Reviewer's report

Title: The ANTOP Study: Focal Psychodynamic Psychotherapy, Cognitive-Behavioral Therapy, and Treatment-As-Usual in Outpatients with Anorexia Nervosa: A Randomized Controlled Trial

Version: 2 Date: 8 December 2008

Reviewer: Tim J Cole

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The protocol is for a study to test the efficacy of two treatments for anorexia nervosa, compared to a “treatment as usual” control group.

1. The Abstract is unclear is several respects, and some points are not clarified in the later text. For example, what is the exact research question relating to the two interventions – are they to be compared with each other, or are they compared separately to the control group? Is there equipoise for the two interventions versus treatment as usual? Why is the treatment period 10 months? What is the follow-up period after treatment has stopped? Why 237 patients? What does the final sentence mean, “Treatment as usual is systematically investigated as a control group”?

2. Page 7 paragraph 2. The definition of treatment as usual implies that if patients ask they are given the names of therapists, but if they don’t ask they get nothing. Can this be made explicit, as it means that for a proportion of patients treatment as usual means no treatment. Will consultants and their patients be happy to be randomised to the trial on this basis, i.e. is there equipoise?

3. Page 7 last paragraph. The primary hypothesis is that both the interventions are effective. This is odd, linking the performance of one intervention to that of another. I don’t see the clinical relevance, as patients are unlikely to be treated with both interventions together, or even a random choice of the two, so why link them in this way? A more straightforward research question would be test whether each one separately was effective.

4. A slightly different approach would be to split the comparisons between the three groups into two orthogonal (independent) contrasts, where the first contrast compares the average of the two interventions with control, and the second compares one intervention with the other. This approach uses the two available degrees of freedom and can be powered on either the first or the second contrast. It also avoids the need to split the 5% type I error into two, which is again non-standard.

5. On pages 7 and 8, the discussion of the hypotheses to be tested is uneven in its reference to the various study endpoints. The primary hypothesis relates to T2, the end of treatment, while a secondary hypothesis, that the two interventions do not differ, involves both T2 and T3, the end of follow-up. The third hypothesis
involves time T1, four months after the start of intervention. It is quite unclear to
me why the various hypotheses are pegged to different endpoints – surely the
point of the intervention is to achieve longterm improvement – presumably T3 –
and the trajectory by which it is or isn’t achieved is not relevant? It is worth
pointing out that T3 is only 3 months after the end of treatment, surely insufficient
time to count as evidence of longterm success of the intervention.

6. Re Figure 1 it is worth pointing out that 10 months is not the same as 40
weeks, which is implied by the two flow diagrams.

7. The primary outcome is change in BMI from T0 to T2, the end of treatment.
The analysis of change requires an adjustment for baseline BMI, as else
regression to the mean operates.

8. For medical complications, cases in either of the intervention groups are
hospitalised and treatment interrupted if their BMI falls below 14. There is no
mention of the control group here – is the assumption that they will also be
hospitalised, but that this is viewed as treatment as usual? This needs to be
made clear. If there is an improvement the treatment is resumed, but what is the
definition of “improvement”? Is it an increase in BMI, and if so how much?

9. Morgan-Russell is spelt with two ‘l’s in the text, but one ‘l’ in Table 2. I suspect
that the text is correct.