Author's response to reviews

Title: Improving recruitment to a study of telehealth management for long-term conditions in primary care: two embedded, randomised controlled trials of optimised patient information materials

Authors:

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Author's response to reviews: see over
RE: 1585397909147257 - Improving recruitment to a study of telehealth management for long-term conditions in primary care: two embedded, randomised controlled trials of optimised patient information materials

Pleased fine attached our revised manuscript and supporting documentation.

We believe that these revisions address all the points raised by our referees. Our point by point response is attached below. Our response to editorial requests is detailed at the end of the document.

Thank you for your help in guiding this manuscript through the review process.
Yours sincerely,

Jo

Dr Jo Rick | Project Manager - MRC START & SWANS

Point by point response to referees:

Referee 4 MC

Major Compulsory Revisions

The Conclusion in the abstract claims that the evidence form the two trial suggest “modest beneficial effects”. This does not reflect to overall pattern of findings in the studies reported which observed only marginal improvements in the optimised condition. All but one of the NHST conducted were non-significant. By convention (various sources) even the greatest magnitude of OR reported here would only just reach the threshold for a ‘small’ effect in Cohen’s terms (usually taken to be somewhere around 1.5). The interpretation of the findings in the abstract is therefore skewed and overly positive. The author should adapt the language to reflect the overall pattern and scale of effects observed.

We accept that our presentation may have been overly optimistic, so we have made the requested changes to the abstract and highlighted the overall pattern of a lack of effects.

The authors should revise the first paragraph of the Discussion to give a more representative view of the overall pattern of findings, which were almost exclusively non-significant.

Again, we have revised the language as requested and highlighted the overall pattern of a lack of effects.
Minor Essential Revisions

The authors should provide some comment on the sample used during ‘user testing’ and the implications this has (e.g. for the effectiveness of the optimised materials in different clinical samples).

Details have been added to page 9 of the revised draft on the composition of the participants in the user testing rounds.

On page 12, the last three sentences that describe the randomisation process is a little unclear (especially with regards to “the first 25 eligible patients to complete this process at each practice were randomised”). The authors should clarify this process further.

This has been rewritten and the process has been clarified.

On page 15 under Data Analysis, gender is introduced as a potential moderator variable. No prior rationale is provided for examining gender. The author should provide this rationale.

One of the major limitations with embedded studies is that trials will differ significantly in terms of potential moderator variables, as they will measure many different baseline characteristics. Gender is one variable which will be present in all data sets and always coded identically. There are potential reasons why the effects of recruitment interventions may vary by gender, but the core reason for its adoption as a moderator is the pragmatic issue that the data are always available. We have clarified this in the revision, although we have placed this in the discussion rather than the methods.

Discretionary Revisions

During the trial there was an administrative error in the Depression study such than individuals randomised to optimised patient materials, and who did not respond to the first letter, were sent the usual (non-optimised) patient materials as a reminder. This is a substantial deviation from the protocol and could have had a substantive effect on the findings. There are at least two potential mechanism by which this could have affected the findings, and which pull in opposite directions. Explanation 1: the ‘dose’ of the intervention was effectively diluted and therefore differences between trial arms would be diminished. Explanation 2: the difference in patient materials between the first letter and the reminder could have operated along the lines of the Hawthorne Effect whereby change per se rather than the nature of the change (or content of the intervention) drive beneficial outcomes. These two alternative mechanisms have important implications for the interpretation of the trial, especially since it was in the depression study where the only significant p-value as observed. Without resulting to inferential tests, the authors could explore these two alternative explanations by examining the proportion of responders after the initial letter (across trial arms in the depression study) and comparing this with the reported proportions that represent the final response after initial (optimised) and reminder (non-optimised) letters were sent, compared to the control arms (non-optimised only). Differences in proportions at ‘time 1’ and ‘time 2’ might suggest whether it was the optimised materials or the change in materials that drove any difference between trial arms.

The error was unfortunate and we agree that it could have a variety of effects, although we think that explanation 1 is the more likely.

Although the suggested secondary analysis would potentially be interesting, we note that the reviewer has labelled it as ‘discretionary’, and on balance we are not in favour of including it. The requested additions from all 4 reviewers have already made the paper longer, and we feel that it will add significant complexity to the paper, as the interpretation is likely to be very complex.

We have slightly expanded the section on these issues in the discussion and we hope this is sufficient.
Referee 2 LC

Thank you for the opportunity to read this interesting and well-written article reporting on two embedded randomized controlled trials of optimized patient information materials. I think that the work of the START group is important and more attention to improving recruitment materials is required, and similarly, that increasing recruitment rates to trials (and other studies) is something all of us working in trials should be keen to learn more about. As such, I am convinced that the article seeks to answer an important and well-defined research question, and one that warrants further empirical study.

Thank you for your kind comments.

The reporting is at a high standard, and the methods used are appropriate and well described according to CONSORT checklist. There are a number of areas where further detail is required (please see list of revisions below for more information). There is, of course, the problem with the administrative error whereby the standard reminder letter was sent to all non-responders to the Healthlines Depression mail-out, but despite this, I still feel that the article is suitable for publication, following relatively minor revisions.

No response required.

The data appear to be sound and their representation in the article raises no major questions. I would argue that elements of the discussion and conclusion should be reconsidered and refined. There is no issue with the claims that they are making, but rather, a couple of points of clarity are warranted. These are explained below also.

I do not have any revisions that are required before a decision on publication can be reached.

No response required.

Major compulsory revisions

Minor essential revisions

Page 6 – The host trial – the Healthlines study

Minor typing error – comma not required after ‘two’ in sentence one.

We have reworded as requested.

Page 8 – Methods

Sentence two is a little confusing. I suggest that the final clause is edited to read ‘...and within Healthlines Depression only, the proportion actually randomised.’

We thank the referee for this helpful rewording.

Page 20 - Interpretation of the findings in the context of the wider literature. Minor typing error in sentence 2 – this should be ‘CVD’, not ‘CVS’.

We have corrected the typo.

Discretionary revisions

Page 7 – The host trial – the Healthlines study

Would it be possible to provide justification for the summary of recruitment issues, perhaps using references from the START group itself?
We thank the reviewer for bringing this to our attention, and have now added three sentences around recruitment issues on page 7 and several references to support our claims. We chose to focus our examples on participant in telehealth research, since this is most relevant to The Healthlines Study. We also acknowledge that some patient groups are especially difficult to recruit due to the nature of the affected condition, such as depression. Again, this is relevant to The Healthlines Study, since one of the trials was specifically recruiting patients with depression.

Page 9 – Development of the recruitment intervention

I am aware that this is not the precise purpose of this article, but would it be possible to say a little more about recruitment of the healthy volunteers to the optimization process. Perhaps this could be included as one of the additional files?

As above, comments added on page 9.

Page 10 – Development of the recruitment intervention

It is useful to see extracts from the standard and optimized recruitment materials for Healthlines Depression, but I think it would be helpful to include the full PIS, unless there are clear and legitimate reasons for not doing so. If that is the case, perhaps a short note explaining the nature of what is included would be helpful.

We would prefer to make examples of the PIS available as Figures with the publication and to make full versions available only on request from the authors.

Page 11 - Description of the Healthlines host trials...

The eligibility criteria for individuals is clearly explained, however, it would be useful to include an explanation of how the three GP practices were recruited, and why this differed from the four that it was intended would be recruited. This is highlighted as a limitation in the discussion section of the paper, but is not covered here.

We appreciate that we could have made GP practice recruitment clearer, and so have modified page 12 with more details on this. In particular, we have now specified that recruitment was carried out with the help of the Primary Care Research Network (PCRN), as well as the criteria we had supplied the PCRN with (socio-demographic and urban and rural location mixture, large practices, using one of three computer systems, in one of three regions of the South West).

We have also now further clarified in this ‘Sample size’ section why the intended number of recruited practices differed from the actual number of recruited practices. This seemed a more appropriate place to discuss the difference between the actual and intended number of practices, since it relates to the power calculation. We thank the reviewer for drawing this to our attention.

Due to a delay in the Ethics approval process, one practice had already been recruited and had started mailing prior to the different versions of the PIS being approved for use.

It was intended to recruit four practices as this gave the required sample size to show any observable effect.

Page 16 – Results

Please can a table of baseline characteristics for both trials be added? In addition, please can a summary of numbers included for analysis be added to the flowchart and supporting text. The analysis appears to include all participants, but it would be useful to be explicit on this issue.
We have added tables of baseline characteristics as requested (Tables 1 and 2) and have clarified in the text that all participants were included.

Page 18 – Discussion

The introductory paragraph summarises the findings as they pertain to depression, but makes no mention of CVD, which is surprising given that the authors have gone to great lengths to include both study populations in the rest of the reporting.

We have made changes to the initial part of the discussion in response to referee 1, which hopefully addresses this concern.

Page 18 – Limitations

Given that there was a prior awareness of the importance of aligning the host and embedded recruitment trials, could the authors expand their explanation of why this didn’t happen in Healthlines? Do they have any recommendations for readers of this particular paper, or could they incorporate any recommendations from the Graffy et al (2010) paper here?

We accept that, as written, it appears that we did not take our own advice. We have highlighted that early linking of host and embedded trials is always preferable, and have reiterated this in the revision. However, the reality is that this is not always feasible, and we would argue that some compromises are justified given the parlous state of the evidence base for recruitment.

Page 20 - Interpretation of the findings in the context of the wider literature.

The interpretation of findings around increased rates of randomization and how this relates to different clinical populations is difficult to follow at present. On the one hand, the authors explain that it wasn’t possible to test rates of randomization in CVD, but then the two clinical groups are compared and contrasted on this basis. In addition, the higher levels of overall acceptance in CVD compared to depression is presented discussed in slightly confusing manner, and this could be brought together with the second paragraph in a better way.

We have tried to rewrite this section as requested, and hope the revised version is clearer.

Page 21 – Implications for recruitment practice

Whilst it may be difficult to quantify improved understanding and patient satisfaction as they pertain to optimized recruitment materials, this is something ripe for qualitative exploration, so perhaps its appropriate to highlight this, and suggest as a potential area for future research?

We thank the referee for this suggestion and have added a short note to this effect on pages 21-22.

Page 22 – Conclusions

I felt that this conclusion lacked substance and should be reconsidered and redrafted by the authors. The conclusion of the abstract provides a helpful starting point for this.

We have rewritten the conclusions as requested, using the abstract as a basis.

General point: Aims

I do have a concern about the dual reporting of the Healthlines Depression and CVD trials, given that they have (for very pragmatic reasons) different outcome measures. I wonder whether separate reporting may provide greater clarity to the key message of the paper that optimized recruitment materials can have a small impact on recruitment rates. Perhaps the authors could justify why both trials are included in this paper, other than the seemingly obvious reason that they are both part of the Heathlines study?
We accept that there may be advantages to a separate presentation, but we did feel that it is important that the context of the embedded trial in the depression and CVD studies had significant similarities (the trial design, team, practices etc), and we also felt that the combined presentation had the advantage of highlighting that the effects of the same recruitment intervention may vary by population.

Referee 3 DF

Thank you for inviting me to review this paper.

Major compulsory revisions:

1. Whilst the authors note that the requirements of research ethics committees can result in long and complex patient information documentation, they may like to consider that many research funders (e.g. NIHR, Marie Curie) require extensive PPI within the research they fund. As a consequence, it could be assumed that many researchers collaborate with patients and the public at large when developing their information sheets, and to pilot them before commencing the study. The current paper seems to overlook this which is to presume that others have not undertaken these steps. Depending on the degree that this has been undertaken in a host study, the benefits cited, and the results achieved may be significantly impacted.

We accept this point. We have clarified that trials will differ in the degree to which PPI will have informed trial materials, and that the amount of PPI input may place limits on the degree to which enhanced PIS may lead to improvements. However, we would also point out that, although PPI input and our enhancement process may lead to similarly improved materials, the processes are not interchangeable and may have different effects. For example, our process does involve formal testing of the effects of the enhancement on information transfer, which is rarely done formally in PPI. Studies that have involved extensive PPI may thus be compared with our enhancement process and it is possible that either is superior. We have discussed this on page 20.

2. In the background the authors identify that there has been little quantitative research in this field. As the authors are trying to overcome barriers to patient recruitment to studies would a mixed method approach not yield valuable information?

We accept that a mixed methods approach will yield additional insights, and have added this useful suggestion together with some illustrative references.

3. The authors identify that they use ‘expertise in writing for patients and graphic design’ - it would be beneficial for readers if you could identify how this expertise is defined. It could be argued that many researchers have a degree of expertise in writing for patients, but does the expertise utilized in this paper go beyond the norm and if so, how?

Comments added to page 9 and page 20.

4. The paper does not describe how the original materials were developed by the host research team – was there any patient involvement? Was it piloted with the patients? Who developed the materials? What was their level of experience and expertise in regard to writing for patients? There needs to be a clearer explanation of the baseline patient information development before the optimization process.

The original patient information sheet was designed by the Healthlines research team in accordance with guidance documentation supplied by the National Research Ethics Service (NRES). The original patient information sheet went through several revisions through discussion amongst the Healthlines research team. We also based the trial patient materials on a patient survey study we had conducted earlier in the Healthlines research programme. Prior to the patient survey, the patient information sheet was reviewed and checked for plain language by an external researcher with relevant expertise and training. We have updated
the manuscript with further information around how the original patient information sheet was constructed and agree that this is important information to include.

5. The process is described as ‘iterative’ when it should perhaps be classed as ‘sequential’ as there appear to only be three stages of testing: original materials, first draft of ‘optimized’ materials, and final round of ‘optimized’ materials following revision. Iterative suggests that there would be multiple rounds of testing of optimized materials which is not the case.

Thank you. What we intended to put across is that the tested materials are amended as required as per the user testing results. The next version is then tested. We don’t think that ‘sequential’ really captures this and suggest ‘repeated’. (Text amended).

6. The cost of generating the optimized materials is identified as £10,000 yet there is no identification of how this cost was calculated. Given this high cost, could it be minimized for smaller trials? How does this cost relate to the cost of the trials concerned? What is the cost per additional patient recruited? It would be useful to have more of an economic evaluation of this process.

Apologies – the costs was approximately £7,000 and this figure has been added. The £7k cost comprises the combined cost of user testing and graphic design. We have not conducted an economic evaluation of the process – this may be more valuable when there are several similar nested trials (as in START), for which an economic evaluation would be both more valuable and robust.

7. The cited benefits of the process (page 21) include patient satisfaction, but this is not discussed earlier in the paper, is not included in the outcome measures, and there is no indication as to how this has been evaluated. If this was tested it would be useful addition to the paper.

The point made by the referee is correct. We do have interest in extending the range of outcome measures to include measures of satisfaction and shared decision-making, although in many cases trials are resistant to adding measures, and recruitment outcomes have the significant advantage that they are already collected. We have added a note to discuss this limitation.

Minor compulsory revision:

1. The time to develop the materials is noted as a limitation, but the duration is not specifically identified.

We estimate this time to be approximately 6 weeks. Details have been added to page 19.

Referee 1 MP

Overall this is a clearly reported manuscript describing the findings of two well conducted randomised trials of patient recruitment strategies embedded in trials of telehealth interventions in primary care. The rationale for the study is convincing, the methods are rigorous, the interpretation of results is reasonable and the implications for future trialists are thoughtful and appropriate. I have only a couple of suggestions to improve what is already an impressive manuscript.

No changes required.

Minor essential revisions

1. More information could be provided under “Methods – Development of the recruitment intervention”. It was unclear to me whether all 20 factual questions had to be answered correctly by each of the 10 participants in each round in order for modifications to be made to the patient information materials. Also, were the 10 participants the same in each round? What was the response rate for user testing (i.e. how many people were invited to review the materials)? And are the characteristics of user testing participants likely to have affected how the optimised patient
information materials were developed? Perhaps summary data on the results of each round could be provided (either within the manuscript or as an Additional file).

We would prefer not to include the User Testing data in the appendix – they are small data sets and are indicative (meaning that interpretation is also influenced by the commentary from the person who did the user testing). We have added comments to page 10.

User testing participants were different in each round – we have now clarified that on page 9. Participants were from a database – ie people who had already given their name as being interested in readability studies, and so the notion of ‘response rate’ does not apply.

Editorial requests:

Please include all author names, email addresses and affiliations on the title page of your manuscript and on the author details tab in the submission system.

We have corresponded with the editorial team on this issue and received the following guidance:

Thank you for your email, and please accept my apologies for the delay in getting back to you on this matter. It appears that you have been unfortunately misinformed, and we apologies for any confusion this has caused you. Although we do allow groups to act as authors, we do still require at least one author to be named. For instance, *Author* on behalf of *group*. Please note however the “on behalf of” will not appear on PubMed.

With regards to the Authors’ Contributions section, this section will need to include the contributions of all within the group who class as an author (and the Acknowledgements section will need to include a list of any other members of the group who were not authors).

We have therefore revised the title page to read Mei-See Man on behalf of the Healthlines Study Group and Jo Rick on behalf of the MRC START Group. The authors contribution section already includes details of the contributions of all those classed as an author and the acknowledgements section includes all other members of the group who were not authors. We trust that this now the editorial policy on group authorship.

Please include the dates of registration with the trial registration numbers at the end of the Abstract.

These have been added.

Please include a statement in your Methods section explaining that you obtained informed consent from each participant of the second trial.

Informed consent was not sought for participants in the embedded trial. This is described in the MRC START protocol and was approved by research ethics for both the MRC-START research programme and the specific MRC-START in Healthlines embedded trial.

Please remove the figure from the main manuscript document. This should only be included in a separate file.

This is now included as Additional file F.

Please move the tables below the reference list.

This has been done.