Author's response to reviews

Title: Guided and unguided CBT for social anxiety disorder and/or panic disorder via the Internet and a smartphone application: Study protocol for a randomised controlled trial

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

Thank you for considering our manuscript, “Guided and unguided CBT for social anxiety disorder and/or panic disorder via the Internet and a smartphone application: Study protocol for a randomised controlled trial”, for publication in *Trials*.

We are grateful to have received such thorough, constructive and rapid peer-review by Dr Perrin. We have revised according to our reviewer’s suggestions and agree that the revisions have resulted in a stronger manuscript. Please see below for comments, point-by-point. All changes unrelated to basic formatting are marked in the manuscript using the track-changes function. Please see below for additional changes made not related to Dr Perrin’s comments.

We look forward to hearing from you at your earliest convenience.

Kind regards,

Philip Lindner
Ekaterina Ivanova
Kien Hoa Ly
Gerhard Andersson
Per Carlbring
A. In the introduction, it would be extremely useful if the authors could set out the observed effect sizes - preferably, intent-to-treat/controlled for iCBT (with or without apps and therapist involvement) in relation so SAD/PANIC or any relevant outcome. The purpose of this information is to help set up the power analysis in the Methods section and to contextualize the findings.

We agree with the reviewer that effect sizes should be explicitly mentioned. We have chosen to include this not in the Background, but rather in the Method section where the iCBT treatment modules are described.

Previous randomised controlled clinical trials using the same core treatment modules have demonstrated post-treatment, between-group Cohen’s d effect sizes in the range of d = 0.79\(^a\) [34] and 0.98\(^b\) [35] for SAD and d = 1.44\(^c\) [36] and 1.97\(^d\) [37] for PD when contrasted against waiting-list control groups. [Page 7]

In relation to the latter, it would be helpful to have a sentence or two to say how effect sizes for iCBT in previous studies compare with those obtained in RCTs of face-to-face CBT for SAD/Panic when patients are recruited directly from clinics and/or internet/newspapers. The purpose of this information is to point out that effect sizes/outcomes for iCBT for patients recruited from the internet are comparable (within the confidence interval) for outcomes obtained in treatment trials of clinically referred patients.

As we understand the reviewer’s suggestion, he would like to see the manuscript mention (A) how iCBT compares to regular CBT for SAD/PD; and (B) how iCBT with community-recruited samples compares to iCBT with clinically referred patients. We believe that point (A) is addressed by an already-included sentence in the Background section (page 3, in italics below) explicitly stating that iCBT effect sizes have been found to be near-equal or equal those of regular CBT. We have added an additional reference here (number 9 in the manuscript) to strengthen the claim.

The addition of a therapist to guide the patient through the self-help program has been found to increase effect sizes [6, 7] to near-equal or even equal to those of traditional, face-to-face CBT [8, 9]. [Page 3]

Regarding point (B), we acknowledge that it would be beneficial to the external validity of future trial findings to note that iCBT appears to work equally well with clinically referred patients. We have now added a sentence stating this in the Background section:

Guided iCBT has demonstrated both efficacy and effectiveness [10], with similar effect sizes seen when implemented in routine psychiatric care, e.g. in treatment of panic disorder [11, 12]. [Page 3]

B. In the Methods section, the power analysis section needs to make reference to the previous observed effect sizes to say how the trial N was arrived at – and any software uses to achieve this N. It is important that the authors distinguish between the power required to detect superiority between the two active treatments, and superiority of both treatments versus wait-list.

We are grateful to the reviewer for pointing out the need to clarify aspects of our power analysis. The section now includes a power analysis for the post-hoc, two-group comparisons (i.e. each
treatment versus waiting-list, and treatment versus treatment) and also references the previously published effect sizes of treatment versus waiting-list. We also mention the statistical software used for power analyses. The section now reads as follows:

This study aims to detect a moderate sized, post-treatment between-group difference (Cohen’s d = 0.5) with 80% power, which will require 150 participants distributed evenly to the three groups. In the post-hoc analyses contrasting any two groups, there will be 80% power to detect a d = 0.66 effect size when Bonferroni-adjusting the p values for the three possible post-hoc comparisons. When comparing each treatment group with the control group, we hypothesise effect sizes larger than d = 0.66 based on previously studies reporting higher effect sizes for the same core treatment program compared to a waiting-list control group [34–37].

Since all self-reported data is collected using the online platform, there is no risk of missing data, or loss or distortion of data. All analyses will be conducted on an intention-to-treat basis using a mixed models approach [49]. Power calculations were performed using the pwr package (http://CRAN.R-project.org/package=pwr) for the R statistical environment (http://www.r-project.org/; version 2.15.3). [Page 10]

2. This is an extremely well-written manuscript that will be a valuable addition to the literature. The authors can remove the box around the abstract.

We have removed the box around the abstract, as suggested.

Other revisions

- The “Trial status” in the manuscript has been updated.
- We have corrected some minor typos.
- Two additional references (not related to the revisions suggested by the reviewer) have been added to strengthen a claim made in the manuscript (page 4).
- Significant change in the study protocol: Second follow-up assessment will be after 36 months, not after 24 months as previously stated. The manuscript and the protocol registered in Clinicaltrials.gov have both been updated to reflect this change.
- Non-significant change in the study protocol: Primary diagnosis (panic disorder or social phobia) will be assessed using the structured clinical interview, not using the scores on the symptom self-rating scales. The manuscript has been revised (page 6), but there is no need to update the Clinicaltrials.gov register.