Reviewer's report

Title: Natural history of colonization with methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE): a systematic review

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Reviewer: James McKinnell

Reviewer's report:

Major Compulsory Revisions

The authors should be commended on their review of the literature related to MRSA colonization and VRE colonization. The authors are correct that estimates of duration of colonization are not readily available in the literature. Furthermore, these estimates are of crucial importance to cost-effectiveness research, health policy analysis, and infection control policies.

However, I have two major concerns about the manuscript, as submitted. First, I think the systematic review could have been improved. Why was the Medline search not complimented with EMBASE or other search engines? Also, why did the authors not review the bibliographies of full-text manuscripts to help identify additional manuscripts. Lastly, why did the authors of the current investigation not contact authors of primary data manuscripts that did not meet criteria or did not present the correct data in the primary manuscript to see if they had additional data that could be included. In a review of a recent publication related to MRSA/VRE colonization, I found multiple references that could have possibly met their inclusion criteria.

For example, why was the recent report by Almyroudis et al not included in the review? PMID 21515980. Or the sentinel paper by Donskey et al on antibiotics and recurrent VRE colonization? PMID: 12186208. Or, similar work by Donskey in VRE colonization dynamics.

The authors should pursue: 1) the above multiple recommendation to expand their search. Further, I would suggest a broader initial search strategy. A Pubmed search including “((enterococcus) OR VRE) AND (((screening) OR testing) OR screen) OR test) OR swab) OR surveillance)” limited to English, Adults, and Humans resulted in over 1400 results; far more than the 284 records found in the authors search.

Second, the Almyroudis and Donskey articles also raises some conceptual limitations of the paper, principally related to colonization dynamics. The loss of colonization typically represents “clearance” of the original colonizing strain, which as the authors comment may only represent reduction of colonization below detectable levels of routine culture, i.e. culture versus pcr.

The concept of test sensitivity may be particularly relevant to VRE as there is specific research by Donskey et al on the impact of antibiotics on VRE density in
stool. The authors comment on antibiotic exposure and duration of VRE carriage, but do not provide any statistical analysis. The authors should i) pursue the large and growing literature on antibiotic impacts on VRE colonization and ii) provide formal calculations or describe this more completely.

The authors do not comment on the underlying dynamics of failure to clear as being the result of sustained colonization with the individual strain, versus acquisition of a second isolate. Although they may not be appropriate for inclusion in the current review, there is a literature on strain typing of MRSA colonizing isolate and VRE colonizing isolate, including the idea of multi-strain colonization that should be commented on in the discussion.

Although I think the conceptual framework and the systematic review for this manuscript could be improved, I would like to re-iterate how valuable this research effort is to the medical literature. Having pursued less formal searches of the literature for these same numbers, I heartily encourage the authors to consider my suggested revisions.

Minor Essential Revisions
- Did the authors make a distinction between VRE. faecalis and VRE.faecium? see Ruiz-Garbajosa J Clin Micro 2009.
- Figures 3, 4, and 5 are referred to Figures 2A, 2B, and 2C respectively in the text. Consider “Percentage of patients with documented clearance of MRSA colonization” on y-axis of Figure 3.
- References 8, 14, and 15 were excluded from the time-restricted analysis for MRSA clearance, but it is unclear whether three other studies that had duration to clearance times in excess of 43 week (References 9, 19, and 20) were excluded as well.
- Citation needed in Introduction, 3rd sentence: “…the growing pools of colonized and therefore isolated patients affect patient care and burden the healthcare system”
- Space needed between “time” and “period” in Methods, 5th sentence.
- Study Selection: Clarification needed whether screening methods and locations were consistent within individual studies.
- Comparison of MRSA and VRE Pooled Clearance Rates: References 8, 14, and 15 were excluded from the time-restricted analysis for MRSA clearance, but it is unclear whether three other studies that had duration to clearance times in excess of 43 week (References 9, 19, and 20) were excluded as well.

Discretionary Revisions
Consider “Percentage of patients with documented clearance of VRE colonization” on y-axis of Figure 4

Data on cohorts of MRSA colonized versus cleared cohorts could be presented and compared using simple descriptive statistics or multiple logistic regression, if appropriate. These data could be interesting in light of recent publications relating to risk factors for MRSA colonization.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

None