Reviewer's report

Title: Assessing the role of undetected colonization and isolation precautions in reducing Methicillin-Resistant Staphylococcus aureus transmission in intensive care units.

Version: 2 Date: 16 July 2009

Reviewer: Martin Bootsma

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I feel this is a well-performed analysis of clinical data obtained in a non-study setting, which tries to answer a relevant medical question. Unfortunately, despite reasonably long study periods, the data do not allow a clear conclusion about the effect of isolation measures.

Minor Essential Revisions

Abstract:
- Remove comma in last line of introduction.
- Methods: If the admission cultures consisted of nasal swabs, add the word “Nasal” as first word.
- Methods: Add that the ICUs consisted of single beds. This is important for the interpretation of the term isolation.
- Conclusions: I think the conclusion is a bit too strong. No ICU showed significant evidence of a benefit of isolation and neither did the pooled estimate, so I would avoid terms like clinically significant reductions.

Materials and methods:
- Given the huge difference between countries in MRSA prevalence, I would prefer if the country and city of the tertiary academic medical center were provided in the first sentence.
- It was not completely clear to me which sites were cultured on admission.
- Mention more clearly that clinical cultures are also used for the analysis and mention which cultures are used (only blood cultures and wound cultures, or also urine cultures, this influence the interpretation of the low sensitivity of detecting MRSA by non-nasal cultures. Also mention somewhere the frequency (or the total number) of clinical cultures.
- What was the size of the ICUs? This can be inferred from table 1, but I think explicit mentioning is useful to provide the readers with a feeling of the data.
- The study period mentioned is incorrect. September 2003-January 2004 is only 5 months, not 17.
- Was the cleaning protocol for the room identical after discharge of an MRSA-positive or MRSA-negative patient?
- From the discussion it can be inferred that conventional microbiological tests were used to detect MRSA colonization. I think this should be mentioned in the methods.

Data analysis
Stochastic model
- In the definition of \( \lambda(t) \), the cross transmission terms do not depend on the total number of patients in the unit (i.e., \( \lambda(t) \) is not \( \lambda_0 + \lambda_1 C(t)/N + \lambda_2 I(t)/N \).)

First, comment somewhere to what extent the number of patient within an ICU changes over time. Second, inclusion of the total number of patient in the unit in the formula for the force of infection rescales the estimates of \#1 and \#2. Although the sizes of the ICUs seem to be more or less identical (same number of total patient days, as suggested by Table 1), a remark on this is useful (for instance to interpret the sentence in the Results that the estimates of \#1 were fairly consistent).

- What are the assumptions about the sensitivity and specificity on clinical cultures? If a clinical culture is positive, the patient is considered to be MRSA positive, but what are the assumptions if a clinical culture is negative?

- Is the likelihood of the observed data computationally intractable if the specificity of a test is assumed to be 100% and subsequent test results of a single patients are assumed to be independent?

Results:
The estimates of \#1 seem to differ a factor 3 between wards, which is quite a lot. Mention the results of the swab sensitivity also in the text. Especially, that nasal cultures have a sensitivity of 60% of detecting MRSA colonization (at any site) is a relevant result, which is worth mentioning.

Discretionary Revisions
Explain the abbreviation ICU.
Last word of the abstract: replace the intervention with isolation.
Second paragraph of the introduction: to minimize the number of unknown MRSA-positive patient days; and to minimize MRSA transmission from known carriers.
Data analysis: Stochastic model. Is Poisson process the right term (as only one infection event can occur per patient)? Percentage of new admissions already colonized: Remove “having had”? Discussion: Remove “we calculate that only about”

**Level of interest:** An article whose findings are important to those with closely related research interests
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.