up conversion of NC

Figure : Amyloid+ (CSF or PET) predicts longer-term risk of MCI

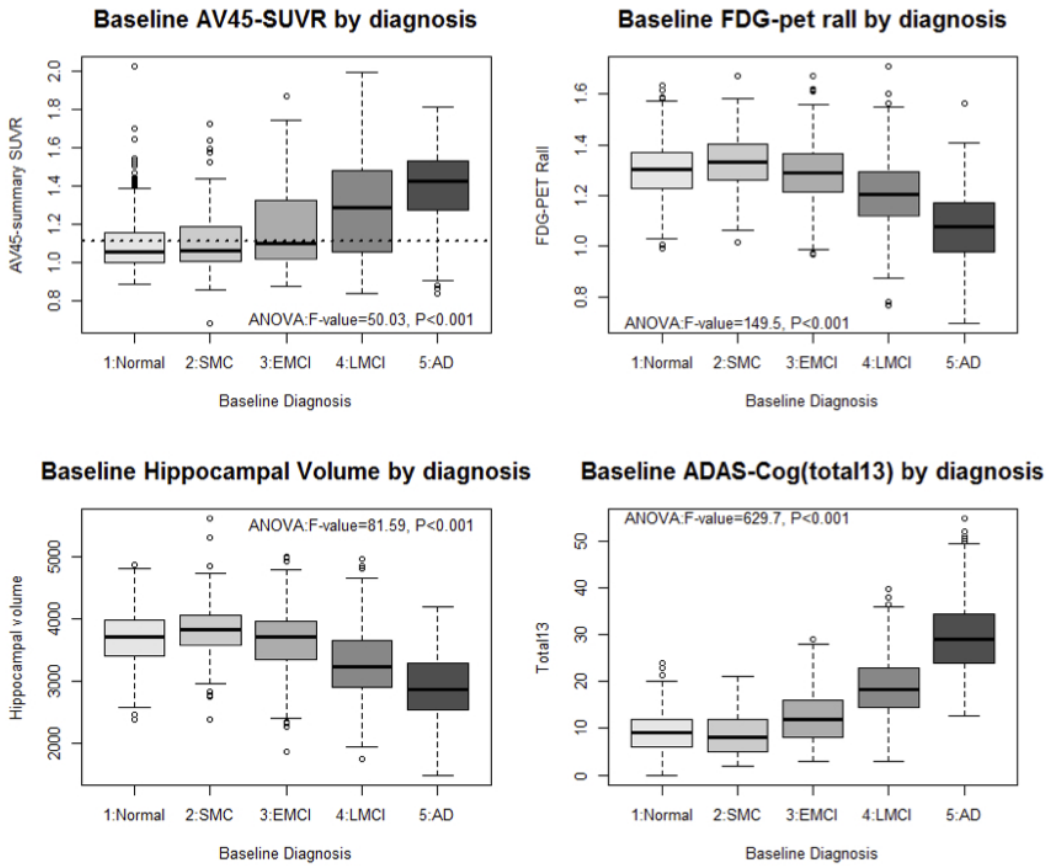


Two new groups added since ADNI-1: eMCI and SMC

- Goal was to fill in gap between NC and later MCI.
- Are some biomarkers already bad in eMCI and SMC?
- Do some problems not show up until later in MCI?
- We tried to get later MCI and AD groups to be "pure" but it's harder in earlier stages.
- What have we learned about heterogeneity of subtle, early clinical problems?
- Can we start to see change in these groups, or in subgroups?

New groups fill in the gaps between NC and MCI

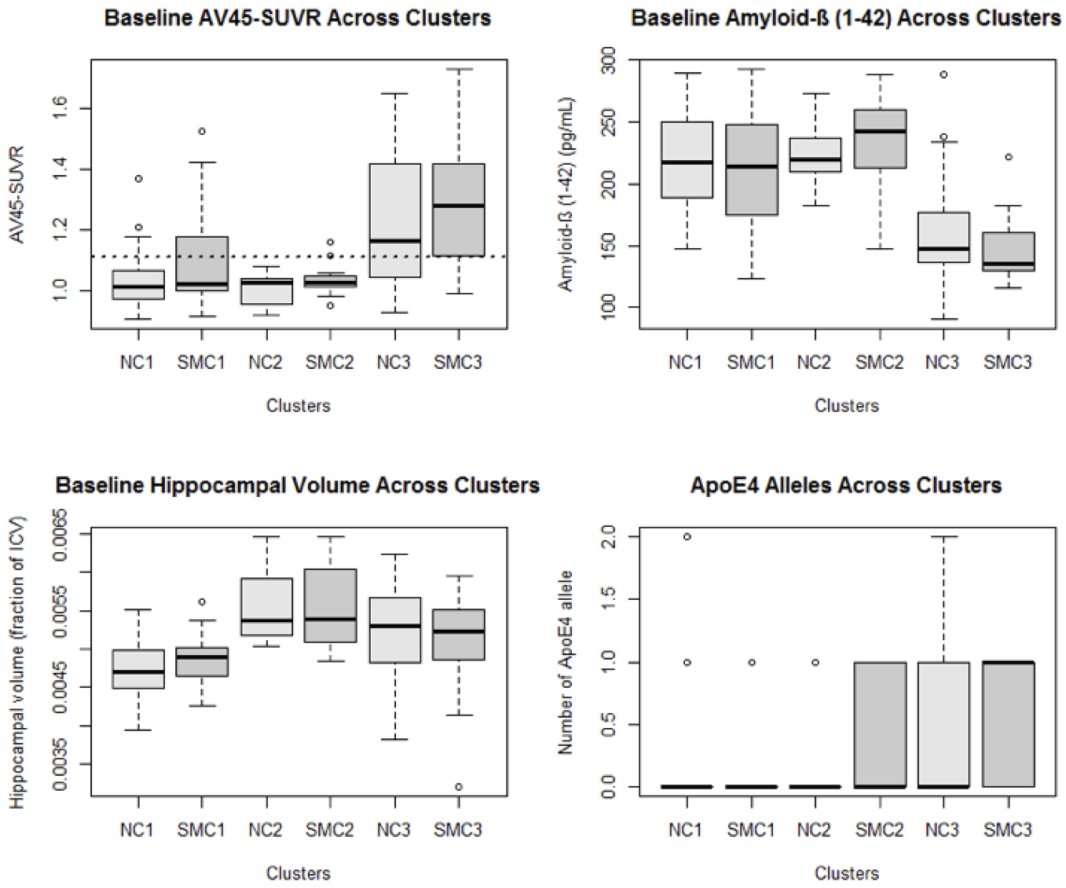
Figure : SMC and eMCI fit in between NC and MCI, as expected



SMC similar to NC but both are heterogeneous

- We used unsupervised clustering to look for subgroups in ADNI-2 NC and SMC.
- Similar method to Nettiksimmons 2010 in ADNI-1 NC, 2014 in ADNI-1 MCI.
- Clusters based on volumetrics, CSF measures.
- Similar results to Nettiksimmons for both NC and SMC.
- Three subgroups in each diagnostic group, quite similar.

Clusters look healthy, pre-AD-like, and maybe vascular

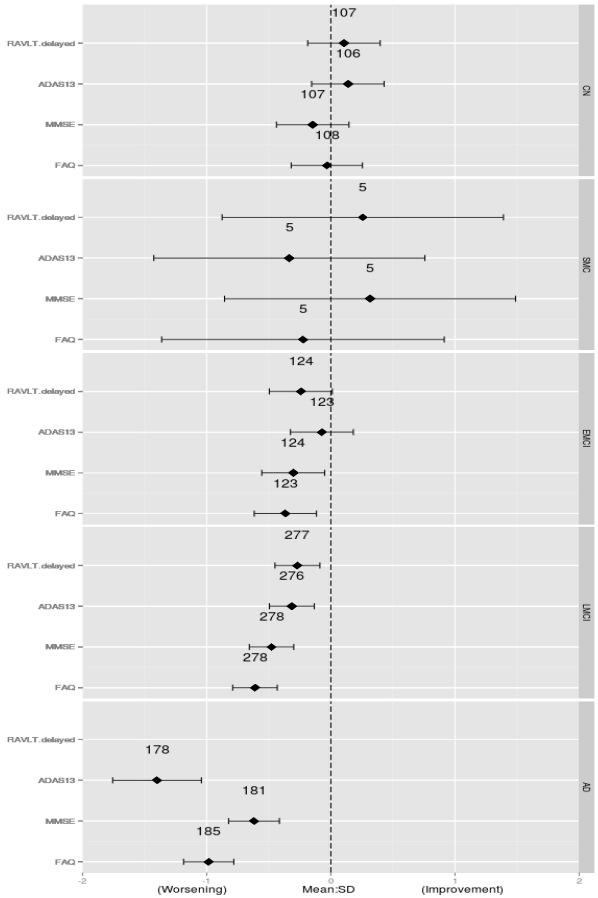


Can we pick up change in new groups?

SMC look similar to NC at baseline, and EMCI intermediate.
What do they look like at 12 months?

- Focus on group most likely to change: ApoE4 carriers.
- Summary for 4 measures:
  - RAVLT delayed (memory)
  - ADAS-COG13, MMSE (general cognitive function)
  - FAQ (functional)

12-month change in 4 measures, by group

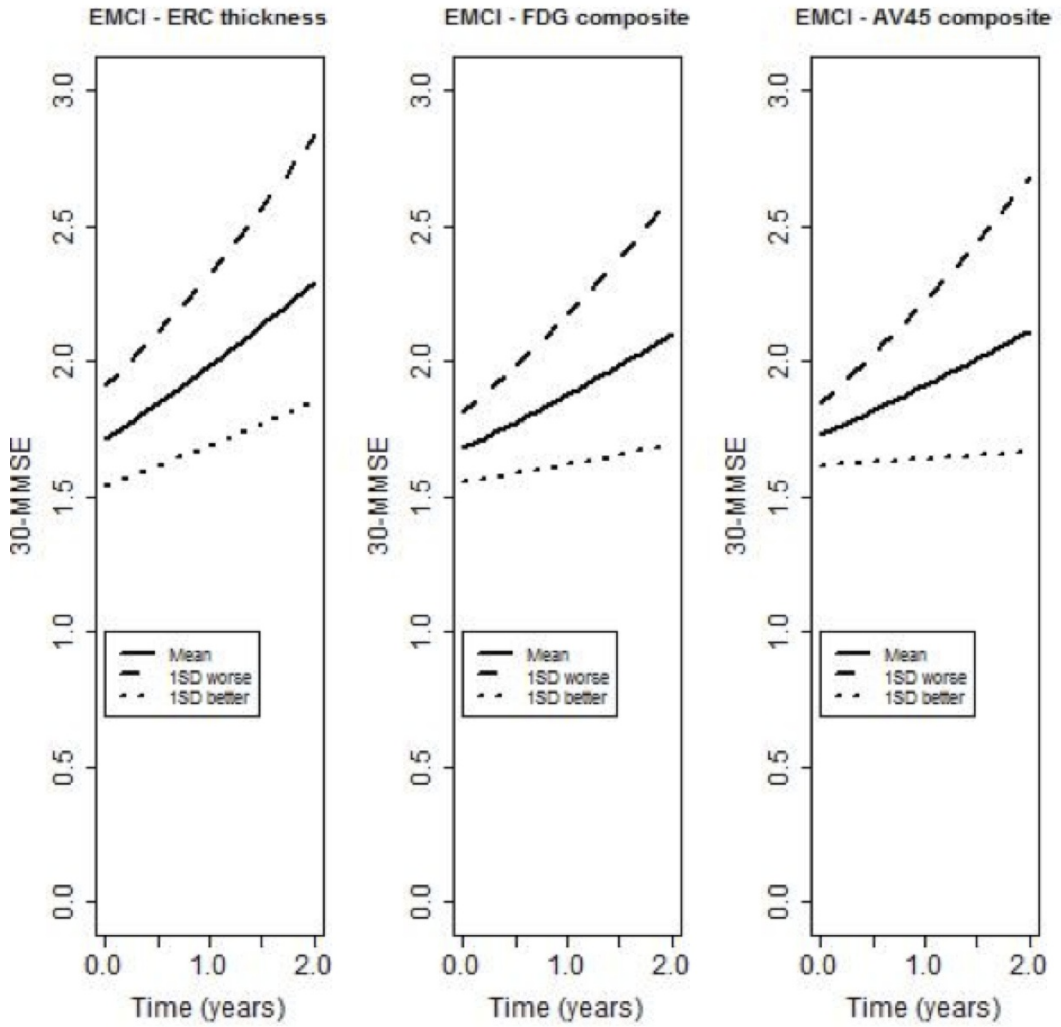


- 5 panels, top to bottom: NC, SMC, EMCI, LMCI, AD
- 4 tests in each panel, top to bottom: RAVLT, ADAS, MMSE, FAQ
- All tests on standard scale: 0=NC baseline mean, 1=NC SD.
- worsening <— x — > improving

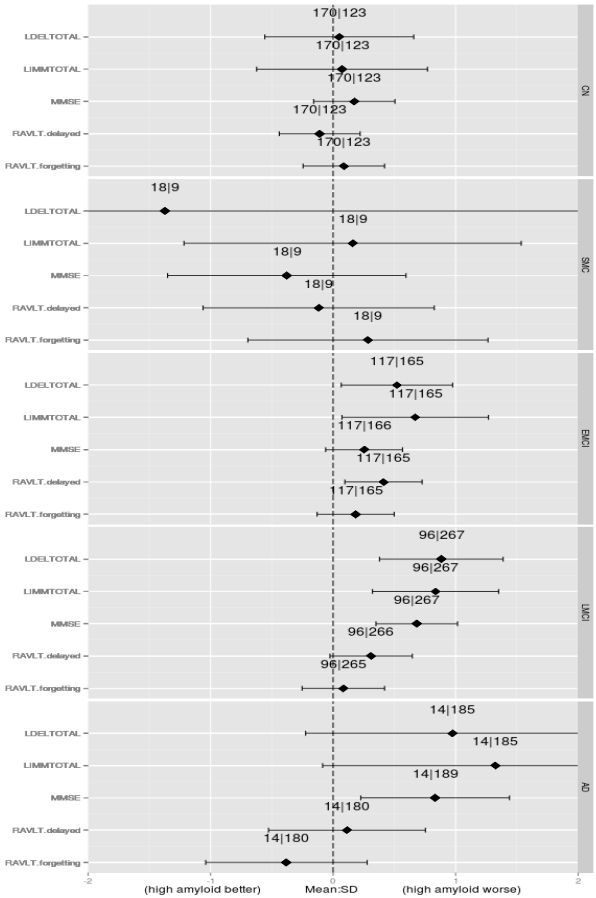
We also added new measures: are they prognostic?

- Amyloid imaging now done on everyone.
- What is prognostic value?
- Does it truly show up really early? How early?
- It's early to see much in NC or SMC.
- But eMCI have been followed longer.

New measures have prognostic value even in eMCI



Another look: Amyloid +/- difference, memory tests



- 5 panels, top to bottom: NC, SMC, EMCI, LMCI, AD
- 5 tests in each panel, top to bottom: LDEL, LIMM, MMSE, RAVLTDEL, RAVLTFORGET
- All tests on standard scale: 0=NC baseline mean, 1=NC SD.
- At 12 mo, amyloid+ is: better $<$ — x — $>$ worse

Thank you!

All done! Any questions?