Reviewer's report

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

Version: 2  
Date: 2 September 2015

Reviewer: Neal Dickert

Reviewer's report:

This paper addresses an interesting topic, and the authors are to be commended for a thorough search of literature related to consent and alternatives to consent in the emergency care research context. As reflected in my comments below, the two major concerns I have with the manuscript have to do with the lack of clear contextualization or analysis of many of the findings and the lack of clarification regarding the range of pandemic research and the ways in which these findings really are or are not helpful in the context of such studies.

- Major Compulsory Revisions

1) The range of clinical studies on pandemic disease and the nature of the ethical and regulatory challenges that these studies might raise is not made clear. For example, a vaccine study in the context of a pandemic may raise challenges with regard to the rapidity with which review has to occur, uncertainties about preliminary data, etc. However, the consent process that would occur with individuals in that kind of study is not complicated by severe symptoms or concrete time limitations in the way that emergency care research is. As the authors state, there are certainly pandemic situations where consent processes are complicated and barriers do exist due to severe acute illness. However, there is no obvious reason to think that one would treat the consent process in those circumstances (and acceptability of alternative processes that are widely used in emergency care research) any differently in the context of a pandemic than other emergency care research settings. Rather, it seems more likely the case that what really distinguishes pandemic research is not consent limitations but rather the urgency to design, review, and launch a trial. Most emergency research, in contrast, is very heavily scrutinized and very thoroughly reviewed, with lengthy community consultation processes in many regions, for example. There are also often very strict standards with regard to adequacy of preliminary data, etc. The authors actually document the increased review that seems to occur but don’t call attention to the fact that the available time for such processes may be exceedingly limited in the context of pandemics.

2) Related to #1, the context of emergency care trials is essential to evaluating the appropriateness of different approaches to consent. In this respect, the findings from particular studies may be heavily specific to the condition or the study (TBI vs MI vs. stroke for example). Almost no context is provided for
pandemic research, making it very difficult to assess how the findings/studies reviewed really apply in the context of pandemic research.

3) There is very little contextualization of the results of the review independent of the connection to pandemic research. The results read simply like a list of results in different categories with very little to explain how studies relate to each other or don’t, how contexts vary, etc. And it is not clear why some data (such as likelihood of attending a public meeting) are in any way relevant to this study that is intended to focus on pandemic research. Where contextualization or interpretation of results is offered, it seems at times quite arbitrary.

For example, one piece used to support the claim that deferred consent is acceptable to patients is reported to have found that 48% of patients indicated deferred consent is acceptable. I would argue that this does not support this claim.

Similarly, with regard to the impact of risk on acceptability, “92% willing to enroll on greater than minimal risk study, 97% for a less than minimal” is taken to indicate significant effect of risk. These differences are in fact quite trivial from a “clinical” perspective.

Also, the following statement regarding third party consent is problematic in its failure to contextualize findings. “Fewer than half of patients (45% of 11) and clinician proxy decision makers (46% of 13) felt consent was necessary at all under emergency research conditions, while 71% of 17 spouses felt some form of consent was necessary [36].” This was a study evaluating perspectives on consent for a study of prehospital initiation of therapeutic hypothermia in the context of cardiac arrest. In addition to incredibly small numbers of participants, this is a highly specific context where decision making is exceedingly rapid, acuity extremely high, and the setting particularly problematic (out of hospital). Its applicability to many other acute care settings is likely limited.

4) While the full body of studies looking at attitudes across acute care research have not been put together, many “sections” of this review have been performed in large part before. It is thus not clear how novel the results are.

- Minor Essential Revisions

There are some more minor conceptual and contextual issues within the paper that do distract in an important way.

1) The statement early on that informed consent is an essential “safeguard against unethical research practice” seems to misconstrue the role of consent. Unethical studies are not made OK by informed consent. Rather, consent is an essential element of most ethical research for a variety of reasons (opportunity to refuse, protection of one’s own interests, etc.). This is likely simply loose wording, but being clear about the role of consent is important if one is examining ethical aspects of doing research without it.
Similarly, the following statement – “in addition, pandemic research frequently offers access to novel treatments and may confer a benefit not only to the participants but also to the wider population”- seems to misconstrue research outside of the context of pandemics, most of which is precisely designed to benefit the population rather than individual participants.

2) A bit more discussion of the variation in practices and approaches within Europe and in other regions could be helpful.

3) It is important to recognize that “deferred consent” and “waived consent” are really not discrete practices. In the US, for example, studies conducted under the exception from informed consent (called waiver in the paper) almost always require consent for continued data collection and sometimes use. Deferred consent has been pointed out on numerous occasions to be a bit of a misnomer because it is just an absence of prospective consent with later consent for data collection and/or use (you can’t consent later to something that has already happened). I recognize that the term deferred consent is used in many countries’ regulatory structure, but I would hope that this study would clarify that it is really not a discrete approach in general. This is not to dismiss it as an approach, just to say it is the same approach as waived consent in almost all cases.

4) The introduction is very difficult to follow. Most importantly, it does not address the nature of consent challenges in pandemic illness, and the connection to situations like comparative effectiveness research on standards of care is particularly unclear.

5) The basis for inclusion of pediatric studies but not neonatal studies is not clear.

6) It would be helpful to provide the full search strategy in an appendix.

7) Commonly some method of checking reliability or ensuring quality of data extraction is employed.

8) Box 1 is poorly organized. Additionally, waiver of consent under the US exception from informed consent for emergency research does not require that a study be considered minimal risk, though there are other provisions that must be met. The minimal risk requirement in order for waiver or alteration to be allowable is for studies that do not fall under this exception for emergency settings.

9) Table 1 is also poorly organized (alphabetical rather than by consent model, for example) and provides little helpful data from each study (such as a key finding or rate of acceptance).

**Level of interest:** An article of limited interest

**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