Author’s response to reviews

Title: Researcher and study participants’ perspectives of consent in clinical studies in four referral hospitals in Vietnam

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Author’s response to reviews:

Dear Reviewers and Editor,

Thank you for the extensive review of our paper. Kindly find the responses below each comment.

Best,

Jennifer
Reviewer reports:

Johannes Van Delden (Reviewer 1):

This is an article on the consent process for research in four hospitals in Vietnam. It describes the results of surveys and interviews with 41 individuals, both participants (4), family members (11), doctors (14), EC members (11) and one nurse. Data were collected in 2013-14, so rather old.

I would suggest to the authors to include descriptive data about the respondents in a table 1.

--We included more descriptive data regarding the respondents and created corresponding tables 1 and 2.

Also, at present all answers of the research stakeholders are lumped together. This is understandable because it concerns a small number of respondents, but in case of some results it might be good to know who held which opinion. For instance who were the 11 individuals who thought that it is not essential to inform about changes in the protocol?

--We decided to keep the research stakeholders lumped together in the table but in the text, we explain in more detail about certain results. We also made the text more explicit about which participants held multiple roles (e.g. physician and EC member).

It seems to me that there is also a gap between the current and desired level of knowledge of these stakeholders.

--This is a fair point. We added this in the discussion section.

In general the statistical testing doesn't help much with such small numbers.

--We agree and removed the stats column.
As such, this is a small descriptive study on an ethically relevant subject matter in a heterogenous group in a local context. There is some room for such studies in the academic literature, although this room is limited because it is often unclear what others who operate outside this context can learn from it. This is precisely the weak point of this manuscript: in its current version it isn't clear what we can really learn from it. This problem already starts in the introduction where the research question is formulated as 'accounting for the broader context of a study and the participants' lives...’. It would perhaps help if the gap that the authors mention in the next sentence is elaborated on.

--We edited the introduction to clarify the gaps from the site. We also edited the section surrounding the broader context as this was meant to reflect an overview of the literature findings.

In the discussion the reader is told that he needs to understand the broader social and economic constraints of the participants. Sure! But please explain what you learned from the data, and what others can learn from it too.

--We added some of what we learned into the discussion. I think the take away (which was not clear in the past draft) is that the stakeholder groups often operate with different motives and understanding of what the consent process should mean and while at times they stated the “right” answer, they also spoke about how they practiced consent, which did not always connect.

My other problem with the manuscript is that the findings are not critically discussed. It is alright to search for a better translation of the word research into Vietnamese but it is not at all alright to 'provide just enough information so that participants feel comfortable and safe but not too much so that they become scared of the research' as EC members and study doctors apparently said. In stead of concluding that these stakeholders were wrong, the authors state in the conclusion that in a hospital patients may suffer from the therapeutic misconception. I would say that this is precisely why it is so important to make it absolutely clear that the patient is invited to participate in research. The fact that research stakeholders 'argued that the word for research should be modified to increase acceptance of joining research studies' goes uncriticized as well, where it should have been. This goes for a lot of the quantitative findings.
--We added more critical discussion regarding the results in the discussion section including the findings about both the level of information, as well as the opinion to modify the consent discussion to increase participation. We also presented more of the quantitative findings in the results section.

Henry J. Silverman (Reviewer 2):

The authors report their findings are an important subject involving the consent process in Vietnam. The study design involved a mixed method approach: surveys and semi-structured interviews that were obtained simultaneously rather than in a sequential manner.

My general comments are as follows:

1. I encourage the investigators to provide further characteristics of the setting and of the participants and the relatives of child participants who gave informed consent. Regarding the setting, the authors mentioned that the study was conducted in "referral hospitals", it might be useful to know whether these hospitals were public or private hospitals". Regarding the 4 study participants and the 11 family/relatives of child participants, what were their educational levels, severity the health status and the economic status.

--We did not capture economic or education levels of the participants, however, we added information on the study disease and the trials under which they had participated.

2. Adult study participants might hold different perspectives and attitudes from parents/relatives of child participants. The literature has reported on certain of these characteristics, for example, it has been reported that parents of children expect benefits from participation and are very concerned with risks. As such, it might be helpful to know whether there were appreciable differences in their perspectives/attitudes on the interview responses.

--We did not see differences in these data, however, this topic was not fully probed upon in the interviews.
3. Why did the authors conduct the study with "relatives" of child participants and not the parents?

--Within our contexts, it is often the relatives who would bring in potential patients and they were the ones who consented for the participation of the children in the study. We focused the data collection on the person who provided consent, in many cases a representative, not the parent, as they were the ones accompanying the children.

4. Information regarding the type of study to which study participants gave consent to participate in might be helpful in understanding their responses in the interviews. For example, studies have shown that responses of study participants differed according to the perceived risk associated with the study: for example, perceived risks differed between between survey/interviews, blood sampling, and experimental drugs and as such, responses differed accordingly.

--Integrated into table and text.

5. The authors use the following terms interchangeably and somewhat inconsistently: perspectives, attitudes, opinions, experiences, and values. For example, the title states "perspectives", but there are many places in the text where the authors refer to the responses as "attitudes", "opinions", and "experiences". In general "perspectives" refer to as to what individuals "see" in the world, whereas "attitudes" refer to how individuals "evaluate" their perceptions. It appears that the authors obtained both perspectives and attitudes and I encourage the authors to clarify which of the responses represented either of these two categories.

--We edited the terminologies and kept it consistent throughout.

6. How did the authors determine the sample size for the surveys? Also, regarding the interviews, was they the sample size determined by when the point at which "saturation was reached?
We added more details on sampling in the methods section.

But the sample size overall was determined in part based on the timeline/budget of the bursary project, as well as the point at which saturation occurred (during interviews). They collected the survey and interview data during the same data collection time point so she was able to summarize key points (see also point 13 about probing).

7. I suggest several ways in which the organization of the manuscript can be improved, thus enhancing clarity. For example, results regarding recruitment are reported in the methods section rather than the results section. Also, the authors tend to interpret some of their findings in the results section rather than the discussion section (e.g., their discussion regarding the existence of choice in lines 247-256).

We moved the recruitment results to the results section and we moved interpretations into the discussions section, as well as several other small edits in the study setting/procedures sections for clarity and better flow.

8. In several places in the manuscript, authors make reference to how medical care and research can be blurred and gave examples of when the interview responses reflected such "blurriness". Did the authors find the therapeutic misconception to be a prominent theme? For example, on page 9, the authors mentioned "The delineation of clinical care and nghien was not clear for this patient".

We expanded the discussion on therapeutic misconception in the discussion as this was a prominent theme but perhaps brought on by the research stakeholders’ manipulation of the consent process (e.g. using different terms, not relaying all the details about a study to increase enrollment).
9. The authors discuss in the results section the use of the word neghien to build trust, but at the end of this section on page 9 the authors comment on how research in "trusted institutions" is a starting point for increased trust in the research process. As such, the authors intermingle two distinct points: use of the word neghien to build trust and the presence of trust a priori to enhance the acceptance of research.

--We reworked this section so that the text more clearly outlines our conclusions regarding how the word research and the extent of information to relay to patients impacted voluntariness and trust building – see also point 12 below.

10. One of the survey questions regarding the importance of the elements of informed consent asked about the "inclusion of the word research". Did survey used the word neghien for this question?

--Yes, the survey used the same word for research.

11. The results of the survey showed that 73.3% % of the study participants thought that the use of the word "research" was essential, but it appeared that many of these participants expressed negative attitudes of the use of this word. It would be helpful if the authors can discuss more about this discrepancy. This would also be important in understanding why study participants held such negative attitudes of the word research, especially since these participants had given consent for participation in research.

--Thank you, we agree that this clarification is necessary. We included more detail and context for this section. Some of the negative attitudes toward research were from the past experiences and/or an overall history of abuse and ethical violations in research while more explicitly, in interviews, the study participant stakeholders often spoke about what they perceived their community’s meaning of research. The research stakeholders often spoke of how they perceived participants to understand research. We added text to clarify.

12. In lines 240-242, the authors state that the use of the work neghien cicu would ensure that the study participants would realize that the participants had a choice. I am not sure of the basis of this conclusion.
We reworked this section so that the text more clearly outlines our conclusions regarding how the word research and the extent of information to relay to patients impacted voluntariness and trust building. (see section on this finding)

13. Beginning on line 200, the authors state that it was difficult to determine from the interview data whether providing limited information was a strategy to provide sufficient information to a population that had limited understanding or was a strategy to hide information that might be scary. I am wondering why this issue was not unpacked during the interview process itself.

--Unfortunately, the interviews were analyzed after the data were collected therefore the PI (who was a bursary student; also the second author) missed some of the probing opportunities during data collection. Methodologically, the PI learned several key lessons about collecting qualitative data: one of which was to probe into more detail and reflect and analyze while data collection is ongoing. We added a limitation section to the discussion section to highlight a few of the limitations of the results we present in this paper.

Other comments:

1. In the results section, the author would use the word "many" and "other" when referring to the responses. It might be helpful to provide the exact number of these responses.

--We added more quantification for the responses for qualitative data, when appropriate (edited throughout)

2. The authors refer to researchers, members of research ethics committees and study coordinators as "stakeholders" and the individuals who gave consent for research participation as "participants". To reflect the current thinking that both groups of individuals are equal partners in the research enterprise, I suggest that individuals who participate in the research should also be considered as stakeholders.
Yes, we agree with this point and have revised the paper to include all participants when we talk about stakeholders and then designated whether they were study participants or researchers, as appropriate. This is also outlined in the tables for more clarity. (edited throughout)

3. On line 246, where the authors refer to the setting of the interviews, the word "privacy" is probably a more appropriate word than "confidentiality", which refers to the obligations of researchers "after" data are obtained.

--Good point. Edited.

4. The authors mention they obtained "written" informed consent. Several research regulations mention that when the only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality, then waiving documentation of the signature would be appropriate. The authors should explain why written consent was obtained instead of verbal consent, which is ethically preferable.

--We obtained written consent because this was a requirement of the EC committees who approved the study at that time. I added a brief fragment about this in the text to clarify. This requirement is changing somewhat at Hospital for Tropical Diseases (e.g. for a recent study, the committee approved verbal consent) but this study was approved several years ago and the committees did not approve verbal consent for any type of study then. Added brief statement.