Author’s response to reviews

Title: Treatments for Irritable Bowel Syndrome: Patients’ Attitudes and Acceptability

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Author’s response to reviews: see over
Title: Treatments for Irritable Bowel Syndrome: Patients' Attitudes and Acceptability

Many thanks providing reviewers comments for the above manuscript. We are delighted that both reviewers felt that the material in the paper was original and informative. We have addressed each point made and attach a revised version of the manuscript. A summary of changes is provided underneath each point below.

We look forward to hearing from you regarding the publication of this paper

Yours sincerely
Dr Lesley Roberts and Dr Lynsey Harris

Reviewer 1:

MAJOR COMPULSORY REVISIONS
The Qualitative part of the survey is very interesting and informative. However, there seem to be many weaknesses that reduce enthusiasm over this part of the paper. Most importantly all qualitative analyses were undertaken by 1 of the authors possibly introducing considerable bias. Although this is acknowledged in the discussion section, time and cost limitations are not a valid reason for omitting essential steps to reduce bias.

We agree that the presentation of this aspect of the work may have caused concern. All data was reviewed by both researchers and we acknowledge that our description of the analysis in the limitations section was misleading. We have therefore rewritten this section to clarify that both researchers reviewed all data and moved the section to the methods as per your latter instruction. We have further expanded the limitations section to explain why we feel researcher bias has been minimised.

There appears to be considerable overlap between categories which may be a sign of bias:
1. Fear of side effects was mentioned under “Barriers to acceptance-internal factors” (e.g., skin allergies) as well as under “Dislike of treatment modality-dislike due to side effects”.

The data pointed to two distinct barriers – one being dislike due to side effects of therapy and the other being co-existing conditions such as eczema contra-indicating certain treatment modalities. We have therefore retained these as distinct categories but have clarified in the text that the first of these categories refers to other co-existing conditions.

2. Time commitment was mentioned under “barriers to acceptance-external
factors” and under “dislike treatment modality-reasons which relate to specific treatment methods”.

Time commitment was a barrier to multiple therapies, whilst it was the concept of personal commitment (much more broadly) that related to the specific therapy of yoga. We have adjusted the text in the section on specific treatment modalities to reflect that this theme related to personal commitment (e.g. quote relating to will and energy) and removed the quote referring to not bothering to continue as taken out of context we agree this is misleading and probably underpinned the reviewers comment.

3. Discomfort/awkwardness of applying medications is mentioned in Figure 2 (2l&m; Dislike of treatment) as well as Figure 4 (4b, Barriers to acceptance). As per point 1 above. These concepts related to different situations patients found themselves in. The former theme related to general discomfort and awkwardness e.g. feelings of embarrassment and personal thresholds whilst the latter related to physical awkwardness of some modalities in patients with other health conditions or limited mobility. We have clarified the concepts in the text and included context to underpin the quote relating to physical awkwardness.

In addition, in the “dislike treatment-general dislike” category the text states that this is “more evident in reference to hypnotherapy, homeopathy, and suppositories”. But most examples in Figure 2 concern medications. Thank you for highlighting this – we have included additional quotes to support this statement.

Have authors noticed these discrepancies and how have inconsistencies in coding been handled? Thank you for pointing out apparent discrepancies – we hope that the additional clarification now provided confirms that these are not discrepancies in the data or thematic framework but lack of clarity in the written paper, which we hope we have now addressed.

I would highly recommend the authors look beyond concepts and themes and think about what this may mean. What is the theory? For example, how do these results fit into the more traditional and prevalent view that distinguishes body from mind? Whereas most CAM is based in integrative medicine that accepts mind/body interactions? For excellent reviews on these topics in IBS see the writings by Dr Drossman and colleagues (e.g., in the Textbook of Gastroenterology, 2003). We agree entirely that a different analytical approach may provide additional evidence. As a questionnaire study we intended to explore the data thematically and feel that a more theoretical analysis would have required a different approach to data collection. Data obtained in this way lacks a degree of depth and does not allow broader exploration of emerging themes. We do agree that such a study would add to the evidence base and have therefore included this as a recommendation at the end of the paper.

MINOR ESSENTIAL REVISIONS
Some references are not included in the text but rather it states “Error! Bookmark not defined”. This has now been corrected.

Figure 1 shows only empty boxes. We are not sure why this figure did not transmit. We have removed colour from the figure in case this was masking text. We have provided the word document as previously and also submit a pdf to prevent the loss of information during upload. We are happy to provide this in any form the editorial team require.

P4. Please state which country the Department of Health document is from. We have clarified in the text that this relates to the UK.

P6. Can the authors give N of how many of the 8646 patients responded to the postal questionnaire (include all patients not only the IBS patients) This is now included in the text.

P6. Can authors specify how many patients were excluded for each reason? This information has now been added.

P8. Please specify exact age groups and race/ethnic groups used for analyses. Categorisation of age, education and employment has now been included in the text. Ethnicity was not considered in analyses.

P8. Please specify who undertook the identification of themes in this section so this is clear before people read the result section. Please refer to first point above – this information is now included in the methods section in a clearer form.

P9. Please test the differences between treatment acceptability and report p-values. P values have now been included in the table comparing acceptability for each treatment modality compared to tablets (the most acceptable form of treatment).

p.9 For age groups please report which post hoc tests were used comparing the groups and which groups were significantly and not significantly different. In all cases comparisons reported are between two groups. This is now clarified in the text.

P9/10 Please show data and p-values for comparing conventional vs CAM vs lifestyle on age. These have now been included.

In the discussion the authors draw conclusions on data that was not presented in the result section. For example, p.17 “There was consensus that time and financial costs were central to acceptability”. Nowhere in the results section is
presented how often certain concepts or themes appeared among individuals. We agree that our choice of words here implies some frequency count. We have now amended this sentence to read ‘For some individuals time and financial cost…’

Or p.18 “Results from this study showed that patients were more inclined to accept any of the treatments if recommended by a physician”. Again this data is not presented in the results section. The results section does state that for all treatments acceptability was greatest when recommended by a clinician. In the table we have reported acceptability under any condition as a better reflection of the underlying acceptability of therapeutic options, but do confirm this point in the text.

Discretionary revisions
In the Quantitative part of the survey treatment preferences have been associated with age and gender. Although this is informative, it would be more interesting to show analyses that look at the association with clinical variables such as duration of disease, severity of symptoms and treatment modalities these patients have used in the past. If the authors have this data this I would strongly recommend to report these analyses.

We agree that these additional analyses may further enhance the information presented in the paper. Whilst some data is available on symptom severity it relates to severity at one point in time – given the fluctuating nature of IBS we feel that use of this data to explore associations with therapeutic choices would be misleading.

P5. “However, many patients still seem adverse to alternative management strategies”. Do the authors have a reference to back up this statement? If not can they explain if this statement comes from their own clinical experience or perhaps is derived out of data that show low usage of hypnotherapy/relaxation strategies (see BMC Complement Altern Med. 2008 Jul 24;8:46)? If the latter is true a lot of other factors play a role beside patient’s adversity to CAM. For example, limited accessibility to CAM is a huge issue as well as physician’s reluctance to suggest CAM as a treatment option.

This statement is evidence based and has now been referenced.
Reviewer 2:

The questionnaire is not fully described or attached to the manuscript, this could be a limit for the full comprehension of the reader. After review of the outcome measures section we feel the questionnaire is well described with only a lack of clarity relating to provision of free text responses. We have therefore addressed this in the text. Whilst we do not believe the questionnaire itself adds to the information provided we would be happy to provide this at the editors request.

Inclusion criteria are not well defined and selection bias could be a problem. Of those who responded, it is quite unclear the total number of contacts, if they were doctors or patients. Only 40% responded and the majority were females. Although IBS preferably affects females this could have influenced the results. Inclusion was limited to individuals who participated in the previous study which is referenced. We do not see that selection bias is a potential problem as all individuals who were alive and contactable were sent the questionnaire. We do agree that a low response rate and therefore responder bias may be a problem. Given that we have provided comment on the demographic similarity of responders and non-responders and have drawn attention to this in the limitations section we feel that this issue has been adequately addressed.

Among the possible therapies herbal remedies have not been mentioned, but they are quite commonly used as beverages. Homeopathy can include the use of tablets, how has it been handled? Why didn’t consider the herbal medicines? The aim of the study was to explore acceptability of broadly defined modalities of treatment and tried to include examples which were largely heterogenous in nature. The study was conducted in the UK where herbal medicines are perhaps less widely used than in other locations and this is why this was not selected as an example. We accept that homeopathic treatment often utilises ‘tablets’ although again given the UK population we felt that the term tablet was when used in the questionnaire more locally appropriate than other terms like medication or drug therapy. We have clarified in the text for non-UK audiences that this term is used to refer to a drug therapy rather than alternative form of treatment.

Why the significant levels have been set at 0.001? Significance levels were not set at 0.001 but at 0.01 to reflect multiple testing which occurred in the exploratory analyses.

Considering different pattern of patients could be of interest: did the Authors consider patients having prevalent diarrhea or constipation? What about disease duration? And what about disease activity? Please refer to response to reviewer 1’s comment about inclusion of symptom severity. We agree that in many research areas the importance of IBS sub-types is critical to interpretation of findings. However given that the focus of this study was on acceptability of broad modalities of treatment without reference to the symptoms they may control we do not feel that this would add to the current paper.
Ageing is a problem in our society: however, the definition of youngers for all patients under 60ys is somewhat grossly. Considering at least 3 groups could be a good compromise.

We agree that this dichotomisation of the data is a gross over-simplification. This was an artefact of a relatively small sample size and the relatively ‘older’ (mean age 55.9) make-up of the sample. Such a simplification was essential to facilitate analyses but we acknowledge the reviewers concern and have therefore included this as a study limitation.

Qualitative analysis: it should be interesting to know how many patients declared treatment unacceptability and the possible correlation with age or other factors. Treatment acceptability is described in table 2 – this has been expanded to include confidence intervals around proportions to enable the reader to determine difference in acceptability of different modalities. We agree that for individual therapies exploration of correlations with age and other factors would be interesting but small numbers declaring unacceptability of some options prohibited such analyses.

If the patient dislikes tablets, does it depend on type of drug?
Again a very interesting question but one we did not aim to explore within this study.

Why did you include patients with chronic pain and not patients with other type of gastrointestinal diseases?
The paper focuses on IBS and all patients with other gastro-intestinal disease e.g. colitis were therefore excluded to prevent contamination of findings.

Foot of page 16: female respondents were 73% not 80%
Thank you for highlighting this error which has been corrected.

Any information about costs and efficacy?
The aim of the paper is purely to comment on acceptability of broadly defined treatment modalities – we therefore do not attempt to provide information about costs or efficacy as this is beyond the remit of the study.

Different studies demonstrated that CAM users do not inform their physicians, and many of them do not care about physicians’ opinion!
A very valid point although in this study it was demonstrated that in our general population sample physician recommendation was associated with enhanced acceptability.

Not able to read figure 1
Response as per identical comment from reviewer 1

Below you will find more specific comments.
1) page 5, lines 7-8; this assumption should be the result of a previous study, cite
This is an assumption rather than being an evidenced based statement. We have prefaced the assumption with ‘It is possible’ to reflect lack of evidence.

2) page 5, lines 19-20; this assumption should be the result of a previous study, cite it and eventually the percentage of patients
As per response to reviewer 1’s comment this has now been referenced.

3) page 6, lines 11-12; this assumption should be the result of a previous study, cite it
This is now referenced.

4) page 6, line 13; what’s the total amount of patients indexed in the registers used to randomize participants in the study?
This study comprises follow-up of an existing research cohort. We have not described the original study in full as this is in press and referenced. We feel that this information is superfluous to the current paper and have not expanded further on the 2001 prevalence study in this text.

5) Page 6, line 14; how many patients responded?
The absolute number of responders has now been included.

6) Page 6, lines 15-16; how many patients had a Rome II diagnosis and how many two or more Rome II symptoms?
These numbers have also been included.

7) Page 6, lines 19-20; in what cases contact was deemed inappropriate?
We have expanded this section to clarify the numbers deceased and uncontactable. We are unable to provide a full breakdown of the reasons GPs excluded patients as this was entirely due to GP discretion. In many cases this would be due to severe mental illness, recent bereavement etc but to protect patient confidentiality and under the terms of our ethical approval GPs did not provide these data.

8) Page 6, lines 20-21; wasn’t possible to use the contact details used in the previous study?
The previous study was conducted in 2000/2001 – this group reflects those who have transferred GP during the intervening period. Without knowledge of the current GP we could not confirm the patient’s status. Whilst a few may have transferred GP without relocating we were obliged to confirm status of the patient prior to recontact. We agree that our wording ‘with no contact details available’ is confusing and we have therefore corrected this to acknowledge that we could not confirm the status of the patient.

9) Page 6, last line; it could be better to inform the reader that it has been used a questionnaire to collect data
We have rephrased this line

10) Page 7, lines 3-4; are you sure it is not necessary to calculate the sample size.
The study was exploratory in nature and largely qualitative. Given these factors and the fact that we were limited to the size of the existing cohort from the 2001 study we did not feel a useful sample size calculation could be presented. Upon reflection we still feel this to be the case as the primary aims of the study are not comparative or related to accurate estimate of prevalence etc.

11) Page 7, description of the intervention; explain if the questionnaire is anonymous or not and if information about the purpose of the study have been given to participants and if an informed consent form have been signed by patients or an authorization of using personal data have been given
Sections addressing these queries have now been added to the intervention section.

12) Page 9, description of results on demographic data; it could be better to give all the results, please present all the collected data in the two groups of patients (respondents and not respondents)
Details of non-responders have now been included in Table 1

13) Page 9, line 11; change the order of result according to percentage (from the highest to the lowest)
We have changed the order as per your recommendation.

14) Page 9, line 15; why do you put the cut off at 60 years? Why don’t you use the media or the median age?
We agree that dichotomisation of groups should have been undertaken using the median age value. We have re-run all age analyses using the median age of 55 years as the categorisation point.

15) Chapter results; did some patients accepted all (or none) treatments presented in the questionnaire? Do they have been excluded from the subsequent analysis? The age of respondent patients seems very high, it could be better to present different ages’ frequency
All participants were included for all analyses as proportions are presented for each modality independently. We have included the numbers accepting all treatment options and no options in the text. The issue of sub-diving the cohort further by age bands is addressed previously.

16) Page 10, line 11; explain with examples “general barriers”
We have clarified the meaning of this term with examples

17) Page 16, lines 11-12: this assumption should be the result of a previous study, cite it
This reference is now included.

18) 13-15; an important bias could be the impossibility to know if the accepted treatment have been previously used or not by the patient: only in the case the patient accept a treatment that he never used before, the option could be
described as hypothetical
We agree the use of the term ‘hypothetical’ is misleading here. We have replaced this with ‘potentially available’ to better reflect the point we were trying to make about removal of cost barriers.

19) Page 16, last but one line; this assumption should be the result of a previous study, cite it
This reference is now included.