Author's response to reviews

Title: Sequential introduction of single room isolation and hand hygiene campaign in the control of methicillin-resistant Staphylococcus aureus in intensive care unit

Authors:

Vincent CC Cheng (vcccheng@hkucc.hku.hk)
Josepha WM Tai (taiwm@ha.org.hk)
WM Chan (chanwm4@ha.org.hk)
Eric HY Lau (ehylau@hku.hk)
Jasper FW Chan (jaspchan@gmail.com)
Kelvin KW To (kelvinto@hkucc.hku.hk)
Iris WS Li (dririsli@yahoo.com.hk)
PL Ho (plho@hkucc.hku.hk)
KY Yuen (kyyuen@hkucc.hku.hk)

Version: 3 Date: 22 June 2010

Author's response to reviews: see over
Dear Dr Melissa Norton, MD
Editor-in-Chief
BMC-series journals

Re: Sequential introduction of single room isolation and hand hygiene campaign in the control of methicillin-resistant *Staphylococcus aureus* in intensive care unit

Thank you for revising our manuscript. The responses to our reviewers are listed in the point to point reply below. The revision is marked in yellow in the revised manuscript.

Thank you for your kind attention.

Dr. Kwok-Yung Yuen
Department of Microbiology
The University of Hong Kong
Corresponding author
Reviewer’s report

Title: Sequential introduction of single room isolation and hand hygiene campaign in the control of methicillin-resistant Staphylococcus aureus in intensive care unit

Version: 2 Date: 17 May 2010

Reviewer: Henrik Westh

Reviewer's report:

This is a very interesting study and adds important information to the value of MRSA isolation in single rooms.

Major Essential Revisions

The study period is quite long. It would therefore be very good to have some data on the prevalent MRSA types during the study period. Changing clones might be a confounder?

Ans: Thank you for the enquiry. The MRSA isolates are not stored routinely in our AICU. We agree that changing clones of MRSA might be a potential confounder for nosocomial transmission. Therefore, we have critically discussed our previous studies on the molecular epidemiology of blood cultures isolates of MRSA in five hospitals in Hong Kong, including our centre. The MRSA strains related to the CC8/SCCmec III/IIIA had decreased from 81.3% before year 2000 to 26.5% in year 2006 to 2008, whereas the CC45/SCCmec IV/V clone had increased from 16.6% to 42.6% in the corresponding period, which was associated with an increasing trend of MRSA bacteremia from 0.05 per 1000 bed-days in 2004 to 0.09 per 1000 bed-days in 2006-2008.

It might be one of the reasons why the pre-ICU onset MRSA infection was significantly increased from phase 2 to 3. However, with a combination of single room isolation and enforcement of hand hygiene practice in phase 3, a further reduction of ICU onset MRSA infection was observed despite an increase in colonization pressure in AICU.

This point has been critically discussed in our revised manuscript (last paragraph of Discussion, page 17-18).

I would like to see the absolute numbers of ICU onset nonbacteraemic and bacteraemic MRSA infection in results. As I read it all infections are for the whole study period not for each phase?

Ans: Thank you for the suggestion. The absolute number of ICU onset nonbacteraemic and bacteraemic MRSA infection are listed in the revised figure 3.

Not knowing how many MRSA patients enter the ICU is a lack of important knowledge. If the general burden of MRSA has been decreasing at the hospital this might be reflected in the MRSA bacteraemia rate for the whole hospital? This would be worthwhile looking into.

Ans: Thank you. The pre-ICU onset MRSA infection (defined as the MRSA infection diagnosed before or within 48 hours of ICU admission) was presented. This not only included the number of MRSA patients entering the ICU, but also the patients who are incubating the MRSA infection at the time of ICU admission. With this demarcation, we can have a better assessment of ICU-onset MRSA infection (refer to Method, page 7).

Minor Essential Revisions
The consumption of antibiotics is measured in DDD or Defined Daily Doses.
Ans: Thank you. We have made this amendment (refer to Method, page 6).

Bottom page 9 and top page 10 should be im methods.

Ans: Thank you. We have added the number of ICU-onset MRSA infection being managed in AICU in different phases of intervention so that it can be presented in “Results” (refer to Result, page 11-12).

The statement in the Abstract line 3 and 4 is overly ambitious. It should probably be their hospital not all of Hong Kong

Ans: Thank you. We have revised the statement as “an enhanced infection control program was conducted to control the spread of methicillin-resistant Staphylococcus aureus (MRSA) in our hospital” (refer to Abstract).

**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:**
I declare that I have no competing interest.
Reviewer’s report

Title: Sequential introduction of single room isolation and hand hygiene campaign in the control of methicillin-resistant Staphylococcus aureus in intensive care unit

Version: 2 Date: 30 May 2010
Reviewer: Jan A kluytmans

Reviewer’s report:

This paper describes an important issue: the use of single rooms to control the spread of resistant micro-organisms. The findings are impressive. Unfortunately there are several methodological weaknesses that are only partially addressed by the authors.

1) the fact that no admission screening is performed makes the interpretation of the results difficult. Temporal trends outside of the ICU can therefore not be controlled for. This especially important because the epidemiology of both MRSA and ESBL is currently changing. Both used to be hospital associated pathogens but are now increasingly found in individuals with no healthcare history. This limits the value of ESBL as a control group as well. The authors should discuss this more extensively.

Ans: Thank you for the comment and we have addressed this limitation in the last paragraph of the Discussion (page 17).

2) No typing is performed and therefore it is impossible to judge if the interventions limit the amount of cross-infection. A lower rate is observed but it is impossible to judge the effect on cross-infection. If the isolates have been stored this may be done additionally. If this is not possible it should be discussed critically.

Ans: Thank you for the comment. Unfortunately, it is impossible to perform the molecular typing because we have not stored the MRSA isolates routinely. We agree that without the molecular typing of the MRSA isolates among the patients with ICU-onset MRSA infection, it is impossible to judge if the interventions had reduced the incidence of cross-infection despite a lower rate of MRSA infection was observed during the study period. However, in our previous studies on the molecular epidemiology of blood cultures isolates of MRSA in five hospitals in Hong Kong, including our centre, the MRSA strains related to the CC8/SCCmec III/IIIa had decreased from 81.3% before year 2000 to 26.5% in year 2006 to
2008, whereas the CC45/SCCmec IV/V clone had increased from 16.6% to 42.6% in the corresponding period, which was associated with an increasing trend of MRSA bacteremia from 0.05 per 1000 bed-days in 2004 to 0.09 per 1000 bed-days in 2006-2008.


It might be one of the reasons why the pre-ICU onset MRSA infection was significantly increased from phase 2 to 3. However, with a combination of single room isolation and enforcement of hand hygiene practice in phase 3, a further reduction of ICU onset MRSA infection was observed despite an increase in colonization pressure in AICU.

This point has been critically discussed in our revised manuscript (Discussion, page 17-18).

3) A quasi-experimental study (before after design) should be analyzed using segmented regression analysis to control for trends. This is a minimal requirement for these kind of studies and the authors should redo their analysis.

Ans: Thank you. Interrupted time series with segmented regression analysis was used to control for trends in our quasi-experimental study before and after interventions. However, there was no significant change in the level and trend before and after the intervention, despite the fact that the incidence density of ICU onset MRSA infection were significantly reduced from phase 1 to phase 2 by Poisson regression analysis.
We believe that the outbreak of severe acute respiratory syndrome (SARS) in 2003 2Q, resulting in the death of 8 healthcare workers in Hong Kong, greatly enhanced the infection control compliance among all frontline healthcare workers, especially on handwashing. Therefore, the incidence density of ICU onset MRSA infection had already decreased in the second half of phase 1 (2003 2Q to 2004 2Q).

This change in habit could be a confounder underscoring the effect of single room isolation using interrupted time series analysis. In fact, the incidence density of ICU onset MRSA infection had a significant change in level and trend before and after SARS.

This finding illustrates an important principle that the compliance of infection control practice by healthcare workers is determined by the perception of our staff on whether their own personal safety was threatened. The outbreak of SARS may undermine the contribution of using single room isolation in the control of MRSA infection. However, the incidence density of ICU onset infection due to ESBL producing organisms was steadily increasing soon after the outbreak of SARS when patients colonized or infected with ESBL-producing organisms were not managed in the single room.

We have also critically discussed this important confounder in the first paragraph of discussion in the revised manuscript (page 14).

Redo-analysis with interrupted time series with segmented regression analysis was presented in the Method (page 9), Statistic method (page 10), Result (page 13), Table 2, and Figure 4 and 5.

**Level of interest:** An article of outstanding merit and interest 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