Author’s response to reviews

Title: Successful reduction of hospital-acquired methicillin-resistant Staphylococcus aureus in a urology ward: a 10-year study

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Author’s response to reviews: see over
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Version: 1 Date: 1 July 2013

Author's response to reviews: see over
First of all, I greatly appreciate the reviewers taking their precious time to review our paper and making constructive suggestions. Please take a look at the following comments, each of them corresponding to each of the reviewers’ comments, and review our revised manuscript once again. Please take a look at attached word file of the revised manuscript, in which revised parts are written in red. I would greatly appreciate the reviewers’ second review.

Reviewer’s report #1 (Dr Bidya Shrestha)

Minor essential revisions

Result: Line 23-24 (page 15, paragraph 2, line 5-6) states that after introducing surveillance culture, the number of culture increased to 61% in 2008 (Fig 3D). Figure 3D shows an increase in number of MRSA culture in 2008, decrease in 2009 and then increased again in 2010. The content in the text and that shown in the figure should match.

Figure 3a, 3b, and 3c show MRSA incidence in decreasing trend with the minimum in the year 2010. However, 3D shows an increasing trend in number of culture from 2006-2010 with a slight decrease in 2009 compared to 2008 and 2010. Does 3D show the MRSA colonization? If yes it should be clearly stated.

Thank you for your fine suggestion. Because of our unclear explanation, we have caused misunderstanding. Figure 3D showed annual total number of bacteriological culture submitted from the urology ward to the laboratory division, including MRSA positive and negative culture. It did not show number of MRSA culture. We would like to show how comprehensively we did bacteriological cultures before and after initiating...
surveillance cultures with Figure 3D.

We re-created Figure 3D and showed the submission rate of bacteriological cultures in the urology ward, which was calculated as a total number of submitted bacteriological cultures divided by total number of admissions during a year. We added the sentence in the results section (line 11 - 17, page 15 in the revised manuscript)

“Figure 3D shows the submission rate of bacteriological cultures in the urology ward, which was calculated as a total number of submitted bacteriological cultures divided by total number of admissions during a year. Before initiating surveillance cultures, those were obtained in 20% of admitted patients in 2006 that were at risk for carrying MRSA. After introducing surveillance cultures, the submission rate of bacteriological cultures increased to 61% in 2008.”

Methods: Is there any purpose/ or significance behind changing the antibiotic in two different years in clean, and clean and contaminated surgeries?

First, for the sake of patient safety, we have gradually reduced AMP in clean urological surgeries for patients without infectious risk. After we confirm that perioperative infection had not increased, we extended the range of application of reducing AMP including clean-contaminated urological surgeries.

We added the sentence in the methods section (line 2 - 3, page 10 in the revised manuscript)

“After we confirmed that perioperative infection had not increased, we extended the range of application of reducing AMP.”

Minor comments
There are some typographical mistakes and they are:
Discussion, line 43 (page 18, paragraph 2, line 1): control use should be replaced by controlled use.
Discussion, line 46 (page 18, paragraph 2, line 4): S aureus should be replaced by S. aureus.
References: Staphylococcus aureus is not italicized anywhere. The reference
numbers to be corrected are: 2, 3, 5, 6, 7, 18, 19, 27 and 29.

Reference number 26: Title is in the square bracket.
    We appreciate the reviewer pointing out our mistakes. We corrected those and revised parts were written in red.

To be added in list of abbreviations:
Methods, avoidance and reduction of AMP, line 14 (page 9, line 14): LVFX for levofloxacin? Method, avoidance and reduction of AMP, line 20 (page 10, line 5): TAZ/PIPC for Tazobactam/piperacillin?
    We appreciate the reviewer pointing out our mistakes. We added LVFX and TAZ/PIPC in list of abbreviations.

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Reviewer's report #2 (Dr Debra E. Irwin)

Major Compulsory Revisions

Methods Section – Statistical Analysis: The incidence rate is expressed as the ‘annual number of cases per 1000 patient years’. The authors should add a sentence that explains how patient-years were derived. Is it derived from length of stay in hospital?

At first, we apologize that we incorrectly used “annual number of cases per 1000 patient years”, and corrected it as “the annual incidence of MRSA per 1000 patients days”. However, drift of an argument has never changed. The annual incidence of MRSA is calculated as a total number of newly identified MRSA cases per 1,000 patient days that is the sum of inpatient days of all patients during a year.

We added the sentence in the methods section (line 2-4, page 13 in the revised manuscript)

“The annual incidence of MRSA is calculated as a total number of newly identified MRSA cases per 1,000 patient days that is the sum of inpatient days of all patients during a year.”

The Poisson regression model needs more explanation. For example, the independent variable ‘years of diagnosis’ – do you mean the actual year of diagnosis for each case or something else? How is ‘number of patient days at risk’ defined? Is it the length of stay in hospital or something else? The dependent variable is described as ‘the number of MRSA cases’ – is it truly the total number of cases?

We greatly appreciate the constructive comments. We explained the Poisson regression model more detail and clarified those variables. As pointed out, the actual year of diagnosis for each case was the independent variable, the logarithm of patient days was an offset and the number of MRSA cases per year was the dependent variable.

We described the formula for the model and the interpretation of the coefficient. In the result section, we added the coefficient with 95% confidence intervals.

We added the sentence in the methods section (line 5-15, page 13 in the
“Given that MRSA cases are rare compared with the number of admissions, we used Poisson regression model to obtain temporal trends in the incidence of MRSA between 2000 and 2010 [25]. In the model the number of MRSA cases per year was the dependent variable, the actual year of diagnosis was the independent variable, and the logarithm of patient days was an offset [26, 27].

The model was

$$\log (\text{Number of MRSA cases}) = \log(\text{Patient days}) + B_0 + B_1 \times \text{Year}. $$

$B_0$ is the overall intercept and $B_1$ is the coefficient for Year.

If the estimation of the coefficient for Year is significantly positive, that indicates the incidence of MRSA significantly increases with time.”

“Although the incidence of MRSA increased throughout the entire hospital (coefficient for Year, 0.016; 95% CI, 0.0062 to 0.027; $p = 0.002$), it decreased significantly in the urology ward (coefficient for Year, -0.12; 95% CI, -0.18 to -0.068; $p < 0.0001$).”

“In the urology ward, the incidence of acquired MRSA decreased significantly over time (coefficient for Year, -0.18; 95% CI, -0.25 to -0.11; $p < 0.0001$), whereas imported MRSA did not change over time (coefficient for Year, -0.020; 95% CI, -0.11 to 0.072; $p = 0.66$).”

“The incidence of CSMI decreased after the stepwise implementation of the strategies (coefficient for Year, -0.17; 95% CI, -0.25 to -0.087; $p < 0.0001$).”

Seems like some of the results could be due to unmeasured confounders. Was there any other data collected on the patients? Would it be possible to create a table that shows simple demographic and clinical data (eg: surgery type or infection control strategy, etc…) on all of the MRSA cases and non-cases during this time? If so, this table should be added and some of those variables may be relevant to put in the models. If not, this fact should be clearly stated and acknowledged as a limitation.
Thank you for a constructive proposition. On all patients in the entire hospital, data that we collected were mean duration of hospital stay, number of admissions and number of surgeries. We re-made figure 2 of the annual number of those, which increased in proportion to the year (Figure 2). On 134 MRSA patients in the urology ward, we showed characteristics of them including surgery type and antibiotics use (Table 1).

We could not collect clinical data on a large number of MRSA negative cases. Therefore we could not set up a case control study nor put some variables into the model. It is possible that unmeasured confounders, such as the staff compliance to the hospital-wide standard precautions, the number of contaminated surgeries, underlying comorbidities as infectious risk and antibiotic consumption, were associated with the incidence of MRSA. We addressed that as a limitation in the discussion section (line 6-13, page 19 in the revise manuscript).

“Second, this study was not a case control study and it is possible that unmeasured confounders, such as the staff compliance to the hospital-wide standard precautions, the number of contaminated surgeries, underlying comorbidities as infectious risk and antibiotic consumption, were associated with the incidence of MRSA. Therefore, we could not clarify the impact of the reduction or avoidance of AMP and minimally invasive surgery on the incidence of MRSA because of the observational design.”

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:

No conflict of interest.
Reviewer's report #3 (Dr Asaf Biber)

GENERAL COMMENTS:

The authors state that the reduction of MRSA cases (by their definition) was a result of reduction or avoidance of AMP in minimally invasive surgery. They should be careful in assuming that; this statement requires case control study and ignores other variants and factors, especially the ward staff compliance for the hospital-wide standard precautions. In addition it may be more appropriate to show the yearly incidence for all surgical classes (clean, clean-contaminated etc.) separately, it may illustrate the trends for each group by their AMP changes.

Thank you for a constructive proposition. We acknowledged that this study was not a case control study and it is possible that many unmeasured confounders such as the staff compliance to the hospital-wide standard precautions including hand hygiene, number of contaminated surgeries, underlying comorbidities as infectious risk and antibiotic consumption affected decreased MRSA incidence. We could not clarify the impact of the reduction or avoidance of AMP and minimally invasive surgery on the incidence of MRSA because of the observational design.

As we did not collect surgical data on MRSA negative cases, we could not show the annual incidence of MRSA according to surgical classes. On 134 MRSA patients in the urology ward, we showed characteristics of them including surgery type and antibiotics use (Table 1).

We addressed that in the discussion section (line 2-6, page 16, line6-10, page 17 and line 6-13, page 19 in the revise manuscript).

“Our study demonstrates that a large-scale, long-term stepwise infection control strategy that includes the reduction or avoidance of antimicrobial prophylaxis in minimally invasive surgery contributed to a reduction in hospital-acquired MRSA and clinically significant MRSA infections in a urology ward,”

“These findings indicate that a reduction or avoidance of AMP in minimally invasive urologic surgery could contribute to the management of MRSA in the urology ward. We believe that the minimally invasive surgery itself also was associated with the favorable outcomes.”
“Second, this study was not a case control study and it is possible that unmeasured confounders, such as the staff compliance to the hospital-wide standard precautions, the number of contaminated surgeries, underlying comorbidities as infectious risk and antibiotic consumption, were associated with the incidence of MRSA. Therefore, we could not clarify the impact of the reduction or avoidance of AMP and minimally invasive surgery on the incidence of MRSA because of the observational design.”

SPECIFIC COMMENTS:

1. It should be mentioned what the abbreviations stand for when they first appear in the paper, i.e. levofloxacin (LVFX).
   We appreciate the reviewer pointing out our mistakes. We added CSMI, clinically significant MRSA infection; LVFX, levofloxacin; TAZ/PIPC, tazobactam sodium/piperacillin sodium; CI, confidence interval in list of abbreviations.

2. Page 11, "Skin has been closed by subcuticular suture without additional dressing and postoperative bedside treatments are not usually performed." The second part of the sentence is not clear.
   Thank you for a constructive proposition. Before that time, we had changed a surgical dressing every day after surgery. After introducing the subcuticular suture, daily bedside treatment including change of the dressing, which is associated with the nosocomial transmission of MRSA, has been no longer required.
   We add the sentence in the methods section. (line 1-5, page 12 in the revise manuscript).
   “Since April 2008, skin has been closed by subcuticular suture without additional dressing. After introducing the suture, daily bedside treatment including change of the dressing, which is associated with the nosocomial transmission of MRSA, has been no longer required.”

3. P.14, second paragraph, first line "Of these patients, 3,719, including 134 urology patients, were diagnosed with MRSA”. It should be mentioned if they
were diagnosed with MRSA infection, colonization or both. This is repeated through the results and discussion.

We greatly appreciate the constructive comments. We clarified terms of MRSA. An MRSA case was defined as a patient from whom MRSA was recovered from any site, including a patient infected or colonized with MRSA. We unified the terms about MRSA in the manuscript and added the sentences in the methods and results section (line 9 - 11, page 8 and line 9-10, page14 in the revised manuscript)

“An MRSA case was defined as a patient from whom MRSA was recovered from any site, including a patient infected or colonized with MRSA. “

“Of these patients, 3,719, including 134 urology patients, were infected or colonized with MRSA.”

4. "Clinically significant MRSA infection" was well defined, but "Major clinically significant MRSA infections" (p.14, third last line) was not defined.

We would like to describe the major type of clinically significant MRSA infection. We added the sentence in the results section. (line 5 - 6, page 15 in the revised manuscript)

“The major type of CSMI were surgical site (33%), genitourinary tract (22%) (Table 1).”

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