ADNI Biostatistics Group call, 7 February 2012

Present on call: Laurel Beckett, Naomi Saito, Arnold Huang, Mike Weiner, Peter Quarg, David Verbel, Nandini Raghavan, Mike Donohue,

Update on data:
Clinical data are coming into LONI more or less in real time.
We have 120-140 eMCI for clinical; we have about the same for freesurfer, ApoE4, AV45 (over 100 of summary data on each.) We have also Bill Jagust's FDG-PET data. We do not have any CSF results yet. They are planning a big upload soon.

We are planning analyses for the New Orleans presentations.
Brief overview:
Mike Donohue is going to look at some power calculations to detect 50% change in the eMCI group, based on clinical and imaging data to date. He will also look at the conversions, and at the people in ADNI-1 who meet a clinical definition at some point after baseline. He will also look at MOCA and how it compares to ADAS-COG.

Mike W notes that there are a lot of amyloid positives, depending on group: 30% in controls up to 60% in MCI. It depends on the definition. Bill's group has one definition, in their papers and on web site. Cutoffs are, of course, arbitrary and depend on the methodology used.

Mike W has not updated freesurfer to give the longitudinal version for 2, 3 or more scans because it is so labor intensive. They are trying to decide at what point to apply this methodology. For the time being, we will use the separate freesurfer analyses.

The Davis group has 3 projects: 1) summarizing AV45 and getting a better handle on what it tells us (does it predict change in MRI volume or cognitive clinical measures and how does it correlate with other markers). We can do that both using the AV45 composite as a continuous measure, but also by using the cut-off (which we believe is 1.22) to split folks into amyloid positive and amyloid negative (which is of clinical interest); 2) establishing where eMCI fall in terms of baseline and trajectories relative to NL and LMCI in particular (ADAS, FAQ, other neuropsych, CDRSum, whole brain, ventricles, entorhinal cortex, and hippocampus); and 3) characterizing ECog baseline and change in the different groups and seeing how it predicts decline particularly in the eMCI and LMCI groups.

We have submitted 3 abstracts to the Joint Statistical Meetings, in Aug in San Diego. One looks at optimal designs for detecting change/ conversion (Dan Tancredi); a second looks at Mallows models for partially ranked data to detect agreement with a sequence of events (such as the Jack model) versus a mixture of sequences (Laurel); the third will present our approaches for comparison of biomarkers (Danielle).

Nandini asked whether there have been any publications comparing the use of repeated cross-sectional free-surfer measures with the smoothed longitudinal estimates. Mike W suggested looking at the free-surfer website. He notes that the means basically don't change, nor do the between-subject variation, but within-subject stuff gets smoothed out. What the FDA would think is another question. There are arguments on both sides for whether to use the smoothed data or the raw data. Interested parties could email Mike W directly and he could put people in touch. The guy to talk to is probably Bruce Fischl

(sp?) in Boston. Note also that Nick Fox's boundary shift image uses co-registered images to get a rate of change. Freesurfer is an extension of this. All data on ADNI uses registration and templates in one way or another.

Our next call is Tuesday, March 6, 10 AM Pacific time.