Author's response to reviews

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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Version: 6 Date: 1 May 2014

Author's response to reviews: see over
Authors to the Editor:

We have greatly appreciated this reviewer’s careful reading and comments throughout the various rounds of review and we appreciate it has greatly contributed to a better manuscript overall. At this point, however, we believe that we have responded to all the reviewer’s comments and have already edited the manuscript to the best of our abilities, while also remaining consistent with our original intent and nature of this work.

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.

Version: 5 Date: 11 April 2014

Reviewer: Leigh Anne Shafer

Reviewer’s report:

The paper is much improved in terms of readability. However, I still have a large concern about the model, some smaller concerns about what simulation results you are choosing to present, and some minor edits.

Major

1) In mathematical modelling, the key is the force of infection. Everything else is easy. Please explain more fully your force of infection (the FH and FC) parameters. It appears from your equations – lines 169 and 170 on p. 8 – that you are assuming that each susceptible patient has contact with just 1 other hospital patient. So you have provided the proportion of hospital patients who are infected – (CH + CHV)/N – and multiplied this by the transmission rate – BCH – to get the FOI. Why do you assume in the equations that each patient only has contact with one other hospital patient?

Authors: We have already responded to this question the reviewer has asked in an earlier round of reviews (Version: 2 Date: 30 September 2013). Formulation of the FOI is basic and typical for this class of models [Refs. 23, 24, 26 in the text]. As per the original model [23, 24], Betas here are effective transmission rates, with units of 1/time, which are compound parameters that implicitly represent the contact rate multiplied by the transmission risk per contact.

2) Further with the force of infection (FOI) equations. You state in the text that susceptible patients could get infected through infected patients, fomites, or health care workers. Where is the portion of infections that occur through fomites or health care workers shown in your FOI equations?

Authors: Such proportions can not be quantified explicitly in this context. The transmission parameters here are meant as proxies in a lumped compound way, across all possible routes of transmission, as per the original model in [23, 24]. (See also

Less Major, but needs to be addressed

3) How far prior to admission do you expect that the vaccine would need to be given? How often could patients be identified and thus given the vaccine, prior to admission? This needs discussion in the introduction or discussion of the paper.

**Authors:** We have already addressed this in the Discussion section (lines 398-404) and included relevant references.

4) It seems that the most important scenario to be discussed would be the impact of the vaccine when other prevention measures are very high. Surely it would be cheaper to improve the other prevention measures than to develop a new vaccine. For this reason, I believe that in the abstract and the paper, we should report and emphasize the impact that the vaccine would have in scenarios of, for example, 90% or above hygiene, 90% or above decolonization, and 90% or above screening. If you disagree with this and think that it would be impractical to believe that we could achieve such high preventive measures, or that developing a vaccine might be cheaper than the effort required to achieve such high preventive measures, then this argument and its reasons should be provided in the paper. If you agree with this, then your main outcome results (in both abstract and main paper) should discuss the impact of vaccine in a setting of very high levels of the other preventive measures.

**Authors:** We are not quite sure why the most important scenario would be one with other prevention measures being very high. Please see paragraph in the Discussion section, lines 327-340. We believe that an average case scenario for preventative measures in place is the most appropriate to serve as an illustrative realistic example here. Related costs of different possible control strategies are not within the scope of this manuscript.

A few of the edits that I found:

In Abstract: “… to assess potential of a …” should be “… to assess the potential of a…”

Intro: “… following 3-year intervention period.” should be “… following a 3-year intervention period.”

“… reported 62% and 45% decrease in rates…” should be “… reported 62% and 45% decreases in rates…”

“… but to rather serve…” should be “… but rather to serve…”

**Authors:** Thank you for highlighting these edits, which we have corrected in the manuscript.