ADNI Biostatistics Conference Call
12 February 2008

Present on call: Laurel Beckett, Danielle Harvey, David LastShera, Hao Zhang, Mike Weiner.

Danielle reported on the data status. She will be checking and reporting weekly (every Wednesday) on what numerical summary data are available on LONI for image summaries and biomarkers. We have asked the sites creating those summaries to provide longitudinal data by 15 March, to give us time to do analyses and circulate for comments and then do final analyses before the April 14 meeting. Some data are available but other groups have either not submitted data, or are working out forms with ADCS and LONI. Once the forms are completed, data submission is fast. We have longitudinal data from hippocampal volume, boundary shift integral, and ROI glucose metabolism from Bill Jagust's lab. We also have some from Norm Foster's PET lab (stereotactic surface projection; may not yet be available through LONI but has been submitted to ADCS). Charlie DeCarli's white matter hyperintensities and stroke are at ADCS with data table under construction. The data are still being fine tuned, so make note of when you download and note that new versions will come out.

We had an extensive discussion on the template handout. Mike asked us to add some clarifications on the scenario for which we are evaluating power. We went over the template, discussed briefly what we propose to present in the April 14 meeting (essentially page 5 table with some illustrative pictures and explanations, and probably some graphics.) We need to be very clear about the limitations of this early analysis.

Mike raised a question about the fact that ADCS uses multiple time points for measuring ADAS COG for their clinical trials, but our example shows same power for two designs. This was right at end of call so answered at greater length via email, inserted here:

1. As I said on the call, under some very specific design and model constraints, the three-time-point (0, 6 and 12 months) requires the same sample size as the 2-time point. The assumptions are: a) no missing data in either study, b) all the variation is fully accounted for by linear trend, between-person differences in overall level, and within person "noise", and c) you do a two-sample t test on the differences if you do the two time point, and a repeated measures difference in slopes model assuming the correct simple model.

2. Any change in these assumptions will alter the balance. If, for example, you have non-linearities like learning effects or rapidly increasing rates of decline later in study or non-linear treatment effects, then you may benefit from more observations and a more elaborate linear model. If you have drop-out, you might be grateful for partial data on people who couldn't otherwise be analyzed (e.g. those who stick around for the six-month but not the 12-month). Anthony mentions several of these.

3. Even under the assumptions above, more observations will make a difference - four is better than 3, 5 better than 4 - but not a lot better.

4. If the variance sources are systematically different from the simple assumption, e.g. autocorrelated, then you can gain substantially from more data; even the 3 vs. 2 observation setting will be a gain.

5. We have very limited data so far - 3 time points on a modest number of people over a short

period (12 months.) Anthony's group has more intensive data collection and longer data projects from a number of large studies, focused on people who would be expected to show declines. Thus he has much more powerful data to elucidate subtle patterns and design more powerful studies.
Based on our limited data, we aren't seeing much yet... just a little hint here and there, as Anthony has mentioned. But I expect to see more pattern as we get out to the two-year mark.

Our next call will be Tuesday, 26 February, same time.