Reviewer's report

Title: Prevalence and acquisition of MRSA amongst patients admitted in a tertiary-care hospital in Brazil

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Reviewer: Ben Cooper

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The manuscript describes a prospective non-interventional study to estimate baseline prevalence of MRSA carriage on admission to a 749 bed tertiary hospital in Brazil, and to estimate the incidence of new colonizations. It also includes an analysis to identify risk factors for colonizations.

This type of study, though simple, is important for setting infection control priorities and developing a basic understanding of the epidemiology of MRSA, and can be particularly important in settings, such as this one, which lack routine MRSA screening. The epidemiology of MRSA is also greatly under-researched in developing country settings, and for this reason the manuscript represents an important piece of research.

Major compulsory revisions

In most respects the study appears to have been conducted well, and reported appropriately. I have only a single major concern (which might require a substantial revision) and a number of minor concerns which are more easily addressed. The major concerns relates to the statistical analysis. The authors report (on page 6) that "To determine potential risk factors for colonization at admission or acquisition of colonization, we performed, respectively, Poisson regression with robust variance and survival analysis with Cox Regression." First, why was Poisson regression used to look at risk factors for being colonized on admission? Poisson regression is appropriate when there are count outcomes (i.e. 0,1,2,3,...events in a given exposure period) and the chance of an event occurring at one time point is independent of the chance at another time point. However, when considering risk factors associated with being colonized on admission surely we have a binary outcome(either a patient is colonized on admission or s/he isn't) and a logistic regression is required. If Poisson regression was used to account for the fact that some patients had multiple admissions there is still a major problem which is that the chance that the same patient is colonized on admission at subsequent admissions will not be independent (and would be expected to be very highly correlated). For these reasons, the Poisson regression doesn't make much sense to me. A simpler and more appropriate strategy would be to use logistic regression, and consider only the first documented admission for each patient (thus overcoming the problem of dependency in patients with multiple admissions).
There are more subtle problems with the use of the Cox Regression for the acquisition analysis. A key assumption of such an analysis is that censoring is uninformative: i.e. the chance of censoring (which is presumably hospital discharge here) is unrelated to the chance of the patient experiencing the outcome (acquiring MRSA), but I think this is questionable at best given that the when patients are discharged it is usually because they are well and might therefore be expected to have less HCW contact, be receiving fewer antibiotics etc and therefore have lower risk of acquiring MRSA. Such informative censoring can severely bias the results and for this reason competing risk models (where the probability of becoming infected/colonized and of being discharged are considered simultaneously) should be considered preferable (see, for example, Crit Care. 2008;12(2):R44. Epub 2008 Apr 2).

Minor essential revisions

1. Abstract should describe the hospital setting

2. Abstract should specify whether the risk factors reported come from the multivariate or univariate analysis.

3. p3 "The colonization pressure (CP) of MRSA can overcome other measures, thereby causing pathogen transmission to continue". Meaning of this is not clear - please revise. Certainly increased CP would be expected to increase the total amount of transmission, but I am not sure I understand what the authors mean by overcoming control measures. Higher CP increases transmission because there are more patients who can transmit, but many control measures (hand hygiene, cleaning, appropriate antibiotic use) would be expected to be just as effective at preventing transmission from each colonized patient in a setting with a high CP as they would in a setting with a low CP.

4. p3 "Recently published trials have given conflicting results". I think this paragraph needs to be substantially revised. First, the word "trials" is usually reserved for RCTs. I don't think any of the three papers cited are RCTs. Secondly, it is not clear that the results are conflicting. As the authors do later acknowledge, they are not comparing the same things. The three studies listed were in different types of settings, evaluated different interventions, and used different study designs with different control groups. It is important to be clear about these precise differences when comparing the studies. I.e. the authors need to describe the interventions in the groups being compared and the study designs and say something about the study settings. For example, the authors state "while another study in an intensive care unit (ICU) showed no reduction of MRSA infection rates with screening and isolation of colonized patients [9].", but as it stands this is misleading as screening and isolation of colonized patients were carried out in both intervention and control periods in this study, only the method of isolation changed. The study therefore showed that there was no evidence of differences in the effectiveness of the isolation methods used in the different study periods. It certainly does not preclude the possibility that screening and isolation greatly reduced transmission in all periods.
5. p5 "patients were not included. Patients admitted to the emergency room (ER) who were expected to stay for longer than 48h in the hospital…". How was this assessed?

6. p5 "Three adults and two children were randomly selected ". How was this random selection accomplished?

7. p6 Insufficient detail given on sample size calculation.

8. Standardized prevalence and incidence should be defined.

9. p8 "The median number of days from admission until positive cultures were obtained from children was 8 days". Is this median just for those patients who were not colonized on admission, or for all patients?

10. p9 "Even thought [sic] we did not find association with length of stay in survival analysis" This sounds peculiar, as survival analysis assumes an association of outcome and exposure time (and it would therefore make no sense to include exposure time as covariate in such a survival analysis). So I am not sure what analysis this sentence refers to. Please clarify and correct analysis if required.

Discretionary revisions

1. p4 "There is no screening for MRSA colonization". None at all? Even in outbreaks?

2. p10 "A Brazilian study observed that patients colonized or infected with multidrug-resistant bacterial organisms had a higher length of stay than controls in the ER, and a higher associated mortality ". There are many such studies, but most do not show causality, due to both selection bias (patients are colonized/infected often have many other risk factors for long stays and mortality) and time dependent bias (increased length of stay would also be expected to increase the risk of colonization or infection). A causal association is of course plausible, but recent analyses have shown that most estimates are likely to suffer from considerable bias.

3. p9 "Two other studies in Brazil have also shown a high rate of colonization [12, 13], although they were in ICU settings, where patients are more exposed to invasive procedures (intravenous catheters, urinary catheters and mechanical ventilation) and have higher rates of colonization." Is the second "colonization" intended? Should this be something else, eg. antibiotic use?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests