Author’s response to reviews

Title: A prospective observational study of the prevalence and risk factors for colonization by antibiotic resistant bacteria in patients at admission to hospital in Singapore

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Author’s response to reviews:

Dear Philippa,

Many thanks to yourself, the reviewers and BMC for considering our manuscript for publication.

We greatly appreciate the reviewers insights, and have considered in detail all the points raised and how to best revise our manuscript. We believe the result is a better communication of the study findings, and a useful contribution to the field.

Please find below a point-by-point response to each of the reviewers comments. The name of the ethics committee has also been added in the Methods section, as advised.

Many thanks,

Barny

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Reviewer 2

1. As described in Introduction section, the authors’ team intended to enroll three major MDRO species (MRSA, ESBL-E and VRE) for analysis. However, only 18 MRSA isolates/1006 patients were obtained, and no VRE isolate detected at all. As the prevalence of MRSA and VRE is low, increasing sample size is essential. Otherwise, case-control study is recommended.

   - Our intention with this study was primarily to determine the colonization prevalence of ESBL-E, MRSA and VRE, and explore some of the associated risk
factors. We agree that the high prevalence of ESBL-E in different risk groups is the main finding of this study, and have reorganized the analysis to this effect. We also fully agree that a case-control study would help elaborate the risk factors for MRSA and VRE – and this was discussed as a limitation of our prospective study design.

2. In the meantime, molecular typing approaches is recommended to support the hypothesis that subsequent infection was caused by MDRO previous colonized on the same patient. Otherwise, nosocomial horizontal transmission cannot be excluded as cause of MDRO infection.

- After considerable thought, this small section has been removed from the manuscript. Our study was not designed to assess this hypothesis and we agree that confounding factors and bias limits interpretation of these results. In addition, we are unable to perform the molecular studies recommended as the relevant clinical isolates are not available.

3. Abstract: it is not appropriate to conclude “High rates of colonization with ESBL-E among patients at admission are significant challenges to infection control and empirical antimicrobial therapy.” based on evidence from the present study.

- The abstract conclusion has been amended

4. Background, paragraph 3: need solid supports for “As many infections derive from host flora, colonization by multi-drug resistant organisms (MDROs) is a risk for multi-drug resistant infections.”

- Appropriate references have been provided

5. Methods, “Participants and setting”, paragraph 1: how many ED visits average per month?

- Added to paragraph 1

6. Methods, “Participants and setting”, paragraph 3: the author mentioned that “Positive culture results within the 12 months following admission for each participant were extracted from the hospital microbiology database.” However, some useful data, e.g. patients’ length of stay in hospital and final outcomes (died or not) was not given. Therefore, it is hard to judge if there’re any potential bias in sampling.

- We have removed this section – see above for a full discussion.

Reviewer 1

1. The conclusion of the abstract is not in agreement with the rest of the manuscript;

- Amended (see above)
2. The use of the expression multidrug resistant is not appropriate in this study since, no multiple drug resistance was studied or detected;

- This has been changed – all references to MDRO (where ESBL-E/MRSA/VRE is intended) have been removed

3. How many patients and how were they monitored again after Hospital admission? Please give these numbers and described the procedures used;

- This section has been removed (see above)

4. How can the authors say they had MRSA without mecA testing? The procedure used in not adequate and mecC should be tested. Please note that there are coagulase positive staphylococci other than S. aureus;

- We agree that the bacteriological techniques in this study, while widely used, have limitations and this has been discussed in the manuscript. However the prevalence of coagulase positive non-aureus Staphylococcus is expected to be low and hence not likely to significantly alter the findings of this study.

5. Figure 1 can be deleted as it does not add anything new to the results presented in the tables.

- We believe the data presented in figure 1 provides an interesting visual illustration of one of the main findings from this study. This data is not evident from either of the tables as it combines and analyses two of the main risk groups (healthcare contact and antibiotic use).

6. The results observed in this study should be discussed based on studies of resistance prevalence and incidence in the community and healthcare facilities in Singapore.

- This has been added to the discussion mainly focussing on the prevalence of ESBL-E, MRSA and VRE in the healthcare setting in Singapore where