Author's response to reviews

Title: Informed consent in Sri Lanka: a survey among ethics committee members

Authors:

Athula Sumathipala (spjuats@iop.kcl.ac.uk)
Sisira Siribaddana (nipuna@stmail.lk)
Suwin Hewage (suwinhewege@yahoo.com)
Manura Lekamwattege (projects@sysnet lk)
Manjula Athukorale (athukoralam@gmail.com)
Chesmal Siriwardane (chesmal@gmail.com)
Joanna Murray (Joanna.Murray@iop.kcl.ac.uk)
Martin Prince (Martin.Prince@iop.kcl.ac.uk)

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Author's response to reviews: see over
Dear editor

We have replied in bold to the reviewer’s comments and changes done in the original manuscript are shown *below in italics.*

**Reviewer's report**

**Reviewer:** Samia Hurst

**General**

This is an interview study of ethics review committee (ERC) members in Sri Lanka, regarding requirements for informed consent in human subjects’ research. The authors present data based on 29 interviews in a context where little data exists. This makes their contribution valuable. However, there are currently several points in the manuscript that require strengthening.

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**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

1. It was not clear to me what the interest of this study’s results were. On second reading, it does seem clear that this is an interesting project, but the authors could clarify their purpose to a greater degree. Is the primary goal to contribute to shared experience of ERC members? To contribute to critique/local adaptation/validation of the WHO check-list? To provide a perspective on adaptations necessary in a context such as Sri Lanka? The goals should be clearer both in the introduction and in the discussion.

**Reply**

We have clarified our aim (purpose) more clearly in the background section

“This study specifically aimed to examine current practices and views of ERC and EC members on the issue of informed consent in the local context and in comparison to international requirement.”

2. This study seems to use a mixed quantitative-qualitative methodology. This is fine, but does merit greater clarification of methodology. Was a random sample selected,
or was recruitment based on methods of qualitative research, such as snowball sampling? How were open-ended responses coded?

**We did not use a random but a purposive sampling.** The method and the number were predetermined during the protocol development stage by series of consensus meetings. Open ended responses were entered in SPSS using ‘string’ value and then coded manually after pasting on a word file.

3. The question of what research subjects have understood prior to enrollment is indeed important, but it is not specific to developing countries. Studies after study in industrialized countries have found similar gaps in information and understanding. (1-6) This should be clarified as part of the context.

**Thanks, we appreciate the comment and necessary changes are done in the introduction**

“A number of studies in industrialized countries have shown the existence of gaps in the information provided and the understanding of research participants [9]. It would be fair to assume that this issue is more pronounced in a developing country setting where poverty, low literacy and large needs gap make the participants more vulnerable to exploitation [10]. “

4. Discussion of ERC members’ views on the requirement of written consent for illiterate, debilitated, or mentally handicapped research subjects does seem to merit discussion. This is currently short enough that the authors’ intentions are not clear. Do they believe that the ERC members who would exempt illiterate subjects from the requirement of written consent are correct? Are misguided, perhaps even showing how capacity building in bioethics is needed? Are signaling a logistical problem with a requirement of consent (rather than written consent) that they do not question fundamentally even in cases where they believe that such consent cannot be in written form? I am outlining these different possible interpretations simply to highlight the need for greater clarity as to what the authors make of this result.

**We acknowledge this point and have discussed these problems in detail in the discussion**

*The majority of participants stated that not all research needs written consent.*

*Elaborating on the research types that do not warrant written informed consent most*
participants mentioned research that has little or no risk to the participants. All the above factors appear to be reflecting on the inadequate resources to review all research. Additional concern voiced was that written informed consent might limit participation even in research that has minimal-risk [15].

Three ERC members were of the opinion that illiterate, debilitated or mentally handicapped participants need not provide written consent. These groups are highly vulnerable participants in research and needs special protection like prisoners and children. Because the questions were pre-agreed and finalized before the interview this controversial statement was not probed further. However, they also proposed alternative methods for obtaining consent. Illiterate participants cannot sign or thumbprint a form they cannot read [16]. Participants’ significant other, clinic nurse who are not involved in the research or a patient representative can be involved during the consent process. Ombudsman structure was proposed by us not only when the participants are vulnerable (debilitated, mentally handicapped or illiterate) but in developing world where there is an exaggerated asymmetry in knowledge and authority exists between researchers and participants [16]. Verbal consent is an alternative but proof of it is an issue. With more than 90% literacy, illiterate research participant in Sri Lanka may be a rarity but due to adverse socioeconomic conditions and free health care, the asymmetry between physician researcher and patient participant will always be an issue”

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

5. On page 7, it is not clear whether “leaflets” refers to information leaflets written by investigators, or to the standard format offered by the ERC. Though it becomes clearer later in the paragraph, it is still not clear how respondents answered this
question. Did they give an opinion on a range of different information leaflets? Or did they choose a “representative” one, or a recent one?

This was a question about ‘What do you think about the quality of the information leaflets and consent forms that you receive?’ We have made it clear that this was about information leaflets they receive.

Discretionary Revisions (which the author can choose to ignore)

6. Were respondents who agreed that there should be uniform format members of the ERCs that provided them?

I have provided the raw data below. We have done the necessary corrections in the text.

<table>
<thead>
<tr>
<th>Members of ERCs that require information leaflet and consent form</th>
<th>Believe in uniform format for info. leaflet &amp; consent form</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>applicable-not members of ERCs</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>yes</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>no</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>14</td>
</tr>
</tbody>
</table>

“Six participants who believed there should be a uniform format was from the ERCs that provides a standard format for information leaflets and consent forms. Only one participant from such ERCs disagreed about uniform format.”

7. Page 8: what does “studies where the participants are at the same level as researchers” mean?

This is clarified

“………..participants are at the same academic or professional level as researchers. “

8. Results include the view among respondents that “constraints on reviewing all studies would be, human resources and time available” (p8). The discussion then mentions the importance of “capacity building on bioethics” (p10), but no longer the need for
more material resources. As the strength of results regarding capacity building in bioethics and regarding the need for resources seem equally strong, it is strange to see only one reflected in the discussion.

This is an interesting argument, but we were not clear about what would be the material resources are. I think in USA, ERC members are professional or at least they get paid for it. In Sri Lanka all ERC members work honorary as a part of their academic or professional job. Other material resources such as stationary, phone, fax, computer and transport facilities are essential for efficient functioning of ERCs. We also believe academic environment with reference material, books and journals should be available for ERC members. Sri Lanka and most of the developing countries lack adequate training and academic resources (books, journals and reference material) to perform ethics review. This was what we meant by capacity building, getting more people trained, increase awareness and attract more academics so there is sufficient critical mass.

“Increased and continuous training, adequate educational and reference material, increased awareness and attracting more academics will increase the critical mass and increase capacity in existing ERC members. “

Reviewer's report

Reviewer: Akira Akabayashi

Reviewer's report:

General

In this study, members of Sri Lanka’s ethics review committees were interviewed about the design of printed explanations and consent forms. While discussion of international research review design is important as design standards currently vary by country, this paper would require many revisions before being considered for publication.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. First, it is not entirely clear what is new or important about this study. Though the authors offer a discussion on how the content of printed explanations and consent forms can be problematic in the approval of international research
involving Sri Lanka and the UK, the discussion does not sufficiently highlight the novelty or importance of this topic.

To our knowledge exploration into

2. “ERC” is used to designate both “ethics review committee” and “ethical review committee.” The expression “ethics committee” also appears in the manuscript, which is confusing.

ERCs have been used throughout to identify Ethical Review Committees.

“Ethical Review Committees (ERC) reviews research and Ethics Committees (EC) carry out other ethics related activities. At the time of conducting this research, there were ERCs in 5 out of 7 medical schools in Sri Lanka [1]. In addition, there were three ERCs and two ECs in professional associations and research institutions.”

3. It is not clear when this study was conducted or what selection criteria were used for inclusion of committees in the study

The study was conducted in 2005 and 2006. There were no selection criteria.

“These interviews were conducted over a period covering the latter part of 2005 and early 2006.”………………………………….. “The only selection criteria was participants have to be members of either ERCs or ECs, available and agree to be interviewed. “

4. It is also unclear why subjects were interviewed about the WHO checklist. Additional information about each of these points should be included in the manuscript.

The WHO has been trying to improve the quality of information leaflets from developing world. They provide a checklist for any study that requires ethical approval by them. This was an itemized list about contents necessary for information leaflet and we thought it would be a good reference standard to monitor the quality of information leaflet. First it was produced by a body (WHO) that has special interest in developing world health and research and second it was itemized into individual components very succinctly. For our study on Common mental disorders, alcohol intake and suicidal intention among twins and singletons in Sri Lanka we also obtained ethical approval from WHO Secretariat Committee on
Research Involving Human Subjects (SCRIHS). This made us to alter our information leaflet according to their guidelines. There are many published studies that has taken ethical approval from this body in the WHO (Semba R. D., Muhilal & Nasrin E. G. Integration of vitamin A supplementation with the Expanded programme on immunization does not affect seroconversion to oral polio vaccine in infants. J. Nutr. 1999;129:2203-2205)

“The next part of the questionnaire contained components of WHO Secretariat Committee on Research Involving Human Subjects (SCRIHS) checklist on information leaflet. These components were rated on a 4 point likert scale (ranging from extremely important to not important) about their relevance in the local context.”

5. On page seven, the authors state that the SLAAS ethics committee is not a research ethics committee. The reason for including interviews with members of this committee should be reviewed.

Members of SLAAS ethics committee comprises members from non medical field and is an apex body of scientist in Sri Lanka. Not interviewing them would be unethical as well as ignoring a body that has voiced their opinion on aspects of bioethics that others have not (e.g. animal rights and ethics of animal research). They do not review research proposals but are active in eth field of ethics.

6. There are also a number of language and spelling errors which require review and correction.

In addition, references must be consistent; it is not appropriate to quote from works still in the submission process (Ref 12).

We have removed the reference although now it is accepted

7. Finally, the quality of the discussion is poor overall. While studies from Sri Lanka are welcome, I look forward to more refined submissions.

Discussion is redone and is more refined now

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Typo (examples)
p. 4 top: Back ground --> Background
p. 4 line 5: ERCs primary duty --> ERCs' primary duty
p. 5 line 1: the ERC members views --> ERC members' views
p. 9 line 9: non invasive --> non-invasive
p. 9 line 14: without written consent --> need period
p. 9 line 20: safe guard --> safeguard
p. 11 line 7: minimal-risk [15] --> need period

All typos corrected

Discretionary Revisions (which the author can choose to ignore)

Reviewer's report
Reviewer: Dominique Sprumont
General
Globally, both the topic and the article are interesting. As such the paper can be published with minor revisions.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. One problem concerns the sampling of the participants in the study. First, in the background (back ground?) section, it is mentioned that there are 5 Research Ethics Committees (RECs) in Sri Lanka plus 5 other ethics committees, while in the strategy for data collection section there are 8 RECs identified while in the results section, there are 9 RECs with a 10th ethics committee mentioned as not being a REC. At the end, it is unclear how many RECs there are finally in Sri Lanka: 5, 8, or 9?

We acknowledge the confusion in numbers and have clarified it. At the time of this research there were 10 committees. Eight ERC that reviews research proposals and two ECs that do not review protocols but engage in other activities related to ethics.
Now there are much more. We have interviewed members from 5 ERCs and one EC. This is clarified in the manuscript.

2. Second, the sampling size was supposed to be originally 20 out of the 60 members of all RECs in Sri Lanka. The final number of participants is 29. How was the sampling done? Did all RECs were invited to participate in the study, respectively were all RECs members contacted as mentioned on p. 6 (point 4 of the strategy for data collection)? It would be important to specify how this number of 29 participants was reached: are the 29 the only ones who answered the questionnaire or were they actually selected?

All 29 have answered the questionnaire. There was no selection.

“A purposive sampling method was used in the selection of respondents from ERCs. More than 30 individuals were approached initially as some may not be available or agree to participate. The only selection criteria was that participants had to be currently serving members or who had served in the recent past in either ERCs or ECs, agree and available to be interviewed.

Interviewers initially setup an appointment with each member requesting their participation in the study. The research project and what was expected from them were explained. Then we provided an information leaflet about the project and the opportunity to contact the main investigators if further clarifications were required.

Some directly consented and participated in the interview. Some requested authorization for participation from the ERC they represented. This resulted in formal approval being requested from some of the ERCs. “

3. This issue should at least be addressed in the discussion section, especially if the questionnaire was send to more than 29 participants it would be useful to explain why some did not answer and give the percentage. Third, to what extend the sampling is representative of the RECs composition in Sri Lanka. Unless this
last point is clarified, the conclusion can not pretend to present the opinion of all
RECs members in Sri Lanka.

The questionnaires were not send RA visited the respondents and obtained answers.
“Twenty-nine participated in the study, exceeding the sample size of 20 decided as
sufficient during the consensus meetings. They were drawn from approximately 60
members of five ERCs and one EC that functioned in Sri Lanka at the time of the study.
Medical as well as non-medical members were interviewed. The strategy of over
sampling of lay members did not succeed as most ERCs had none or very few lay
members.

Members of the ERCs from Sri Jayewardenepura (5), Ruhuna (3), Peradeniya (5),
Kelaniya (5) and Colombo (1) medical faculties and the Medical Research Institute (5)
and members of the EC of Sri Lanka Association for the Advancement of Science –
SLAAS- (2) and Sri Lanka Medical Association (3) were interviewed. Members in two
ERCs neither declined nor participated.

Participants in this study were professionals from diverse fields such as Parasitology,
Sociology, Zoology, Biochemistry, Psychiatry, Community Medicine, Physiology,
Microbiology, Pathology, Biotechnology, Veterinary Medicine, Forensic Medicine and
Pharmacology. Five participants were microbiologists, making it the most represented
area while Community Medicine and Physiology had three representatives each. There
were 22 male and 7 female participants. There were eight professors among the
participants. Five members of the ECs did not answer the first three questions, as they
do not review research proposals. The first two paragraphs below describe results only
from 24 participants who were members of ERCs.

4. Another problem is linked to the presentation of the results. It should be
harmonized. For instance on page 8, in the need for ethical approval section,
figures are first mentioned as followed: 20 (69 %), and then three lines under (10;
48.7%).
We have corrected this
“The majority, 20 (69%), believed that all research need ethical approval. According to them, downside of reviewing all studies are limitations in human resources and time 8 (40%), and lack of capacity 10 (50%).”

5. Sometimes, numbers are in letter (again page 9 in the same section) or not.

We have used uniform style in describing numbers. All numbers less than 10 are spelt out and more than 10 Arabic numeral is given except at the start of the sentence. There are some exceptions when describing table numbers and sequence of numbers

6. The presentation of the tables could as well be improved and simplified.

We have tried to simplify the tables

7. This is also the case for the list of abbreviation which should separate more clearly the abbreviations from their definitions.

We have added list of abbreviations

8. Some notes should also be revised, for instance there seems to be a problem with the note 11.

This note is removed

9. The discussion and conclusion only reflect part of the results. The limits of the study are not presented, neither the bias in the selection of the participants (see comments above) and in their answers (do they answer what they know or what the interviewer wants to hear?). Some questions in the interview guide (Q2 – Q5) are open and their answers should therefore be more varied than the ones discussed in the paper.

The limitations are discussed in a separate paragraph and the discussion is more refined now. We have not discussed the obvious biases in a questionnaire study but limited it to characteristics in this sample and pre agreed structured questionnaire. The answers to the questions were varied but we have summarized it into salient findings presented in the manuscript.

Discretionary Revisions (which the author can choose to ignore)
10. If the study remains mostly descriptive, we would have found interesting to have a discussion on the difference between the answers of the participants and the ethical requirements on informed consent as recognized in the main international documents of references in research ethics.

This is a very good point and we plan to do this in another study analysing the data.

As that will be rather long for a modern research paper

11. For instance, when some participants consider that illiterate, debilitated or mentally handicapped need not provide written consent. Of course, this is based on the fact the subjects are deemed incompetent, but it does not solve the issue of who should consent for them, normally their legal representatives. There is the same problem with the issue on verbal consent and the need to keep a written proof that the consent was obtained.

We have discussed this issue in more detail fashion. Please see the 4th point raised by Samia Hurst and our reply to it.