ADNI-2 Accomplishments: Highlights of Biostatistics Accomplishments

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Outline

1. ADNI-2: Continuation: More years, more people.

2. ADNI-2: More diagnostic categories.

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

![Graph showing CN/SMC to IMCI progression rate with number of normal and elevated cases over years]

- Amyloid
  - Normal
  - Elevated

\[ p = 0.00357 \]
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 \( < \rightarrow \rightarrow \rightarrow \rightarrow > \) 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, RAVLTFORGEST
- 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?