Reviewer's report

Title: International Study to Predict Optimized Treatment for Depression (iSPOT-D), a Randomized Clinical Trial: Rationale and Protocol

Version: 4 Date: 27 October 2010

Reviewer: John Geddes

Reviewer's report:
	his is an ambitious project and will possibly be a great source of exploratory data. Although you say it has been through peer review I suggest you get more evidence of this as the funder is a company who see this trial (iSPOT) as one of their "products" - see website.

Further some of the investigators are on the advisory board of MyBrainSolutions who fund the trial so they need to clarify this

the statistical section is clearly inadequate - it simply says that they aren't using a traditional approach but there are no hypotheses, proper power calcs - or analysis plans (essential when you are looking at genetic/biomarker data - enormous potential risk of false positives.

But it they can put all this right and be more explicit about the science, then worth publishing