

ESPS Manuscript NO: 27464

Response Letter to Peer Reviewers' Comments

Dear Editors of *World Journal of Methodology*,

The comments from the reviewers have been carefully addressed point-by-point both in the manuscript and in this response letter (yellow highlighted) as follow.

We hope that this revised version should meet the requirements for being published in *World Journal of Methodology* and eventually contribute to the ever-enhancing impact of your journal.

In addition, a list of changes/corrections made:

- We made any editorial corrections in compliance with the Guidelines and Requirements and Format for manuscript revision.
- We checked our revised manuscript using the Grammarly free program available at <https://www.grammarly.com> instead of CrossCheck and we check the final title using Google Scholar at <http://scholar.google.com> as suggested.
- An audio core tip has been provided.
- A signed copyright assignment has been attached.
- The supplementary file was revised.
- The scientific research process PDF file was uploaded

Reviewer 1 (code 00068723)-R1

_R1C1: Grade C (Good); Grade B: minor language polishing

R1A1: The entire article was edited, improving the language and grammar. The co-author Prof. Nehmat Houssami is a native-English speaker and she carefully revised the text.

_R1C2: If there is any issues specific to imaging. It would add more values to this manuscript to discuss the points. Problems dealing imaging data should be discussed in Introduction in detail.

R1A2: We thank the reviewer for the comment, a useful suggestion to improve our manuscript. We have inserted the suggestions in the text, as indicated below (line 152), adding appropriately references [] :

Imaging in research is increasingly involved. The use of imaging data in clinical research can provide a lot of scientific benefits, but can result in additional complexities leading risks, biases and errors[13]. As indicate by Erickson BJ et al.[14],the use of imaging data in CTs may be a part of the solution to reduce cost and increase the efficiency to conclude in time the CT. A frequent problem with a radiological clinical trial consists of the quality of the clinical trial data: multicenter CTs need reproducible, quality assured data with postprocessing methods supported by an operational infrastructure.

In the hospital, medical subject's imaging data are managed in the clinical picture archiving and communication system (PACS) via the digital imaging and communications in medicine (DICOM) protocol. Clinical PACS could separated from the research PACS.

PACS are extremely limited in their support for research imaging: they are DICO-centric and generally don't support alternative file formats widely used in research. It is essential to guarantee a high quality of the entire process that images for CTs are collected using uniform image acquisition and measurement methods to minimize the variability.

Reviewer 2 (code 02441737)-R2

Comments to the manuscript entitled: Radiological Clinical Trials: proposal of a problem-solving approach to improve study success. By Francesca Valdora et al. This is an interesting study because it was undertaken in Genoa, Italy, to develop a survey helping how to define the main problems in radiological clinical trials. *Comments Introduction Improve the wording, especially the syntax.* Methodology: 1. In addition to describe the number of subjects they included in the study, It is important that the authors describe the number of subjects who refused to participate, the number of data that had to be dropped from the sample because of missing information. 2. Also to describe, the reasons why the authors did not make a selection of hospitals from different socioeconomic strata. 3. Mention if normality tests were conducted to quantitative variables. Results 1. Complete the title of Table 1, write down the name of the City where the study was conducted. If it is possible remove the word "our". 2. In Table 1, type the standard deviation of the mean value among respondents. Discussion 1. It would be interesting if the authors discuss the limitations in the development of clinical trials in the area of radiology, are different when comparing the work carried out in developing and in-development Countries? 2. Mentions possible differences in difficulties or problems in radiology clinical trials, made in the present compared to those developed in the past?

R2C1: Grade C (Good); Grade B: minor language polishing

R2A1 The entire article was edited, improving the language and grammar. The co-author Prof. Nehmat Houssami is a native-English speaker and she carefully revised the text.

R2C2: Introduction: Improve the wording, especially the syntax.

R2A2: We thank the reviewer for the kind comment. We made the necessary corrections to improve the reading of the text.

R2C3: Methodology: 1. In addition to describe the number of subjects they included in the study, It is important that the authors describe the number of subjects who refused to participate, the number of data that had to be dropped from the sample because of missing information

R2A3: As requested, the number of subjects included in the study is 19 and the number of the subject that refused to answer was 1.

R2C4: Methodology 2. Also to describe, the reasons why the authors did not make a selection of hospitals from different socioeconomic strata.

R2A4: The reason why we didn't make a selection of the hospital as suggested was due to lack of funding for the present research. We added this potential limitation in the discussion (add to line 317).

R2C5: Methodology 3. Mention if normality tests were conducted to quantitative variables.

R2A5: We didn't conduct normality test because it was not considered necessary by our statisticians.

R2C6: Results 1. Complete the title of Table 1, write down the name of the City where the study was conducted. If it is possible remove the word "our".

R2A6: We have removed the word our and we made the suggested change as follow:

Previous: "Table 1 List of main issues and problems identified during the conduct of **our** Clinical Trials. The **scoring** is from 1 (no problem) to 10 (serious problem)."

Revised: "Table 1 List of main issues and problems identified during the conduct all Clinical Trials. The score system is ranging from 1 (no problem) to 10 (serious problem)."

R2C7: Results 2. In Table 1, type the standard deviation of the mean value among respondents.

R2A7: We add the Standard deviation value as suggested.

R2C8: Discussion 1. It would be interesting if the authors discuss the limitations in the development of clinical trials in the area of radiology, are different when comparing the work carried out in developing and in-development Countries?

R2A8: As suggested by the reviewer we add this sentence and a new reference [] in the discussion (line 306):

"In larger multicentre studies requiring gathering data from different centres, even minor differences in population, culture, nomenclature and medical practice can be possible causes of variability.....". As indicated by Willis-Shattuck et al.[21] in a systematic review facing the issues related the recruitment in developing countries, they reviewed all studies investigating the link between motivation and retention of health workers in developing countries. They concluded that motivational factors are influenced by context and the successful completion of a study depends on the number of resources available.

It is commonly thought that the public health sectors of many countries suffer of a surplus of workers who are not particularly productive because they did not receive an adequate training. In fact a survey presented at RSNA 2013 by Rehani B et al[22] confirms that radiologists in developing countries need an accurate training program.

R2C9: Discussion 2. Mentions possible differences in difficulties or problems in radiology clinical trials, made in the present compared to those developed in the past?

R2A9: As suggested by the reviewer we add this sentence in the discussion (line 270):

Clinical Trials have rapidly evolved during the past decade. As we discussed above, radiological clinical trials can be affected of different types of bias, concerning imaging technology and recruitment strategies. Bias can result from differences in the methods in which information is collected or in the manner in which data are obtained during the recruitment process. In the past, radiologists often have limited direct patient interaction, depending on other specialists to refer

patients for enrollment: inadequate approaches to patient recruitment could introduce bias. In fact, the main strategies employed for recruitment were: flyer distribution; brochure pick up; internet posting-ads or poster distributions without a direct contact with the patients. Now the technology allowed us to have a different approach and a direct interaction with the patients monitoring the follow-up or response.

We thank all reviewers for the kind comments, constructive criticisms and useful suggestions for which we have used to improve our manuscript. We have re-read the whole manuscript once again and made any editorial corrections.

Thank you for the helpful review once again.

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Response Letter to comments of journal's editor-in-chief

Dear Editor in chief,

We hope that this revised version should meet the requirements for being published in *World Journal of Methodology* and eventually contribute to the ever-enhancing impact of your journal.

- **Question1**

Page numbers are missing

Answer: I provided to add the page numbers, as requested

- **Question 2**

Request to modify the title in “Radiological clinical trials: propose a problem-finding questionnaire to improve study success”

Answer: done

- **Question 3**

Request to revise and edit the entire manuscript by a professional standard English service

Answer: Done, I enclosed the Language Certificate.

With best regards,

Prof. Alberto Tagliafico and Dr.Francesca Valdora

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