Reviewer’s report

Title: Delivering internet-based exposure treatment for irritable bowel syndrome in a clinical setting: a randomized controlled trial.

Version: 1 Date: 7 March 2011

Reviewer: Yanda van Rood

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Major Compulsory Revisions

1. The authors state: "Our aim was to investigate the feasibility and effectiveness of ICBT within regular clinical practice." However, only data on the effectiveness of ICBT are presented. Since, ICBT has already been shown to be more effective for IBS than waiting list, data on the feasibility (and cost effectiveness) of ICBT would be of more interest.

2. Abstract. An abstract is missing.

3. Background. Page 2 "Recent studies that have included extensive self-help material combined with qualified therapist contact through telephone [13], the internet [14], or a reduced number of sessions [15] have demonstrated effects at par with face-to-face treatments." Please include references demonstrating that these interventions are as effective as face-to-face treatments.

4. "This study is reported in accordance with the CONSORT statement for nonpharmacological trials [20]." However, there is no mention of trial registration. Please include the registration number if the trial has been registered.

5. Exclusion criteria. The reasons for including exclusion criteria g and k need to be explicated. Specifically, the authors should explain what makes patients highly unsuitable for ICBT other than not having access to internet, and not reading or write Swedish. In total 7 patients were not suitable for ICBT, i.e. 5% this needs explanation.

6. By excluding all patients with severe diarrhea, the IBS patient group is not any more representative for IBS patients in general. Patients type of IBS, diarrhea, constipation or mixed according to the ROME III criteria should be described in table 1. In the discussion this limitation should be described.

7. The authors violate their own inclusion criteria by including 2 patients who first visited the clinic outside the specified period. These patients should not have been included.

8. Please explain how 5 patients could be unreachable if they visited the clinic in the specified period. If patients were phoned after their first visit this should be described in the recruitment procedure.
9. The following sentence is not clear. "GSA is defined as "the cognitive, affective, and behavioral response stemming from fear of gastrointestinal sensations, symptoms, and the context in which these visceral sensations and symptoms occur" [21] and is proposed to be a maintaining and exacerbating factor in IBS." GSA is already anxiety, i.e. an affect. The cognitive, affective and behavioral response are part of the fear response. They do not stem from it.

10. "Dysfunctional behavioral responses to IBS, such as excessive symptom controlling or avoidance behaviors, can also increase the awareness of symptoms and lead to a decreased quality of life, which further worsens the symptoms [22, 24]." Selective attention, anxiety, muscle tension all can increase or maintain symptoms directly. Please explain how a decrease in quality of life might worsen the symptoms.

11. Symptom reduction and increase of quality of life are presented as primary goals. The authors might want to describe the increase of quality of life in line with the outcome measures as a secondary goal, i.e. if symptoms are reduced the quality of life will increase.

"In the long run, acceptance of symptoms instead of control or avoidance behaviors will increase quality of life. Together with the change in GSA this will lead to a decreased burden of IBS symptoms." The primary goal of treatment now seems to be an increase in quality of life, whereas before symptom reduction was the primary aim of treatment. The authors might want to check the text for consistency on this matter.

12. "Exposure can be defined as exposing oneself to an aversive stimulus and simultaneously engaging in a behavior that is inconsistent with the emotion that the stimulus elicits. This serves to reduce the strength of the emotional reaction when exposed to the stimulus in the future [25]." The authors give a unusual definition of exposure. What they describe is usually known as systematic desensitization or counterconditioning. In both techniques an aversive stimulus is associated with a new neutral or positive stimulus. A stimulus which elicits an emotion which is not consistent with the emotion elicited by the aversive stimulus. Mindful acceptance is, as is the relaxation response, not compatible with anxiety and can be used to change the acquired negative valence of the stimulus (i.e. gastrointestinal sensations and symptoms). Exposure with or without response prevention can be used to falsify catastrophic expectations or to extinguish the fear response, depending on the working mechanisms that are supposed to play a role. This form of exposure is indeed an integral part of most CBT treatments. Counterconditioning techniques are much less often explicitly mentioned.

13. It is not clear how mindfulness exercises are used in the exposure exercises and what rationale is given to patients to motivate them for treatment. A table in which the content of the sessions is presented would be most welcome.

14. Exposure can be very effective, however in clinical practice many patients do not start treatment or drop out during treatment because they find the exercises
to challenging. This might be brought forward in the discussion.
Exposure exercises need to be tailored to the patient. How was this done?
Where there individual goals set and if so, how many patients reached all their therapeutic goals.

15. Patients were encouraged to send at least one message per week. The intensity of the contact, i.e. how active the patient was in treatment might explain the observed effect. In the results section the authors might want to describe how many contacts the patients on average did seek per week as well as the range. This is at least as interesting as the amount of therapist time spent per week. Here the range is of interest too.

16. Treatment consists of different steps and patients only could go to a next step if they finished the last one. This is an important aspect of the treatment and the authors might want to consider to present the statistics (average and range). The same holds for the number of steps in the treatment and the number of patients that finished all treatment steps.

17. As the authors point out in their discussion a major limitation of the study is the use of a waiting list control condition. To control for the placebo effect which is known to be large in IBS patients the control condition needs to include an activity that is as credible to the patient as the activity in the experimental condition and the time spend on the activity must me comparable to control for attention. Not only do they not control for the placebo effect, but waiting for treatment when one expects to be treated (as is the case in normal clinical care) may have a negative effect on symptom severity. Indeed patients in the waiting list condition deteriorate on the MADRS-S, GSRS-IBS and IBS-QOL. It can not be ruled out that the group by time effect is significant for GSRS-IBS and IBS-QOL as a result of a worsening of symptoms of patients in the waiting list condition. The authors might want to include this aspect in the discussion.

18. A psychiatric assessment was conducted before randomization. Please explain at what time, by whom and for what reason in the recruitment procedure the psychiatric assessment took place. If it was used to check on exclusion criteria this should be described in the paragraphs on exclusion and inclusion. If the psychiatric assessment was carried out with the aim to collect data, e.g. psychiatric diagnosis, than the results should also be presented.

19. 2 patients were included who were seen outside the time frame reserved for inclusion. The data have to be analyzed again with 131 patients.

20. "Since IBS symptoms are known to vary considerably over time [36], the mean score of four weekly assessments of GSRS-IBS was used to get reliable estimates of the participants’ symptom levels at each assessment point." If patients filled in the GSRS-IBS at the first visit and every week for three weeks after that before they started ICBT this might be stated in the method section.

21. The IBS-QOL and the SDS both assess symptom induced disability / interference. Why are both included in the study? Why did the authors include an
instrument for depressive symptoms. Generally IBS patients are not depressive. The scores indicate that most patients indeed were not depressed. Another point of consideration is that the correlation between MADRS-S and physicians' MADRS is moderate (r = 0.54, p < 0.001) indicating that MADRS-S is complementary rather than redundant to the MADRS (ref: The self-reported Montgomery-Asberg Depression Rating Scale is a useful evaluative tool in Major Depressive Disorder. Fantino B, Moore N. BMC Psychiatry. 2009 May 27;9:26.). So it can not be used for the diagnosis of depressive disorder. Since no specific hypothesis was formulated concerning the outcome on the MADRS-S and taking into account the above point, the authors might want to consider to eliminate the data on the MADRS.

22. Follow-up: the scores on the MADRS-S increased during follow-up. Please present the p-values and other relevant statistics for all follow-up measurements.

23. In the first sentence of the discussion an other aspect of the study not explicitly mentioned before is highlighted, i.e. that before it was an self-selected sample and now it is a consecutively recruited sample. If this is the most important difference with the study done before it should be mentioned in the background paragraph. How the clinical usefulness might be evaluated has not been defined. This should be done and the results need to be reported.

24. "Clinical guidelines recommend that IBS patients should be referred to psychological treatments primarily if they show depressive symptoms, anxiety, or poor coping strategies and wish to undergo such a treatment [7, 48]. However, in this study we deliberately did not let the gastroenterologists select the patients that they deemed would benefit from a psychological treatment." These points are unrelated. It is unlikely that the selection criteria used by gastroenterologists are the same as the mentioned criteria (depressive symptoms, anxiety, or poor coping strategies and wish to undergo such a treatment).

25. On page 16 the authors give as a possible explanation for the lower effect sizes than they observed in their earlier study the supposedly lower motivation of these patients. The authors might want to objectify this by reporting the number of patients that completed all steps of the treatment.

26. The discussion might be extended by including the negative effect of being on a waiting list, the non-representativeness of the IBS patients, and the unacceptability of exposure exercises as another possible explanation for the high number of drop outs.

27. The title in it self is contradictory, suggesting that one can have a RCT in clinical practice (without changing clinical practice).

28. Conclusions. "These results might indicate that a larger proportion of IBS patients than is usually presumed might benefit from psychological treatment." On what grounds do the authors draw this conclusion? If this is indeed a conclusion data supporting this should be presented and discussed in discussion section.
Minor Essential Revisions

1. Page 4. Power calculation. The authors state: "We aimed at having a power of at 85% to detect a standardized mean difference between the active treatment and waiting list of 0.8, which gave a sample of at least 60 participants." Words seem to be missing; i.e. the outcome measures used to calculate the necessary number of patients.

2. Page 4. Inclusion criteria. Criterion c precedes b and the order might be changed accordingly.

3. Page 5 first sentences breaks between 'in' and 'Stockholm'

Page 5. "However, if the gastroenterologists judged ……. Etc" is one of the exclusion criteria and has been explained already. Sentence may be deleted.

4. Page 5. "To ensure that the effects of this basic IBS management ….. , we applied at least a one-month "washout" period ...." The word “washout” is confusing because it refers to medication use. Please clearly explain what was done.

5. Page 6. "However, for 16 eligible patients……." This sentence should follow after the following sentence ...".. period, and 131 of these were eligible according to their medical record."

6. Page 7. "GSA is defined as “the cognitive, affective, and behavioral response stemming from fear of gastrointestinal sensations, [and] symptoms, and the context in which these visceral sensations and symptoms occur” [21] and is proposed to be a maintaining and exacerbating factor in IBS." Delete punctuation mark and insert and.

7. Page 8. "In ICBT the patients learn about the treatment interventions by reading self-help texts that contain both educational material and instructions on how to perform the exercises that constitute the treatment. The general principle is that the treatment should reflect face-to-face therapy in terms of content, but using an online therapist to guide the participants through the course of the treatment. The format allows for large patient volumes to be treated and an increasing number of controlled studies indicate that for common psychiatric disorders ICBT is as effective as face-to-face delivered treatment [30]." The authors might want to consider to place this paragraph in the introduction, page 2 last sentence.

8. Page 10. "The waiting list completed assessments immediately after and 12 months after having been crossed over to and finishing treatment and a psychiatric assessment of all patients was conducted before the randomization and at 12-month follow-up." This sentence is not clear. Suggestion: The waiting list completed assessments immediately after and 12 months after having been crossed over to and finishing treatment. A psychiatric assessment of all patients was conducted before the randomization and at 12-month follow-up.
9. Page 13. "Of the 30 patients in the ICBT group, 20 (67%) completed the 12-month follow-up assessment. One of these patients had not completed the post-treatment assessment and one patient completed all follow-up questionnaires but GSRS-IBS. Thus 24 patients were included in the analyses of change between post-treatment and follow-up, with 5 patients having missing data." Confusing sentence. Suggestion: One of the patients who completed the 12-month follow-up assessment did not complete the post-treatment assessment, but was included in the analysis of change between post-treatment and follow-up resulting in 24 patients in this analysis. Of these 24 patients 5 had missing data.

10. "…. and one patient completed all follow-up questionnaires but GSRS-IBS." No information is given on the other patients with missing data. The authors might want to consider to leave this information out here.

11. Page 16 "….. with a few exceptions relating primarily to age [include: of onset], presence of inflammatory bowel disease, severe diarrhea, poor language skills, and patient willingness." Patient willingness however was not defined as a inclusion criterion.

12. Page 16 From ... "It has been difficult to empirically determine which patient characteristics ....[to the end of the paragraph]" might be placed after "Of 131 eligible patients 77 (59%) were included in the study. An inclusion rate of 59% stands in contrast to the estimated 25% of IBS patients that will benefit from a psychological treatment [48]."

13. According to the instructions to the authors, tables should not be submitted as figures but should be included in the main manuscript file.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

'I declare that I have no competing interests'