Key points from the analysis of the PACE trial raw data for "recovery"

Margaret Williams 21st September 2016

The following extracts are taken from:

"A preliminary analysis of 'recovery' from chronic fatigue syndrome in the PACE trial using individual participant data".

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Key Points

1. There was no committee approval for the re-definition of "recovery".

2. "Recovery" rates for CBT and GET were not statistically significant.

3. The PACE PIs originally reported "recovery" rates of 22% for CBT and GET.

4. The published "recovery" rates were based on thresholds that deviated substantially from the published protocol and were inflated by an average of four-fold.

5. In contrast to the published paper by the PIs, the recovery rates in the CBT and GET groups are not significantly higher than in the SMC (standard medical care) group alone.

6. APT (adaptive pacing therapy) was a highly modified version of "pacing" (preferred by patients).

7. 13% of participants at baseline simultaneously met the trial entry criteria for "significant disability" and the revised "recovery" criteria.

8. The Investigators excluded drop-outs, which is not recommended practice in clinical trials.

9. Logistic regression (used by the PIs) has been shown to be an inappropriate method of analysis in randomised trials.

10. The figures originally given by the PIs for the four groups were:

    SMC 7% (but according to the protocol are 3%)
    APT 8% (but according to the protocol are 2%)
    CBT 22% (but according to the protocol are 7%)
    GET 22% (but according to the protocol are 4%)

11. "Our findings therefore contradict the conclusion of White et al (2013) that CBT and GET were significantly more likely than the SMC group to be associated with 'recovery' at 52 weeks".

12. "The multiple changes to the recovery criteria had inflated the estimates of recovery by approximately 2.3 to 5.1-fold, depending on the group, with an average inflation of 3.8-fold".

13. When using the revised recovery criteria, 8% of the "recovered" participants still met trial eligibility criteria for "significant disability".

14. "The changes made by the PACE investigators after the trial was well under way resulted in the recovery criteria becoming too lax to allow conclusions about the efficacy of CBT and GET as rehabilitative treatments for CFS".

15. "This analysis, based on the published trial protocol, demonstrates that the major changes to the thresholds for recovery had inflated the estimates of recovery by an average of approximately four-fold".

16. "It is clear from these results that the changes made to the protocol were not minor or insignificant, as they have produced major differences that warrant further consideration".

17. "The PACE trial provides a good example of the problems that can occur when investigators are allowed to substantially deviate from the trial protocol without adequate justification or scrutiny".

18. "It seems prudent that the published trial results should be treated as potentially unsound, as well as the medical texts, review articles, and public policies based on those results".