Author's response to reviews

**Title:** Prediction of symptomatic improvement after exposure-based treatment for irritable bowel syndrome.

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**Author's response to reviews:**

We would like to thank the Reviewer and the Editor for providing more comments on our manuscript and the Editor for clarifying the remarks that were made on the first submission. We are also happy to note that the Editor found the manuscript to be improved and that the Reviewer seems to be satisfied with the major revisions we have made.

Comments from Associate Editor:

**COMMENT**

1. In the authors' response to my comments they discuss analyses using clinically significant improvement (yes/no). I did not ask for these analyses, I asked what is a clinically significant change in GSRS-IBS score. Is a change of 2 clinically interesting (probably not) or 30 (probably yes). This information is of importance for evaluation of the results (see my point 3)

**RESPONSE**

We appreciate this clarification and we believe that the Editor has an important point. As there are no recognized standards for clinical significant improvement on the GSRS-IBS, we have chosen to address the Editors comment 1 and 3 in the discussion, where we speculate on the possible significance of the differences in outcome between depressed and non-depressed participants.

**COMMENT**
2. The authors write in their response: "Testing for only one of the predictors while controlling for pretreatment score did not change the results". I recommend to add this sentence in the paper, it is valuable information.

RESPONSE
We have now added a sentence about this alternative analysis in the results section (alternative model no 4).

COMMENT
3. The discussion of a type II error is still missing. The results indicate that subjects with major depression (scored yes/no?) and depression (high scores for MADRS-S) have less effect of the treatment (but not statistically significantly) The CI for major depressive disorder is -2.32:12.94 which means that changes in GSRS-IBS in this interval is not statistically significant. If a change in GSRS-IBS <= 12.93 is of clinical significance (see point 1), a clinically significant effect could have been missed (=type 2 error).

RESPONSE
As stated above, we appreciate this clarification and we agree in principle. A minor note is that the confidence interval indicates that a difference above about 7.6 points (not 12.93) would have been statistically significant (estimate 5.31 + lower CI 2.32). However, in the discussion we now focus on the possible significance of the estimate of 5.31.

COMMENT
4. The discussion has two statements that should be rephrased: "...ICBT for IBS is suitable for most subgroups of IBS patients...." and "...ICBT is highly effective..." My personal opinion is that the results are very disappointing, the reduction in GSRS-IBS from 47.74 to 32.58 (a reduction of 32%) is in the same order as the placebo response reported in many trials in patients with IBS.

RESPONSE
Although we believe that our study in AJG, 2011 (where we compared ICBT with a credible control condition) actually showed that the ICBT does lead to larger improvement than can be explained by placebo response, we agree that this study in itself does not provide evidence that ICBT is “highly effective” for IBS. We have therefore made both these statements more modest. We would also like to add that this comment (together with reviewer comment #4) led to some general rearranging and shortening of the Discussion section.

COMMENT
5. Read the comments from the reviewer carefully and make necessary changes, with special reference to point 4 about the conclusion.

RESPONSE
We hope that you will find that this has been done.
Reviewer: Wijnand Laan

Minor Essential Revisions:

COMMENT
1. Trial registration should not go into the abstract section, now it appears like the paper describes a trial. Just add it to the methods section like this: This study included 79 self-referred participants with a diagnosis of IBS who had participated in a randomized controlled study (ClinicalTrials.gov: NCT01171053) of ICBT for IBS, where they were randomized to either treatment (n=39) or waiting list control (n=40) for 10 weeks [27].

RESPONSE
Changed accordingly

COMMENT
2. The 'sentence' starting on line 2, page 7 does not make any grammatical sense: 'Trial registration ClinicalTrials.gov NCT01171053'. Please rephrase it so it contains at least one verb.

RESPONSE
Contingent on Comment 1, this 'sentence' has now been removed.

COMMENT
3. Line 24, page 16: The sentence reads like the main conclusion of the paper is the fact that study is important (We believe the findings of the present study to be important). I think the conclusions should be related to the results, not to whether the study itself is important or not).

RESPONSE
We have rephrased in accordance with the reviewer’s comment.

COMMENT
4. I feel the conclusion of a paper should be limited to a few lines only as is it should present only the conclusion. Now the authors present a discussion within the conclusions (line 6 and 7, page 17: However, it is possible that (....)). I would strongly suggest to limit the number of lines in the conclusion section to a maximum of five.

RESPONSE
We agree that the conclusion got lost. We have moved most of the text further up in the discussion and the Conclusion section is now five lines long.

Discretionary Revisions:

COMMENT
5. Line 11 page 5: GSA should not be included in the [brackets] of the reference
but (get their own). This is repeated on further on in the paper several times, I do not think is proper referencing to include the abbreviation in the citation brackets as this is commonly done with author names. I will not make further remarks regarding this.

RESPONSE
We have made all these bracketed abbreviations separate from their respective references.

COMMENT
6. The sentence starting on line 12, page 6 is obsolete given the sentence starting on line 6 of the same page.

RESPONSE
Changed accordingly.

COMMENT
7. Line 12 page 7 (and throughout the whole paper): Table is not to be written with a capital T.

RESPONSE
We have looked at previous papers published in BMC Gastroenterology and found that tables and figures are referenced both with and without a capitalized first letter. The instructions for authors (http://www.biomedcentral.com/bmcgastroenterol/authors/instructions/researcharticle#preparing) do suggest that Table should be written with a capital T, but this is not expressed clearly. We therefore wish to leave this decision to the Editor.

Once again, we thank the Editor and the Reviewer for these comments.