

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

|                            |                                                                                                                                                                                                                           |
|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>TITLE (PROVISIONAL)</b> | Consideration of antimicrobial resistance and contextual factors in infectious disease guidelines: a systematic survey                                                                                                    |
| <b>AUTHORS</b>             | Stalteri, Rosa; Santesso, Nancy; Bognanni, Antonio; Darzi, Andrea; Karam, Samer; Piggott, Thomas; Baldeh, Tejan; Schunemann, Finn; Ventresca, Matthew; Morgano, Gian Paolo; MOJA, Lorenzo; Loeb, Mark; Schunemann, Holger |

### VERSION 1 – REVIEW

|                        |                                                                 |
|------------------------|-----------------------------------------------------------------|
| <b>REVIEWER</b>        | Araujo da Silva, André Ricardo<br>Federal Fluminense University |
| <b>REVIEW RETURNED</b> | 31-Jan-2021                                                     |

|                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>GENERAL COMMENTS</b> | <p>Dear authors. I received the article entitled: "Antimicrobial Guidance: the need to consider antimicrobial resistance and context" for review. Despite the relevance of the manuscript, some aspects need to be clarified in order to improve his quality.</p> <p><b>Abstract</b><br/>Objectives: The objective should be reviewed in order to be applied to the prevalent infections studied ( tuberculosis, gonorrhoea and respiratory tract infections). The authors did not evaluate other conditions. For this reason, the objective should be related only to guidelines studied.</p> <p><b>Introduction</b><br/>Last paragraph: Please modify the sentence in order to specify that the authors are studying guidelines for tuberculosis, gonorrhoea and respiratory tract infections</p> <p><b>Methods</b><br/>Please justify why only guidelines in English language were included</p> <p><b>Conclusion</b><br/>I'm not sure if the last sentence of conclusion is related to the aim of the article. Please review it.</p> |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                        |                                                                                        |
|------------------------|----------------------------------------------------------------------------------------|
| <b>REVIEWER</b>        | Bailey, Pamela<br>University of South Carolina School of Medicine, Infectious Diseases |
| <b>REVIEW RETURNED</b> | 26-Feb-2021                                                                            |

|                         |                                                                                                                         |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------|
| <b>GENERAL COMMENTS</b> | Overall, I found the paper interesting and the PICO/PICAR question relevant, with the study well designed to answer it. |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------|

|  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  | <p>There were a number of awkward transitions through the paper and odd word choices, I would strongly recommend rereading and adjusting some of the language.</p> <p>I could not find some of the figures references in the text, my proof only has figure 1, 5, 6. This is worth noting as multiple places throughout the text, figures are noted that I cannot review.</p> <p>The second paragraph of the discussion/summary of findings is worth expanding on how the compliance of recommendations is unsatisfactory--support with your data/findings. In the third paragraph, I would include the "high proportion" number of WHO and NICE guidelines.</p> <p>In limitations, was a kappa statistics between reviewers considered?</p> <p>In the introduction, second paragraph, defining 'values' as well as 'medicine policies' would be relevant.</p> <p>In "Data Extraction and Quality Assessment," would reference the table after the first sentence of paragraph 2. While it is addressed in the limitations, it would also be worth noting what went into picking 60% as the cutoff for acceptable quality.</p> <p>In table 2, the 95% CI in proportion of recommendations with AMR consideration seems unnecessary.</p> <p>In table 3, would note the language is confusing. Suggest 'mean domain score % (SD)' and similar throughout--more standardized.</p> |
|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

### VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Name: Dr. André Ricardo Araujo da Silva, Federal Fluminense University

3. "Abstract - Objectives: The objective should be reviewed in order to be applied to the prevalent infections studied (tuberculosis, gonorrhoea and respiratory tract infections). The authors did not evaluate other conditions. For this reason, the objective should be related only to guidelines studied."

Response: We modified the objectives to reflect that we analyzed tuberculosis, gonorrhoea, and respiratory tract infection guidelines in the abstract and the introduction.

The revised text reads:

The objectives were to analyze a) how, and to what extent, tuberculosis, gonorrhoea, and respiratory tract infection guidelines are considering antimicrobial resistance; b) are of acceptable quality; and c) whether they can be easily contextualized to fit the needs of specific populations and health systems.

4. "Introduction - Last paragraph: Please modify the sentence in order to specify that the authors are studying guidelines for tuberculosis, gonorrhoea and respiratory tract infections".

Response: Thank you for this great suggestion. We modified the objectives to reflect that we analyzed tuberculosis, gonorrhoea, and respiratory tract infection guidelines in the last paragraph the

introduction.

The revised text reads:

Our objectives were to analyze how, and to what extent, tuberculosis, gonorrhoea, and respiratory tract infection guidelines are considering antimicrobial resistance; are of acceptable methodological quality; and if they can be easily contextualized to fit the needs of specific populations.

5. "Methods - Please justify why only guidelines in English language were included."

Response: We added an explanation for restricting to guidelines published in English language. We suspect the reviewer considers this to be a limitation of our study and we added this as a potential limitation.

The revised text in the methods reads:

We restricted to English language guidelines because, from a practical standpoint, English language publications would be the simplest to contextualize for most international groups and the major international organizations like WHO publish their guidelines at least in English.

And

However, but by focusing on three domains and a relatively low score cut-off we were more inclusive although we also focused on English language publications only.

6. "Conclusion - I'm not sure if the last sentence of conclusion is related to the aim of the article. Please review it."

Response: Thank you for this comment. We reviewed the last sentence, "This may preserve the remaining and essential medicines we have left, and the future of new classes of antimicrobials", and still feel that it relates to the aim of the article, given our work in the context of the Essential Medicines List. In the abstract, we state that "Guidelines that include antimicrobial recommendations should explicitly consider contextual factors that influence antimicrobial resistance and their downstream effects on resistance selection." If there is careful consideration of AMR when developing recommendations, this may have an indirect impact on the preservation of antibiotics and may help manage resistance. We replaced the word "preserve" with "help protect" in the last sentence to better reflect the above relationship.

Reviewer 2

Name: Dr. Pamela Bailey, University of South Carolina School of Medicine

7. "There were a number of awkward transitions through the paper and odd word choices, I would strongly recommend rereading and adjusting some of the language."

Response: Thank you for this advice. We re-read the entire article and adjusted the language, reflected by the track changes.

8. "I could not find some of the figures references in the text, my proof only has figure 1, 5, 6. This is worth noting as multiple places throughout the text, figures are noted that I cannot review."

Response: Thank you for pointing this out. Some of the figures were mentioned in the online supplement. Figures 1, 2, 3 and 4 are referenced in the article and labelled accordingly. Figures 5 and 6 are intended for an online supplement (now labelled as supplement 1, Figure 1 and supplement 1, Figure 2). We labelled them clearly in the manuscript now.

9. "The second paragraph of the discussion/summary of findings is worth expanding on how the compliance of recommendations is unsatisfactory--support with your data/findings. In the third paragraph, I would include the "high proportion" number of WHO and NICE guidelines."

Response: Thank you for these suggestions. We reworded the second paragraph to include support from our findings. We also included the number of WHO and NICE guidelines providing the necessary information to addressing contextual factors in the third paragraph of the discussion/summary of findings. We also added an additional sentence at the end of the third paragraph to summarize the performance of other organizations.

The revised text reads:

There is an emerging consensus that reporting of Evidence to Decision dimensions is ethically and scientifically essential. Unfortunately, reporting these dimensions is not always seen in practice. Our review highlighted that some of the proposed dimensions seemed to be adopted by guideline developers (i.e., values and resource use were most considered), while others were less so (i.e., acceptability, feasibility, and equity were the least considered). Further, the quality of these guidelines varied and there were inconsistencies between regions and guidelines promoted/sponsored by different entities.

The use of the GRADE Evidence to Decision framework by the WHO and NICE seems to positively influence the consideration of contextual factors in the guidelines we reviewed. A high proportion of WHO (n=5/7) and NICE (n=1/5) guidelines contained complete information necessary to provide optimal guidance on how to use antimicrobials in the considered syndromes. Other regional organizations provided limited information addressing contextual factors – most addressed one (n=6/21) or two (n=6/21) contextual factors and a good proportion did not address any (4/21).

10. “In limitations, was a kappa statistic between reviewers considered?”

Response: We did not calculate the kappa statistics following Cochrane guidance (“We do not recommend the use of statistical measures of agreement (such as kappa statistics) to describe the extent to which assessments by multiple authors: <https://training.cochrane.org/handbook/current/chapter-07>”). Given the lack of any prior guidance for inclusion of articles of interest, our approach to set a low threshold for potential inclusion by starting a consensus process if one of two reviewers thought an article was potentially eligible reduced the potential for inadvertently exclusion of eligible guidelines.

11. “In the introduction, second paragraph, defining 'values' as well as 'medicine policies' would be relevant.”

Response: Thank you for this suggestion to define values and medicine policies. We defined ‘values’ and ‘medicine policies’ in the second paragraph of the introduction along with the definitions of the other evidence to decision dimensions.

The revised text reads:

For example, guideline recommendations are likely to better support effective use of antimicrobials in specific contexts when they account for how much people value the affected health outcomes (“values”), antimicrobial resistance burden, public health infrastructure, local medicine policies for consistent access to safe, effective, affordable medicines, and equitability of antimicrobial regimens (9).

12. “In “Data Extraction and Quality Assessment,” would reference the table after the first sentence of paragraph 2. While it is addressed in the limitations, it would also be worth noting what went into picking 60% as the cutoff for acceptable quality.”

Response: Thank you for this comment. Originally, we referenced table 1 at the end of paragraph 2 and realize that this may have not been apparent. Therefore, we moved the reference to table 1 to after the first sentence of paragraph 2. We also described why we chose 60% (guidance by the authors) as our cut-off for acceptable quality at the end of the 4th paragraph in the methods section

and provided the relevant reference.

13. "In table 2, the 95% CI in proportion of recommendations with AMR consideration seems unnecessary."

Response: We believe this information does not convolute the table and some readers will find the information useful. However, if the reviewer and editor insist, we can remove this information.

14. "In table 3, would note the language is confusing. Suggest 'mean domain score % (SD)' and similar throughout--more standardized."

Response: Thank you for this suggestion. We replaced 'mean domain score (SD) as %' to 'mean domain score % (SD)'.

Technical editor changes and responses:

1. Please cite affiliation 8 is missing in author list on your main document file.

Done

2. In Research Ethics Approval: Human Participants

You have selected "NO" in the ScholarOne system. If consent for participation was not obtained and NO is selected, please provide an explanation in the free text field. Otherwise you can put Not applicable in your Research Ethics Approval.

Response: stated Not applicable

3. Please embed your 'Ethics approval statement' in your Main document. Please note that the statement in the ScholarOne system and main document should be the same.

Response: Done.

4. Data sharing

- Please provide a data availability statement in your main document. Kindly specify what unpublished data are available and where it can be accessed. If there are none then you can simply state "No additional data available".

Please note that the statement in the ScholarOne system and main document should be the same.

Response: Done

5. Please include figure legends at the end of your main manuscript.

Response: included.

6. Please change the label of your Images and cite it as "Figure 1", "Figure 2", "Figure 3" and "Figure 4" to avoid confusion. Please also ensure to cite it all in the main text of your main document file and please include Figure legends at the end of your main manuscript.

Response: Done

## VERSION 2 – REVIEW

|                        |                                                                                        |
|------------------------|----------------------------------------------------------------------------------------|
| <b>REVIEWER</b>        | Bailey, Pamela<br>University of South Carolina School of Medicine, Infectious Diseases |
| <b>REVIEW RETURNED</b> | 25-May-2021                                                                            |

**GENERAL COMMENTS**

Much clearer and easier to read/follow/understand in this draft.  
There are still scattered grammatical issues, but a much improved manuscript.