Reviewer's report

Title: Improving recruitment into clinical trials: a mixed methods study investigating the ethical acceptability, feasibility and recruitment yield of the Cohort Multiple Randomised Controlled Trials design.

Version: 1 Date: 14 April 2014

Reviewer: Clare Relton

Reviewer's report:

Major compulsory revisions

This is an interesting and timely study. The main point I think that needs to be emphasised is the hypothetical nature of this study. This needs to be explicit in the title and the abstract...... and the impact of the hypothetical nature of this study discussed more fully.

I suspect that the hypothetical nature of the questions being asked will have affected the confusion expressed by the clinicians who were asked to recruit participants and also the low percentage of patients who were approached..... 131 vs 752 (if something is hypothetical then no one stands to lose or gain by participating - so why bother?)

In the discussion section it would be good to refer to other articles that attempted to assess the acceptability of a trial design using a hypothetical scenario, and also perhaps discuss their applicability to the real world.

Abstract

In the abstract you state that the cmRCT is proposed as a way of 'embedding the principle of research participation into routine health service setting's - am not clear where this was said in the original BMJ article describing the design - can you provide a direct quotation?

I am unclear as to what the 'principle of research participation' means here - this is referred to several times in the article - can you be explicit

Main text: BACKGROUND section

Paragraph 1

I suggest that patients don't "reject the principle of randomisation", but rather "reject the idea of their treatment being allocated by chance"

Paragraph 3

Rationale for intro of Zelen design was multiple..... " To address the reluctance of potential research participants for RCT enrolment' is too simplistic...... is the term 'reluctance being used as a euphemism here.
The randomised consent design was originally proposed by Marvin Zelen, as a way of maximising recruitment by only seeking consent to participate from those already randomised to the intervention arm, thus helping overcome the discomfort for physician and patient of explaining equipoise and acknowledging uncertainty (Zelen, 1979). It was hoped that the design would maximise external validity and statistical power while maintaining an acceptable level of internal validity.

"randomised without prior consent....' please define which particular consent is being referred to here

Not exercising informed choice" - please define the information that is being withheld here ....... and then how that information relates to what you refer to as the 'fundamental principle of ethical research conduct' - please describe which principle you referring to in full....

I dont think that the reference for the single consent design should be Campbell 2005. suggest you use Zelen 1979 instead or one of Torgersons earlier articles on the design

Paragraph 4
1st sentence is v unclear
I don't think single randomised consent design article mentions the term 'cohort'. The concept of embedding multiple single randomised consent design trials within a cohort is part of the innovation of the cmRCT design.

'Both these designs do not seek consent from participants randomised to the treatment as usual control conditions' - suggest rephrase as 'Neither design provides information about the trial treatment to the treatment as usual group'

Paragraph 5
Line 5 - Remove "about"
Specify what type of consent is sought - 'consent to accept the trial treatment'?
Line 10 - be specific about exactly what people are not told
line 13 - delete 'who are'

Paragraph 6
last sentence 'cmRCT design'

Paragraph 7
What do you mean by 'general consent' - be specific

Paragraph 8 RQs
The Trials Test - suggest revise to 'to being prospectively randomly selected to receive the offer of new treatments'
METHODS section

3rd paragraph

The three levels of consent from participants is interesting and useful. However level (3) is quite a mouthful - 'Randomly allocated active treatment procedures in future unspecified trials' - I wonder if this contributed to clinician reluctance to take part? - this type of terminology just would not be used with patients in a real world routine clinical setting........ I imagine it would be more along the lines of 'in the future, can we offer you treatments that we are testing? (but you wont be offered all the treatments that we will be testing)

Paragraph 4

Is the cmRCT really a 'system'?

Make clear that 'feasibility' here refers to hypothetical

Paragraph 5

when and how did thy invite them??

RESULTS SECTION

Paragraph 3 - 'consented to being randomised' does not feel very clear - do you mean 'consent to be chosen at random to be offered a treatment that is being trialled'

this phrase recurs during the article - please make it clear each time what is being referred to

Paragraph 7

Do you say what questions therapists were asked?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

As an author of the BMJ article describing the cmRCT design I have an obvious interest in research relating to the design. However I do declare that I have no competing interests as defined