

Peer Review File

Article information: <http://dx.doi.org/10.21037/tp-20-310>.

Reviewer A

Comments to the authors:

The authors have written a nice review/opinion piece on the challenges of recognizing and managing sepsis in children in low and middle income countries. This is of particular importance as LMIC bear the brunt of the burden of sepsis. They offer potential solutions, primarily focused on advocacy and education, and a template for a potential sepsis management algorithm for LMIC that takes into account some of the aspects of sepsis care that are unique to this care setting. Similar to the recently published Pediatric Surviving Sepsis Campaign guidelines, this algorithm is mostly based on expert opinion and weak quality of evidence. Additionally, it was not derived from a formal meta-analysis or consensus conference or similar panel of experts. Caution should be highlighted in the exploratory nature of this algorithm. The manuscript is clear and logical, however, it is quite long and there are areas of redundancy that could be edited to make it more concise. There are also minor grammar issues and formatting that sometimes make it unclear where paragraphs start and stop.

Specific comments:

1. Comment: There is an incomplete sentence in line 50
Response: Thank you. The incomplete sentence has been deleted (Abstract line 12)
2. Comment: A reference is needed for the sentence that ends on line 85
Response: Reference has been inserted (page 4, line 12)
3. Comment: The abbreviation RLA (first used on line 179) should be defined
Response: Thank you. RLA has been replaced by LMIC and has been defined earlier, Page 7, line 17.
4. Comment: The sentence on lines 362-364 is a duplicate of the prior sentence (with a slightly different first few words).
Response: Thank you. The duplicate line has been removed (page 13).
5. Comment: In the paragraph on Universal Vaccinations starting on line 365, the authors may want to consider adding how to overcome vaccine hesitancy and

mistrust in some LMIC.

Response: Thank you for this suggestion. We have added these lines on Page 13, line 20-28.

“Unfortunately, a growing section of the society has become vaccine-hesitant because of the risk-benefit concerns that are raised related to political motives and social media (59). Because of its negative influence on vaccination confidence, the availability of misinformation on social media should be identified as a threat to the public’s health.

In a vaccine-hesitant atmosphere, health education that supports the government campaigns against vaccine refusal are essential in changing attitudes(60). This requires a climate of respectful mutual trust between science and society to be fostered, where scientific knowledge is not only preached but also cultivated and sustained thanks to the emphatic understanding of citizens worries, needs of reassurance and health expectations.(60)”

6. Comment: The abbreviation LRS (first used on line 427) should be defined

Response: Thank you. This has been changed to LMIC, page 15, line 8.

7. Comment: The section on critical care practitioners making pragmatic modifications (lines 446-452) is redundant without a clear solution proposed.

Response: Thank you for pointing this out. This is an introductory statement to the sentence that follows. We have added a sentence to clarify the intent, page 15, lines 32-34.

“and local critical care leadership in various regions must tailor a pragmatic diagnostic, prognostic, and therapeutic approaches to a range of settings. We have outlined a few suggestions below”

8. Comment: The sentence on lines 506-509 (Regarding mortality prediction...) doesn’t seem to fit with the rest of the section, and seems to go against what they are saying about availability of critical care resources and lab testing. I’m not sure this sentence adds to their point.

Response: Thank you. We agree that these lines on mortality prediction add limited value and have deleted the sentence.

9. Comment: Line 605 references figure 1, I believe this should be figure 2.

Response: We have deleted the original Figure 1, so this is now Figure 1

10. Comment: The sentence on lines 685-687 (This procedure might avoid...) is a duplicate of a sentence on lines 677-679.

Response: Thank you. We have deleted the duplicate sentence.

11. Comment: Do the authors have permission to duplicate figure 1, which is taken from another journal article? Also the figure is blurry.

Response: We agree that Figure 1 is fuzzy, and have deleted it.

12. Comment: I recommend that the authors stress that their management algorithm in figure 2 is one possible suggestion that is untested and urge caution in its use.

Response: Thank you for this prompt. We have added the following sentences to emphasize that the algorithm in Figure 2 is untested, Page 21 lines 12-15.

“This physiologically-driven pathway is modified from the WHO algorithm for management of shock in areas with limited resources, with elements based on the authors’ own work demonstrating a fluid-sparing effect of early norepinephrine use in pediatric septic shock (42) (81) (82). However, this treatment pathway is untested in large trials, and we urge caution in its use.”

Reviewer B

Comments to the authors:

I compliment the authors on writing a nice review and recommended guidelines. My only comments are:

1. Comment: Can the paper be shortened a bit (maybe by 20%)? I think it is possible and still carry the same message.

Response: Thank you for this suggestion. The manuscript has been shortened by about 15%, however the new Table has slightly increased word count.

2. Comment: Maybe a Table be included for the problems/challenges faced in resource limited settings.

Response: Thank you for this suggestion. We have included a new Table 1 on page 8 entitled “Pediatric Sepsis-Summary of Challenges and proposed Solutions in Resource Limited Regions”