Author's response to reviews

Title: Internet-based cognitive behavior therapy for obsessive compulsive disorder: A pilot study

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Author's response to reviews:

Dear Editor. Please, find enclosed our revised paper "Internet-based cognitive behavior therapy for obsessive compulsive disorder: A pilot study" (Clinical Trials reg. NCT01348529). We would like to thank the reviewers for careful reading of our manuscript and valuable comments. We have considered all the comments given and made substantial revisions of the manuscript in accordance with them. Below, we detail our response point by point.

Reviewer 1:

1a) Abstract, Results: “did not longer fulfill” should be “no longer fulfilled”
   Comment: Changed accordingly.

b) Introduction, first para., between refs. [14] and [15-18], “report” needs an “s.”
   Comment: Changed accordingly.

c) Intro, second para., second sentence: “of computerized treatment where” would be better as “… treatment in which….”
   Comment: Changed accordingly.

d) Same para., third sentence, “one single” should be “a single.”
   Comment: Changed accordingly.

e) Next sentence, redundancy at the end.
   Comment: Very important note. The last part of this sentence has been deleted.

f) Next para., first sentence, “and/or with” would be better as something like “and/or have featured very….”
Comment: We have changed this section to “Previous self-help trials on OCD have been strictly computer-based and/or have featured very limited therapist support. There are, to our knowledge, no published data on ICBT in the treatment of OCD.”

g) Method/Participants, 2nd para, (c) should read “4th” not “4:th”
Comment: Changed accordingly.

h) 3rd para, sentence after [35], colon after “a and b” should be semi-colon
Comment: Changed accordingly.

i) Last para before Conclusions, first sentence: replace “might be” with “is”; “suggested” is sufficiently tentative.
Comment: Changed accordingly.

2) In the Intro, 2nd para, last sentence—how/why would Internet-based OCD treatment reduce stigma?
Comment: We agree with the reviewer that this is not clear. To avoid confusion, we have changed the sentence, clarifying this: “Therefore, ICBT has the potential to be a cost-effective alternative for OCD and increases treatment accessibility [1].”

3
a. Was there a minimum Y-BOCS for study entry?
We did not have any minimum Y-BOCS criteria. Our main inclusion criteria was instead only a primary OCD diagnosis. In retrospect however, it would have been better to have an established Y-BOCS cut-off score such as 12 or 16.

b. Why was “extreme” OCD excluded?
Comment: The reason for excluding severe OCD was because of ethical reasons. OCD is known to be hard to treat and we found it ethically problematic to give these patients an untested method of delivery. It is also common for ICBT to be developed for patients with a light to medium symptom burden (e.g. ICBT for depression). The reviewer still points to something important and future studies should investigate whether this really is a plausible exclusion criteria.

c. Which results might have “suffered from floor effects”? It seems like a greater threat in light of relatively low baseline OCD severity would have been null treatment results, which were not found. The low starting point also suggests that the results are unlikely to be attributable to regression.
Comment: We agree with the reviewer on this point. We have deleted the sentence regarding floor effects and instead added the following: “One possible consequence is that the effects in this trial are lower because we had less room for Y-BOCS change. Another possible consequence is that this population was easier to treat because they had lower symptom burden. Thus, the lower
baseline means could have affected the results in both ways.”

d. What was the range of Y-BOCS scores at baseline?  
Comment: The Y-BOCS range was 10-30.

4. Please discuss the limitation that one psychologist treated all participants, especially given the crucial question of how effective this treatment would be if implemented by other therapists.
Comment: This is indeed an important issue and also pointed out by reviewer 2. We have added a part in the discussion clarifying this: “First, only one psychologist (EA) treated all patients and the limited therapist time achieved in this study is perhaps not fully generalizable to other therapists. However, the time to treat the patients was about 9-10 minutes per module which is in line with previous research studies of ICBT with therapist support [2].”

5. Were assessors blind to time point? If not, please add to the limitations in light of no control group.
Comment: We agree with the reviewer and have added this to the limitation: “Finally, as this was a pilot study, there was no randomization to a control condition, which rendered it difficult to claim any improvements were caused by the treatment alone. Furthermore, the assessors were not blinded to time point. However, OCD is regarded as a stable and often chronic disease [3] and, considering the large effect sizes on both the clinician and self-administered instruments, it is unlikely the overall treatment results could be due spontaneous remission.”

6. Average number of completed modules was about 10 of 15. Why? This number seems somewhat low to me. Also, were some modules more likely not to be completed than others?
Comment: We have added a sentence in the discussion clarifying this important issue put forward by the reviewer: “…the time to treat the patients was about 9-10 minutes per module which is in line with previous research studies of ICBT with therapist support [2].”. The particular modules not completed were 11-15 because the modules were given consecutively.

7. Results, second sentence: “Some participants” had daily contact…. How many?  
Comment: Depending on the definition of “daily”, we would estimate the sample to about 20-30% of the participants. However, since this figure varied considerably in the treatment, we have not attempted quantify this figure.

8. Same para., “Three participants did not begin ERP exercises.” Do you know why not?  
Comment: This is a very good point by the reviewer and we have added information about those participants in this section: “The reasons for not
beginning ERP reported by these participants were lack of time and difficulties getting started with the active treatment."

9. Cost offset analysis: mean time spent with study therapist is provided; what were range and median? Was time spent with therapist associated with improvement? I would guess it would not be given that some patients likely spend more time with therapist because they’re struggling.

Comment: We agree with the reviewer and have added a part in the sentence clarifying this further: “...(range: 25-203 minutes, median: 80 minutes).”. The reviewer is also correct in that more therapist time were not associated with improvement.

10. Para. that begins “The effect sizes in this trial”: I do not understand the logic connecting the high accessibility to the therapist with participants’ working intensively with the treatment and achieving rapid results. Please clarify.

Comments: We agree with the reviewer that this part is not very clear. We have therefore changed this section: “The effect sizes in this trial were in the same range as the effects of traditional face-to-face CBT for OCD [4], even though this trial used much less therapist time (92 minutes over the 15-week treatment) than traditional face-to-face treatments, and had higher in-group effect sizes than most trials with strictly computer-based treatments [5-9]. One possible explanation for the large effects in this trial was the high accessibility and possibility to have an intensive contact with the therapist during treatment. Intensive contact and increased access to the therapist has been investigated in face-to-face CBT with effect sizes comparable to other trials of CBT for OCD [10]. Furthermore, the therapist input has been found to be an important factor in ICBT [11]. The therapist in this trial was very active and had sometimes had daily communication with the participants. As a result of this very active therapist input, some participants worked intensively with the treatment and achieved therapeutic benefits (i.e. successful ERP) within a couple of weeks. In addition, the screening and post-treatment assessment interviews were conducted face-to-face by a psychiatrist and this could also have affected the treatment adherence and outcome. “

11. Conclusions section: Unless required for the journal I would jettison this section since it’s mostly redundant with the previous concluding paragraph.

Comment: As this is a mandatory part of the BMC journal, we have chosen to keep this part but deleted the last sentence in the discussion. We then changed the conclusion sentence to: “Despite several limitations, the results suggest that ICBT has the potential to reduce OCD symptoms, depressive symptoms and possibly produces societal cost-offsets. Controlled trials are needed to further validate ICBT for OCD”. We thank the reviewer for making the discussion much clearer.

Discretionary Revisions
1. Some readers might wonder, as I did, why the SCID was used for OCD and the MINI for other diagnoses.
Comment: We have added information about this in the method section: “The reason for conducting the SCID on OCD criteria was that the SCID provides more detailed questions than the MINI.”

2. Table 3: Although not impossible, it seems really unlikely (something like 1/10,000 chance) that the Y-BOCS (clin) would be exactly 20 (Pre) and 10 (Post) to two decimals; was that the case?
Comment: We admit this look peculiar but, after have crosschecked two times, the means are indeed exactly 20.00 and 10.00 respectively.

Reviewer 2:
1. There are many measures of the effects but there is no (Bonferroni) correction for findings by chance.
Comment: This is an important mark by the reviewer. We have added Bonferroni corrections on the significant outcomes in method and results section (table 3).

2. The authors define clinical significant reduction as the % of patients with 30% reduction in symptomatology. This is not the correct way to define clinical significance. This percentage should be described as meaningful response. It would be correct to use the more conservative Jacobson and Truax criterion: two standard error reductions in combination with change from above the cut-off score of clinical symptomatology to below.
Comment: We agree with the reviewer and have added the Jacobson and Truax criteria in method, results, abstract and discussion. We thank the reviewer for helping us making the results clearer to the reader.

3. The suggestion of cost-effectiveness seems too self-serving. There are 5 measures in the TIC-P, only one of them (hours of help from the family) shows a nearly significant reduction between pre- and posttest. If the Bonferroni correction would have been applied, even that measure would not show a trend in cost-effectiveness. Yet, the means of the TIC-P measures suggest improvements, but they do not come close to significance. This might be related to the large SD’s at pretest. The authors might reflect on this: were the SD’s in this study larger than in other studies, or do the scores reflect a psychometric problem of TIC-P?
Comment: We agree with the reviewer on this point and have added a section in the discussion, reflecting on this issue: “The fact that the health economic analysis did not came out significant could be explained by large standard
deviations on the subscales. Large standard deviations is a common phenomenon when using TIC-P [12] and is also regarded as a general problem in health economic evaluations [13]. Future studies should therefore focus on using alternative statistical ways to handle this problem (e.g. Markov simulations). “.

4. The study is an open pilot trial with only 23 participants. In the discussion, the authors state this as limitations. I would not call it that way. Pilot studies as these can be helpful and even necessary. But even an open pilot study should include a follow-up period, in order to investigate to what degree improvements sustain. Especially since an unknown but probably considerable percentage of the patients did not complete treatment and accordingly did not follow the relapse prevention module.

Comment: This is indeed a valuable reflection, however pilot studies can be designed in many ways. We could have done a small randomized pilot study but chose not to do this. Not incorporating a control group (even if the study is very small) is still a limitation. We have changed this part and hope that the reviewer and the editor agrees with our decision: “Finally, as it was a pilot study, there was no randomization to a control condition, which rendered it difficult to claim any improvements were caused by the treatment alone. Furthermore, the assessors were not blinded to time point. However, OCD is regarded as a stable and often chronic disease [3] and, considering the large effect sizes on both the clinician and self-administered instruments, it is unlikely the overall treatment results could be due spontaneous remission.”

5. Due to the omission of a follow-up period the interpretation of the costeffectiveness is also questionable. This should not be measured during the treatment but in a (longer) follow-up period.

Comment: We agree with the reviewer and we have added the following limitation: “Fifth, this study did not include any long-term follow-up data. Our recommendation for future studies is therefore to include follow-up periods and further investigate long-term efficacy of ICBT. This is especially important since TIC-P covers a time period of 4 weeks retrospectively.”

6. The authors mention an average completion of slightly less than 2/3 of the 15 modules. What does this mean? After a pilot, we would expect a detailed description on where the people stopped and why? Didn’t they need further response prevention exercises? It would be interestingly to explore whether there are indications (not tests) whether the ‘completers’ (a term they do not use) have a higher rate of reduction in symptoms in comparison to those who left the programme.
Comment: The main reason for not completing all modules was that several participants felt that they had found ERP exercises that worked and focused on doing them and report to their psychologist instead of completing all text material. We have added information about the participants who did not begin ERP: “Three participants did not begin the ERP exercises. The reasons for not beginning ERP by these participants were lack of time and difficulties getting started with the active treatment.”. The average number of completed modules are also in line with previous studies from our research group.

7. The self-help treatment is supported guidance by one psychologist (not clear whether this was done by email and/or telephone contact). Altogether 92 minutes during the treatment on average. This amounts to an average of about 6 minutes per module. Since patients could seek contact whenever and how often they wanted this could happen a few times during one module. This calls for more description and more reflection than the authors provide: To what degree may the results of this psychologist be generalized to other psychologists as he/she must have been a sort of genius. After all, in maybe two or three minutes he must have been able to read the report of the patient, think about it, give meaningful feedback and motivate the patients to proceed. The description in the manuscript should also be clear about the way of measuring the support time, exactly where did it start and end and how reliable was it measured. The more so, since only one psychologist was involved.

Comment: The reviewer is correct in that the use of one therapist is a limitation. We have therefore added the following limitation in the discussion: “First, only one psychologist (EA) treated all patients and the limited therapist time achieved in this study is perhaps not fully generalizable to other therapists. However, the time to treat the patients was about 9-10 minutes per module which is in line with previous research studies of ICBT with therapist support [2].”.

We have also added the following sentence in method section, further describing the way we measured the therapist time: “Therapist time (i.e. read the reports and write feedback) were logged automatically in the treatment platform.”

In addition, we added the following sentence in the treatment section to clarify that no face-to-face contact was made with the therapist: “The treatment lasted for 15 weeks and included e-mail contact only with the therapist.”

8. Finally, the programme was mainly online, but the patients were seen by a psychiatrist. The authors sure have their reasons for this but it also constitutes a limitation in a study on pure online treatment. What is the effect of this face to face intake? How much of a threshold it causes to participate in the online programme? How does it affect the outcome? Does the client/therapist interaction during the diagnostic interview influences the outcome? Shouldn’t we
add the time of the diagnostic interview to the 92 minutes? Wouldn’t it be possible to conduct the screening entirely online and telephone?

Comment: This is indeed an interesting discussion point. Theoretically, it is possible to have both the inclusion and the treatment online. However, our experience from implementing this to real-world psychiatric practice (www.internetpsykiatri.se) is, that it is necessary to meet with a clinician before included to ICBT. Furthermore, the Y-BOCS clinician version is validated on face-to-face basis. Thus, the reason for having psychiatrist visits in this study was to a) resemble real psychiatric practice and b) increase validity of primary outcome. The assessors were psychiatrists and were not involved in the active ICBT treatment. We have added information in method, further clarifying that the psychiatrist was an independent assessor: “Of the 55 individuals screened, 34 individuals continued to a face-to-face diagnostic interview with a psychiatrist (independent assessor)...”. In line with the reviewer’s recommendations, we have also added the following sentence in the discussion: “In addition, the screening and post-treatment assessment interviews were conducted by a face-to-face psychiatrist and this could also have affected the treatment adherence and outcome.”

Our recommendation is to not incorporate the assessment time in the 92 minutes. This would blur the results regarding active treatment time and also make them less comparable with other studies. In the current MS, the reader understand that the active ICBT treatment was 92 minutes but that extra time was also spent on assessment with a psychiatrist. We think this information is sufficient

Conclusion: The points made above could and should be addressed in the description of the study, in the abstract that should be more cautious, and in reflections in the discussion. The discussion should focus more on what the authors learned from this pilot than on the outcome. The authors should focus on the real limitations and not on the limitations that are not real (pilot study, no randomization)

Comment: We want to thank the reviewer for giving such comprehensive feedback. We have added a section in the discussion with our reflections and ideas from conducting this study: “If controlled trials confirm that ICBT with therapist support is indeed effective compared to a control condition, one possible venue for future applications could be to combine face-to-face CBT with Internet support. This would combine two important elements in therapy, the possibility to be flexible using a face-to-face therapist but also opportunity increase and reinforce ERP frequency between the sessions. Other possible applications would be to add weekly videoconference sessions as an adjunct to ICBT. This would in turn expand the treatment arsenal and further increase treatment accessibility for patients suffering from OCD. “.

Reviewer 3:
1. The Y-BOCS, MADRS, AUDIT and DUDIT were delivered to the participants through the internet. Are those measurements validated for online screening? Please add information about online psychometric properties (reliability, sensitivity, specificity and cut-off scores) of those instrument to the method section, as they might be different (e.g. Buchanan, T., 2003. Internet-based Questionnaire Assessment: Appropriate Use in Clinical Contexts. Cognitive Behaviour Therapy 32, 100-09), although results are mixed (e.g. Carlbring, P., Brunt, S., Bohman, S., Austin, D., Richards, J.C., Öst, L-G., Andersson, G., 2007a. Internet vs. paper and pencil administration of questionnaires commonly used in panic/agoraphobia research. Computers in Human Behavior 23, 1421–34). Which cut-off scores are used (based on paper-pencil or on internet)? If those measures are not validated for online usage yet, please mention this in the limitations as well.

Comment:

The screening procedure: The Y-BOCS, MADRS, AUDIT and DUDIT were administered online but inclusion was made in the psychiatric interviews (i.e. the MINI, SCID and Y-BOCS) and not primarily based on the Internet-administered questionnaires. The use of previously mentioned measures was just to get an indication of OCD severity, depression, alcohol and drug abuse. Thus, the inclusion was based on face-to-face psychometric properties.

Outcome measure: We agree with the reviewer that the online main outcome measures should be discussed in the manuscript. We have therefore added information for each outcome measure:

SCID & MINI: The SCID has shown to have acceptable reliability with Cohen’s Kappa coefficients ranging .70-1.00 [14] and the MINI has high diagnostic concordance with other diagnostic tools [15]. The reason for conducting the SCID on OCD criteria was that the SCID provides more detailed questions than the MINI. The Clinical Global Impression Scale (CGI) [16] and Global Assessment of Functioning (GAF) [17] were used to measure global improvement. Although not previously validated for an OCD population, both CGI [18] as well as the GAF [19] has shown satisfactory reliability in other psychiatric populations.

Y-BOCS: “There are moderate correlations between the clinician and the self-rating version of the Y-BOCS, with the obsession subscale having lower convergence between the two versions [20]. However, another study has shown a correlation between the computer and clinician administered Y-BOCS of .88 [21].”.

MADRS: Previous research has shown that the psychometric properties of the MADRS-S remains unchanged after transformation to online use [22].”.

EQ-5D: The computer administered EQ-5D correlates highly (.85) with the paper and stencil version [23]."
QOLI: “The online version of the QOLI has been compared to the paper and stencil version with mixed results [24, 25].”

PSWQ: “and the computerised version has shown high convergence compared to the paper and stencil version [26].”

The remaining outcome measures are added in the limitations: “Finally, some of the outcome measures (OCI-R and TIC-P) used in this study has not been validated for online use. Thus, the administration format could have affected the results.”

Discussion

2. How can one person be included in the program with drug and alcohol abuse, while the psychiatrist conducted a face-to-face diagnostic interview with this person? What was his/her score on the AUDIT and DUDIT? I assume that a trained psychiatrist is able to diagnose validly and reliable with the SCID, but that there is always a chance of missing out a diagnosis or wrongly diagnose a ‘healthy’ person. However, this issue about the validity of the diagnoses has to be addressed in the discussion.

Comment: The participant originally included had a DUDIT score of 18 and the psychiatrist knew this at the time of the assessment interview. However, the participant also claimed that she had been clean for a year and that she had misinterpreted the online questions. The psychiatrist (with over 20 years of experience in OCD diagnostics) made the decision to include the participant based on the psychiatric interview (in spite of the high DUDIT score). This was done as we did not have any cut-off scores on the Internet-administered questionnaires. The main function of the Internet-administered questionnaires was merely to give background information. We have added a sentence to clarify this issue: “Two weeks after inclusion, one participant reported serious problems with drug and alcohol abuse which had not been detected at the psychiatrist visit. This participant was retrospectively excluded from the study and all data analyses.”

3. See comment 1. If the screening questionnaires are not validated for online usage yet, please mention this in the limitations as well.

Comment: We agree with the reviewer and have added a limitation in the discussion: “Finally, some of the outcome measures (OCI-R and TIC-P) used in this study has not been validated for online use. Thus, the administration format could have affected the results.”

Minor Essential Revisions

Background

4. page 3/4: To stress out/ underline that therapist support in ICBT appears to be more beneficial compared to unguided ICBT, the background might be improved

We have partly highlighted this issue in introduction “…Hence, therapist support appears beneficial in this treatment format which is in line with what has been observed for several other conditions [11].”. We have also added the following sentence in line with the reviewer’s comment: Self-help treatments with therapist support has been found to be equally effective as face-to-face treatments [27] whereas studies without the therapist have lower effects [28].” And also: “Previous self-help trials on OCD have been strictly computer-based and/or have featured very limited therapist support. This is important as evidence suggest that self-help treatments are more effective when guided by a therapist [11]. There are, to our knowledge, no published data on ICBT with therapist support in the treatment of OCD.” We thank the reviewer for making this clearer to the reader.

5. page 4 last paragraph: The paragraph begins with the sentence: “previous self-help trials on OCD have been….. with very limited therapist support”. Then, the current study is described: “therefore, an open pilot study was conducted to evaluate the value of ICBT for OCD”. Consider adding guided or supported to ICBT, so it is immediately clear this study is with therapist support (as opposed to previous self-help trials on OCD).

Comment: We agree and have added information in line with the reviewer’s recommendations: “Therefore, an open pilot study was conducted to evaluate the value of ICBT with therapist support for OCD before moving on to a controlled trial.”

6. Page 4 second paragr: “The patient’s work with the treatment is supported by regular contact”. Please change the word ‘is’ to ‘can be’, as unguided self-help is also a form of ICBT.

Comment: We have added information clarifying this: “Internet-based CBT
ICBT) with therapist support is a type of computerized treatment in which the patient logs onto a website and works with written self-help material and homework assignments [11, 29]; the patient’s work with the treatment is supported by regular contact with an online therapist.”

Methods
7. Page 7: Diagnosis and global functioning: who (therapist, psychiatrist?) conducted the SCID and MINI and were they trained for these interviews?
Comment: We have added information regarding this issue: “Of the 55 individuals screened, 34 individuals continued to a face-to-face diagnostic interview with a psychiatrist (independent assessor) who had extensive training in OCD diagnostics.”

8. Please add some information about the psychometric properties of the SCID-I for OCD.
Comment: We agree with the reviewer and have added information about both MINI and the SCID in the method section: “The SCID has shown to have acceptable reliability with Cohen’s Kappa coefficients ranging .70-1.00 [14] and the MINI has high diagnostic concordance with other diagnostic tools [15].” However, we have not found any isolated validation studies on SCID for OCD and have therefore excluded this from the article. The reason for choosing the SCID is also added in the article “The reason for conducting the SCID on OCD criteria was that the SCID provides more detailed questions than the MINI.”. We hope that the reviewer and editor agree with this decision.

9. What is the reason for using a MINI and a SCID? Why not only use one diagnostic interview?
Comment: As commented above, we have added information about this in the method section: “The reason for conducting the SCID on OCD criteria was that the SCID provides more detailed questions than the MINI.”

Discretionary Revisions
Abstract
10. Consider adding “with guidance of a therapist” to the abstract methods. So it is immediately clear the intervention is guided.
Comment: We agree with the reviewer and have changed this accordingly: “An open trial where patients (N=23) received a 15-week ICBT program with therapist support consisting of psychoeducation, cognitive restructuring and exposure with response prevention.”

Background
11. Page 3: consider briefly addressing some possible reasons for limited access to CBT.
Comment: We say that there is a lack of CBT therapists and give references for
this claim. We regard this as sufficient as the reasons for this lack is not a main aim of the article, rather just an important background information why we want to test ICBT. We hope that the reviewer and the editor agree with this.

Methods
12. Page 9: “one psychologist (EA) treated all participants..”. On page 4, it is described that the main function of the therapist is to provide support. Therefore, I would suggest to change the word “treated” to “gave support”

Comment: We have changed the sentence in line with the reviewer’s recommendation: “One psychologist (EA) treated all participants and provided feedback and support on homework assignments within 36 hours during weekdays. “

Again, we would like to express our gratitude to the reviewers for the comments and hope that this revised version of manuscript will be approved for publication in BMC Psychiatry.

Kind regards

Erik Andersson