ADNI Biostatistics Core: Conference Call, 22 April 2008

Present on call: Laurel Beckett, Danielle Harvey, Hao Zhang, John Kornak, Mike Weiner, David Shera,

Danielle updated us on the analysis training. She emailed all the people who have expressed interest in future training (those who had already participated) to ask whether they are interested in future training and what format (web vs. in person). The general preference is for a web format to avoid travel. Last time was teleconference but this time we will try for a web conference so people can view screen live, and try things themselves.

Laurel summarized the Chicago meeting. The presentation was very well received and had lots of discussion – many thanks to Hao and Danielle for all their hard work in preparation. The "bad" news is that we have been asked to present an update in July, at ICAD in Chicago again. We are already working on this. We have circulated a list to labs of all the participants, and how many have images ready to process, and how many of the labs (and which labs) have provided summaries, by patient. We are targeting those with lots of summaries already to try to complete a full set of summaries on each patient so we can, if possible, get a maximal subset with data from all labs. A second project is to look hard at the clinical data and develop some composite measures of clinical data. We are already doing analysis for this, based on our work on baseline data with Ron Petersen and David Salmon.

Mike suggested reminding the labs and giving them a firm date on when to have the data analyzed on common data set.

Mike also asked whether we would go beyond the analyses presented last time. We will do all that was done then and try to add two things: 1) better assessment of clinical correlation (likely including more stable composite clinical measures), 2) some direct comparisons, at least via having them on same subset of patients, possibly more sophisticated if time permits.

Other questions Mike raised: 1). The clinical measures of change that FDA requires as primary outcome variables are things like CDR, ADAS-COG. If the primary outcome fails, the whole trial fails. Can we improve the power of the primary measures? One idea would be to look at baseline measures that might predict clinical decline, and incorporate those as covariates to reduce unexplained variation in clinical measures. Anthony is working on this problem at ADCS. Laurel will ask Anthony about it. He is skeptical about whether it will be fruitful. We will continue to talk but Laurel thinks the composite measure approach is more promising. 2.) How do we deal with multiple comparison issue? Laurel points out that we have already posted the cross-validation sets (both 60-40 split and leave-10%-out), and a plan for doing that. Mike was worried about Eric Reiman's lab; they presented data on ROI that was post-hoc but did not do cross validation for April meeting. Danielle says that Eric knows very well about the cross-validation and is planning to do it but just didn't have enough data yet to do it. John and Danielle will remind folks but it will probably have to wait till there is enough data and it is not clear that PET will have enough by July. The labs will have to do this themselves; then they will provide summaries to us. They will remind labs that they will have to implement this ultimately. John adds a reminder that cross-validation is not a magic pill

for multiple comparisons, either. If someone picks the best out of 50 regions, that is still an issue not addressed by the multiple comparisons.

Anthony and Laurel discussed statistical methodology papers at the meeting and we are going to try to get several out as a group, during the next year, with different folks taking lead on each paper. We plan to try to get the biostat folks at west coast ADNI institutions together informally to talk about this and work on it, maybe at end of WNAR.

Next call is Tuesday, 6 May, at 10 AM Pacific time.