Reviewer's report

Title: The SPIRiT study protocol: a randomised controlled trial comparing specialist rehabilitation and care assistant support with specialist rehabilitation alone and usual care for people with Parkinson’s living in the community.

Version: 2 Date: 9 September 2011

Reviewer: Peter Sandercock

Reviewer’s report:

1. The primary hypothesis of the study and the primary outcome are not clearly spelt out.
2. Table lists two primary outcomes; are these co-primary outcomes? How will this be handled in the analysis if the patients get better but the caregivers get worse?
3. Why was the PDDS chosen as opposed to the PDQ 39 scale used in the PDMED trial?
4. Inclusion of a usual care group – was this discussed with lay / patient representatives and was it regarded as acceptable?
5. Who will confirm PD diagnosis/check eligibility and obtain informed consent? This aspect of subject enrolment was unclear.
6. Eligibility criteria did not specify a minimum severity of PD. For patients only recently diagnosed with PD, especially if only minimally affected there is little scope for benefit and hence the trial will be underpowered.
7. Balance of key prognostic variables at baseline – no inclusion of severity as minimisation stratification factor; this needs to be justified.

In a small trial imbalance in severity at baseline can wreck any chances of detecting a treatment effect (since post randomisation adjustments are statistically inefficient)

8. Please clarify the method used to generate the randomisation sequence and what strategies will be used to ensure that the study statistician maintains allocation concealment.
9. Please clarify what strategies will employed to avoid cross-contamination of the intervention between groups.
10. Sample size – do the proposed effect sizes represent a clinically significant effect (this should be set out more clearly in the protocol)
11. Trial management structures unclear; who is the trial chief?
investigator, who is the trial coordinator, who is the data manager. Who will enter the data, who will chase missing or overdue data, is there a link to an accredited trials unit?

12. This trial imposes a huge questionnaire burden for the subjects, with lots of data per patient. This may prejudice data completeness

13. The huge data collection poses a substantial data management problem, but the arrangements for data management (data entry, data verification, chasing missing data, query resolution, etc) were unclear. 270 patients x 3 assessment points x 21 questionnaires = 17010 forms with goodness knows how many individual data items! = how will all this be managed?

14. Planning a trial which anticipates 10% LTFU is unwise since when trying to detect a modest treatment effect, the proposed effect size is small and impossible to detect if LTFU is so high.

15. What will the analytic strategy be overall (there is very little detail), how will allowance be made for multiple comparisons and what strategies will be used for minimising bias in the handling of missing data?

16. Role of, members of, steering committee not stated

17. Justification for not having a Data monitoring committee or periodic review of safety during the trial?

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.