SESSION 8 - Discussion points on SCAST results paper
(Lancet 2011; 377: 741-50)

1. The trial had two co-primary endpoints. An events-based one, as it was hoped that the trial would confirm the unexpected results from ACCESS, and one based on functional outcome (the modified Rankin Scale, mRS) since this is the outcome conventionally used in Phase III stroke trials.

2. The sample size calculation for the mRS endpoint was based on a conventional fixed dichotomy (death or major disability versus better), to be conservative, although it was planned from the outset to perform an ordinal analysis of the mRS.

3. The precise method for the ordinal analysis was not decided at the onset. It was discussed at several meetings of the Trial Steering Committee. The method was fully pre-specified in the Statistical Analysis Plan which was published before the trial was completed and unblinded (reference 17 in the Lancet paper).

4. The chosen method was ordinal regression assuming a proportional odds model. The sliding dichotomy and the conventional binary analysis were included as sensitivity analyses.

5. When the six month mRS was not available but the one month mRS was recorded then the one month value was 'carried forward' for the analysis. This is not a great way to handle missing data, but as it only concerned four patients it was judged that it was not necessary to get involved in imputation or any other alternative approach.

6. The trial was stopped early on administrative grounds (funding exhausted!), but the numbers recruited were sufficient that with the ordinal analysis the power for the mRS endpoint was at least equal to the original target. (The relevant power calculations for ordinal analyses will be discussed in Sessions 9 and 10).

7. It turned out that the proportional odds model gave an excellent description of the treatment effect (see Figure 4), albeit that the effect went in the wrong direction!

8. There are interesting issues for interpretation with the p-value for the mRS analysis being statistically significant at conventional levels, but not being significant when allowing for the two co-primary endpoints.

9. As one might anticipate, and on the assumption that there is indeed a deleterious effect on mRS, the proportional odds analysis was more sensitive than the sliding dichotomy which was more sensitive than the conventional dichotomous analysis (See Sessions 9 and 10, later).

10. Towards the end of the discussion section there are some comments on the interpretation of odds ratios. This was in response to a referee who believed very forcefully that odds ratios have no place in reporting trial results. Their main concern seemed to be that everyone (wrongly) interprets odds ratios as relative risks, and so authors should report relative risks to stop their readers misinterpreting their results. At one level this is just silly, but it does raise the interesting point that if the proportional odds model does hold then since there is a common odds ratio wherever the scale is dichotomised, the relative risk must vary according to where one dichotomises the scale. So how, for example, does one report a common odds ratio in terms of a measure similar to a number needed to treat?