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: Laura Temime

Reviewer's report:

In this paper, the authors investigate the impact of a hypothetical S. aureus vaccine on MRSA infections in a hospital setting, using a modeling approach. Because of the current interest in developing such a vaccine, being able to assess its potential impact is an important issue, especially taking into account the other infection control strategies that are already being used. To my knowledge, this is the first study to do so. In addition, mathematical modeling is an obviously pertinent approach in this context, as no data is available yet.

Minor essential revisions

1. p.8, line 162. I think "eta" actually works as a composite parameter, describing both hygiene compliance and hygiene efficacy. This should be clarified.
2. It is fine to refer the reader to the paper by Webb for "technical details" and mathematical equations (provided the choice to keep the exact same model is valid, see comment 8). However, I would still have liked to find some more explanation of the model structure and parameters without having to refer to the Webb paper (for instance in the legend of Figure 2 or in the Methods).
3. p. 13, line 279. The paper should specify how many doses are assumed to be necessary per person, and possibly discuss this assumption which may impact model predictions.
4. Table 1. The description of parameters betaCC, betaCH, betaIC and betaIH is unclear and should be reformulated.

Major compulsory revisions

5. Even though the basic control strategies are fully described in the original papers by D'Agata and Webb, I think that this should also be the case in the current paper. In particular, the reader shouldn't need to refer to the original papers to be able to understand exactly how these strategies translate in terms of model parameters (and equations).

For instance, it wasn't clear to me why a screening and decolonization strategy with assumed 100% screening compliance and decolonization efficacy did not lead to total disappearance of MRSA infections, because I had not understood that screening was assumed to occur among already hospitalized patients rather than at admission.

6. On a related note, why wasn't a "screening at admission" strategy
investigated? It seems to me that this a relatively frequent control strategy which has been explored using modeling approaches before, and could prove to be more efficient than the other investigated strategies, hence changing the main results.

7. I couldn't find a precise description of the chosen model outcomes in the paper. While the authors mention that they are looking at "the number of MRSA infections" and at the reduction in these infections, they do not specify over which time period they do so. I gather that these are steady-state outcomes? This should be clarified.

8. More importantly, I am not convinced that the choice of the model developed by D'Agata and Webb et al. is pertinent here. This model was developed specifically for exploring CA-MRSA transmission dynamics within hospitals, in competition with HA-MRSA. Not only is exploring the CA-MRSA/HA-MRSA dynamics not part of the objectives of the current study, this aspect is actually completely ignored here by assuming identical vaccine effects on these two strains (which is a fully justified assumption, considering that the vaccine is still hypothetical). Hence, I think that using a simpler model with MRSA described as a whole would have been more appropriate. This could have been done by using either another (possibly older) MRSA transmission model, or a simplified version of the D'Agata model in which the CA-MRSA and HA-MRSA compartments would be fused together.

The authors justify their use of this specific model by writing that it “minimizes the number of assumptions” and “reduces bias”. However, in this case, while it is indeed true that many baseline parameter estimates were obtained from epidemiological data in the original study by D'Agata et al., this was not the case for the transmission parameters, for which no source was provided except for in-vitro studies. In the D'Agata et al. study, this was made necessary by the absence of available data on relative CA-MRSA vs. HA-MRSA transmissibility. In the current study, this seems to me to be a relatively large assumption, which may have a large impact on model predictions, and which could have been avoided had the authors used a simpler MRSA-only model (for which robust estimates of the transmission parameters are available).

For instance, simply using a simplified version of the D'Agata model (as suggested earlier) would also allow to use those among the parameters that are well documented, while avoiding the introduction of unnecessary uncertainty in this study.

9. In this study, vaccination is assumed to occur before hospital admission, "in a timeframe to allow an adequate immune response". While this seems a reasonable enough hypothesis, I think it has implications which are not fully taken into account in this study. As mentioned by the authors, such a vaccination procedure would only be possible in individuals identified as high-risk, or in cases of planned hospitalizations. Hence, investigating a vaccination coverage as high as 100% (or even 75%) is probably unrealistic. It seems to me that it should be possible to compute a rough estimate for a realistic upper bound for this vaccination coverage, based on available data on hospitalization causes (i.e.,
what portion of hospitalized patients do high-risk patients and patients with planned hospitalizations actually represent?). If it is indeed lower than 75%, this realistic upper bound should then be used in model simulations instead.

Another important parameter is the necessary duration between vaccination and immunity. Depending on this duration (and in particular whether it is superior to the average delay between a hospitalization is planned and hospitalization actually occurs), vaccine coverage may be lower than expected.

Discretionary revisions
10. p.9, lines 182-184. I am not sure that this introductory paragraph is necessary.

11. The discussion could include a paragraph on possible applications of this work for cost-effectiveness analyses, which would no doubt prove necessary before systematic pre-hospitalization vaccination is recommended.

**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.