Author's response to reviews

Title: Collaborative Care for Patients with Bipolar Disorder: a randomised controlled trial.

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Author's response to reviews: see over
Dear reviewer,

Thank you for your valuable remarks. We discussed your comments in our group and hereby react.

**Title:** Collaborative Care for Patients with Bipolar Disorder: a randomised controlled trial.

**Version:** 1

**Date:** 23 June 2011

**Reviewer:** Gil L’italien

**Reviewer’s report:**

*Reviewer:* Design is adequately presented.

*Our reaction:* Thank you for your positive comment.

*Reviewer:* The postulated sample size seems small. I would challenge the authors to find some published studies to better inform the sample size. What about the Simon (ref 16,17) and Suppes (18) intervention studies referenced by the authors? Appropriate sizing is critical since authors admit that knowledge of CC by CAU patients/providers might reduce the effect size; this could lead to an uninterpretable or erroneous finding.

*Our reaction:* Our power calculation was driven by the idea that, to be worth implementing at a larger scale, the intervention should have at least a clinically relevant effect. Using the literature on power calculation (Cohen 1988), a clinically relevant effect size (Cohen’s d) is generally met at d = 0.5. Using conventional levels of alpha = 0.05 and beta = 0.8 and two-sided tests, this yields a minimum of 63 participants in each arm of the study.

Besides this, the Simon and Suppes study implemented a different collaborative care intervention then the one we developed. E.g. we added Problem Solving Treatment (PST; Bell et al., 2009) and, in case patients remain depressive, we add a specialised form of PST aimed at solving inactivity. PST has shown good effects on depression and as depression is...
the condition which seems to be not influenced by the Simon and the Suppes intervention we expect to make a difference here.

Effects we might find could be reduced by the fact that respondents in the control group have knowledge of the intervention. We agree with you, and we take several measures to avoid this. E.g. the details of the intervention are not known to professionals nor caregivers in the control group, and CC will not be implemented in this group.

**Reviewer:** One major limitation to the study which should be acknowledged in the discussion is the fact that it will not be possible to discern which components of CC are contributing most (or least) to the benefit (if seen). This is unfortunate since the economic component of this analysis might benefit from an assessment of the more versus less cost intensive components of the intervention. Those components with the greatest benefit might justify a greater cost.

**Our reaction:** We fully agree with you on this point, although we consider it unavoidable in complex interventions like this. We added this remark in the discussion paragraph.

**Reviewer:** Also what is meant by: “These interventions will be tailored to the individual needs of the patient.” For example, will some patients receive more intensive lifestyle coaching if they request it, or respond to it? Greater clarity is needed here. This could contribute to overall effects which are related to the patient characteristics and thus may not be generalizable to other groups of patients with differing characteristics.

**Our reaction:** We recognise your concern. However, this is an intervention in a real life situation, and we measure the effects in a pragmatic trial. We have developed a flexible intervention that can be tailored to the needs of the patient. However, we are certainly doing all we can to standardise the intervention. To achieve this we developed a manual which guides the professional in performing the intervention. We provide many forms and lists to fill in by the patient and the nurse, which also are means of standardisation.
To be able to account for this, we will keep record of to what degree patients are exposed to the intervention and we document fidelity to the manual in the experimental group. This will be reported when we publish our results.

In our study we may indeed find that the effect of the intervention co-varies with characteristics of the patient. Effect modification is an important area of research and we will look into factors that modify the effect of the intervention.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

We hope we have provided satisfying reactions to your questions and concerns. If not we will be glad to hear from you.

With kind regards, on behalf of all authors,

Trijntje van der Voort

References