PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A mixed methods feasibility study to evaluate the use of low-intensity, nurse delivered Cognitive Behavioural Therapy for the treatment of Irritable Bowel Syndrome: Study Protocol.
AUTHORS	Dainty, Andrew; Fox, Mark; Lewis, Nina; Hunt, Melissa; Holtham, Elizabeth; Timmons, Stephen; Kinsella, Philip; Wragg, Andrew; Callaghan, Patrick

VERSION 1 - REVIEW

REVIEWER	Sayed Abbas Haghayegh Isfahan Univerrsiry of Medical Sciences
REVIEW RETURNED	20-Apr-2014

- The reviewer completed the checklist but made no further comments.

REVIEWER	David Ekers Durham University
REVIEW RETURNED	25-Apr-2014

GENERAL COMMENTS	Study aim is rather confusing and could be more clearly articulated will the study objective be to assess the costs of treatment or estimate? Methods In general I felt the methods section read more like an essay rather than a research protocol. Some of the discussion areas would need to be excluded or moved to the introduction area. The methods (study design) should be a factual description of the methods to be used and brief rationale for choices made (for example lines 12-13 page 5 and the intervention). Recruitment processes are not clearly defined and are mixed in with sample size. Whilst the choice of a nurse to deliver the intervention is excellent and very interesting little description is made of this. It would appear a central factor in the study, why a nurse, rationale for choices and training. Is this replicable which I would presume is a key issue in feasibility studies. The nurse received substantial training. It may help if there are separate sections on interventions and therapists. Outcomes This section needs more structure, measures

	There is no mention of how cost data will be collected although in objectives. The numbers in each group seems small to be used to estimate sample size. The use of LOCF is mentioned which is a rather unpopular approach to missing data. I wonder if a statistician has been involved in this section and if not should one be involved. What are the criteria to be used to define the success of feasibility? In general I think this is an important study and will produce very interesting data on feasibility. In conducting the review of the study protocol I have tried to avoid too much discussion over the trial methods as this is down to the study team to agree. I do feel however as it is presented it does not provide a sufficient clarity on the process to be accepted. It requires more structure, attention to a clear and concise description of the process. There does appear to be some overlap between feasibility and pilot study objectives within the protocol.

REVIEWER	Ching-Liang Lu Div. Gastroenterology Taipei Veterans General Hospital, Taipei, Taiwan Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan
REVIEW RETURNED	29-Apr-2014

GENERAL COMMENTS	This protocol aimed to compare the efficacy of low intensity (nursing staff- administered) and high intensity (psychotherapeutics administered) CBT on IBS symptoms. Two other treatment arms with self-help treatment workbooks and treatment as usual will be also included. A total of 60 IBS patients will be enrolled. Here is my comment about this protocol. Major points 1. Though CBT has been demonstrated as an effective modality in treating of IBS symptoms, wide application of CBT therapy is limited by a lack of trained psychotherapist and associated time and costs invested in specialist psychological therapy. If the authors can demonstrated a non-inferior efficacy of low intensity nursing staff administered CBT when compared with high intensity ones, it would provide an important basis for the future treatment arrangement in IBS patients. 2. Will the patients be blinded to low or high intensity CBT? The study results may be biased if the IBS patients were not blinded to the therapist, i.e. nursing staffs vs. psychotherapeutics. As is well known, IBS patients are often co-existed with psychological comorbidities and the placebo effect in the IBS treatment is extremely huge. It is very likely that that IBS patients will take it for granted that the therapeutic effect from nurse-administered low intensity CBT may be less effective than that from the high intensity ones, especially the protocols are different between low intensity and high intensity CBT. Blinding between the low and high intensity CBT treatment is necessary.

	3. Quality control of the CBT is important. The authors should let us know how to judge the nurses who will administer the low intensity CBT are capable to perform the CBT therapy. 4. The primary and other therapeutic endpoints (such as, complete spontaneous bowel movement per week, Bristol stool form scale, 11-point NRS-scale,……) should be clearly defined in the protocol. 5. What are the definition for responders and non-responders in this study? This should be clarified. Minor points: 1. Page 4, method and analysis: lines3 last two words: there are double 'of's. One of them should be deleted. 2. Page 6, line 2: What is 'second generation' psychological therapy? A more detailed explanation should be addressed. 3. Are the usual treatment allowed in the 3 other treatment groups? This point should be clarified. 4. Page 10, a downward arrow was missed in the 'Nurse delivered CBT'

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 Sayed Abbas Haghayegh
No author response required. Thank you for reviewing our protocol.

Reviewer: 2 David Ekers
Thank you for highlighting potential areas for the improvement of our manuscript which relate largely to a lack of clarity regarding the aims of the study and the study related processes, the outcome measures used and the quality of the statistical methods employed. We have carefully considered your comments and have amended the aims and objectives. Some text has been excluded or revised to improve accuracy and clarity as recommended. However, it is acknowledged that this study is complex in nature and may require an extensive rationale for the use of the Mixed Methods design in order to satisfy readers of the scientific quality of this work. The nursing intervention sections and outcome measure descriptions have been amended. Whilst we acknowledge cost effectiveness as an important issue regarding the delivery of these interventions, a limitation to this study is that cost data will not be collected during feasibility, this has been made clear within the study protocol. As this is a protocol that is in the early stages of being implemented, the statistical methods anticipated will be subject to further review with our appointed trial statistician when the time comes to analyse the data. The issue of LOCF is subject to critical commentary and debate in the literature and there is, as yet, no robust consensus on the issue. At present, we remain persuaded that this method will satisfy the requirements of the proposed study. Nevertheless, we will keep this issue under review.

Reviewer: 3 Ching-Liang Lu
We note concerns regarding the lack of blinding participants to their allocated mode of treatment, particularly in relation to High-Intensity or Low-Intensity CBT. We had considered these issues during the design of our study, but feel that our ethical obligations to participants require us to be explicit in relation to what is involved in taking part in the study. We therefore feel that we were unable to blind patients to the intensity of the various treatment approaches as these factors would help patients make an informed decision regarding their participation in our study. We also acknowledge that some participants may prefer the low-intensity or self-help formats which may be more suitable for people

with work or family commitments. We hope to observe some of these phenomena within the qualitative study data. We agree that the high level of placebo response seen in patients with IBS is worth noting, and may potentially be a cofounding factor in this regard. This is a feasibility study and should this issue be apparent in the study, we will consider how to address it in a future stage three trial.

We have tried to demonstrate a level of competence has been acquired by our nurse therapist by linking the training of the nurse to the nationally recognised CBT curriculum used for the education of Psychological Wellbeing Practitioners in the UK. Indeed, one of our concerns regarding other therapeutic trials for IBS is that training mechanisms for professionals delivering such interventions are often unclear. We hope our training mechanism has ensured that our training will be easily replicable in future trials. We have further clarified concerns regarding the definition of treatment responders, outcome measures and have corrected the minor typographical errors as suggested.

VERSION 2 – REVIEW

REVIEWER	David Ekers Durham University UK
REVIEW RETURNED	28-May-2014

GENERAL COMMENTS	the authors have responded to my issues. I wish them well with the study and look forward to reading their findings.

REVIEWER	Ching-Liang Lu Institute of Brain Science National Yang-Ming Univeristy Div. Gastroenterology Taipei Veterans General Hospital Taipei, Taiwan
REVIEW RETURNED	02-Jun-2014

GENERAL COMMENTS	The authors had answered my questions and critics clearly. I got no more comment.