Author's response to reviews

Title: Effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing total hip replacement: feasibility study for a randomised controlled trial

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Manuscript: Effectiveness and cost-effectiveness of a group-based pain self-management intervention for patients undergoing total hip replacement: feasibility study for a randomised controlled trial (MS 1114703254101119)

We would like to thank the reviewers for their valuable comments and suggestions on this manuscript. Please find below responses to the reviewers’ comments and actions taken to address the issues raised. We have edited and amended the manuscript in line with all comments and all changes are highlighted using track changes. Page numbers used below refer to page numbers in the revised manuscript.

REVIEWER 1 (DAVID BEARD)

Reviewer comments
The paper reports the findings of a feasibility study to assess the effectiveness and cost effectiveness of pain self-management for hip replacement patients. This aim is laudable. This area is interesting and research is needed. As expected (for this capable group) the paper is well ordered and very nicely written. There are no issues with rigour or attention to appropriate detail. The report is neither verbose nor lacking in granularity. I am a firm believer that sort of work should be disseminated at some level to help the development of clinical trials in surgery. I would therefore support publication.

However, my one minor criticism is that the paper, as it stands, does not offer any unique methodological aspect or substantial insight into general feasibility for a trial of this type. What it does show (and very well) is that 1. feasibility studies for trials with humans are essential (we already know this – hence the conduct/completion of this feasibility trial - especially for this type of intervention). 2. the location of delivery for any self-help intervention is important (again intuitive), and 3. there is some disparity in acceptance between those that do not wish to engage and those taking part (i.e. those who found the course very useful). I suspect that this is also expected (and not really a new finding). Hence, the overall impact of the paper could be questioned by those with an agenda. It could be seen as merely getting something out of some rather distressing findings (i.e. that the intervention looks to be unworkable as it presently stands - but this is important information in itself). The report is certainly critical for NIHR purposes, but could be argued perhaps less so for the wider community.

The paper is certainly acceptable as is and is enjoyable to read, but I wonder if the authors might consider focusing or emphasising just one aspect to make it a little less mundane and obvious. Is there anything novel that the feasibility highlighted that could be further drawn out? (Although
they may have done all they can!). I suspect that a higher level journal such as Trials may be looking for such “colour” or a unique methodological slant. That said, the quality of the research in itself is certainly sufficient for publication and I would not allow my comments, intended to only enhance/improve the impact of the work, prevent publication.

One writing error noticed.
P9. “in conjugation with a physiotherapist,”
I believe this should be in “conjunction”!

Authors’ response
Thank you for your positive and constructive comments on our manuscript. We appreciate your view that this manuscript should be published and agree with your suggestion that the manuscript could be improved by drawing out a novel finding from the study. As you point out, our study shows that feasibility studies are essential, the location of the intervention is important, and there is some disparity in acceptance between those that do not wish to engage and those taking part. We agree that while these findings are important, we need to ensure that we highlight the novelty of our study. There are a number of findings from the study which we believe add a novel methodological contribution to the literature, and we have increased the description and discussion of these:

1.) Brief interviews with non-participants are valuable to gain insight into barriers to participation. We believe that this point could contribute the most to the design of future studies because very few previous feasibility and pilot studies have included detailed coverage about findings relating to recruitment (Shanyinde et al 2011). We have expanded our discussion to include a more detailed consideration of the value of brief interviews with non-participants. We have highlighted the lack of previous feasibility and pilot studies which have given detailed coverage of issues with recruitment and discussed the benefits of using brief interviews vs. other forms of data collection e.g. structured questionnaires, in-depth interviews. The paragraph in the discussion about barriers to participation now concludes with a sentence in which we advocate that brief interviews with participants should form a core component of feasibility studies (page 14-15).

2.) Carrying out feasibility studies can be of high value for money to health care research funding bodies. When planned trials show to be unfeasible, they provide high savings in wasted research funds.

We have amended the manuscript to include consideration of the importance of feasibility studies to research funders. In the abstract (page 3), we have added a final sentence to say that the information gained from this feasibility study is of value to researchers and
funders in the design and commissioning of future research. In the introduction, we have added a sentence (page 5) to highlight that feasibility work can increase the efficiency of research funding by evaluating the likely success of processes within a definitive trial. We have expanded our concluding paragraph (page 19) to state that feasibility studies can present high value for money to health care providers and funding bodies by identifying areas for concern to consider when deciding to commission research of similar interventions.

Other novel findings from our study include the challenges of implementing measures to improve recruitment rates while remaining in keeping with preferences of the NHS research ethics committees, the problems with using resource use diaries to collect self-report data on resource use, and the need for flexibility in scheduling group-based interventions to facilitate attendance. We hope our last paragraph in the conclusion highlights these key messages, and the importance of piloting trial procedures and data collection tools to carry out feasible evaluations of the effectiveness and cost-effectiveness of health care interventions in large randomised trials.

We hope our amendments enhance the manuscript and strengthen the potential impact it may have on the design of future feasibility and pilot studies. And many thanks for noticing our typo on page 9, we have now corrected this!


**REVIEWER 2 (ASHLEY JONES)**

**Comment 1**
The title of the study states that the study that has been conducted is a feasibility study, I would question this and based on the definition of a feasibility study and a pilot study as described by Arain I would think this is a pilot study (What is a pilot or feasibility study? A review of current practice and editorial policy BMC Medical Research Methodology 2010, 10:67), I would also suggest that this reference is added to the bibliography.

**Authors’ response**
Thank you for raising this important point. The article by Arain and colleagues provides useful definitions of a pilot and feasibility study and we have added this reference to the bibliography (reference 19). While there are similarities between our feasibility study and a pilot study, we
would argue that our study is a feasibility study, based on the National Institute of Health Research (NIHR) definition of feasibility and pilot studies (http://www.ccf.nihr.ac.uk/RfPB/Documents/Feasibility and pilot studies.docx) and the guidance provided in the article by Arain and colleagues. The main factors which make our study a feasibility study rather than a pilot study are:

1.) We conducted this study to find out whether it would be possible to do a definitive RCT, rather than running the definitive RCT in miniature to test whether the components of the main study can all work together. The decision to run a feasibility study rather than a pilot study was informed by previous literature which reported difficulties in running trials of similar interventions (described in paragraph 2 of the introduction, page 4).

2.) We did not have a primary outcome, or analyse any of our outcome data, as we were interested in the feasibility of running the trial, rather than the collecting data to inform the sample size for a definitive trial (described in the analysis section, page 10). A pilot study of this particular intervention, for example, would have had a longer follow-up to mock a definitive trial (12 months) and collect long-term preliminary estimates of outcome parameters to estimate minimum clinical differences of interest and the size of the full trial. We were more interested in learning about patients’ acceptability of the intervention and processes for successful recruitment and data collection. A feasibility trial with shorter follow-up would be of greater value to inform our main areas of uncertainty around the issues we faced when attempting to design the full scale trial.

3.) Our sample size was based on the estimated number of patients needed to give us an estimate of recruitment and retention rates and explore the acceptability of the intervention (described in the sample size section, page 10).

4.) We had no plans to use this data as internal or external pilot data.

While we acknowledge that feasibility studies do not need to be randomised, we included randomisation in our study to explore whether patients were willing to be randomised and ensure that retention was similar in both the intervention and standard care groups.

We hope this clarifies our description of the study as a feasibility study rather than pilot study.

Comment 2
The extremely poor consent rate raises a number of interesting questions which could be discussed further:
a. Is the method of identifying potential patients the most suitable?
b. Do the patient information sheets that were sent out need to be changed in any way?
c. How generalizable are the results given that such a large percentage of participants refused to take part?
d. How many participants were contacted who did not wish to take part?

Authors’ response

We agree that the reasons for the low recruitment rate into this study are important as they could provide useful information to inform future studies. We had included a discussion of this within the manuscript (page 15-16) but your comments have raised additional points which warrant further consideration. Please find below our responses to each point raised.

a. Is the method of identifying potential patients the most suitable?

We believe that our method of identifying potential patients was suitable and that we identified an adequate number of eligible patients. We used an established method within our centre which we have used for previous research studies. Using this method we identified 385 eligible patients over a one year period, which demonstrates this was a successful method of identification.

b. Do the patient information sheets that were sent out need to be changed in any way?

You raise an important and topical point about the patient information leaflet and the potential impact it may have had on recruitment rates. This highlighted to us a recent article in *Trials* (Gillies et al. Patient information leaflets for UK randomised controlled trials: a feasibility study exploring whether they contain information to support decision making about trial participation. 2014; 15:62), in which the authors found that many patient information leaflets used in UK RCTs lack information to support good quality decision making.

The patient information leaflet used in our study was designed in collaboration with a patient and public involvement group, who thought the patient information leaflet was clear, conveyed the necessary information and was easy to read. They made some suggestions for improvement which we incorporated into the patient information leaflet; these included a diagram to explain randomisation, emphasis on the valuable contribution of patients randomised to the standard care group, and inclusion of a contact e-mail address for the research team and Arthritis Care. Patient representatives also suggested that we should offer one year free membership to Arthritis Care for all participants but as we discuss on pages 15-16, the ethics committee asked us to remove this from the study protocol.

Therefore, although there is the potential that our patient information leaflet contributed to the low recruitment rate, we believe that collaboration with our patient and public involvement group in the design of the patient information leaflet minimised this risk. We have amended the manuscript to clarify the input from patient representatives into the design of the patient information leaflet on page 6 in the methods section and page 16 in the discussion section.

c. How generalizable are the results given that such a large percentage of participants refused to take part?
The finding that a large percentage of patients declined participation was a core finding of this study, and underpins the interpretation of the findings. As you rightly point out, this will influence how generalisable the results are to the wider patient population. However, as this was a feasibility study, this is a result in itself and we openly discuss this finding in the results (page 11) and discussion (pages 15-16). The fact that the majority of patients would refuse to take part in the study is a major finding, one that would impair the generalizability of our treatment effect estimates should we continue to have such low uptake in the definitive trial. This result was one of the main factors contributing to our decision to not go ahead with a definitive trial.

**d. How many participants were contacted who did not wish to take part?**

We contacted 385 eligible patients and 297 patients did not return a reply slip and consent form which was taken as a proxy that they not wish to participate. This information is provided in the CONSORT flow diagram (Figure 1) and we have also now added it into the text within the results section (page 11).

**Comment 3**

Has there been a systematic review of the previous existing evidence? Does there need to be? It seems with several trials that one is warranted.

**Authors’ response**

A systematic review and meta-analysis of pre-operative interventions for patients with hip or knee osteoarthritis awaiting joint replacement surgery has been published (Wallis et al. Pre-operative interventions for patients with hip or knee osteoarthritis awaiting joint replacement surgery-a systematic review and meta-analysis. Osteoarthritis and cartilage, 2011. 19: 1381-1395; reference 13 in bibliography). This systematic review identified two previous trials of self-management interventions for patients on the waiting list for joint replacement, but did not identify any trials evaluating the effectiveness of a pain self-management intervention in this patient population. This is described in the second paragraph of the introduction (page 4).

**Comment 4**

I think the introduction needs more structure and some of the information reported here is not required and some is repeated.

**Authors’ response**

We have amended and rewritten the introduction to clarify structure, improve the content and reduce length (word count has been reduced from 674 to 498). The structure is now:

- Paragraph 1: Introduction to hip replacement and the problem of pain management while patients are on the waiting list for surgery.
• Paragraph 3: Purpose and importance of feasibility work.
• Paragraph 4: Aims of the study.

We have also updated the figures on the number of hip replacements performed to reflect the latest report from the National Joint Registry.

Comment 5
I was surprised to see that there was no objective to estimate parameters for a sample size calculation. Has this information already been collected? This should be discussed as this is one of the key pieces of information for any future trial.

Authors’ response
As described in our response to comment 1, the aim of this study was to assess the feasibility of conducting a definitive trial rather than to conduct a pilot study. In light of this, and combined with the findings that such a trial was not feasible, we have not chosen one of the outcome measures administered as a primary clinical outcome nor estimated the sample size for a future definitive trial.

Comment 6
There was also nothing with regards to developing core outcomes, are all the outcomes in this area well established? (see Williamson PR, Altman DG, Blazeby JM, Clarke M, Devane D, Gargon E, Tugwell P: Developing core outcome sets for clinical trials: issues to consider. Trials 2012, 13:132.)

Authors’ response
Thank you for raising this point. Core outcomes are important to improve quality and consistency in the assessment of outcomes in clinical trials. We are currently involved in developing a core outcome set for the assessment of chronic pain after knee replacement (manuscript currently under review, study registered at http://www.comet initiative.org/studies/details/291?result=true). Through this work, we are aware that there is not a core outcome set for patient-reported outcomes after total hip replacement. While we acknowledge the need for the development of a core outcome set to guide assessment of patient outcomes after hip replacement, this was beyond the scope of this study.

Comment 7
This pilot study was conducted in only one centre, how generalizable are the results to other centres?

Authors’ response
We acknowledge that our feasibility findings on patients’ acceptability of the intervention, recruitment and retention from a single-centre study may have limited generalisability to other centres. We have included a sentence in the discussion section to acknowledge this limitation.
Our patient group had similar socio-demographic characteristics to the cohort of patients undergoing hip replacement (National Joint Registry 10th Annual report 2013, available at: http://www.njrcentre.org.uk/njrcentre/Reports,PublicationsandMinutes/Annualreports/tabid/86/Default.aspx), which may suggest that our feasibility results may extend to the same patient group in other centers.

Comment 8
Further information needed on the randomisation procedure.
Authors’ response
We have extended the randomisation section to provide further details on the randomisation procedure, including details on the minimisation variables used in the allocation of patients to the intervention or standard care group (page 7).

Comment 9
For baseline characteristics would means and standard deviations be a more appropriate way of describing the parametric data?
Authors’ response
Thank you for highlighting this, and we agree that it would be more appropriate to describe the baseline characteristics with means and standard deviations, rather than means and 95% confidence intervals. We have amended Table 1 and the related text on pages 10 and 11 to report standard deviations.

Comment 10
Page 10, for the 37 females, could a percentage be given.
Authors’ response
Many thanks for highlighting this omission. We have added the percentage of patients who were female (65%) on page 11.

Comment 11
The retention of participants section should refer to the consort diagram. It would be more useful if the withdrawal reasons were split by group.
Authors’ response
Thank you for the reminder. We have added a reference to Figure 1 in this section to refer readers to the CONSORT diagram. Details of withdrawal reasons have been rewritten so that they are split by group (pages 11 and 12).

Comment 12
The high amounts of missing data and the low retentions rates of the intervention suggest that this method is not suitable or needs to be changed considerably to be rolled out in a larger trial. I don’t think this is discussed in enough detail.

Authors’ response
This is an important point which we agree requires further discussion within the manuscript. Based on our findings, we believe that the roll out of the feasibility study to a definitive trial in its current design at our centre would not be feasible. Further research would be necessary to evaluate strategies to improve recruitment rates and increase flexibility in the scheduling of the group-based intervention. However, we did find that questionnaire completion rates, retention of participants and satisfaction with the intervention were all high, suggesting that further methodological work could lead to a feasible trial design. We have added a paragraph discussing the feasibility of the definitive trial on pages 17-18.

Comment 13
There are high amounts of missing economic data, again suggesting that this is not feasible or worthwhile yet the authors do not seem to agree?

Authors’ response
Many thanks for this comment. The aim of the economic evaluation feasibility work was to check whether it was feasible to collect resource use data from patient-reported questionnaires for an NHS and a societal perspective. Economic evaluations are prone to missing data (Noble et al, 2012). As cost is a compound variable, when one item of resource use is missing, the full cost is missing. There are methods to deal with missing data frequently used by health economists, such as multiple imputation models (Briggs et al, 2003). We found that the less completed categories of missing data were questions relating to the patients’ private costs component of the societal perspective. The level of completeness of NHS resource use categories indicated that an economic evaluation from an NHS perspective using patient-reported questionnaires was feasible. We have discussed this in page 16 of the manuscript. In addition, we have added a sentence at the beginning of this section to explain that economic evaluations within trials are prone to missing data.

Patient-reported questionnaires are often only one source of data collection for economic evaluations and resource use data can be collected in a myriad of ways in the same trial (Ridyard 2010; Martin et al 2011). Should this feasibility work have continued to a full-scale trial, we would have endeavored to employ research staff to collect the majority of NHS resources from medical records and shorten the patient completed questionnaires to capture only use of social services. This would have allowed a higher completion rate for the NHS + Personal Social Services perspective, as advised by NICE guidelines. Productivity losses data completion levels indicate that measurement of time off work and leisure activities would have been feasible to collect by patient questionnaire in a full-scale trial, and it would have provided valuable information for a sensitivity
analysis. However, as this feasibility study highlighted that a definitive trial was not feasible, further discussion of this was deemed to be beyond the scope of the manuscript.


Comment 14
There is no discussion on completeness of particular outcomes within the questionnaire, just the return of the questionnaire themselves, were all questionnaires that were returned 100% complete?

Authors’ response
We did consider including completion rates of the individual questionnaires but decided against this because the outcome measures themselves weren’t the primary focus of the study. Also they are widely used measures and there is published data in much larger studies than our own, which provide information about rates of missing data. For example:


Comment 15
The discussion describes the barriers that were faced in a constructive manner but does not discuss whether or not a future trial is actually manageable and if so what should be the key objectives of such a trial.
Authors’ response
We hope we have provided a satisfactory response to this comment in our response to comment 12.

Many thanks for your comments. We hope we have clarified your queries and provided satisfactory amendments to the manuscript. We feel that our manuscript is now much improved as a result.