Reviewers report

Title: Key stakeholder perceptions about consent to participate in acute illness research: a rapid, systematic review to inform epi/pandemic research preparedness

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Reviewer: Mihaela Matei

Reviewers report:

NH Gobat and collaborators addressed a major ethical issue recently encountered during the Ebola epidemic: what is the model of consent ethically acceptable in case of a pandemic research. The authors conducted a “rapid” evidence review of publications (from 1996 to 2014) dealing with consent models used in acute illness/emergency research. Out of these publications, they only found one paper specifically related to pandemic research.

The question of consent to epi/pandemic research is a very important and timely topic. For instance in Europe and this seems also to be the case in the USA, the current regulations don’t provide a specific ethical and legal framework for this type of research. In the absence of specific rules regarding the informed consent in pandemic research, the authors suggest that researchers, ethic committees and other stakeholders should apply the existing consent models such as emergency research consent model. The aim of this paper is to analyze the stakeholders “acceptability of different consent models for emergency research participation to inform pandemic research planning”.

At the very moment when human subject research regulations are revised worldwide (e.g. France, USA, EU), regulators should consider whether the existing legal and ethical frameworks are enough to protect patients in epi/pandemic situations while allowing researchers and public health authorities to address these specific issues in a rapid and ethical way. Even though this is not the position defended by the authors, their analyses of existing literature could inform the debate on the revision of the current legal and ethical frameworks relating to research on human subjects.

However, several key points of this paper need further clarification and discussion.

Main issues:

1. Regarding the scope of the paper, it is not clear whether the intention of the authors is to focus their analysis on pandemic research or, more broadly, on acute illness research.

   If their objective is the epi/pandemic research rather than acute illness research, the literature review conducted by the authors are not relevant for consent issues
in epi/pandemic research since only one paper out of 52 initially selected by the authors is related.

This point needs further clarification and new developments. For instance, following Ebola outbreak, several publications have recently appeared dealing with research ethics in infectious diseases outbreaks.

Having considered the above, I see two possibilities: one possibility would be to concentrate the paper on “acute illness” research with no mention of pandemics. One paragraph in the discussion section could mention and discuss the relevance of the study to pandemic research. Another possibility would be to remain in the field of pandemics and to update their review by extending the search to recent publications on Ebola.

2. In addition, it is not clear why the authors decided to focus their review only on consent models used in emergency research. They seem to imply that the practical and ethical issues raised by the inform consent process in epi/pandemics or acute illness research are similar to the issues encountered in emergency research. Some authors have already pointed out the specificities of epi/pandemic research and argue that the two situations are not “ethically” equivalent. For instance, Ruth Macklin et al. argue that “procedures for obtaining consent from individuals in a outbreak situation could depart from those typically used in other investigations and still be ethically acceptable” (Conducting Research in Disease Outbreaks, PLOS, April 2009, e333) This option is not considered and not even discussed in this paper.

For instance, pandemic disease research in developing countries (e.g. Ebola virus epidemic) raises specific consent issues related to cultural characteristics. In addition, cluster research methods are frequently used in this context raising distinct ethical issues.

Therefore it might be relevant and useful to consider and discuss in this paper alternative consent models, such as consent in cluster randomized trials.

2. Regarding the discussion, this section is mainly dedicated to recommendations. The specific ethical questions raised by this type of research are not addressed, in particular the ethical issues in relation to informed consent in pandemic/acute illness research.

In addition, if potentially important issues are mentioned in the first paragraph of the Discussion, like the discrepancy between participants’ and regulators’ views, comments on this point are rather scarce.

Another interesting finding of the study, which could be developed, is the importance of a direct experience of the third party consent model versus hypothetical scenarios.

Minor ones
1. (p.5, line 10) The “rapid review” methodology is not necessarily known from every one. Even if corresponding and pertinent references are given (ref 12-14), it could be further explained in a few sentences.
2. (p. 12, line 6) Another interesting finding of the study not discussed is the negative correlation between the rate of acceptability of enrolment using deferred consent and the level of risk.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

none