

REPLY TO REVIEWERS COMMENTS

April 2, 20142

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9306-editedR2.doc).

Title: World health dilemmas: orphan and rare diseases, orphan drugs and orphan patients

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Name of Journal: *World Journal of Methodology*

ESPS Manuscript NO: 9306

The manuscript has been improved according to the suggestions of reviewers:

A. Format has been updated

1. The title has been reduced to 12 words and has been changed to “World health dilemmas: orphan and rare diseases, orphan drugs and orphan patients”
2. A Running title has been included “World health dilemmas and orphan drugs”
3. The affiliation of authors have been included
4. The author contributions have been included
5. The key words were placed after the abstract
6. A Core tip of 100 words was included
7. All reference numbers were changed to superscript format
8. Changes in the revised manuscript including English language are shown in bold lettering

B. Revision has been made according to the suggestions of the reviewers

Reviewer 1

We thank the reviewer for the comments.

Regarding the specific formatting suggested by the reviewer, the page numbers have been included in the manuscript.

Regarding the “flow” of ideas in the review, this is characterized by the appropriate sub headings with a global view and the specific examples of the topics presented. All the sub heading are related to the issues described in the title and the abstract. The same issues support the statements made in the recommendations and the conclusion sections.

Corrections on English language were carried out throughout the manuscript including the examples presented in the reviewing report and the use of “etc”.

Regarding the abstract, we believe that the presentation of essential facts and figures provides the real dimension of the global health problems and allows for the right conclusions to be drawn and recommendations to be made for improving the present situation. Therefore we believe that the abstract is not “hodge-podge of facts and figures” but it represents the major issues and provides suggestions for improvements. The term annual is clearly described in the abstract.

Regarding the introduction, we believe that a brief description of the major issues discussed in the review, are clearly addressed including the example of the orphan iron chelating drugs. The introduction was reduced in size according to the referee’s comments and the sentence quoted was modified.

The “New outlook of health issues affecting morbidity and mortality worldwide” is summarised in Table 1 and was described in the section under this title.

Regarding the “subsequent sections”, these are clearly described. The recommendations and conclusions are

clearly defined in the last two sections.

Regarding the review summary, such as corrections in English and in the format, these were carried out as requested. In contrast to the reviewer's comments about "tremendous amount of dogma" in the manuscript, we believe that we have provided sufficient evidence to show that the health problems we describe are real and it is unavoidable if they seem to go against present dogmas. Furthermore, it is emphasised that there is a need for the implementation of the appropriate policies to improve drug development and global health care.

Reviewer 2

We thank the reviewer for the comments and for recognizing the importance of the topics presented on global health care including drug safety.

Regarding other comments, it should be noted that

1. According to the journal instructions for authors, there are no restrictions on the length of the manuscripts submitted. Similarly, the information provided in the introduction on orphan drugs is sufficient and is fully described in the section "Developing concepts of orphan drugs and orphan diseases"
2. We consider that the topics and examples presented in the manuscript provide the general picture of the major global health issues. Many other important topics such as the methodological issues or analytic approaches to the complex problem of orphan drugs could have been included but this is beyond the scope of the present manuscript.
3. The analytical or methodological approaches for studying the global health issues are an important topic but also beyond the scope of the present manuscript. We believe that some of the presented subsections provide in depth analysis of the major issues and also methods for improvements. The recommendations and the conclusions presented in the last two sections could offer solutions to some of the global health problems.

Reviewer 3

We thank the reviewer for the comments and for recognizing the importance of the topic.

2. The introduction was reduced in size according to the referee's comments. We believe that the major issues discussed in the review are clearly addressed in the introduction, including monetary issues, the poverty and disease problems in the developing countries and also orphan iron chelating drugs.
3. The issues addressed in the manuscript are very complex and could be used for further research covering each topic separately including those suggested by the reviewer on national and international policies, research and organization. We believe that the manuscript as it stands gives the essential background on the issues addressed and could be used for further research on each of the separate topics presented or on combination of topics
4. The information provided in the manuscript was derived from recent available information at the time it was written. It is certain that more recent available information has become available since then, but is unlikely that such information will change the main messages of the topics and issues presented and discussed in the submitted manuscript.

C. References were corrected

Thank you for considering publishing our manuscript in the *World Journal of Methodology*.

Yours sincerely,

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