Author’s response to reviews

Title: The feasibility and acceptability of an early intervention in primary care to prevent Chronic Fatigue Syndrome (CFS) in adults: randomised controlled trial

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Thank you for allowing us the opportunity to respond again. We are pleased that reviewer 2 had no further comments, and reviewer 3 just thought the comments were minor. We have responded as below:

Reviewer reports:

Reviewer #2: None

Reviewer #3: Thank you for your responses to the first review. Most of these responses adequately cover my original concerns; however, two of the issues remain (albeit more minor than major).
Original review comment: &gt;Figure 1 starts from the 90 'potential recruits who may or may not be eligible' but the problem with the recruitment process stems higher, which is missed in the flowchart - and hence I feel is somewhat misleading. The above point leads to the major problem with the recruitment process and that is regarding the loss of potential patients from the 1711 figure to the 90 that were actually referred. Is there any information available to ascertain why this dramatic loss has occurred? Could any data (e.g. age / gender / index of multiple deprivation) be compared between the 90 referred and 1621 non-referred, albeit possibly at the level of aggregated data?  
Response of authors: We have no information on patients that were not recruited to the study. Our paper points out that few of them were recruited, and then discusses the reasons why from the qualitative work.  
Further comment: Figure 1 should include the top level figure of people that consulted and had the relevant code (i.e. 1711) [this will help show the drop-off in numbers from being potentially eligible to numbers referred]. The follow up responses and losses should be broken down in relation to 12 weeks and 6 months.  
Thank you. Sadly, we do not know if these 1711 were consulted or not. We were very surprised at the very low number of potential patients identified as this is very low compared to population surveys (for example the first one we quote which is that GPs should be seeing a large case load as 10-24% of patients should be eligible). We therefore went back to see if, perhaps, these GP practices didn’t see any eligible patients which is when we looked at the number of TATT patients.  
We have made this clearer by putting the paragraph on the data provided at the end of this section. We have added an additional paragraph to expand on this which now reads: “We wanted to understand whether the problem with recruitment was because there were no eligible patients. We therefore explored this question by examining how many patients consulted their GP with fatigue. Data was provided by…” The detail on 11 (not 13) practices and the different dates then makes more sense.  
Original review comment: [Lines 173-179, page 7]: "The following inventories were completed by participants at their assessment with the researcher (baseline) and then at 12-week and 6-month follow-up… and a health resource-use questionnaire, developed for this study which asked questions about health service use and travel costs most relevant to the CFS/ME population.”  
&gt;Firstly, only 6 month outcome results are presented descriptively in this paper Secondly, the information on health resource use and travel costs relating to the health economics are not presented here.  
Response of authors: Thank you. Given the sample size, we did not feel it was appropriate to do any form of statistical analyses as this would be likely to lead to erroneous conclusions. As this was a feasibility study, the outcomes of interest are feasibility. Given the small sample size, we couldn't perform any type of analysis. However, in the methods, we described all the outcomes collected for transparency.  
Further comment: Whilst accepting that this is feasibility study and hence does not warrant a full statistical analysis, in my view whatever outcomes are collected should be reported descriptively. Hence, 12-week descriptives as well as any descriptive data that relate to resource use (including response/ completion rates of items) would help to give the full picture from the data collected.
For example, if there are clear/large descriptive differences in the data for the two study groups (e.g. at 12 weeks) this may still persuade researchers that the underlying clinical question may be worth pursuing (albeit via a different methodological approach to recruitment).

We have carefully considered this. Our view is that the purpose of this study was to see if we can do a trial testing an early intervention. Given we describe the assessment data (time 0) and the primary end point (6 months) which straddle the three month data, we don’t think adding 3 month data will enable researchers to have any insight into whether the trial may be feasible. Follow up was worse at 3 months compared to 6 months. So we think there is the risk of confusion and reducing the readability of the paper.

We have added a sentence about the lower return of data at 3 months to the results section and changed the subtitle from Six month outcomes to Outcomes. The added sentence is:

Return of follow up questionnaires was generally low but was marginally better at 6 months (primary time point, see table 3, 36/44 returned) compared to 3 months when only 35/44 returned any questionnaires and only 34/44 (77%) returned the SF-36 physical function subscale.