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# Pre-emptive contact precautions for intubated patients reduced healthcare-associated meticillin-resistant *Staphylococcus aureus* transmission and infection in an intensive care unit

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SUMMARY

Healthcare-associated infection by meticillin-resistant *Staphylococcus aureus* (MRSA) is still a great concern in an intensive care unit (ICU). Our surveillance data in the ICU revealed that intubated patients were at eight times higher risk of acquiring MRSA than non-intubated patients, so we hypothesised that pre-emptive contact precautions for all intubated patients would prevent healthcare-associated infection by MRSA in the ICU. Patients staying in our ICU for >2 days were included in this study. The study period was divided into two periods. During 2004 (1st period), contact precautions were performed only for patients with MRSA. During 2005–2007 (2nd period), contact precautions were applied to all intubated patients regardless of MRSA infection status. Patients were defined as MRSA-positive on admission when MRSA was detected by surveillance or clinical culture on enrolment. Other MRSA-positive results were defined as healthcare-associated MRSA (HA-MRSA) transmission. HA-MRSA infection was diagnosed according to the National Nosocomial Infections Surveillance Manual. The 1st period comprised 415 patients, and the 2nd period comprised 1280 patients. In intubated patients, HA-MRSA infection rate decreased significantly in the 2nd period (1st period 12.2%, 2nd period 5.6%; $P = 0.015$). HA-MRSA infection of all patients decreased from 3.6 to 2.3 incidents per 1000 patient-days ($P < 0.05$), despite a significant increase in the rate of patients MRSA positive on admission in the 2nd period (1st period 2.9%; 2nd period 6.1%). Pre-emptive contact precautions for intubated patients would be helpful in reducing HA-MRSA infection in ICU.



## Introduction

Meticillin-resistant *Staphylococcus aureus* (MRSA) infection in critically ill patients is associated with prolonged intensive care unit (ICU) stay, increased medical cost, and high mortality.[1–3] To prevent healthcare-associated (HA)-MRSA infection, in 2006 the US Centers for Disease Control and Prevention (CDC) published the guideline entitled *Management of multidrug-resistant organisms in healthcare settings* which recommends infection control precautions such as standard and contact precautions and surveillance of multidrug-resistant organisms (MDRO).[4] The CDC also noted that individual facilities should seek appropriate guidance and adopt effective measures that fit their particular circumstances and needs.

In this study, we aimed at reducing HA-MRSA infection in our combination medical, surgical and trauma ICU, and performed active surveillance of MDRO in the 1st period. In the 2nd period, we adopted pre-emptive contact precautions for all intubated patients based on our surveillance data, and then evaluated the effect of these measures on prevention of HA-MRSA infection and cost for infection control.

## Methods

All patients who stayed in our combination medical, surgical, and trauma ICU during January 2004 to December 2007 were

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included in the present study. Patients who stayed for less than three days were excluded. The study period ran from January 2004 to December 2007 and was divided into two periods: 1st period (January to December 2004) and 2nd period (January 2005 to December 2007).

Our ICU consists of two private rooms and a 17-bed main area. The distance from bed centre to bed centre in the main area was ~5 m, which does not allow direct contact between patient and patient or bedside instruments. The following infection control precautions were performed for all patients' care through the two study periods; standard precautions, hand hygiene with alcohol gel or soap before and after patient care, isolation of patients with MDRO. As contact precautions, the ICU staff were required to wear a disposable apron and gloves for patient care. During the 1st period, contact precautions were required only when ICU staff caring for patients were found to have MDRO. In the 2nd period, the contact precautions were applied to all intubated patients' care regardless of MDRO colonisation (Table I). Other infection control precautions were not different between the two periods.

We performed surveillance culture of sputum, nasal excretion and urine when patients were admitted in the ICU. The surveillance culture was continued once per week while the patients were staying in the ICU. Other clinical cultures were performed when needed. Those patients whose surveillance cultures were positive for MRSA at the time of enrolment were defined as 'MRSA-positive on admission'. Other patients, whose surveillance or clinical cultures became positive for MRSA >48 h after admission in the ICU were defined as 'HA-MRSA transmission'. Transmission includes apparent infection and colonisation of MRSA.

CDC criteria for nosocomial infection were used to determine which clinical isolates represented colonisation and which represented true infection.[5]

We evaluated the rate of HA-MRSA transmission and apparent infection, and we also evaluated the cost of contact precautions and antibiotics administered to treat MRSA infection. Segmented Poisson regression analysis was also performed to evaluate the level and trend change in monthly HA-MRSA infection rates after intervention.[6,7]

Continuous variables were analysed by Student's $t$-test or non-parametric test, as appropriate. Categorical variables were analysed by $\chi^2$-test or Fisher's exact test, as appropriate. The incidence of infection per 1000 patient-days was analysed on the assumption of Poisson distribution. $P < 0.05$ was considered to be statistically significant. Statistical analysis was performed with SPSS version 16.0 for Windows (SPSS, Chicago, IL, USA).

## Results

### *Patient characteristics*

Admissions to the ICU comprised 760 patients in the 1st period and 2351 patients in the 2nd period (Figure 1). We excluded 345 patients during the 1st period and 1071 patients during the 2nd period because of short stay (<3 days) in the ICU. The remaining 415 patients in the 1st period and 1280 patients in the 2nd period were the subjects of this study.

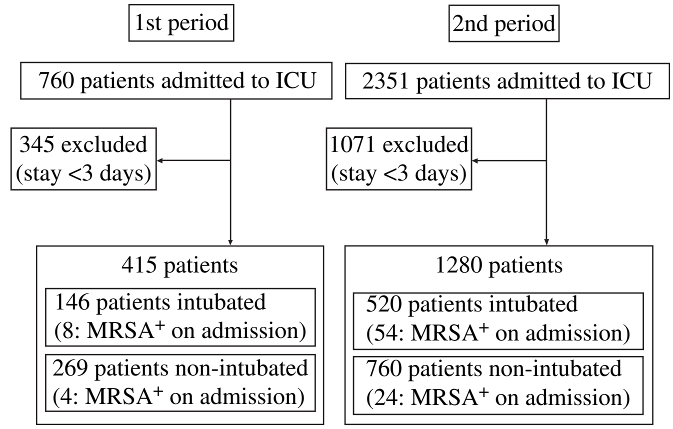


**Figure 1.** Schematic of the study. MRSA$^{+}$, meticillin-resistant *Staphylococcus aureus*.

Patient characteristics are presented in Table II. Patient age in the 2nd period was higher than that in the 1st period ($P < 0.05$). There was no significant difference in sex and mean length of ICU stay between the two periods. The number of intubated patients within 24 h of admission was 146 (35.2%) in the 1st period and 520 (40.6%) in the 2nd period. The percentage of intubated patients was significantly higher in the 2nd period. The number of patients MRSA positive on admission was significantly higher in the 2nd period (78, 6.1%) than in the 1st period (12, 2.9%).

### *HA-MRSA transmission and infection*

The incidence of healthcare-associated transmission (colonisation and infection) by MRSA is shown in Figure 2. In the 1st period, the incidence of HA-MRSA was 23.7% in intubated patients compared with 3.0% in non-intubated patients. In the 2nd period, when pre-emptive contact precaution was performed for all intubated patients, the incidence of HA-MRSA transmission decreased to 16.1% (non-significant). The incidence of HA-MRSA in the 1st period was more than 10 times higher in intubated patients in comparison with non-intubated patients (intubated 12.2%, non-intubated 1.1%); the infection rate in intubated patients decreased significantly to 5.6% in the 2nd period. No difference was found in non-intubated patients between the two periods.

HA-MRSA infection of all patients also decreased from 3.6 to 2.3 incidents per 1000 patient-days ($P < 0.05$), despite a significant increase in the rate of patients MRSA positive on admission in the 2nd period (1st period 2.9%; 2nd period 6.1%).

Details of HA-MRSA infections are shown in Table III. The incidence of critical infection was lower in the 2nd period (non-significant).

**Table I**
Precautions for preventing healthcare-associated infection in the 1st and 2nd periods

| Patients | Precautions | |
|---|---|---|
| | 1st period (2004) | 2nd period (2005–2007) |
| Intubated | Standard | Standard + contact |
| Non-intubated | Standard | Standard |
| MDRO$^{+}$ | Standard + contact | Standard + contact |

MDRO$^{+}$, positive for multidrug-resistant organisms.

**Table II**
Patient characteristics

| | 1st period | 2nd period | $P$-value |
|---|---|---|---|
| Age (years) | 50 ± 22 | 55 ± 22 | <0.05 |
| Sex (% male) | 68.4 | 63.1 | NS |
| No. of patients | 415 | 1280 | – |
| Patient-days | 5457 | 16 381 | – |
| Mean ICU stay (days) | 13 + 21 | 13 + 20 | NS |
| No. of intubated patients | 146 (35.2%) | 520 (40.6%) | <0.05 |
| No. of patients MRSA$^{+}$ on admission | 12 (2.9%) | 78 (6.1%) | <0.05 |

NS, non-significant; ICU, intensive care unit; MRSA$^{+}$, positive for meticillin-resistant *Staphylococcus aureus*.

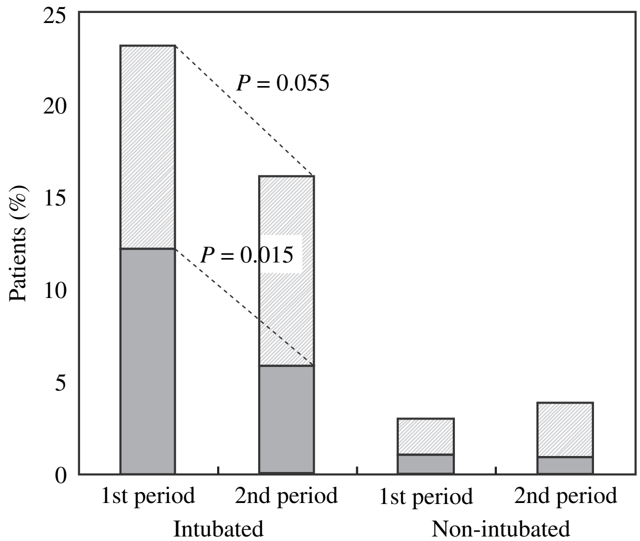


**Figure 2.** Percentage of healthcare-associated meticillin-resistant *Staphylococcus aureus* (HA-MRSA) transmission [colonisation (light grey bars) and infection (dark grey bars)] in intubated and non-intubated patient groups.

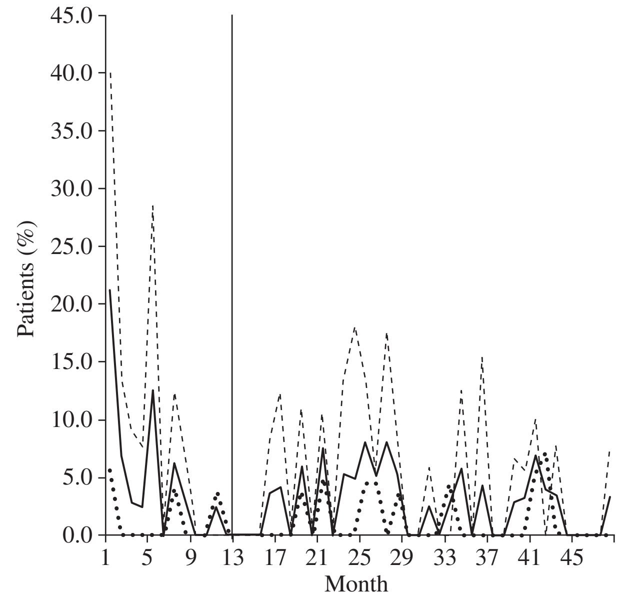


**Figure 3.** Monthly healthcare-associated meticillin-resistant *Staphylococcus aureus* infection rates during the study period. Vertical line represents the time of intervention. Dotted line: non-intubated; dashed line: intubated; solid line: total.

Figure 3 shows monthly HA-MRSA infection rates during the study period. Pre-emptive contact precaution was initiated at the 13th month. Variation of infection rate was observed during each period, but the infection rate decreased after the intervention, which was also indicated by segmented Poisson regression analysis (Table IV). Level of HA-MRSA infection rate was significantly decreased after intervention in total patients, and trend of infection rate was also changed after intervention. These findings suggested that pre-emptive contact precaution had beneficial effects on HA-MRSA infection rate. Analysis in total patients indicated that intubation was significantly associated with the increase in HA-MRSA infection. Segmented Poisson regression analysis showed that neither the level nor trend changed after intervention in non-intubated patients, whereas both the level and trend changed in intubated patients. These results indicate that the decrease in HA-MRSA infection rate in the total patients was due to the result of intubated patients.

As to the MDRO other than MRSA, we found one patient with extended-spectrum β-lactamase (ESBL)-producing *Klebsiella pneumoniae* in the 1st period and five patients with ESBL-producing *Escherichia coli* in the 2nd period. MDR *Pseudomonas aeruginosa* was detected in five patients (none in the 1st period vs five in the 2nd period), and vancomycin-resistant enterococci (VRE) were not detected throughout the study period. These small numbers meant that no evaluation of the effectiveness of our intervention on those MDRO was possible in the present study.

**Table III**
Details of the healthcare-associated meticillin-resistant *Staphylococcus aureus* infections

| Infection | 1st period | 2nd period |
|---|---|---|
| Pneumonia | 7 (1.69%) | 19 (1.48%) |
| Surgical wound | 5 (1.20%) | 6 (0.47%) |
| Bloodstream | 3 (0.72%) | 4 (0.31%) |
| Gastrointestinal | 3 (0.72%) | 1 (0.08%) |
| Central nervous system | 1 (0.24%) | 0 |
| Urinary tract | 0 | 3 (0.23%) |
| Sinusitis | 0 | 1 (0.08%) |
| Total no. of infections | 19 (4.58%) | 34 (2.66%) |

*Cost of contact precautions to prevent HA-MRSA infection*

The numbers of both gloves and aprons were increased in the 2nd period, because of the pre-emptive contact precautions performed (gloves: 1st period, 41 pairs, and 2nd period, 49 pairs per patient-day; aprons: 1st period, 15 and 2nd period, 26 per patient-day). The cost of gloves and aprons was $8.2 per patient day in the 1st period and $12.0 per patient day in the 2nd period. The annual cost of gloves and aprons increased from $49,242 in the 1st period to $71,493 in the 2nd period (original Japanese yen values were converted to US$ at the rate of $1 = ¥100) (Table V).

**Table IV**
Segmented Poisson regression analysis for pre-emptive contact precautions for intubated patients

| Variable | Coefficient | SE | 95% CI | | $\chi^2$ | |
|---|---|---|---|---|---|---|
| | | | Lower | Upper | Statistic | *P*-value |
| Intubated | | | | | | |
| Intercept | −0.85 | 0.41 | −1.65 | −0.06 | 4.40 | 0.0360 |
| Baseline trend | −0.29 | 0.10 | −0.48 | −0.09 | 8.49 | 0.0036 |
| Level change after intervention | −1.77 | 0.72 | −3.19 | −0.36 | 6.01 | 0.0142 |
| Trend change after intervention | 0.28 | 0.10 | 0.08 | 0.48 | 7.67 | 0.0056 |
| Non-intubated | | | | | | |
| Intercept | −4.24 | 1.22 | −6.63 | −1.86 | 12.16 | 0.0005 |
| Baseline trend | −0.04 | 0.17 | −0.37 | 0.29 | 0.05 | NS |
| Level change after intervention | −0.29 | 1.64 | −3.51 | 2.93 | 0.03 | NS |
| Trend change after intervention | 0.04 | 0.17 | −0.30 | 0.38 | 0.05 | NS |
| Total | | | | | | |
| Intercept | −2.90 | 0.48 | −3.83 | −1.96 | 36.83 | <0.0001 |
| Baseline trend | −1.56 | 0.65 | −2.83 | −0.28 | 5.74 | 0.0166 |
| Level change after intervention | −0.24 | 0.08 | −0.40 | −0.08 | 8.44 | 0.0037 |
| Trend change after intervention | 0.23 | 0.08 | 0.07 | 0.40 | 7.62 | 0.0058 |
| Intubation | 1.81 | 0.34 | 1.14 | 2.47 | 28.43 | <0.0001 |

CI, confidence interval; SE, standard error; NS, non-significant.

**Table V**
Cost (US$/year) for contact precautions and antibiotics used to treat meticillin-resistant *Staphylococcus aureus* infections

| | 1st period | 2nd period | Change in cost |
|---|---|---|---|
| Gloves + aprons | 49,242 | 71,493 | +22,251 |
| Antibiotics (IV + PO) | 40,628 | 28,932 | −11,696 |
| Total | 89,870 | 100,425 | +10,555 |

IV, intravenous; PO, per oral.

The cost of antibiotics used for MRSA infections was $4.8 per patient-day in the 1st period and $3.9 per patient-day in the 2nd period. The annual cost of antibiotics for MRSA decreased from $40,628 in the 1st period to $28,932 in the 2nd period. When limiting cost analysis to the cost of the aprons, gloves, and antibiotics used for MRSA infection, the annual cost increased by $10,555 in the 2nd period.

## Discussion

HA-MRSA is still a matter of great concern with respect to patients' outcomes and hospital management costs. In comparison with meticillin-susceptible *Staphylococcus aureus* (MSSA) infection, MRSA infection is reported to be associated with longer hospital stays and more treatment failures, producing worse clinical and economic outcomes.[1,2] Capitano *et al.* calculated that management costs for MRSA infection in a long term care facility were six times higher and nursing care costs were twice those for MSSA infection.[3]

Based on the numerous reports dealing with the adverse effect of MRSA infection on patient clinical and economic outcomes, the 2006 CDC guideline recommended infection control precautions such as standard and contact precautions and surveillance of MDRO.[4] With respect to the differences between each facility and patients targeted (e.g. ICU, burn care unit, neonatal ICU, long-term care facility), the guideline also emphasises assessment of local problems to determine proper interventions for controlling MDRO.

We introduced healthcare-associated infection (HAI) control management techniques such as active surveillance for MDRO, standard and contact precautions, and isolation of MRSA-positive patients beginning in 2003. However, HA-MRSA transmission occurred in >20% of intubated patients in 2004, and about half of them developed HA-MRSA infection. Analysis of our surveillance data in 2004 revealed that intubated patients had an eight-fold higher risk of acquiring MRSA than did non-intubated patients. We considered this to be because the ICU staff administered more frequent intensive care such as tracheal aspiration and body position changes to intubated than to non-intubated patients, thus increasing the chance of MRSA transmission by medical staff or equipment to intubated patients. On the basis of this analysis, we hypothesised that the use of extensive (pre-emptive) contact precautions for all intubated patients could prevent HA-MRSA transmission and infection.

Comparing patient characteristics between the 1st and 2nd periods, the percentage of patients intubated within 24 h of admission and MRSA-positive patients on admission was significantly higher in the 2nd period, indicating that the risk of MRSA transmission was higher in the 2nd period than in the 1st period. Nevertheless, HA-MRSA transmission in intubated patients decreased in the 2nd period. HA-MRSA infection also significantly decreased in the 2nd period in both the intubated patients and in total ICU patients. These results indicate that pre-emptive contact precautions for all intubated patients helped to reduce HA-MRSA in intubated patients, which consequently prevented spreading and developing MRSA infection in all of the ICU patients. The percentage of patients who developed HA-MRSA decreased from 52.6% in the 1st period to 36.6% in the 2nd period. The percentage of patients who developed HA-MRSA infection decreased from 52.6% in the 1st period to 36.6% in the 2nd period. The detailed mechanism of this reduction was not clarified in this study. However, we noticed that transmission of MRSA to intubated patients was delayed slightly during the 2nd period, which might affect developing HA-MRSA infection.

The idea of taking pre-emptive precautions to control the spread of MRSA was reported from a burn care unit (pre-emptive barrier precautions) and a diabetic foot care unit (pre-emptive isolation). Safdar *et al.* concluded that in their burn unit, pre-emptive barrier precautions using clean gloves and gowns for any patients found to be infected or colonised by MRSA were highly effective in controlling further outbreaks of MRSA and maintained a very low rate of nosocomial MRSA infection.[8] Lecornet *et al.* reported a significantly lower rate of MRSA acquisition in a diabetic foot care unit during the intervention period in which a pre-emptive isolation protocol was used.[9] Our study focused on intubated patients who were revealed to be at high risk of acquiring MRSA in our ICU, and showed some effect for prevention of HA-MRSA infection. To our knowledge, this is the first report to address pre-emptive contact precautions for intubated patients.

Some investigators have published their experiences with pre-emptive use of precautions for all patients with no beneficial effects. Yap *et al.* reported their intervention during outbreak of severe acute respiratory syndrome, which comprised gloves and gowns used all the time when medical staff worked in their ICU.[10] They showed an increase in the MRSA isolation rate in spite of their infection control policy, and considered that low compliance to the policy was the main reason for the adverse result. Their result suggested that it was important to formulate practicable infection control policy according to the individual healthcare setting. In the present study, we introduced the contact precaution only for the intubated patients based on our surveillance data and explained its significance to our ICU staff through the 2nd period, which we think may have made our intervention more successful. In Bearman *et al.*'s study, efficacy of universal gloving was compared to standard and contact precaution of CDC guidelines.[11,12] The acquisition rate of MDRO was not different between the two phases (phase 1: standard and contact precaution; phase 2: universal gloving). They suspected that low compliance with hand hygiene might affect the transmission of MDRO, and that the short follow-up period was insufficient to reveal a statistically significant difference in HAI rate. We introduced pre-emptive contact precautions with gloves and apron for the intubated patients and followed its effect for three years. Although the compliance with apron and glove was not evaluated, we think the targeted precaution derived from local surveillance data could improve HAI control. Slaughter *et al.* reported the efficacy of universal use of gloves and gowns in comparison with that of glove use alone on acquisition of VRE in a medical ICU.[13] In comparison with our study, the percentage of patients with VRE positive on admission was higher, and the number of patients included was smaller in their study. Barrier precaution bypass and contamination of equipment were also noted in their study, which could affect healthcare-associated transmission of VRE. Our study was not designed to determine the effect of apron and gloves in comparison with gloves alone, so further investigation is needed to clarify the effect of universal use of gloves together with gown or apron to prevent HAI.

In the 2nd period, more than 40% of the patients were intubated, so the number of targeted patients for pre-emptive contact precautions was high, which indicated higher cost for infection control. In regard to the efficacy of preventing MRSA transmission in the ICU, routine MRSA surveillance and infection control protocol are reported to result in marked reduction in the incidence of MRSA bacteraemia in ICU, non-ICU and hospital-wide.[14] Because patients admitted to the ICU usually transfer out of the ICU when they no longer require critical care, target precautions to prevent MRSA transmission in the high risk unit could prevent a large number of MRSA infections not only in the ICU but also throughout the entire institution. In our calculation, the cost for infection control (gloves and aprons) on each patient-day was $12.0, which was $3.8 higher than the cost in the 1st period. The cost of antibiotics used to treat MRSA infection was reduced by $0.9 per patient-day in the 2nd period. Therefore, the total increase in cost was $2.9 per patient-day in the 2nd period. However, the attributable cost for a longer stay in ICU or evaluation and treatment of infection other than antibiotics was not taken into account in this calculation; we speculate that the cost reduction in the 2nd period would be much greater in the real clinical setting. Regarding the cost for infection control, the additional cost for ventilator-associated pneumonia (VAP) was reported to be $10,019 per case, which included the cost for evaluation such as chest radiography, arterial blood gases and blood cultures, and the cost for administered antibiotics.[15] Puzniak *et al*. performed a cost-benefit analysis of gown use in controlling VRE transmission: the annual net benefit of the gown policy was $419,346, and the cost-saving per case of averted VRE was $1,897.[16] They concluded that infection control policies initially increase the cost of health service delivery, but that such policies can result in overall cost savings by averting HAIs and the costs of treatment. Considering the adverse effect and outcome of MRSA infection in critically ill patients, we also think that the cost for gloves and aprons to prevent MRSA transmission is well worth the price in this high risk care area.

Our study includes some limitations. First, this is a historical control study. It is also possible that our ICU staff were more susceptible to MRSA transmission or infection during the 2nd period, as a result of the so-called Hawthorne effect. The differences in patient characteristics between the two periods such as age, percentage of intubated patients within 24 h of admission and the rate of MRSA-positive patients on admission might also have affected the results. Second, we did not present the infection rates by device days in urinary tract infection, central venous line-associated infection and VAP. Although total HAI rate per 1000 patient-days was significantly lower in the 2nd period, the incidence of each infection was too low to show a significant decrease in the 2nd period. Further study is required to determine the effect of pre-emptive contact precaution on each HAI. Third, our study was focused on critically ill patients in the ICU, so our strategy may not be applied directly to other institutions such as non-acute care facilities. As the CDC guidelines recommend, setting a flexible and individual strategy for each facility based on the local surveillance or risk assessment data is necessary to perform cost-effective infection control, and we suppose that educating and feeding these data back to the local medical staff may contribute to the promotion of more rigorous infection control.

In summary, the incidence of HAI by MRSA in the ICU decreased significantly after we introduced pre-emptive contact precautions for all intubated patients. We conclude that infection control based on the local risk assessment would help to reduce HA-MRSA infection in the ICU.

### Conflict of interest statement

None declared.


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