Reviewer's report

Title: Who is the research subject in cluster randomized trials?

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Reviewer: Elina Hemminki

Reviewer's report:

I have both substance and technical comments. The first mentioned are subjective, and cannot be taken into account if the authors disagree. However, the authors could argue their own view clearer.

Substance comments

1. I understood that the authors share the current ethics principles, which ethics committees in many countries use. Many of them, however, may not easily apply to many CRTs, and I had hoped for a more critical / reflective opinion. The current paper is one of a series. The content of the other papers was not available, and it is possible that the other issues will be discussed in the other papers. Particularly I was thinking of informed consent and the distinction between care and research. It might be good to add a short list and description what the other papers deal with and how they may relate to the definition of a research subject.

2. A large number of CRT are made to compare service delivery (including preventive activities), which could be delivered without research. I.e. the option for research would not be “not giving the intervention”, but taking it into practice right away. This questions the logic of participant protection as now presented: which one is better? The definition for separating research and care (p.10) is not valid, particularly in CRT. All care is not just for one patient (example: infectious diseases, children vs. parents, availability of resources) and some research may be care at the same time. Clinician investigators are fine in many CRTs.

3. For example, their view of classifying new service delivery as an individual patient intervention is potentially dangerous. Currently service delivery methods are often taken into practice without evidence.

4. This being so, it is very important that any new research regulation suggested, should not impede CRT (for the above purpose). I would like to have a comments on the impact of this new definition, how it will influence the interest and possibilities to do CRT and to get evidence base health care. It may be that their future articles show that other solutions, such as waivers, solve the research threat. But many/ some countries do not have the possibility of a waiver: if someone is defined as a research participant, informed consent is needed (see also Helsinki declaration).

5. They largely use Anglo-American laws for analyzing the current rules. The rules are not the same in many other countries. The limitation and its potential impact should be acknowledged.
Technicalities
1. The paper is long and written like a story. As a health professional, I found it difficult to read, particularly as many of the concepts and words and not common English, but words with special meaning. I suggest a different structure, allowing readers to read only parts of the text, by their choice, and still get the authors’ point. This could be done by imitating the structure of medical reporting: background, previous literature, etc, current definition, its history, problems of current definition, new suggestions, arguments for the new suggestion etc. Some readers are not interested in the history or variation in different rules, but want to know what is now suggested and what follows from that.
2. The paper could also be shorter, and it could be made clearer by using tables (comparisons).
3. At places, the text goes: there is nothing, but actually there is something, and actually there is one thorough good example (e.g. current definition of research subject). That style is difficult for the reader. Go more straight/ reverse the order.

Details
1. The word “intervention” is used, as far as I understood, to mean an activity made within research. As this word also has a more narrow meaning (“experiment”), not covering “data collection intervention” (data collection by interview or from documents), I suggest changing the term.
2. There are some misspellings/ extra words, so a proof-reading is needed.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
'I declare that I have no competing interests'