Reviewer’s report

Title: What potential could there be for a S. aureus vaccine in a hospital setting on top of other preventative measures? A model-based analysis.

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Reviewer: Leigh Anne Shafer

Reviewer’s report:

In this study, the authors employ mathematical modelling to assess the potential impact of a hypothetical S. aureus vaccine, when used as part of a prevention bundle in hospitals. The topic is good and timely, in order to assess the importance of continued work on developing such a vaccine. The modelling scenarios run answered the question well. However, there are a number of concerns, most of them about the structure of the model and assumptions.

Major Revisions

1. Did you use D’Agata’s model, and update it with the potential to include a vaccine intervention? That is, did D’Agata give you his model (the programming code) and you used it? If so, why isn’t D’Agata a co-author? If you used the description of a model that D’Agata provided in a previously published manuscript, but wrote your own model program, we need more detail. What programming language did you use? How did you incorporate human mixing patterns in the hospital? Although you provide quite a bit of model detail in the methods of the manuscript, we need more. We probably need a detailed appendix of the model that you developed (or modified), so that we can evaluate it. I disagree with your statement that providing the mathematical details of the model is beyond the scope of this paper since the pre-modified model was described previously (p. 12, line 237). You have made enough changes that it warrants a full description of your model.

2. The originally published modelling work provided baseline parameters relevant to a general MRSA infection. You have specific HA-MRSA and CA-MRSA. How did you determine the parameter values for your updated model? Although I agree that explicitly including HA-MRSA and CA-MRSA allows “potential different transmission aspects to be adequately accounted for”, as you state on p. 7 line 118, you need to give much more detail on this model (e.g., an appendix fully describing the updated model), so that we can evaluate how you determined parameter values related to the different transmission aspects.

3. You wrote in the manuscript text that # is the number of hospital admissions per day. Yet, it appears in Figure 2 (hard to tell for sure because it is too blurry when magnified), that you have people leaving the hospital from the two infection states, at a rate of #*(the relevant lambda for the respective hospital leave rate). This cannot be right. If this reflects what the model is doing, then the model needs updating and re-fitting. If it is just a typo, the revision is simple.
4. The FOI is wrong unless you only assume 1 effective contact per time unit (day?). According to p. 8, lines 153-154, your FOI appears to be, essentially, the fraction of hospitalizations that are colonized or infected patients, times their respective (colonized or infected) transmission rate. What happened to the contact rate – number of people each colonized or infected person contacts per time unit? If your betas somehow incorporate the contact rate into the estimated transmission rates, then you need to explain this in detail.

5. The baseline parameter values that you give in your Abstract do not match those from Table 1. For example, in the Abstract, you assume 50% hygiene compliance, but in Table 1, you state that the baseline is 60%. In the Abstract, you assume 50% decolonization, but in Table 1, you state that the baseline is 0%.

6. Explain why there are no already infected admissions to hospital among those vaccinated (figure 1). You don’t assume that vaccination cures those already infected, do you?

7. The figure resolution was too low, so it was almost impossible to see Figure 2, which was key to understanding the model, given your sparse description of it. When I magnified the Figure 2 page size by 250% (so that the words would almost be large enough to be legible), then the figure became too blurry. Anything less than 250% magnification and the words and symbols were too small to read. Also, as a minor detail, you do not have one vaccinated compartment and one unvaccinated compartment, as your Figure 2 headers imply. Rather you have multiple compartments in each group.

8. In your background prevention bundles, how quickly do you assume that screening or decolonization occurs? Please describe the rates used in order to achieve the different scenarios of Figure 3. E.g., what rate was used in order to achieve 100% screening and 100% decolonization? This is necessary in order to assess why 100% screening, 100% decolonization, and 100% hygiene results in ~75% reduction in MRSA.

9. Like Figure 2, Figure 4 was very difficult to read. Resolution is too low and figure is too small.

10. For your analysis of number of vaccine doses (Figure 5), are you assuming that people are vaccinated before each hospital admission, so that people could be vaccinated many times (once for each hospital admission)? So you are assuming a very fast waning rate of the vaccine? Please explain.

Minor Revisions

11. Abstract: Using an existing model with published baseline estimates of model parameters would neither reduce assumptions, nor reduce bias. Assumptions (e.g., assumptions about mixing or about infectiousness of s. aureus) were made in the previously published model, right? And what bias are you talking about? Do you mean that you reduced uncertainty (not bias)? If that is what you mean, using an existing model did not reduce that either. You might have been able to reduce uncertainty by fitting your model to different populations settings, with the same assumptions about things like infectiousness that would not change
between populations.

12. Typo on p. 4, line 77. The word “program” should be singular. On p. 5, line 80. “… during 6-month intervention…” should read, “… during a 6-month intervention…” Throughout the manuscript, some prepositions and articles (“a”, “the”) are missing.

13. Did you consider waning?

14. We have people leaving the unvaccinated susceptible and entering the vaccinated susceptible compartment at a rate of #SV, according to the manuscript text. Yet, this flow of people between unvaccinated and vaccinated states is not seen in Figure 2. Perhaps you simply forgot to add it to Figure 2 because you were only modelling pre-hospital vaccination rates and assumed that vaccination in hospital was 0? So #SV would be 0. However, if this flow is part of the model, it should be depicted even if all of the scenarios for this study had a flow rate of 0.

15. Are the rates in the model per day? Daily rates?

16. On p. 12, line 250, you state that, “…a model-projected reduction of at least 48% can be achieved…” Please explain what you mean by “at least”. From Figure 3, it appears that all of your modelling results are based on just one best-fitting baseline scenario, and varying intervention rates. If your model results are based on a range of good-fitting scenarios, and 48% was the lowest predicted impact of the intervention rates you describe, then you need to explain this in the methods and show this in your Figure 3. This applies to all of the “at least” statements in the manuscript. E.g., “… a reduction of at least 64% is projected…”.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.