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**ARTICLE DETAILS**

| TITLE (PROVISIONAL) | International health research monitoring: Exploring a scientific and a co-operative approach using participatory action research |
|---------------------|--------------------------------------------------------------------------------|
| AUTHORS             | Lang, Trudie; Chantler, Tracey; Cheah, Phaikyeong; Miro, George; Hantrakum, viriya; Nanvubya, Annet; Ayuo, Elizabeth; Kivaya, Esther; Kidola, Jeremiah; Kaleebu, Pontiano; Parker, Michael; Njuguna, Patricia; Ashley, Elizabeth |

**VERSION 1 - REVIEW**

| REVIEWER             | Dr. Anil Kumar |
|----------------------|----------------|
| National JALMA Institute for Leprosy and Other mycobacterial diseases, Agra, India |

| REVIEW RETURNED      | 21-Oct-2013 |

| GENERAL COMMENTS     | The research question "On-site monitoring" as a process to improve research quality is a good idea and authors have tried to explore some of the related questions. One thing could be "Who shall be the person or agency to ensure on-site monitoring as a part of research protocol to make mandatory?. To me this could well be encouraged by funding agency. However there need to be convincing agreement between researchers and funding agencies with the aim of improving rather than threatening. Although the present article as a beginning of novel idea is recommended for publication as a special research article but authors need to elaborate on points clearly from receiving and delivering ends and how effectively funding agencies could translate on-site monitoring in improving quality of research/trials. |

| REVIEWER             | Enriqueta Pujol-Ribera |
|----------------------|------------------------|
| INSTITUT UNIVERSITARI D'INVESTIGACIÓ EN ATENCIÓ PRIMÀRIA (IDIAP) JORDIO GOL |

| REVIEW RETURNED      | 27-Oct-2013 |

| GENERAL COMMENTS     | Seven point should be adapted to studies with qualitative methodology. Based on my knowledge of English, the manuscript is well written, clear and understandable. Nevertheless, I'm not expert in this aspect. |
After a careful review of this manuscript, I have concluded that it is a very interesting qualitative research on the value of a scientific and co-operative approach health research on-site monitoring, which may be accepted. There is a lack of evidence about the study topic, and there is a need for further evaluation trials.

Qualitative methodology and the use of a case study as a strategy to deepen in the dynamics present in the study contexts (the places where the monitoring models are coordinated and applied in Thailand, Cambodia, Uganda and Kenya) seem very appropriate.

The research questions of the study are interesting and relevant. The description of the methods is clear, accurate and transparent. The sampling strategy is appropriate and participants selected are adequate to provide the type of knowledge sought by the study. The type of analysis is appropriate, and the interpretations are clearly presented. The findings are based on a theoretical and conceptual framework. The contributions and limitations of the study are explicitly described and discussed. Based on my knowledge of English, the manuscript is well written, clear and understandable.

I suggest some minor modifications

The authors use many acronyms that hinder the readability of the manuscript. I recommend leaving only those that in the authors' opinion are essential.

Study participants
The sampling strategy is appropriate and explained. Participants selected are adequate to provide the type of knowledge sought by the study. Nevertheless, it would be interesting to know how many potential participants were in EACCR and in MORU, and if someone had refused to participate and why.

The sample size is explained, but not justified. For example there is no reference to whether the authors would reach saturation of the discourse.

Related to ethical aspects, in addition to informed consent, it would be important to know how the investigation team kept the anonymity and confidentiality, if they did. Although according to the type of study, the approval of a research ethics committee may not be necessary, I suggest specify this aspect.

Analysis
Analytic approach is described in depth and justified. Themes were derived from the data inductively. Context and/or meaning are richly detailed. It would be convenient to describe the basis on which quotes were chosen.

Figure 1 and 2
I suggest not using acronyms or to put their meaning at the bottom of the figure so it is self-explanatory

Table 1
I suggest clarifying participants in the Group 1 and Group 2 in EACCR Case Study column, and not to use acronyms or to put their meaning at the bottom of the table so it is self-explanatory.
Overall, this is an excellently written and interesting paper. My reservations are considerably less serious than suggested by my review checklist ratings.

This paper provides an excellent qualitative review of the experiences of both the monitors and the research staff being assessed in two real statistical monitoring exercises. The findings are excellently analysed and presented, and the findings are both illuminating and important. As a statistician, I recognised the concerns expressed about the potential "threatening" aspects of such a review, and I was impressed by the sensitive and helpful way in which these were handled. Equally, the concerns expressed by the monitors, while probably not totally unexpected, were important - and this is possibly the first time these issues have been properly identified and documented. My view as someone who may well be involved in such monitoring from both sides (i.e. both as a monitor and as someone whose work will be monitored) is that the results presented are hugely informative. I have no doubt that this paper when published will have a major impact (for the good) on statistical monitoring practice.

My only concern is that, in my view, the aims of this project are slightly over-stated (closing paragraph of Background section). As indicated above, it is my opinion that the authors provide an excellent documentary of the process of statistical monitoring through the perspective of the monitors and those being monitored - so this aim is achieved totally.

I am not convinced, however, that the authors have been able to determine the value of the two monitoring models assessed, nor have they been able to produce any insight as to how their value can be measured. For this, some evaluation is needed of the impact of the monitoring on the quality of data produced and, indeed, the overall quality of the study. For example, were any processes identified that were having a major negative impact on data quality? - if so, would these have been detected anyway or would either monitoring model have been the only way in which such erroneous process could have been detected and rectified? Were any individuals found to need some additional training or advice on data management/quality? Were any issues identified that could have impacted negatively on patient safety and well-being while participating in either trial?

The authors provide excellent evidence to inform the process of statistical monitoring, which should lead to better practice in future exercises, at least in terms of ensuring that monitoring is done in an appropriately non-threatening manner and that both the monitors...
and those being monitored engage in a professional and mutually helpful manner. For that reason, I believe that this paper is a major contribution and suitable for publication.

However, I would wish to argue for a moderation of the stated aims. Defining "value" as the identification of problems and their rectification, there is no real evidence relating to this in the paper - but this would probably require a slightly different methodology in any case.

With this very minor revision to properly reconcile the aims and the results/findings reported, I strongly support the publication of this paper. It deals with a very under-researched but increasingly important element of clinical research conduct - and provides important empirical data to help improve the conduct of statistical monitoring.

**VERSION 1 – AUTHOR RESPONSE**

Dr. Anil Kumar
The research question "On-site monitoring" as a process to improve research quality is a good idea and authors have tried to explore some of the related questions. One thing could be 'Who shall be the person or agency to ensure on-site monitoring as a part of research protocol to make mandatory?. To me this could well be encouraged by funding agency. However there need to be convincing agreement between researchers and funding agencies with the aim of improving rather than threatening.

Although the present article as a beginning of novel idea is recommended for publication as a special research article but authors need to elaborate on points clearly from receiving and delivering ends and how effectively funding agencies could translate on-site monitoring in improving quality of research/trials.

No specific statistical use is done. However there may be a need to randomize the researchers, KI, Monitors globally to broaden the knowledge and experience on 'on-site monitoring' their agreements and suggestions.

Response from Authors
We appreciate the supportive and constructive comments made by Dr Kumar. In terms of his first point about who should make this mandatory we think that this is well covered in the background section where we explain that appropriate monitoring of trials is indeed a ICH-GCP requirement and therefore this is a given and funding is to be found. However what we have aimed to explore here is some alternative mechanisms for monitoring beyond the expensive one-size-fits all contract research organisation model.

There are no formal power calculations or randomisation because this study uses social science methodology and this is not appropriate.

Enriqueta Pujol-Ribera
1. The authors use many acronyms that hinder the readability of the manuscript. I recommend leaving only those that in the authors' opinion are essential.
2. The sampling strategy is appropriate and explained. Participants selected are adequate to provide the type of knowledge sought by the study. Nevertheless, it would be interesting to know how many potential participants were in EACCR and in MORU, and if someone had refused to participate and why.
3. The sample size is explained, but not justified. For example there is no reference to whether the authors would reach saturation of the discourse.
4. Related to ethical aspects, in addition to informed consent, it would be important to know how the
investigation team kept the anonymity and confidentiality, if they did.
Although according to the type of study, the approval of a research ethics committee may not be
necessary, I suggest specify this aspect. Analytic approach is described in depth and justified.
Themes were derived from the data inductively. Context and/or meaning are richly detailed. It would
be convenient to describe the basis on which quotes were chosen.
5. Figure 1 and 2 I suggest not using acronyms or to put their meaning at the bottom of the figure so it
is self-explanatory

6. Table 1 I suggest clarifying participants in the Group 1 and Group 2 in EACCR Case Study column,
and not to use acronyms or to put their meaning at the bottom of the table so it is self-explanatory.
7. All references follow the rules, but in reference 9, the year of publication is missing.

Authors response
1. We agree and have now used abbreviated terms for the research institutes and limited them
throughout to essential use only
2. One participant was happy to be observed but initially cautious about being interviewed but later
agreed very willing having learnt more about this study. We are not sure whether writing about this
would add anything to this paper because all the participants were happy to take part and were simply
selected because they were the monitors and study staff
3. We appreciate this question because it raises a good point. We analysed the data sufficiently to be
confident about our findings. So yes, saturation of the discourse (or interviews and observations
obtained during case study visits), however in the ‘perfect world’ of a much wider study (that was not
practicable in any sense) we would have added others TRAC sites (i.e. Nigeria or Kongo) or EACCR
sites then we could possibly have learnt more. However this is always the case with this form of
methodology and you have to take a practical decision about how far you can go. However, the
monitors interviewed in MORU and EACCR talked about their experiences in these different places
and so this added to our confidence about saturation.
4. Ethical approval details listed at the end of the paper. A sentence has been added about how the
participant's confidentiality was protects and also a statement on how the quotes were selected.
5. The figures have been changed
6. The Table has been changed
7. The publication year is added

Dr. Brian Faragher
1. My only concern is that, in my view, the aims of this project are slightly over-stated (closing
paragraph of Background section). As indicated above, it is my opinion that the authors provide an
excellent documentary of the process of statistical monitoring through the perspective of the monitors
and those being monitored - so this aim is achieved totally.
2. I am not convinced, however, that the authors have been able to determine the value of the two
monitoring models assessed, nor have they been able to produce any insight as to how their value
can be measured. For this, some evaluation is needed of the impact of the monitoring on the quality
of data produced and, indeed, the overall quality of the study. For example, were any processes
identified that were having a major negative impact on data quality? - if so, would these have been
detected anyway or would either monitoring model have been the only way in which such erroneous
process could have been detected and rectified?
3. Were any individuals found to need some additional training or advice on data
management/quality? Were any issues identified that could have impacted negatively on patient
safety and well-being while participating in either trial?
4. However, I would wish to argue for a moderation of the stated aims. Defining "value" as the
identification of problems and their rectification, there is no real evidence relating to this in the paper -
but this would probably require a slightly different methodology in any case.
5. The authors use many acronyms that hinder the readability of the manuscript. I recommend leaving only those that in the authors’ opinion are essential.

Authors response
We appreciate the reviews complimentary review and highly constructive comments. We specifically value the recognition that this is an un-researched area and this is a novel approach to gathering data in this important area.
1. This is a very fair point and we have changed the wording from evaluate to observe and re-written that whole sentence
2. We think this is also a very good point. However, we do think this research is able to comment on the value of these approaches in monitoring - but perhaps we use the term ‘value’ in a different way? This is a social science study and we have not measured the quantitative impact on data quality. This of course would be an excellent and necessary new study that should be done, as the reviewer recognised and indeed suggested. We do take this point well thought, which is made again in point 4, and so we have addressed this throughout the paper by changing the wording, as can be seen in the manuscript and described below
3. In this study there were no responses that specifically said that there was a safety issue or risk to the data quality. However we firmly agree that there should be further studies that explicitly set out to address these key questions, and here different designs and higher numbers would be needed. We do not think this needs stating in the paper, but agree wholeheartedly with the point made.
4. We do take this point and have therefore worked carefully through the paper as can be seen in the comments and changed the wording so as not to overstate our achievements or the scope. We have changed the wording to reflect this point and we feel this strengthens the paper, and so appreciate this point being made.
5. We have dropped as many acronyms as possible