Author's response to reviews

Title: Empiric guideline-recommended weight-based vancomycin dosing and nephrotoxicity rates in patients with methicillin-resistant Staphylococcus aureus bacteremia: a retrospective cohort study

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Author's response to reviews: see over
To the Editor and Reviewers,

Federico Pea

1. The potential use of different vancomycin assays must be stated in the text as a potential limitation

   This information has been added to the limitations section of the discussion as suggested.

Douglas Ball

1. Include information on the sample size calculation including detectable difference, power, and calculated size.

   Information has been added to the Statistical Analysis subsection of the Methods regarding the sample size calculation including the expected event rate and minimizing the risk of overfitting the model for a multivariable analysis.

2. Include text from the cover letter to the section describing bias.

   This information has been added as suggested in the limitations paragraphs discussion section.

3. Information regarding the automated screening and lack of data regarding reason for study exclusion should be addressed. More clarity is needed in the limitations section to describe the potential effects of this lack of data than external validity that is currently listed.

   A sentence was added to the results section to alert the reader that reasons for exclusion were not collected. We also added a sentence to the limitations paragraph of the discussion to discuss that the lack of this information may limit how other institutions are able to use our findings.

4. Include the number of patients from each hospital and event rates. Also, discuss how inter-hospital differences and clustering were addressed in the discussion.

   These data were added as hospital A, B, and C to protect the anonymity of the institutions. Information regarding differences and clustering have been added to the discussion/limitations section.

5. Clearly state in the methods that only the first/initial vancomycin trough was used in the analysis.

   This information has been added as suggested.

6. Give information on how vancomycin TDM was conducted at each hospital. Describe in the bias paragraph in the discussion if patients without TDM were less complex patients?
Information regarding TDM was added to the methods section. Less complex patients do tend to receive less TDM, which has been added to the discussion (limitations paragraphs). Thank you for the suggestion.

7. Guideline
   a. State the date of the guideline.

      The date of the guideline (2009) has been added to the text on pages 5, 9, and 13 of the manuscript.

   b. Make it clear that the retrospective evaluation examines past dosing practices.

      We have attempted to make this clear by adding the guideline date in several areas. We already mentioned the study period in the methods section. We also added a sentence in the limitations part of the discussion to address this issue.

   c. Use “weight-based vancomycin dosing as recommended in the new guidelines” at times

      Thank you for the suggestion. This phrase has been added at times throughout the text.

8. The potential use of different vancomycin assays must be stated in the text as a potential limitation.

      This information was added as suggested to the limitations section of the discussion.

9. Discuss that heavier patients could be at a higher risk of nephrotoxicity due to higher absolute vancomycin doses

      Heavier patients were not at a higher risk of nephrotoxicity due to higher doses according to an analysis of our data. Patients weighing ≥ 100 kg received 1941 mg/day versus 1919 mg/day for patients weighing < 100 kg (p = 0.72).

10. Include the response to exclusion of renal dysfunction and/or prior MRSA infection in the text.

      This information is now included in the methods section.