Author’s response to reviews

Title: Improving the relevance of randomised trials to primary care: a qualitative study investigating views towards pragmatic trials and the PRECIS-2 tool.

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Author’s response to reviews:

Reviewer reports:

Reviewer #1: This is a well written and interesting paper which would make a good contribution to the literature. It is likely to be highly cited as the study has an interesting and novel finding.

Specific points

1. In the introduction you say that the NIHR, NIH etc all aim to fund pragmatic trials. Is this really so? Can you provide some evidence to back this claim up. PCORI might be the exception here - but i don’t think that the NIHR for example has any specific remit or advice on how and if the trials it funds should be pragmatic. Maybe it is the word "aim" here and perhaps simply saying "funds" would soften this statement.

It is the case that the NIHR, NIH and PCORI actively aim to fund pragmatic trials. We have added references for each funder to the second paragraph of the manuscript and describe the evidence in more detail below for the NIHR and NIH:

For the NIHR we have added a reference to the NIHR HTA document “HTA Is an intervention ready for HTA evaluation?” (see https://www.nihr.ac.uk/documents/hta-is-an-intervention-ready-for-hta-evaluation/22003) This states that the NIHR HTA funding stream aims to fund pragmatic trials stating:
“HTA trials determine whether an intervention is effective and cost-effective when delivered in typical NHS or social care settings with typical NHS or social care users. The programme therefore needs to be convinced that the intervention is ready for this type of pragmatic evaluation.”

For the NIH we’ve added a reference to Weinfurt et al “Pragmatic clinical trials embedded in healthcare systems: generalizable lessons from the NIH Collaboratory” which describes lessons learnt from an NIH funding stream which aims to fund pragmatic trials.

2. One person from each category seems too low. The authors attempt to defend this by saying that the study targeted an elite group - even if this is the case the findings of this study will still be highly limited when only one group member was included.

When designing the study we prioritised targeting a higher number of categories of potential interviewees to ensure that we obtained a broad range of views. A consequence of this was the limited number of interviewees per category. We have acknowledged in the limitations section that we may not have captured all views on the topic of interest due to a limited sample size. Whilst we may not have captured all views the results of the article show that our sample was sufficient to provide an in depth and informative discussion highlighting areas of trial design where there is greater consensus, and areas where what constitutes the best design is more nuanced.

3. There is a very long delay between the study conduct and the submission of this paper.

True. Publication of this study has been delayed by a lengthy review and rejection of the article by a different journal. We believe that the results of this study are still relevant for current researchers. Pragmatic trials are still of interest to research stakeholders. As far as the authors of this study are aware no other work has been published discussing stakeholder views towards trial design in primary care.

4. How did you identify the participants? I don't think this information is included. Related to this, what were participants told about the study at the time of first contact. How many people approached did not want to participate?

The manuscript contains details on how we identified study participants and how many people approached did not want to participate.

In the second paragraph of methods we state “We identified individuals from each category either from appropriate websites or through personal networks of the research team”

In the first line of the results section we state: “Twenty four individuals or groups were invited to participate. Seventeen individuals took part in total, nine via individual interviews - and the rest via group-interviews”
We have added details to the third paragraph of the methods section on the information given to participants at first contact.

5. I'm not a qualitative researcher so this comment might be misinformed - but did you not have to consider if saturation was reached?

There was evidence of saturation in some areas, for example, across the themes of “How evidence is used”, “aspects of trials considered when assessing evidence” and “views on the PRECIS-2 domains. For our fourth theme “perceptions of pragmatic and explanatory trials” we collected a wide variety of views and whilst there was repetition of some of the key ideas we can not be certain saturation was reached. We have added a comment on saturation to the strengths and limitations section of the discussion.

We aimed to recruit an elite sample, covering a broad range of views and did not design the study to recruit until saturation was achieved. While this approach may have missed some views, we are confident that the most important factors are captured.

6. Can you clarify what you mean by 24 individuals or groups (I'm not sure what you mean by groups here)

Some of the invitations were sent to individuals and invitations were sent to groups. We count one invitation per group ie if we invited a group of three people to participate that would count as one invite. To clarify what we mean by this point we have reworded to say “We sent 24 invitations to groups or individuals to participate in the study, we conducted 12 interviews and 12 invitations were declined.”

7. I found the fact that developers of guidelines and clinicians use evidence in different ways very insightful. To me this seems entirely the appropriate way that evidence should be used.

8. Could you give some examples of the misconceptions of the term pragmatic trial. In my own experience, people have come to me thinking that this terms means the trial can be pragmatic and so low quality. So for example, they might say that in the control arm the outcome can be assessed in an unreliable way and more reliable way in the intervention arm. When i protest, they say "well this is a pragmatic trial". It would be good to have some examples of misconceptions - highlighting these can be a way of correcting these misconceptions.

We have added further details of misconceptions that were raised by interviewees and rearranged the article slightly to make other misconceptions presented more clear (p17, section headed “Perceptions of pragmatic”, trials, 2nd paragraph).
Reviewer #2: I am sorry to have to recommend the paper should not be accepted by Trials as I think it needs to be reworked before it can be published. I was a bit unclear exactly what it was that you were exploring in your paper. There is a lot of literature about the differences between pragmatic and explanatory trial design and implications for implementation of the results. Including the stakeholders in a discussion about trial design is interesting but the topic might have been explored in more depth.

We have edited the final two paragraphs of the background section to make the aims of the study and rationale more clear. The aim of the study is not to highlight the differences between pragmatic and explanatory trials but to investigate the interesting and important views of stakeholders in primary care towards trial design.

I was unclear why you didn't include clinicians as a group - the ones included were included because they were in another stakeholder role. As the main implementers of research evidence I would have thought they would be important to interview.

We did not include clinicians as a group as we included clinicians in our sample via other groups. Whilst we acknowledge that our sample is finite and will not capture all views on the topic, we believe that as there were a number of clinicians included in the study we do not fail to cover the views of clinicians on this topic. We discuss this point in the strength and limitations section of the paper.

Specific suggestions:

1. the introduction should really argue the case for doing this qualitative study, especially when the limitations of pragmatic trials are so well explained in other research;

Good point. We have edited the background section to make the rationale for this study clearer and highlighted the absence of research exploring the views of stakeholders in primary care towards clinical trial design. The aim of this study is not to highlight the limitations of pragmatic trials but to find out how researchers can maximise the relevance of their work to primary care by taking into account the views of those who influence practice.

2. the title 'maximising' is not really what you have covered in your results;

We have edited the title to “Improving the relevance of randomised trials to primary care: a qualitative study investigating views towards pragmatic trials and the PRECIS-2 tool.”.

Our results explore the ways in which clinical trials can be designed to make their results more relevant to primary care. We have edited the title, and edited the discussion to make the link between our results and the title more clear.
3. the results needs to be streamlined and synthesised to include only the most relevant data and quotes;

We have streamlined quotes on pages 6 and 7 and removed a quote from the manuscript on page 8.

In writing this manuscript we have tried to strike a balance between including data in the results covering all relevant views captured and prioritising those most relevant to the research. We would be happy to consider streamlining the results further if any more concerns are raised either by the reviewers or editor.

4. include some implementation outcome definitions if that is what you are looking at.

Apologies, we haven’t been clear enough, which has led to a misunderstanding. We have not included implementation outcome definitions in the manuscript as evaluating implementation outcomes was not the focus of our work. As our work focuses on the views of key stakeholders towards the design of clinical trials we have focused our background section on introducing different approaches to designing clinical trials. We’ve edited the final paragraph of the background section to make explicit that our work focuses on the views of stakeholders towards the design of clinical trials.

Reviewer #3: I want to praise the authors for this fine piece of work. I have only minor comments and some suggestions.

Background: The first reference could be supplemented by this reference (Kennedy-Martin T, Curtis S, Faries D, et al. A literature review on the representativeness of randomized controlled trial samples and implications for the external validity of trial results. Trials 2015;16:495), that empirically supports your claim.

We have added the suggested reference to the manuscript.

Methods: the last part of the first sentence needs to be clarified or rewritten "…and on PRECIS-2" Do you mean? "on how best to design trials based on PRECIS-2?

We have reworded to “…, and on views towards areas of design covered by the PRECIS-2 domains”

Line 52-52: word is missing? "…carried out [at] the participants…”

We have added “at” to the manuscript

Results: your results are interesting and a valuable contribution to the understanding of pragmatic trials. Especially the lack of knowledge of pragmatic trials among some interviewees are concerning… (p. 7).
We thank the reviewer for their comment.

Discussion:

in the discussion I think you need to emphasis the importance of good reporting (p. 11, line 57-58), by adding a reference. You are right about the importance of reporting details of the intervention, but this aspect is often overlooked cf. this publication PMID: "29467013 Details to replicate interventions remain lacking, impairing best implementation or meaningful further research. Editorial endorsement of reporting checklists needs to be more extensive") For this purpose, a very useful checklist (and tool) exist: Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014;348:g1687-g1687. doi:10.1136/bmj.g1687. I would strongly recommend you include a reference for this.

We thank the reviewer for bringing these references to our attention and have included them in the manuscript.

Comparison with existing literature: This is a fine section. And it is fine that you also are critical towards some aspects of pragmatic trials. A critique that has been raised (Kent DM, Kitsios G. Against pragmatism: On efficacy, effectiveness and the real world. Trials 2009;10:1-3) is that "...a null pragmatic trial provides little information about whether our treatment has some potential value". Kent & Kitsios raises some questions about pragmatic trials that are often overlooked. This comment is just for your inspiration and reflection (and not necessarily for inclusion in the paper).

Thank you for this comment and for bringing this reference to our attention.

Reviewer #4: This is a useful paper and may help researchers when designing pragmatic RCTs. I recommend it for publication following some corrections or clarifications set out below. Please note, I have used the line numbers, but it was sometimes difficult to line up, so they may be one line out.

General comments

1. The paper focuses heavily on the PRECIS-2 tool and on pragmatic trials and as such I think either PRECIS-2 or ‘pragmatic’ should feature in the title.

We have edited the title to “Improving the relevance of randomised trials to primary care: a qualitative study investigating views towards pragmatic trials and the PRECIS-2 tool.“ including reference to both PRECIS-2 and pragmatic trials.
2. The aim is to study views of people who have an influence on primary care but the views of charities and funders are not included under the theme 'how evidence is used' and therefore it is not clear why they have been included as people who use results from RCTs. I would like their views to be covered in this section, or a comment on why they are not included and also covered in the discussion. There is a lack of clarity as to whether people are included due to their role in using evidence or designing trials and the aim seems to vary slightly across the sections in this regard.

We’ve added further justification to the methods section on why research funders and charities were included in the sample.

We have added details and quotes on how those from the research charity and funders on how they use evidence. The charity used evidence in their advocacy work with the government and help facilitate discussion between clinicians. The funders advocated the use of evidence via the systematic review an guideline process.

We’ve commented in the discussion on how by including these two groups we drew in views from those involved heavily in the design of research.

3. There are no details provided regarding the GP interviewer (as per items numbers 2, 4, 5, 7 and 8 of COREQ).

We have added details regarding the GP interviewer to the methods (credentials and gender) and to box 1 (participant knowledge of the interviewer and interviewer characteristics reported to the participants).

4. Details of framework analysis is unclear. Did one person complete all of the coding of the manuscripts? What was completed by more than one individual; were the results of the analysis just reviewed by the other authors, or did they conduct analysis? Please add a little more detail to this section (page 4, lines 38-45). This should also be commented on in the strengths and limitations section of the discussion.

Coding was conducted by one author (GF) and reviewed with three other authors (SE, KL, and MC). Four of the study authors, GF, SE, KL, and MC were involved in all stages of the analysis, including familiarizing themselves with the manuscript, discussing the thematic framework and reviewing the coding. The final two authors were involved at the stage of forming interpretation of the coded data.

We have edited the methods section to make it more clear who was involved at each stage of the analysis and we have added a sentence to the strengths and limitations section highlighting that multiple people were involved in the analysis.

Abstract:
1. Line 26 - you have said 'people who influence practice in primary care' but have not made it clear that all individuals do have such an influence (charities and funders), perhaps add something about people who design research in primary care (if this is correct).

We have added additional details on why we considered charities and funders to be involved in influencing primary care practice to the manuscript.

Background (page 2):

1. Lines 6–8 - consider re-writing as the second point seems an after thought in this sentence.

We have re-written this sentence as:

“In addition, primary care faces restrictions on resourcing and a need for complex interventions, involving multiple interacting elements; two factors that can further complicate the adoption of new interventions.”

2. Line 22 - consider adding 'often', i.e. 'compromises often have to be made.'

We have added “often” to this line.

3. Line 34 - should 'take design decisions' be 'make design decisions'?

We’ve replaced take with make as suggested.

4. Line 45 - add 'in primary care' at the end of the sentence.

Added “in primary care” to sentence.

Methods:

1. Page 3, line 38 states there are 8 categories of people but only 7 are listed in lines 39–42.

We have corrected page 3, line 38 to read seven categories of people.

2. Page 3, line 53 - missing 'at' and 'another' in '.carried out at the participants place of work or another location.'

We have corrected this sentence as suggested.
3. Page 3, line 54 - consider adding the time range of interviews.

We’ve added the range of times of the interviews: from 45 minutes to 1 hour 15 minutes.

4. Table 1 - consider marking which interviews had the GP present.

We have added a note to the table highlighting which interviews had the GP present.

5. Figure 1 and Box 1 - PRECIS written instead of PRECIS-2

Thank you for spotting this omission, we have edited the manuscript.

6. Page 4, lines 38-45 - add detail as mentioned in general comments.

Further clarification of who did what in the analysis have been added to lines 38-45.

7. Page 4, line 42 - I think it should be NVivo rather than NVIVO. Is there a reference for the software?

We have changed to NVivo and added the version number of the software used.

We are more than happy to add a reference if the editor thinks in appropriate. We have looked at a number of articles published in trials and it is not common practice to include references with the name and version of the software so have not added a reference at this stage.

Results:

1. Page 4, line 50 - Do you have any information about those who did not consent to take part?

We did not record any data on those people we contacted who declined to take part as they did not provide consent for the study.

2. Table 1 - consider indicating which interviews you only had notes for.

We have added note to table 1 indicating the interviews for which only notes were available.

3. Table 1 - under role, interviews K and L are described as 'journal publishing systematic reviews', please add the participant's actual role, e.g. editor/author. Could you also add a role for the representatives of the research charity? What are the individuals responsible for in the charity in relation to research evidence?
We have added the roles for interviewees K and L: editor and clinical director respectively. We’ve added responsibilities for the individuals from the charity, two of the interviewees were members of the research funding team and one was a member of the research policy team.

4. Page 45-6 - as mentioned above, I would like to see the views of the charities and funders under the first theme as the aim of the paper is to understand the relevance for people who use evidence.

We have added details of the use of evidence by the charities and funders to the manuscript.

5. Page 7, lines 25-26 - consider adding a quote to demonstrate the view that pragmatic trials are inferior to more traditional RCTs.

The manuscript includes the quote “Pragmatic can be a dirty word when describing trials, people like to shoot at them…” to illustrate this point. We have edited the paper to make it more clear that this is quote relates to the point that pragmatic trials can be viewed as inferior.

6. Page 7, line 37 - add 'editor/author (or appropriate descriptor)' to description of participant for Interview K. As per point 3, you may want to add some detail to the research charity descriptors as well.

We’ve added detail to the description of interview K and to the research charity descriptors.

7. Page 7, line 55 - 'eligibility, recruitment and setting' should be italicised (they are later, keep consistent).

We have italicised these words, thank you for picking this up.

8. Page 8, line 15-16 - re-write sentence ('bring being people')

We have reworded to “… there was concern that very intensive recruitment could lead to people being included in trials who would not usually present for treatment in routine practice.”

9. Page 10, line 1 - 'primary outcome' and 'primary analysis' should be italicised.

Edit made

10. Page 10, line 22 - brackets on new line as per other quotations.
Discussion:

1. Page 11, line 31/32 - did all interviewees acknowledge a less pragmatic approach for recruitment and follow-up, or just select groups?

Only a subset of interviewees acknowledged a less pragmatic approach for recruitment and follow up. We’ve added this qualification to the discussion.

We mention in the results section for recruitment that not all interviewees gave a view towards recruitment in trials. For follow we have added some more detail on concerns raised by some interviewees about intensive follow up acting as a separate intervention and changing behaviour.

2. Page 11 - as mentioned before, please add something about how charities and funders use evidence for primary care.

We have added details and quotes on how charities and funders use evidence for primary care.

3. Page 12, lines 6-9 - the abstract states that you found a wide range of views, please add this here and consider commenting on any saturation (or the lack of it)?

We have added a comment on the wide range of views we obtained and mentioned that the study was not designed to achieve saturation.

4. Page 12, line 11 - ‘the focus of this study was on the design of randomised trials’ is not in line with the rest of the article which has seemed to focus on the interpretation of results in relation to pragmatic designs. Check this thread is clear throughout.

We have edited the background section to make it more clear that the focus of the study was on the views of those involved in implementing research in primary care towards the design of randomised trials. In response to comments from this reviewer and other reviewers we have taken out the part of the sentence this comment refers too.

5. Page 12, line 12 - you have indicated who is a primary care clinician in Table 1 and so am not sure about this limitation. In regards to designing trials, you could have included more methodologists and trialists. Again, is the focus of the interviews on the interpretation of results, or on designing trials for primary care? The interview questions seem to be about how evidence is used, and then you have applied this to design, which is fine but should be clearer on your aims and interpretation.
The focus of the study was to explore the views of stakeholders involved in influencing clinical practice in primary care towards the design of trials. The interviews began with questions on how evidence is used as we believed this to be relevant to the design of trials. We have edited the background section to make the aims of the study more clear.

We did not aim to include more methodologists and trialists in the sample as the study aimed to investigate the views of stakeholders in changing practice, rather than those conducting research.

We have qualified the limitation regarding not including primary care clinicians as a group adding to the sentence “…a number of clinicians were included ensuring that their contributions are well represented”

6. Page 12, line 25-29 is one sentence and should be re-written.

We have broken this sentence into more than one sentence.

7. Any comment on future research? Where next?

We have added a paragraph suggesting some areas future research.

8. Consider discussing excess treatment costs funding in the UK - providers must fund the intervention in NIHR trials and so has to be more in line with the available primary care resources.

We have added a sentence regarding excess treatment costs to the discussion

Conclusion:

1. Page 12, line 54 - consider adding 'and usual care' to 'particularly details of the intervention and usual care delivered' at the end, as I felt this was apparent in the quotes.

We’ve added a reference to usual care to the final sentence of the conclusions.

Reviewer reports:

Reviewer #1: This is a well written and interesting paper which would make a good contribution to the literature. It is likely to be highly cited as the study has an interesting and novel finding.

Specific points
1. In the introduction you say that the NIHR, NIH etc all aim to fund pragmatic trials. Is this really so? Can you provide some evidence to back this claim up. PCORI might be the exception here - but i don't think that the NIHR for example has any specific remit or advice on how and if the trials it funds should be pragmatic. Maybe it is the word "aim" here and perhaps simply saying "funds" would soften this statement.

It is the case that the NIHR, NIH and PCORI actively aim to fund pragmatic trials. We have added references for each funder to the second paragraph of the manuscript and describe the evidence in more detail below for the NIHR and NIH:

For the NIHR we have added a reference to the NIHR HTA document “HTA Is an intervention ready for HTA evaluation?” (see https://www.nihr.ac.uk/documents/hta-is-an-intervention-ready-for-hta-evaluation/22003) This states that the NIHR HTA funding stream aims to fund pragmatic trials stating:

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When designing the study we prioritised targeting a higher number of categories of potential interviewees to ensure that we obtained a broad range of views. A consequence of this was the limited number of interviewees per category. We have acknowledged in the limitations section that we may not have captured all views on the topic of interest due to a limited sample size. Whilst we may not have captured all views the results of the article show that our sample was sufficient to provide an in depth and informative discussion highlighting areas of trial design where there is greater consensus, and areas where what constitutes the best design is more nuanced.

3. There is a very long delay between the study conduct and the submission of this paper.

True. Publication of this study has been delayed by a lengthy review and rejection of the article by a different journal. We believe that the results of this study are still relevant for current researchers. Pragmatic trials are still of interest to research stakeholders. As far as the authors of this study are aware no other work has been published discussing stakeholder views towards trial design in primary care.
4. How did you identify the participants? I don't think this information is included. Related to this, what were participants told about the study at the time of first contact. How many people approached did not want to participate?

The manuscript contains details on how we identified study participants and how many people approached did not want to participate.

In the second paragraph of methods we state “We identified individuals from each category either from appropriate websites or through personal networks of the research team”

In the first line of the results section we state: “Twenty four individuals or groups were invited to participate. Seventeen individuals took part in total, nine via individual interviews - and the rest via group-interviews”

We have added details to the third paragraph of the methods section on the information given to participants at first contact.

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Specific suggestions:

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2. the title 'maximising' is not really what you have covered in your results;

We have edited the title to “Improving the relevance of randomised trials to primary care: a qualitative study investigating views towards pragmatic trials and the PRECIS-2 tool.”. Our results explore the ways in which clinical trials can be designed to make their results more relevant to primary care. We have edited the title, and edited the discussion to make the link between our results and the title more clear.

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Apologies, we haven’t been clear enough, which has led to a misunderstanding. We have not included implementation outcome definitions in the manuscript as evaluating implementation outcomes was not the focus of our work. As our work focuses on the views of key stakeholders towards the design of clinical trials we have focused our background section on introducing different approaches to designing clinical trials. We’ve edited the final paragraph of the background section to make explicit that our work focuses on the views of stakeholders towards the design of clinical trials.

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Methods: the last part of the first sentence needs to be clarified or rewritten "…and on PRECIS-2" Do you mean? "on how best to design trials based on PRECIS-2?"
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Results: your results are interesting and a valuable contribution to the understanding of pragmatic trials. Especially the lack of knowledge of pragmatic trials among some interviewees are concerning… (p. 7).

We thank the reviewer for their comment.

Discussion:

in the discussion I think you need to emphasis the importance of good reporting (p. 11, line 57-58), by adding a reference. You are right about the importance of reporting details of the intervention, but this aspect is often overlooked cf. this publication PMID: "29467013 Details to replicate interventions remain lacking, impairing best implementation or meaningful further research. Editorial endorsement of reporting checklists needs to be more extensive") For this purpose, a very useful checklist (and tool) exist: Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014;348:g1687-g1687. doi:10.1136/bmj.g1687. I would strongly recommend you include a reference for this.

We thank the reviewer for bringing these references to our attention and have included them in the manuscript.

Comparison with existing literature: This is a fine section. And it is fine that you also are critical towards some aspects of pragmatic trials. A critique that has been raised (Kent DM, Kitsios G. Against pragmatism: On efficacy, effectiveness and the real world. Trials 2009;10:1-3) is that "...a null pragmatic trial provides little information about whether our treatment has some potential value". Kent & Kitsios raises some questions about pragmatic trials that are often overlooked. This comment is just for your inspiration and reflection (and not necessarily for inclusion in the paper).

Thank you for this comment and for bringing this reference to our attention.

Reviewer #4: This is a useful paper and may help researchers when designing pragmatic RCTs. I recommend it for publication following some corrections or clarifications set out below. Please note, I have used the line numbers, but it was sometimes difficult to line up, so they may be one line out.
General comments

1. The paper focuses heavily on the PRECIS-2 tool and on pragmatic trials and as such I think either PRECIS-2 or 'pragmatic' should feature in the title.

We have edited the title to “Improving the relevance of randomised trials to primary care: a qualitative study investigating views towards pragmatic trials and the PRECIS-2 tool.“ including reference to both PRECIS-2 and pragmatic trials.

2. The aim is to study views of people who have an influence on primary care but the views of charities and funders are not included under the theme 'how evidence is used' and therefore it is not clear why they have been included as people who use results from RCTs. I would like their views to be covered in this section, or a comment on why they are not included and also covered in the discussion. There is a lack of clarity as to whether people are included due to their role in using evidence or designing trials and the aim seems to vary slightly across the sections in this regard.

We’ve added further justification to the methods section on why research funders and charities were included in the sample.

We have added details and quotes on how those from the research charity and funders on how they use evidence. The charity used evidence in their advocacy work with the government and help facilitate discussion between clinicians. The funders advocated the use of evidence via the systematic review an guideline process.

We’ve commented in the discussion on how by including these two groups we drew in views from those involved heavily in the design of research.

3. There are no details provided regarding the GP interviewer (as per items numbers 2, 4, 5, 7 and 8 of COREQ).

We have added details regarding the GP interviewer to the methods (credentials and gender) and to box 1 (participant knowledge of the interviewer and interviewer characteristics reported to the participants).

4. Details of framework analysis is unclear. Did one person complete all of the coding of the manuscripts? What was completed by more than one individual; were the results of the analysis just reviewed by the other authors, or did they conduct analysis? Please add a little more detail to this section (page 4, lines 38-45). This should also be commented on in the strengths and limitations section of the discussion.

Coding was conducted by one author (GF) and reviewed with three other authors (SE, KL, and MC). Four of the study authors, GF, SE, KL, and MC were involved in all stages of the analysis,
including familiarizing themselves with the manuscript, discussing the thematic framework and reviewing the coding. The final two authors were involved at the stage of forming interpretation of the coded data.

We have edited the methods section to make it more clear who was involved at each stage of the analysis and we have added a sentence to the strengths and limitations section highlighting that multiple people were involved in the analysis.

Abstract:

1. Line 26 - you have said 'people who influence practice in primary care' but have not made it clear that all individuals do have such an influence (charities and funders), perhaps add something about people who design research in primary care (if this is correct).

We have added additional details on why we considered charities and funders to be involved in influencing primary care practice to the manuscript.

Background (page 2):

1. Lines 6-8 - consider re-writing as the second point seems an after thought in this sentence.

We have re-written this sentence as:

“In addition, primary care faces restrictions on resourcing and a need for complex interventions, involving multiple interacting elements; two factors that can further complicate the adoption of new interventions.”

2. Line 22 - consider adding 'often', i.e. 'compromises often have to be made..' We have added “often” to this line.

3. Line 34 - should 'take design decisions' be 'make design decisions'? We’ve replaced take with make as suggested.

4. Line 45 - add 'in primary care' at the end of the sentence. Added “in primary care” to sentence.

Methods:
1. Page 3, line 38 states there are 8 categories of people but only 7 are listed in lines 39-42.

We have corrected page 3, line 38 to read seven categories of people.

2. Page 3, line 53 - missing 'at' and 'another' in '..carried out at the participants place of work or another location..' 

We have corrected this sentence as suggested.

3. Page 3, line 54 - consider adding the time range of interviews. 

We’ve added the range of times of the interviews: from 45 minutes to 1 hour 15 minutes.

4. Table 1 - consider marking which interviews had the GP present.

We have added a note to the table highlighting which interviews had the GP present.

5. Figure 1 and Box 1 - PRECIS written instead of PRECIS-2

Thank you for spotting this omission, we have edited the manuscript.

6. Page 4, lines 38-45 - add detail as mentioned in general comments.

Further clarification of who did what in the analysis have been added to lines 38-45.

7. Page 4, line 42 - I think it should be NVivo rather than NVIVO. Is there a reference for the software? 

We have changed to NVivo and added the version number of the software used.

We are more than happy to add a reference if the editor thinks in appropriate. We have looked at a number of articles published in trials and it is not common practice to include references with the name and version of the software so have not added a reference at this stage.

Results:

1. Page 4, line 50 - Do you have any information about those who did not consent to take part?
We did not record any data on those people we contacted who declined to take part as they did not provide consent for the study.

2. Table 1 - consider indicating which interviews you only had notes for.

We have added note to table 1 indicating the interviews for which only notes were available.

3. Table 1 - under role, interviews K and L are described as 'journal publishing systematic reviews', please add the participant's actual role, e.g. editor/author. Could you also add a role for the representatives of the research charity? What are the individuals responsible for in the charity in relation to research evidence?

We have added the roles for interviewees K and L: editor and clinical director respectively. We’ve added responsibilities for the individuals from the charity, two of the interviewees were members of the research funding team and one was a member of the research policy team.

4. Page 45-6 - as mentioned above, I would like to see the views of the charities and funders under the first theme as the aim of the paper is to understand the relevance for people who use evidence.

We have added details of the use of evidence by the charities and funders to the manuscript.

5. Page 7, lines 25-26 - consider adding a quote to demonstrate the view that pragmatic trials are inferior to more traditional RCTs.

The manuscript includes the quote “Pragmatic can be a dirty word when describing trials, people like to shoot at them…” to illustrate this point. We have edited the paper to make it more clear that this is quote relates to the point that pragmatic trials can be viewed as inferior.

6. Page 7, line 37 - add 'editor/author (or appropriate descriptor)' to description of participant for Interview K. As per point 3, you may want to add some detail to the research charity descriptors as well.

We’ve added detail to the description of interview K and to the research charity descriptors.

7. Page 7, line 55 - 'eligibility, recruitment and setting' should be italicised (they are later, keep consistent).

We have italicised these words, thank you for picking this up
8. Page 8, line 15-16 - re-write sentence ('bring being people')

We have reworded to “… there was concern that very intensive recruitment could lead to people being included in trials who would not usually present for treatment in routine practice.”

9. Page 10, line 1 - 'primary outcome' and 'primary analysis' should be italicised.

Edit made

10. Page 10, line 22 - brackets on new line as per other quotations.

Interview tag moved to new line

Discussion:

1. Page 11, line 31/32 - did all interviewees acknowledge a less pragmatic approach for recruitment and follow-up, or just select groups?

Only a subset of interviewees acknowledged a less pragmatic approach for recruitment and follow up. We’ve added this qualification to the discussion.

We mention in the results section for recruitment that not all interviewees gave a view towards recruitment in trials. For follow we have added some more detail on concerns raised by some interviewees about intensive follow up acting as a separate intervention and changing behaviour.

2. Page 11 - as mentioned before, please add something about how charities and funders use evidence for primary care.

We have added details and quotes on how charities and funders use evidence for primary care.

3. Page 12, lines 6-9 - the abstract states that you found a wide range of views, please add this here and consider commenting on any saturation (or the lack of it)?

We have added a comment on the wide range of views we obtained and mentioned that the study was not designed to achieve saturation.

4. Page 12, line 11 - ‘the focus of this study was on the design of randomised trials’ is not in line with the rest of the article which has seemed to focus on the interpretation of results in relation to pragmatic designs. Check this thread is clear throughout.
We have edited the background section to make it more clear that the focus of the study was on the views of those involved in implementing research in primary care towards the design of randomised trials. In response to comments from this reviewer and other reviewers we have taken out the part of the sentence this comment refers to too.

5. Page 12, line 12 - you have indicated who is a primary care clinician in Table 1 and so am not sure about this limitation. In regards to designing trials, you could have included more methodologists and trialists. Again, is the focus of the interviews on the interpretation of results, or on designing trials for primary care? The interview questions seem to be about how evidence is used, and then you have applied this to design, which is fine but should be clearer on your aims and interpretation.

The focus of the study was to explore the views of stakeholders involved in influencing clinical practice in primary care towards the design of trials. The interviews began with questions on how evidence is used as we believed this to be relevant to the design of trials. We have edited the background section to make the aims of the study more clear.

We did not aim to include more methodologists and trialists in the sample as the study aimed to investigate the views of stakeholders in changing practice, rather than those conducting research.

We have qualified the limitation regarding not including primary care clinicians as a group adding to the sentence “…a number of clinicians were included ensuring that their contributions are well represented”

6. Page 12, line 25-29 is one sentence and should be re-written.

We have broken this sentence into more than one sentence.

7. Any comment on future research? Where next?

We have added a paragraph suggesting some areas future research.

8. Consider discussing excess treatment costs funding in the UK - providers must fund the intervention in NIHR trials and so has to be more in line with the available primary care resources.

We have added a sentence regarding excess treatment costs to the discussion

Conclusion:
1. Page 12, line 54 - consider adding 'and usual care' to 'particularly details of the intervention and usual care delivered' at the end, as I felt this was apparent in the quotes.

We’ve added a reference to usual care to the final sentence of the conclusions.