PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A primary care Symptoms Clinic for patients with medically unexplained symptoms: pilot randomised trial
AUTHORS	Christopher Burton, David Weller, Wendy Marsden , Allison Worth and Michael Sharpe

VERSION 1 - REVIEW

REVIEWER	Graham Dunn Professor of Biomedical Statistics University of Manchester UK
REVIEW RETURNED	24/11/2011

The reviewer completed the checklist but made no further comments.

REVIEWER	Henriette E. van der Horst, MD, PhD. Head of Department of General Practice, VU medical centre, Amsterdam, the Netherlands. COI I'm currently involved in research into MUS, studying the effectiveness of a mental health care based symptoms clinic in the Netherlands
REVIEW RETURNED	07/12/2011

THE STUDY	In the abstract, and under the heading article focus, the authors state that their fourth aim is to inform power calculations. At the end of the introduction paragraph they state they want to have a preliminary estimation of the treatment effects. Although these two matters are related, they are not exactly the same.The authors report on a pilot study, designed to shed light on some important aspects, such as feasibility, recruitment methods and drop out rate, acceptability, before embarking on a full-blown trial. The items of your review form are not in all aspects compatible with such a manuscript. So, I have some trouble with completing the list, for example the items on statistical methods.
GENERAL COMMENTS	As the authors want to report on the recruitment strategies, I would expect some elaboration of their strategy: for instance are they confident that they found a representative sample? And ow did they check that. And why are people with musculoskeletal MUS less appropriate for the intervention? How much time does it take to perform the search, and especially doctors time in checking the lists? Furthermore, they briefly give some information on possible treatment effects, which they assume to be clinically relevant, based of an estimated effect size of 0.5. However, as a clinician I would like

	some elaboration on the clinical relevance of the estimated treatment effects. In the discussion paragraph, they give some information on the merits of the intervention, however, that is not the focus of the article. I would prefer that they stick to their study aims in the discussion. Comparison to other studies is perhaps not an appropriate paragraph for a report of a pilot study, focussing on feasibility, acceptability. A comparison with other recruitment strategies and acceptability of other MUS interventions would be more appropriate.

REVIEWER	Richard Byng Clinical Senior Lecturer Peninsula College of Medicine and Dentistry, University of Plymouth
REVIEW RETURNED	07/12/2011

THE STUDY	Research question is in form of objectives about feasibility; these are well articulated. I do not think that framing these as a research question would add benefit. The outcomes in terms of feasibility are listed as sub-domains but not with apriori targets. eg regarding identification and recruitment.
RESULTS & CONCLUSIONS	The interpretation is well argued but as discussed in more detail, there is further complementary work required before the intervention is ready to be submitted to a full trial.
GENERAL COMMENTS	General Comments: This paper is timely, addresses an important question and is a significant component in the preparation for a randomised control trial. The paper is well written and clear and I would suggest there are two important additions to be made to the discussion section. These relate to other requirements in preparation for a trial of such a symptoms clinic. Firstly, I would suggest that significantly more work is required to develop, understand and 'protocolise' the intervention. This might take the form of qualitative interviews with practitioners and patients receiving the intervention. The weakness of having one GP with a special interest developing the intervention has been highlighted. However the appropriate response to this has not and could take the form of in depth analysis of processes within the consultation learning from the previous series of papers by Dowrick et al, which are referenced and comparing what has been carried out in the symptoms clinic with examples of best practice from elsewhere. These elements of care would then need to be 'protocolised' and tried out with other practitioners with further evaluation, identifying both whether the translation to other practitioners has been successful and also the identification of other potentially beneficial elements introduced by other skilled practitioners. The use of techniques such as tape assisted recall could be powerful as a way of identifying key components of the intervention which are found useful or less useful by patients within the clinic. Secondly, the range of outcomes tested is possibly not as complete as it could be. There is little evidence as to which outcome should be chosen within such studies. Function is not well measured, nor is quality of life and there is no cost component currently. A significant amount of work may need to be carried out both to allow patients and practitioners to decide on the outcome set appropriate for such a study and potentially a primary outcome measure in a definitive trial, although the latter may not be necessary in an exploratory trial

	which may be the next step for this study. A few further detailed comments are made below: Page 7 – line 52: Exclusion of having a serious illness is pragmatic, but given the possibility of overlay may not be appropriate. Page 9 – Lines 189-20: Base line assessment only should be listed as weakness in discussion. Page 12: The exclusion of more than 12% of potentially eligible patients because of self-harm is worthy of note in the discussion and it is arguable as to whether this is appropriate considering the potential benefit. Page 12 – Line 50: Numbers would be appropriate rather than the word 'appeared'. Page 13 – Line 27: It is not clear how the estimations were made. Page 14 - Line 7: Numbers would be useful instead of a few.

VERSION 1 – AUTHOR RESPONSE

Thank you for the considered and insightful responses of the reviewers. We have addressed the points they raise as follows:

Reviewer: Henriette E. van der Horst, MD, PhD.

1. In the abstract, and under the heading article focus, the authors state that their fourth aim is to inform power calculations. At the end of the introduction paragraph they state they want to have a preliminary estimation of the treatment effects. Although these two matters are related, they are not exactly the same.

This is a fair comment and we have changed to "estimate potential treatment effects" in all three places for consistency

2. As the authors want to report on the recruitment strategies, I would expect some elaboration of their strategy: for instance are they confident that they found a representative sample? And how did they check that.

We have expanded the sentence in the discussion/strengths & limitations referring to our previous studies:

We found that the health related quality of life and prevalence of depression and anxiety in patients recruited into this pilot study were similar to those in our previous descriptive study of a similarly defined patient sample [4,5] . This suggests that the sampling method used in the trial achieved a representative sample .

3. And why are people with musculoskeletal MUS less appropriate for the intervention?

The section in results has been clarified and now reads as follows:
…when we used the criterion of three or more referrals without requiring any specific MUS syndrome, (search B) it identified three patients who on clinic assessment had localised joint pain as their main symptom. While these patients also reported other symptoms on the PHQ-14, it was the localised joint pain which had greatest effect on their functioning. As patients regarded addressing the joint pain (in one case surgically) as their top priority, the symptoms clinic model appeared less appropriate than for patients who were still seeking an explanation for their symptoms.

4. How much time does it take to perform the search, and especially doctors time in checking the lists?

We have added an additional paragraph to results / trial retention and acceptability..

Practices reported experiencing no major problems with the process for identifying or recruiting patients. The searches took less than 30 minutes; and the checking of the resulting patient lists was also quick and straightforward as patients were often well known to the doctors.

5. Furthermore, they briefly give some information on possible treatment effects, which they assume to be clinically relevant, based of an estimated effect size of 0.5. However, as a clinician I would like some elaboration on the clinical relevance of the estimated treatment effects.

This comment has been elaborated.:

Although we are not aware of studies assessing clinically important difference with these scales in a comparable population, a standardised effect size of 0.5 is generally found to represent a clinically meaningful difference [19]. We did not measure subsequent healthcare use in this short-term pilot study but regard this as an important outcome for future studies.

6. In the discussion paragraph, they give some information on the merits of the intervention, however, that is not the focus of the article. I would prefer that they stick to their study aims in the discussion. Comparison to other studies is perhaps not an appropriate paragraph for a report of a pilot study, focussing on feasibility, acceptability. A comparison with other recruitment strategies and acceptability of other MUS interventions would be more appropriate.

We accept this point and have amended the section in the discussion to “Comparison with other recruitment and intervention strategies” . The text has been changed as follows:

Previous studies of primary care interventions for patients with MUS have depended either on questionnaire sampling [9], GP identification and referral [8] or review of consultations by investigators to decide whether the patients symptoms were medically unexplained [10]. None of these methods identify patients with MUS and high healthcare use.. Only one trial has used systematic searching of clinical records; this was a lengthy process carried out by hand [18]. The recruitment strategy we used had the advantage of combining activity data from electronic records (referrals and diagnostic coding) with symptoms reporting on questionnaire.

And, in the next paragraph concerning the intervention, after describing how it differs from reattribution

Recent evidence suggests that patients often actively resist reattribution [22]. Even when they have anxiety and depression patients with MUS may see them as associated with rather than causal to their physical symptoms [23].

Reviewer: Richard Byng

7. The outcomes in terms of feasibility are listed as sub-domains but not with apriori targets. eg regarding identification and recruitment.

As this was a pilot study there were no specific targets in terms of numbers other than the stated aim to recruit approximately 30 patients (sample size and statistical analysis)

The interpretation is well argued but as discussed in more detail, there is further complementary work required before the intervention is ready to be submitted to a full trial.
Please see below

8. Firstly, I would suggest that significantly more work is required to develop, understand and 'protocolise' the intervention. This might take the form of qualitative interviews with practitioners and patients receiving the intervention. The weakness of having one GP with a special interest developing the intervention has been highlighted. However the appropriate response to this has not and could take the form of in depth analysis of processes within the consultation learning from the previous series of papers by Dowrick et al, which are referenced and comparing what has been carried out in the symptoms clinic with examples of best practice from elsewhere. These elements of care would then need to be 'protocolised' and tried out with other practitioners with further evaluation, identifying both whether the translation to other practitioners has been successful and also the identification of other potentially beneficial elements introduced by other skilled practitioners. The use of techniques such as tape assisted recall could be powerful as a way of identifying key components of the intervention which are found useful or less useful by patients within the clinic.

These are valuable comments regarding the way ahead which we have summarised in the discussion / implications for future research section as:

Further work is now needed to better understand patients' views of which aspects of the intervention were most helpful and to protocolise a final version of the intervention before undertaking definitive tests of its efficacy.

9. Secondly, the range of outcomes tested is possibly not as complete as it could be. There is little evidence as to which outcome should be chosen within such studies. Function is not well measured, nor is quality of life and there is no cost component currently. A significant amount of work may need to be carried out both to allow patients and practitioners to decide on the outcome set appropriate for such a study and potentially a primary outcome measure in a definitive trial, although the latter may not be necessary in an exploratory trial which may be the next step for this study.

We have added a sentence to the strengths and limitations section.

In a future trial other outcome measure could be considered. In particular a measure of health care use.

We report SF12 scores as a measure of health related quality of life. In a Cochrane review of interventions for MUS we are currently examining the use of the physical component summary in particular. While we agree with the reviewer's point we consider a detailed discussion of outcome measures beyond the scope of the discussion section here.

10. A few further detailed comments are made below:
Page 7 – line 52: Exclusion of having a serious illness is pragmatic, but given the possibility of overlay may not be appropriate.

We took a cautious view to recruitment for this pilot trial of a novel intervention, no amendment to text

Page 9 – Lines 189-20: Base line assessment only should be listed as weakness in discussion.

see point 9 above

Page 12: The exclusion of more than 12% of potentially eligible patients because of self-harm is worthy of note in the discussion and it is arguable as to whether this is appropriate considering the potential benefit.

Again, we took a cautious view to recruitment in keeping with standard research practice and excluded any patient judged to be at risk of self harm. However given the sample size we prefer not to make anything of this in the text.

Page 12 – Line 50: Numbers would be appropriate rather than the word ‘appeared’.

See response to question 3 (it was three)

Page 13 – Line 27: It is not clear how the estimations were made.

Apologies. We have inserted “from the records” – this is described and referenced [18] in the methods.

Page 14 - Line 7: Numbers would be useful instead of a few.

It was two, but this was from qualitative interviews and an unstructured question, so on balance we prefer to leave it imprecise.

VERSION 2 – REVIEW

REVIEWER	Richard Byng Senior Lecturer Institute of Health Services Research, Peninsula College of Medicine and Dentistry UK
REVIEW RETURNED	06/01/2012

The reviewer completed the checklist but made no further comments.