**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 reviewers’ and associate editor for commenting on our manuscript. We believe that the manuscript is more to the point now that it has been considerably shortened and we have also made the language less difficult to follow.

Comments from Associate Editor:

**COMMENT**

In this explorative study, no significant associations were seen between symptoms (GSRS-IBS) after treatment and comorbid psychological distress following exposure-based ICBT. The main problem with the paper is that a negative study per se never excludes an effect, it has to be documented. What is a clinically significant change in GSRS-IBS? Give the information in the "method" section.

**RESPONSE**

We are not sure why the associate editor requests a criterion for clinically significant change on the GSRS-IBS as there are no instructions on how this criterion would be used. To our knowledge, there are no such criteria defined for GSRS-IBS and we have conducted no analyses using clinically significant improvement (yes/no) as dependent variable so we are slightly confused regarding what the purpose would be. We would be happy to comply with the editor's request but we need more precise instructions.
COMMENT
Does the study really exclude such an effect; give the 95% confidence intervals (CI).

RESPONSE
We have added 95% confidence intervals to the coefficients in Table 2.

COMMENT
For example, what are the CIs of the differences in the improvement of GSRS-IBS in patients with high and low pretreatment scores for GSRS-IBS, MADRS-S, VSI etc. Do the CIs really exclude clinically significant differences?

RESPONSE
Splitting a sample into low and high scorers on the predictors introduces problems (see Steketee & Chambless, 1992) such as reduced power and marginal effects that may distort actual relationships. Interpreting these effects, i.e. if one would split the sample, would also be difficult considering that we already know that the investigated predictors had no overall predictive effect. We believe that the regression analyses provide a robust test of the predictive power of the pre-treatment characteristics in this sample.

COMMENT
Is it correct to use all significant variables in the regression analyses? I guess that the predictors might be highly correlated. Do regression models with GSRS-IBS pretreatment and only one of the other predictors at a time also give non-significant results?

RESPONSE
As detailed in the Results section, we assessed the effect of multicollinearity and tested alternative models where variables that were highly correlated were removed, this did not affect the principal results. Also, testing only one of the predictors while controlling for pre-treatment score did not change the results.

COMMENT
In conclusion, before publication of a negative study it has to be documented that the negative findings really exclude clinically significant associations between premorbid psychological distress and effect of cognitive therapy (exclude a type II error).

RESPONSE
We agree that reporting a negative result does not prove that there is no association. However, we believe that we discuss several limitations of the study and highlight the fact that the sample may be inadequate to find relevant predictors of symptomatic outcome. It should nonetheless be mentioned that power was adequate, as outlined in the Methods, to detect predictors of moderate effect size, thus suggesting that type II errors were unlikely.
COMMENT
In addition, the authors have to read the comments from the reviewers thoroughly and make the necessary changes. The writing has to be improved, several sentences are difficult to understand and there seems to be contradictions. The sections “introduction” and the “methods” are too long and detailed.

RESPONSE
We have shortened both the Introduction and Methods sections and also made the manuscript easier to read. We have also addressed all issues raised by the reviewers and revised the ms accordingly.

COMMENT
Please also state in your revised manuscript the full name of the ethics committee that approved your study, including the approval reference number.

RESPONSE
The name of the committee is actually “the Regional ethical review board in Stockholm” and we have added the reference number.

Reviewer #1
COMMENT
This article is well written with sound methodology and good English (a few inevitable typos need correcting). Statistical analysis appears appropriate. Discussion is written well and some of the limitations are discussed. However, the article does not significantly contribute to the knowledge in the field. There are few significant findings and it may be that the sample size is the main culprit.

RESPONSE
We are happy to note that the reviewer findings the methodology to be sound although he questions the relevance of the results. We comment on this below.

Reviewer #1 2
Major Compulsory Revisions
COMMENT
1. The following line in the introduction (?), page 5 is not clear to me:
As almost no studies of psychological treatment of IBS have used the presence of psychological distress as inclusion criteria<....>. This has allowed for several studies where measures of psychological distress have been used as predictors of outcome after psychological treatment.
What are the authors trying to say, what has allowed for several studies?

RESPONSE
We completely agree. This sentence has been removed.

COMMENT

2. The various ‘Measures’ sections on pages 9 to 12 are too long. Please list them and add a reference for the readers who are interested in the individual Chronbach alphas and possible scores but do not add all this information to the body of the text.

RESPONSE

We have removed all reports of psychometric data.

COMMENT

3. A lot of participants suffer from co-morbid psychiatric disorders, approximately 71% ((15+39)/76=71%) of the participants suffered from a serious psychiatric disorder. Given this information, how valid are the IBS diagnosis? Where they made using Rome–III diagnostic criteria? Without proper diagnostic criteria I fear there might be many ‘false positive’ patients suffering from IBS in the sample.

RESPONSE

The anxiety and depressive diagnoses showed some overlap so the actual number is 42, i.e., about half the sample had a psychiatric diagnosis – this is now clarified in the Results section. The fulfillment of Rome III criteria were confirmed before inclusion, which is now stated in the manuscript. We are not aware of any research that suggests that the presence of a psychiatric disorder makes an IBS diagnosis more likely to be incorrect.

COMMENT

4. Many papers have yet been written on the subject, see the introduction:

We have found four studies that reported a positive association <....>. Eight studies have reported the reverse association<....>. Finally, three studies reported no association <....>.

The authors even state:

Thus, the results in this study largely follow the same pattern of previous prediction studies in the IBS field, with no variable appearing as a clear and consistent predictor of treatment outcome.

The question arises therefore what this study adds the literature, why should it be published?

RESPONSE

As we state in the introduction, this is the first study that explores several types of possible predictors of symptomatic improvement after an exposure-based treatment. The studies that have been published on this new type of psychological treatment suggest that it may have a unique value in treating IBS and may very well be more effective than mainstream psychological treatments that target general distress rather than fear and avoidance of symptoms. We
believe that it is important to explore the possible predictors of treatment outcome for this new type of treatment and the dataset we present has measured several different types of predictors. Therefore, we believe that the analyses were justified and not publishing null findings of justified analyses could impede the search for knowledge about what role these new treatments could have in the IBS care. Our results suggest that simply looking at the level of GSA is not a reliable predictor. Furthermore, the conception that psychological treatments for IBS are best suited for those patients who present with a psychiatric disorder still prevails in reviews in the medical journals. We believe that is important to summarize the very weak support for this assumption and also show that it does not hold for the participants in our previous study.

COMMENT
5. In the conclusion the authors state that:
This is information of high clinical relevance as it supports the use of ICBT for a wide range of IBS patients.
I think this is an overstatement, also given point 6.

RESPONSE
We agree and have removed the sentence.

COMMENT
6. The authors did not write a review article but nevertheless reference 78 articles. I think this is too much for an original research article.

RESPONSE
We have removed more than 20 references.

Minor Essential Revisions

COMMENT
1. The data was collected in a previously published RCT. Please add the Trial Register number in the method sections so readers can quickly assess the aim and methods as originally formulated.

RESPONSE
We have added the Trial Register number to the abstract and methods section.

COMMENT
2. In the ‘Participants’ section: it is not clear why only 93% of the original study subjects were included.

RESPONSE
Because 6 of 85 participants in the original trial withdrew from the study before the post-treatment assessment, only 79 participants (93%) provided data that were usable in the prediction analyses. We have now clarified this.
COMMENT
3. Have the paper read by a native English speaker. The paper is not always easy to read.

Discretionary Revisions

RESPONSE
We have done so.

COMMENT
1. Please add line numbers when submitting an article, this makes it easier for a reviewer to point to a phrase that is not clear.

RESPONSE
We have added line numbers

COMMENT
2. The ‘Introduction’ heading is missing.

RESPONSE
We have added the heading.

Once again, we thank the Editor and the Reviewers for all the helpful comments.