

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Improving the recruitment activity of clinicians in randomised controlled trials - a systematic review
AUTHORS	Ben Fletcher, Adrian Gheorghe, David Moore, Sue Wilson and Sarah Damery

VERSION 1 - REVIEW

REVIEWER	Benjamin Kasenda, MD, Junior Researcher, Matthias Briel, MD MSc, Assistant Professor Basel Institute of Clinical Epidemiology and Biostatistics, Basel, Switzerland -We declare to have no competing interests
REVIEW RETURNED	25/10/2011

THE STUDY	Authors worked according to PRISMA checklist; manuscript is quite well structured in this regard
RESULTS & CONCLUSIONS	Research ethics are not applicable in this systematic review and meta-analysis
GENERAL COMMENTS	Minor comments - Page 5, 2nd para under Quality assessment: Could the authors give a reference for the used CASP qualitative research appraisal tool? - Page 5, 3rd para under Quality assessment "... the results were compared for inconsistency." - Was agreement between reviewers measured (e.g. using kappa)? If yes, what was it? - Page 13, 2nd para of Discussion "Evidential nihilism, where narrow exclusion criteria..." - shouldn't it rather read "narrow inclusion criteria"? - Page 15, 3rd para: The second half of this para practically duplicates a previous para (page 14, para 5) - the authors should consider merging the information from the 2 paragraphs. In addition, the ref at the end of para 3 on page 15 should probably be ref 42 and not 43. - Page 14, para 1, 2nd sentence: "In both studies the intervention increased recruitment, but had no effect on proportion of recruited subjects who accepted allocation...." - when reading this sentence for the first time was somewhat confusing, because in the end the intervention increased the proportion of eligible patients that could be randomly allocated, right? Maybe it is worthwhile rephrasing the sentence.

REVIEWER	Shaun Treweek, Senior lecturer, University of Dundee, UK I confirm that I have no competing interests.
REVIEW RETURNED	28/10/2011

General comments

I enjoyed reading this well-written paper, which makes a useful and important contribution to the recruitment literature. The authors have been ambitious in presenting both qualitative and quantitative data in the same paper but they do a good job of this challenging task. I have a few comments, which are given below, most important first and then by section heading. I don't think any of them should pose too much difficulty for the authors.

Most important points

1. the meta-summary and effect sizes (Table 4 and main text). First, I'm not a qualitative researcher so the following comment may represent my ignorance. While I can see the benefit of trying to rank the qualitative work in some way to highlight the areas to target in future work, saying that, say, 'Understanding of research' had an effect size of 27% while 'Effect on patients' was 36% suggests a precision that is more imagined than real. What is the significance of that 9% difference? My own preference would be a much simpler exercise of counting how often themes arose in the qualitative work and those that came up most are those that we should target, or perhaps, the effects could be grouped into small, medium and large or some other categorization scheme. My key point is that the idea of calculating an effect size presented in % terms doesn't really work for me and I'm sure a simple change to the presentation method would achieve the same result but in a more meaningful way.

2. Results. The authors have a tendency to say there was no difference when the confidence interval has not in fact ruled out a difference. For example, for comparing 2 types of recruiters, the authors state there was no difference for a result of $RR=0.94$, 95% $CI=0.76$ to 1.17 . That CI contains the possibility of important harm or benefit; a good description of the error is Altman's and Bland's 2004 letter to the BMJ: *BMJ* 328 : 1016 doi: 10.1136/bmj.328.7446.1016-b. The Cochrane Collaboration has a very useful set of standard phrases to use and the authors could have a look at Glenton et al 'Presenting the Results of Cochrane Systematic Reviews to a Consumer Audience: A Qualitative Study' *Med Decis Making* 2010; 30: 56-.

3. All of the Appendices were missing. I suspect that these were submitted by the authors but for some reason I didn't get them. 4. Reporting of qualitative results. There are a lot of items in single quotes (eg. 'winners and losers', 'partners in research', 'gatekeepers') and it isn't clear what these single quotes signify. Are these direct quotes from participants mentioned in the article text, or the authors' summing-up of concepts coming from the articles? It would be good to clarify this in the text so that readers know whether these phrases come from research participants or the authors. Finally, in Results if there was anything the authors could think of to separate the quantitative results from the qualitative results that would be helpful. It might be as simple as a bit more white space between the sections and a bigger, clearer heading for the two sections.

Abstract

1. Page 2. The 2nd and 3rd paragraphs of the Methods section seems a bit loose to me and it would be good if the authors could be a bit more concrete. For example, name the standardised tool, be clear whether all data extraction was done in duplicate (this is also unclear in the main Methods section), say a bit more about what 'all results/findings were extracted' means. Also, under Results there is a little bit of inconsistency between the descriptions of the themes abstracted from the data in the Abstract and those in the main text (eg. individual benefits for clinicians vs ..benefits for trialists).

Article summary

1. Page 3, Strengths. The quote beginning "an approach for.." doesn't make sense to me. I realise it's a direct quote but I suggest that the authors don't use the quote and rewrite it in a way that is easier to understand.

Introduction

1. Page 4, 1st paragraph. RCTs are certainly the gold standard for effectiveness studies but it's less clear cut for safety studies where an RCT may well be unfeasibly expensive. I'd be tempted to drop safety from this opening sentence, or define the

types of safety studies that are meant.

2. Page 4, 2nd paragraph. The Cochrane review has been recently updated and the new citation is: Treweek S, Mitchell E, Pitkethly M, Cook J, Kjeldstrøm M, Johansen M, Taskila TK, Sullivan F, Wilson S, Jackson C, Jones R, Lockhart P. Strategies to improve recruitment to randomised controlled trials. Cochrane Database of Systematic Reviews 2010, Issue

4. Art. No.: MR000013. DOI: 10.1002/14651858.MR000013.pub5.

3. Page 4, 4th paragraph. Sentence starting 'Maintaining recruitment activity over time..' looks like a sentence that should end with a reference. Is the reference missing?

Method

Page 5, 3rd paragraph. Minor point but the Box is called a figure in the version of the box/figure I got. I suspect that this is a feature of the journal submission system but it would be good to make sure the box is indeed called a box.

Page 5, 4th paragraph. Were all these abstracts checked by two people? It would be good to clarify.

Results

1. Page 7, 1st paragraph. It would be good if the opening line mentioned the total number of abstracts. Something like 'The search identified 9236 abstracts of which..'

This information is in the figure but it would be good to add it to the text as well.

2. Page 7 and elsewhere. Several of the included studies don't quote RRs so the authors have clearly calculated these themselves. All the ones I checked were correct so there's no problem there but a single line in Methods mentioning this and what was used (RevMan?) would be helpful.

3. Page 8, Liénard study. There's a typo, the study had 302 in the intervention group, not 301 (see Table 2 of the article). This study didn't account for clustering, which is why the Cochrane recruitment review doesn't give RRs for this study's data and simply quotes the result given in the original paper. The authors might consider whether they want to do the same.

4. Page 9, 2nd paragraph. The Donovan 2009 talks about proportions agreeing to be randomized and proportions accepting allocation and it's probably best to stick to this terminology rather than the current text. The Donovan paper isn't completely clear about what represents actual recruitment but my guess is it is those accepting allocation that equate to recruited participants and if true, the authors' current RR of 1.87 for 12 month recruitment is incorrect because this represents those agreeing to be randomized (12 patients at 12 months) but not all accept their allocation (only 8 accept). It's the latter group that is interesting because these are actually recruited (if I'm correct in my interpretation of the Donovan paper). It would be good for the authors to check the Donovan paper and see which interpretation is correct.

5. Page 9, last paragraph. 'do RCTs provide the best available evidence'. Is this a question, or is the 'do' a typo?

Discussion

1. General. The authors have been ambitious in presenting both qualitative and quantitative data in the same paper and this makes the Discussion a challenge to write. The authors have done a good job but I wonder if they could give a bit of thought to how they could discuss the different weight to be given to the various quantitative designs included in the review. There are RCTs but there's also an uncontrolled before-after study and I think it could be a bit clearer that the quality of evidence is different because of these design choices.

2. Page 13, 2nd paragraph. Could the authors list a few examples of the 'logistical, ethical and scientific obstacles' mentioned? I think nested trials could be done more often but there are indeed obstacles and it would be good to state a few explicitly.

3. Conclusion (or lack of). I missed a Conclusion to wrap things up so the paper ends a bit softly when something a bit punchier would be better. There's a Conclusion in the Article Summary section and this could form the basis of a main text Conclusion.

Table 1

I'd be tempted to drop this table.

Conflict of interests

None

VERSION 1 – AUTHOR RESPONSE

Comments from reviewer 1:

[2.1] “Authors worked according to PRISMA checklist; manuscript is quite well structured in this regard”

Response: Thank you for your comments.

[2.2] “Page 5, 2nd para under Quality assessment: Could the authors give a reference for the used CASP qualitative research appraisal tool?”

Response: References have been added for the qualitative and quantitative quality assessment tools used (reference number 17: Effective Public Health Practice Project: Quality Assessment Tool for Quantitative Studies; 2010; reference number 18: Critical Appraisal Skills Programme).

[2.3] “Page 5, 3rd para under Quality assessment “... the results were compared for consistency.” - Was agreement between reviewers measured (e.g. using kappa)? If yes, what was it?”

Response: Results were compared for consistency, and following discussion a final decision on quality was made for each study. This has been clarified in the text. Agreement between the two reviewers was not formally assessed statistically using Kappa.

[2.4] “Page 13, 2nd para of Discussion “Evidential nihilism, where narrow exclusion criteria...” - shouldn't it rather read “narrow inclusion criteria”?”

Response: This should have read “inclusion” and has been changed.

[2.5] “Page 14, para 1, 2nd sentence: “In both studies the intervention increased recruitment, but had no effect on proportion of recruited subjects who accepted allocation...” - when reading this sentence for the first time was somewhat confusing, because in the end the intervention increased the proportion of eligible patients that could be randomly allocated, right? Maybe it is worthwhile rephrasing the sentence.”

Response: The comments about allocation have been removed, and recruitment in this context has been more clearly defined as the proportion of eligible subjects who consented to be randomised into the study.

[2.6] “Page 15, 3rd para: The second half of this para practically duplicates a previous para (page 14, para 5) - the authors should consider merging the information from the 2 paragraphs. In addition, the ref at the end of para 3 on page 15 should probably be ref 42 and not 43.”

Response: The paragraph on page 14 has been removed, and the reference numbers have been revised.

Comments from reviewer 2:

[3.1] “I enjoyed reading this well-written paper, which makes a useful and important contribution to the recruitment literature. The authors have been ambitious in presenting both qualitative and quantitative data in the same paper but they do a good job of this challenging task. I have a few comments, which are given below, most important first and then by section heading. I don't think any of them should pose too much difficulty for the authors.”

Response: Thank you for your constructive comments. Incorporating qualitative and quantitative evidence was challenging methodologically. We hope that whilst investigating recruitment to RCTs, which was the primary focus, the methodological issues dealt with in this review can also help inform future systematic reviews of diverse evidence.

[3.2] “The meta-summary and effect sizes (Table 4 and main text). First, I'm not a qualitative researcher so the following comment may represent my ignorance. While I can see the benefit of trying to rank the qualitative work in some way to highlight the areas to target in future work, saying that, say, ‘Understanding of research’ had an effect size of 27% while ‘Effect on patients’ was 36% suggests a precision that is more imagined than real. What is the significance of that 9% difference?”

My own preference would be a much simpler exercise of counting how often themes arose in the qualitative work and those that came up most are those that we should target, or perhaps, the effects could be grouped into small, medium and large or some other categorisation scheme. My key point is that the idea of calculating an effect size presented in % terms doesn't really work for me and I'm sure a simple change to the presentation method would achieve the same result but in a more meaningful way."

Response: We appreciate the reviewer's comments on this subject. We attempted to defend the use of qualitative metasummary in paragraph 1 on page 6. The percentages are used to show the frequency of studies in which each abstracted findings occur, and we hope that the paper does not suggest that the results are precise, or imply importance or statistical precision. The use of frequency effect sizes goes a step beyond the qualitative convention of using descriptive terms, and hopefully highlights the fact that a predetermined, reproducible method was used for data analysis.

Also, this means of presenting qualitative syntheses follows an accepted method for this type of work (Sandelowski and Barroso, 2007), and we believe that there is merit in maintaining fidelity to their method. Thus, we would like to keep the qualitative effect sizes as percentages.

[3.3] "Results. The authors have a tendency to say there was no difference when the confidence interval has not in fact ruled out a difference. For example, for comparing 2 types of recruiters, the authors state there was no difference for a result of RR=0.94, 95% CI=0.76 to 1.17. That CI contains the possibility of important harm or benefit; a good description of the error is Altman's and Bland's 2004 letter to the BMJ: BMJ 328 : 1016 doi: 10.1136/bmj.328.7446.1016-b. The Cochrane Collaboration has a very useful set of standard phrases to use and the authors could have a look at Glenton et al 'Presenting the Results of Cochrane Systematic Reviews to a Consumer Audience: A Qualitative Study' Med Decis Making 2010; 30: 56-."

Response: Thank you for the additional references on this point. In the text where "no difference" was reported, this has now been changed to "no significant difference", so that a spurious impression of statistical significance is not given where none may exist (or vice versa).

[3.4] "All of the Appendices were missing. I suspect that these were submitted by the authors but for some reason I didn't get them."

Response: We uploaded all of the supplementary data at the time of first submission, but due to our misunderstanding attached them as materials "not for review", but it was not our intention for you to not be able to access them.

[3.5] "Reporting of qualitative results. There are a lot of items in single quotes (eg. 'winners and losers', 'partners in research', 'gatekeepers') and it isn't clear what these single quotes signify. Are these direct quotes from participants mentioned in the article text, or the authors' summing-up of concepts coming from the articles? It would be good to clarify this in the text so that readers know whether these phrases come from research participants or the authors. Finally, in Results if there was anything the authors could think of to separate the quantitative results from the qualitative results that would be helpful. It might be as simple as a bit more white space between the sections and a bigger, clearer heading for the two sections."

Response: The abstracted findings were cited in single quotation marks in an attempt to differentiate them from quotations taken from references. The quotation marks have been removed to avoid confusion.

With regard to separating the Qualitative and Quantitative sections of the results we have added more space between the two sections and hope that this will be reflected in the final copy. The BMJ Open guidelines for formatting titles have been followed throughout the manuscript.

[3.6] "1. Page 2. The 2nd and 3rd paragraphs of the Methods section seems a bit loose to me and it would be good if the authors could be a bit more concrete. For example, be clear whether all data extraction was done in duplicate (this is also unclear in the main Methods section), say a bit more about what 'all results/findings were extracted' means. Also, under Results there is a little bit of inconsistency between the descriptions of the themes abstracted from the data in the Abstract and those in the main text (eg. individual benefits for clinicians vs . benefits for trialists)."

Response: The abstract has been rewritten according to PRISMA guidelines to include more detail on

the methodology followed. The standardised quality assessment tools have been named in the abstract. Language has been cleared up for consistency and to clarify the confusions that were highlighted by the reviewer.

[3.7] “Page 3, Strengths. The quote beginning “an approach for..” doesn’t make sense to me. I realise it’s a direct quote but I suggest that the authors don’t use the quote and rewrite it in a way that is easier to understand.”

Response: The relevant quote has been removed and replaced with: “The purpose of qualitative metasummary is to determine how frequently each abstracted thematic finding occurs in the included studies. Qualitative metasummary is appropriate for synthesising studies that are thematic summaries or surveys of data.”

[3.8] “Page 4, 1st paragraph. RCTs are certainly the gold standard for effectiveness studies but it’s less clear cut for safety studies where an RCT may well be unfeasibly expensive. I’d be tempted to drop safety from this opening sentence, or define the types of safety studies that are meant.”

Response: After discussion among the authors, we concede the point about safety studies. We have removed all reference to safety studies from the text.

[3.9] “Page 4, 2nd paragraph. The Cochrane review has been recently updated and the new citation is:

Treweek S, Mitchell E, Pitkethly M, Cook J, Kjeldstrøm M, Johansen M, Taskila TK, Sullivan F, Wilson S, Jackson C, Jones R, Lockhart P. Strategies to improve recruitment to randomised controlled trials. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: MR000013. DOI: 10.1002/14651858.MR000013.pub5.”

Response: Thank you for providing the updated reference – the reference for the Cochrane review has been changed accordingly.

[3.10] “Page 4, 4th paragraph. Sentence starting ‘Maintaining recruitment activity over time..’ looks like a sentence that should end with a reference. Is the reference missing?”

Response: Apologies for the omission. The reference has been added: [6] S. Wilson et al (2000).

[3.11] “Page 5, 3rd paragraph. Minor point but the Box is called a figure in the version of the box/figure I got. I suspect that this is a feature of the journal submission system but it would be good to make sure the box is indeed called a box.”

Response: “Box” has been replaced with “Figure” in the text.

[3.12] “Page 7, 1st paragraph. It would be good if the opening line mentioned the total number of abstracts. Something like ‘The search identified 9236 abstracts of which..’ This information is in the figure but it would be good to add it to the text as well.”

Response: The text has been changed to include the number of studies identified as well as giving this information in Figure 2.

[3.13] “Page 7 and elsewhere. Several of the included studies don’t quote RRs so the authors have clearly calculated these themselves. All the ones I checked were correct so there’s no problem there but a single line in Methods mentioning this and what was used (RevMan?) would be helpful”

Response: The following sentence has been added to the Data extraction and analysis section of the Methods, “Risk ratios with 95% confidence intervals were calculated using RevMan software, where appropriate, to describe the effect of interventions.”

[3.14] “Page 8, Liénard study. There’s a typo, the study had 302 in the intervention group, not 301 (see Table 2 of the article). This study didn’t account for clustering, which is why the Cochrane recruitment review doesn’t give RRs for this study’s data and simply quotes the result given in the original paper. The authors might consider whether they want to do the same.”

Response: This has been changed in the text. The correct number was reported in my supplementary material. The relative risk has been removed and replaced with the raw data reported in the paper.

[3.15] “Page 9, 2nd paragraph. The Donovan 2009 talks about proportions agreeing to be randomized and proportions accepting allocation and it’s probably best to stick to this terminology rather than the current text. The Donovan paper isn’t completely clear about what represents actual recruitment but my guess is it is those accepting allocation that equate to recruited participants and if true, the authors’ current RR of 1.87 for 12 month recruitment is incorrect because this represents those

agreeing to be randomised (12 patients at 12 months) but not all accept their allocation (only 8 accept). It's the latter group that is interesting because these are actually recruited (if I'm correct in my interpretation of the Donovan paper). It would be good for the authors to check the Donovan paper and see which interpretation is correct."

Response: The reported results of this paper are open to interpretation, and the description provided within the Donovan paper was itself unclear. It can be argued that both those accepting randomisation and those accepting allocation are "recruited" (see response to reviewer 1, number 2.5).

The aim of this systematic review was to identify interventions that ultimately increase the numbers of subjects who consent to take part in trials. In this case the intervention increased the numbers of subjects who agreed to take part (randomisation) regardless of whether they accepted the outcome of the randomisation (allocation). For the purposes of this review, those accepting randomisation will be described as recruited.

[3.16] "Page 9, last paragraph. 'do RCTs provide the best available evidence'. Is this a question, or is the 'do' a typo?"

Response: "Do" has been removed from the text.

[3.17] "General. The authors have been ambitious in presenting both qualitative and quantitative data in the same paper and this makes the Discussion a challenge to write."

Response: Again, thank you for your comments.

[3.18] "Page 13, 2nd paragraph. Could the authors list a few examples of the 'logistical, ethical and scientific obstacles' mentioned? I think nested trials could be done more often but there are indeed obstacles and it would be good to state a few explicitly."

Response: Two sentences regarding challenges for host and nested trials have been included in the first paragraph of the 'methodological challenges' section of the Discussion: "Challenges for host trials include: increasing complexity and management burden; compatibility between host and nested study; and the impact of the nested study on host trial design. Challenges for nested studies include: investigators' concerns that host study investigators might have strong preferences, limiting the nested study investigators control over their research; and concerns about sample size which might limit statistical power."

[3.19] "Conclusion (or lack of). I missed a Conclusion to wrap things up so the paper ends a bit softly when something a bit punchier would be better. There's a Conclusion in the Article Summary section and this could form the basis of a main text Conclusion."

Response: Apologies for the oversight here. A conclusion section has been added that builds upon the conclusion from the abstract.

[3.20] "Table 1 I'd be tempted to drop this table."

Response: Table 1 was included in an attempt to highlight the lack of any real improvement over time in recruitment to RCTs. We think this is important given the attention given to improving recruitment to RCTs. Providing the information in the table gives a clear overview of the difficulties reported in recruiting, and provides the relevant references for anyone who may want more information.