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# Daily bathing with chlorhexidine-based soap and the prevention of Staphylococcus aureus transmission and infection

Melissa A. Viray

*Washington University School of Medicine in St. Louis*

James C. Morley

*University of New South Wales*

Craig M. Coopersmith

*Emory University*

Marin H. Kollef

*Washington University School of Medicine in St. Louis*

Victoria J. Fraser

*Washington University School of Medicine in St. Louis*

*See next page for additional authors*

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**Authors**

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Author(s): Melissa A. Viray, MD; James C. Morley, PhD; Craig M. Coopersmith, MD; Marin H. Kollef, MD; Victoria J. Fraser, MD; David K. Warren, MD, MPH

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## ORIGINAL ARTICLE

# Daily Bathing with Chlorhexidine-Based Soap and the Prevention of *Staphylococcus aureus* Transmission and Infection

Melissa A. Viray, MD;<sup>1</sup> James C. Morley, PhD;<sup>2</sup> Craig M. Coopersmith, MD;<sup>3</sup> Marin H. Kollef, MD;<sup>1</sup>  
Victoria J. Fraser, MD;<sup>1</sup> David K. Warren, MD, MPH<sup>1</sup>

**OBJECTIVE.** Determine whether daily bathing with chlorhexidine-based soap decreased methicillin-resistant *Staphylococcus aureus* (MRSA) transmission and intensive care unit (ICU)-acquired *S. aureus* infection among ICU patients.

**DESIGN.** Prospective pre-post-intervention study with control unit.

**SETTING.** A 1,250-bed tertiary care teaching hospital.

**PATIENTS.** Medical and surgical ICU patients.

**METHODS.** Active surveillance for MRSA colonization was performed in both ICUs. In June 2005, a chlorhexidine bathing protocol was implemented in the surgical ICU. Changes in *S. aureus* transmission and infection rate before and after implementation were analyzed using time-series methodology.

**RESULTS.** The intervention unit had a 20.68% decrease in MRSA acquisition after institution of the bathing protocol (12.64 cases per 1,000 patient-days at risk before the intervention vs 10.03 cases per 1,000 patient-days at risk after the intervention;  $\beta$ ,  $-2.62$  [95% confidence interval (CI),  $-5.19$  to  $-0.04$ ];  $P = .046$ ). There was no significant change in MRSA acquisition in the control ICU during the study period (10.97 cases per 1,000 patient-days at risk before June 2005 vs 11.33 cases per 1,000 patient-days at risk after June 2005;  $\beta$ ,  $-11.10$  [95% CI,  $-37.40$  to  $15.19$ ];  $P = .40$ ). There was a 20.77% decrease in all *S. aureus* (including MRSA) acquisition in the intervention ICU from 2002 through 2007 (19.73 cases per 1,000 patient-days at risk before the intervention to 15.63 cases per 1,000 patient-days at risk after the intervention [95% CI,  $-7.25$  to  $-0.95$ ];  $P = .012$ ). The incidence of ICU-acquired MRSA infections decreased by 41.37% in the intervention ICU (1.96 infections per 1,000 patient-days at risk before the intervention vs 1.15 infections per 1,000 patient-days at risk after the intervention;  $P = .001$ ).

**CONCLUSIONS.** Institution of daily chlorhexidine bathing in an ICU resulted in a decrease in the transmission of *S. aureus*, including MRSA. These data support the use of routine daily chlorhexidine baths to decrease rates of *S. aureus* transmission and infection.

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*Staphylococcus aureus* is a major cause of healthcare-associated infections, particularly among critically ill patients. Methicillin-resistant *S. aureus* (MRSA) has caused an increasing proportion of intensive care unit (ICU)-acquired *S. aureus* infections in the United States over the past 20 years. Compared with methicillin-susceptible *S. aureus* (MSSA), MRSA infections are associated with increased costs<sup>1-3</sup> and mortality.<sup>4,5</sup>

Transmission of *S. aureus* between hospitalized patients has long been felt to primarily occur via the hands of healthcare workers.<sup>6</sup> Multiple interventions have been undertaken to interrupt MRSA transmission in healthcare settings, including improving healthcare worker hand hygiene compliance, instituting contact precautions for patients colonized or infected with MRSA, performing active surveillance to identify

asymptomatic colonization and prompt earlier contact precautions, and decolonizing MRSA-colonized patients.<sup>7</sup> Chlorhexidine gluconate, a topical antiseptic, has been used in preprocedural skin antisepsis and to eliminate MRSA carriage. Recent data have emerged to support the use of chlorhexidine skin antisepsis to prevent the transmission of drug-resistant organisms, such as vancomycin-resistant enterococci (VRE) and MRSA, in ICUs.<sup>8-10</sup> Several studies have evaluated the use of chlorhexidine-based skin antisepsis, with or without intranasal therapy to decolonize MRSA-colonized ICU patients,<sup>11-14</sup> and reported decreases in MRSA acquisition,<sup>11</sup> colonization,<sup>12,13</sup> and infection.<sup>13,14</sup> Additionally, bathing all ICU patients daily with a chlorhexidine-based soap has been shown to decrease acquisition of MRSA,<sup>8,15</sup> colonization with MRSA<sup>16</sup> and MRSA infection.<sup>17</sup> However, few studies<sup>8,17</sup> ex-

Affiliations: 1. Washington University School of Medicine, St. Louis, Missouri; 2. University of New South Wales, Sydney, Australia; 3. Emory University School of Medicine, Atlanta, Georgia.

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TABLE 1. Characteristics of the Intervention and Control Intensive Care Units

| Variable  | Intervention (surgical) ICU<br>(Dec 2002–Dec 2007) | Control (medical) ICU<br>(Jan 2005–Dec 2007) | P <sup>a</sup> |
|---|--|--|----------------|
| No. of beds   | 24   | 19   | NA             |
| Patient days, total <sup>b</sup>  | 35,124   | 18,402                                       | NA             |
| Ventilator utilization ratio, monthly, median (range) <sup>b</sup>              | 0.69 (0.45–0.80)                                   | 0.59 (0.43–0.68)                             | <.001          |
| Central venous catheter utilization ratio, monthly, median (range) <sup>b</sup> | 0.66 (0.44–0.81)                                   | 0.59 (0.46–0.76)                             | .008           |
| Patient characteristics, monthly proportion, median (range) <sup>c</sup>        |  |  |                |
| Decubitus ulcer (stage II or greater)   | 0.23 (0.14–0.38)                                   | 0.22 (0.16–0.34)                             | .08            |
| Tracheostomy  | 0.20 (0.11–0.54)                                   | 0.18 (0.11–0.25)                             | .003           |
| Enteral tube feeding  | 0.28 (0.17–0.69)                                   | 0.22 (0.17–0.40)                             | .004           |
| MRSA colonization at admission  | 0.17 (0.06–0.38)                                   | 0.24 (0.13–0.38)                             | <.001          |

NOTE. ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not applicable.

<sup>a</sup> Determined by Mann-Whitney *U* test.

<sup>b</sup> Patients with more than a 2-day stay in the ICU only.

<sup>c</sup> Proportion of all ICU admissions with variable of interest during ICU stay, per month.

aming the effect of routine daily chlorhexidine bathing on *S. aureus* transmission and infection have accounted for secular trends in colonization pressure because of changes in MRSA prevalence or changes in patient mix among patients admitted to the ICU. Additionally, few studies have concomitantly compared the use of chlorhexidine in intervention units with its use in nonintervention units.<sup>10,18</sup>

The objective of this study was to determine whether a daily bathing protocol with a chlorhexidine-based soap decreased intra-unit MRSA transmission among ICU patients. A secondary goal was to determine whether chlorhexidine-bathing reduced intra-unit overall *S. aureus* (ie, regardless of susceptibility to methicillin) transmission and ICU-acquired *S. aureus* infection. These outcomes were compared with outcomes in an ICU in which bathing with nonmedicated soap was performed. The use of time series methodology allowed us to address potential confounders, such as temporal trends in patient mix and the prevalence of *S. aureus* colonization at ICU admission over time.

## METHODS

This study was performed at Barnes-Jewish Hospital (BJH), a 1,250-bed, urban, tertiary-care teaching hospital in St. Louis, Missouri. During the period of study, the trauma and surgical ICU (SICU) had 24 beds and approximately 1,400 admissions per year. The 19-bed medical ICU (MICU) had approximately 1,500 annual admissions. Patients with a previous or current history of MRSA, VRE, *Clostridium difficile*-associated diarrhea, and certain multidrug-resistant gram-negative bacilli were routinely placed under contact precautions, in accordance with hospital policy.

*S. aureus* (both methicillin-susceptible *S. aureus* and MRSA) active surveillance data were available for the intervention unit (SICU) from January 2002 and for the control unit (MICU) from January 2005. The study intervention was performed in June 2005, and study activities continued through

December 2007. For the purposes of our analyses, all available data from each ICU were included for primary and secondary outcomes.

Nasal cultures for *S. aureus* were performed for all patients admitted to these ICUs for more than 12 hours. Nasal cultures were also performed weekly and at ICU discharge for all patients staying in the ICU more than 48 hours. Decolonization therapy for MRSA with topical mupirocin was not routinely performed at BJH during the study period. Microbiological analysis of nasal specimens has been previously described.<sup>19</sup> Methicillin resistance among *S. aureus* clinical isolates was determined using standard microbiological methods. All positive routine clinical cultures for *S. aureus* (ie, MRSA and MSSA) were recorded.

## Bathing Protocol

Patient bathing in both units before June 2005 consisted of basin baths with nonmedicated soap (Aloe Vesta 2-n-1 Body Wash & Shampoo; ConvaTec) at least daily and additionally throughout the day if needed after bowel movements or other episodes of blood or body fluid soiling. In June 2005, the surgical ICU switched to using 4% chlorhexidine-based soap (Exidine 4%; Cardinal Health) for daily patient bathing. One 4-ounce bottle of chlorhexidine-based soap was added to 4 quarts of water, to give an approximate final concentration of 0.125% chlorhexidine gluconate in the bath water. Bathing was done with wash cloths using a standard method.<sup>20</sup> Chlorhexidine bathing was not performed above the neck, on the perineum, or on open wounds. Bathing compliance in the surgical ICU during the postintervention period was assessed weekly by determining the total number of chlorhexidine bottles used versus the total number of patient-days.

## Data Collection and Definitions

Prospective collection of patient-level data occurred in the surgical ICU from January 2002 through December 2007 and

TABLE 2. Comparison of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Acquisition Rates in the Intervention Intensive Care Unit (ICU), 2002–2007, and Control ICU, 2005–2007

| Variable   | Intervention (surgical) ICU <sup>a</sup> | <i>P</i> | Control (medical) ICU    | <i>P</i> |
|--|--|----------|--------------------------|----------|
| Crude rate per 1,000 patient-days at risk <sup>b</sup> |  |          |                          |          |
| Before intervention                                    | 12.64                                    |          | 10.97                    |          |
| After intervention                                     | 10.03                                    |          | 11.33                    |          |
| Change, %  | –20.68                                   |          | +3.28                    |          |
| Time series model, $\beta$ (95% CI) <sup>c</sup>       |  |          |                          |          |
| Intervention   | –2.62 (–5.19 to –0.04)                   | .046     | –11.10 (–37.40 to 15.19) | .395     |
| Adjusted MRSA colonization pressure <sup>d</sup>       | 30.79 (8.74–52.85)                       | .007     | 22.90 (–13.36 to 59.16)  | .207     |
| AR(1)  | ...                                      | ...      | 0.33 (–0.02 to 0.67)     | .061     |
| MA(4)  | ...                                      | ...      | –0.89 (–1.00 to –0.79)   | <.001    |
| Constant   | 6.75 (2.14–11.35)                        | .005     | 17.72 (–11.61 to 47.04)  | .227     |
| Model parameters                                       |  |          |                          |          |
| Adjusted R <sup>2</sup>                                | 0.14                                     |          | 0.32                     |          |
| Durbin-Watson statistic                                | 2.08                                     |          | 1.84                     |          |
| Q(4) <i>P</i>  | ...                                      | .71      | ...                      | .65      |
| Q(8) <i>P</i>  | ...                                      | .55      | ...                      | .55      |
| Q(12) <i>P</i>   | ...                                      | .62      | ...                      | .73      |

NOTE. The inclusion of autoregressive (AR) and moving average (MA) terms in the model addressed serial correlation seen, as evidenced by the Durbin-Watson statistic and the Box-Ljung  $Q(k)$  tests of the unadjusted model. AR(1), AR variable 1; CI, confidence interval; MA(4), MA variable 4.

<sup>a</sup> Models are based on all available data for the surgical ICU (61 months, 2002–2007) and medical ICU (24 months, 2005–2007).

<sup>b</sup> See “Methods” for definition of patient-days at risk.

<sup>c</sup> In the multivariate time series model,  $\beta$  indicates the magnitude and the direction of the variable in the model, whereas the *P* value and 95% CI indicate the precision and significance of the variable within the model.

<sup>d</sup> Other factors considered for inclusion in the final model included decubitus ulcers, tracheostomy, enteral feedings, central venous catheter utilization ratio, and mechanical ventilator utilization ratio.

in the medical ICU from January 2005 through December 2007 as part of an ongoing study of *S. aureus* transmission that has been previously described.<sup>21</sup> Data collected for all surgical and medical ICU patients included demographic characteristics, hospital and ICU admission and discharge dates, previous admission to BJH in the past 12 months, the patient’s location before hospital admission, and use of contact precautions. Additional data were collected for patients who remained in the ICU for more than 48 hours, including their past medical history, ICU processes of care, and use of mechanical ventilation and/or central venous catheters. Enteral tube feeding was defined as feeding via a nasogastric, Dobhoff, gastrostomy, jejunostomy, or gastrojejunostomy tube.

*S. aureus* colonization at ICU admission was defined as a patient having an admission nasal surveillance culture positive for *S. aureus* or any clinical culture positive for *S. aureus* within 48 hours after ICU admission. To determine the number of patients coming into the unit already carrying *S. aureus*, incoming colonization pressure was defined as the number of patients colonized or infected with *S. aureus* at admission per total number of admissions per month. *S. aureus* acquisition was defined as an admission nasal surveillance culture negative for *S. aureus* and subsequent isolation of *S. aureus* from a surveillance or clinical culture performed more than 48 hours after admission. The *S. aureus* acquisition rate was

defined as the number of acquired *S. aureus* cases per 1,000 patient-days at risk, where a day at-risk was defined as a day in the ICU (not within the first 48 hours after admission) without evidence of any *S. aureus* colonization or infection.<sup>18</sup> ICU-related *S. aureus* infections and device utilization ratio were defined using the Centers for Disease Control and Prevention criteria.<sup>19</sup>

### Analysis

The primary outcome of the analysis was the effect of the bathing intervention on MRSA acquisition in the intervention ICU (SICU) versus the control ICU (MICU). Time series analysis of the primary outcome was performed using data from the intervention ICU (SICU) from January 2002 through December 2007 and from the control ICU (MICU) from January 2005 through December 2007. The secondary outcomes were *S. aureus* acquisition (ie, both methicillin-susceptible and methicillin-resistant bacteria) as well as ICU-acquired infection due to MRSA and all *S. aureus* within the intervention ICU. The unit of analysis for each ICU was 1 month. The monthly proportion of patients admitted to each unit with that characteristic, or who developed it during their ICU hospitalization, was calculated. A time series model was developed for each ICU with use of ordinary least squares regression. First-order serial autocorrelation and higher-order

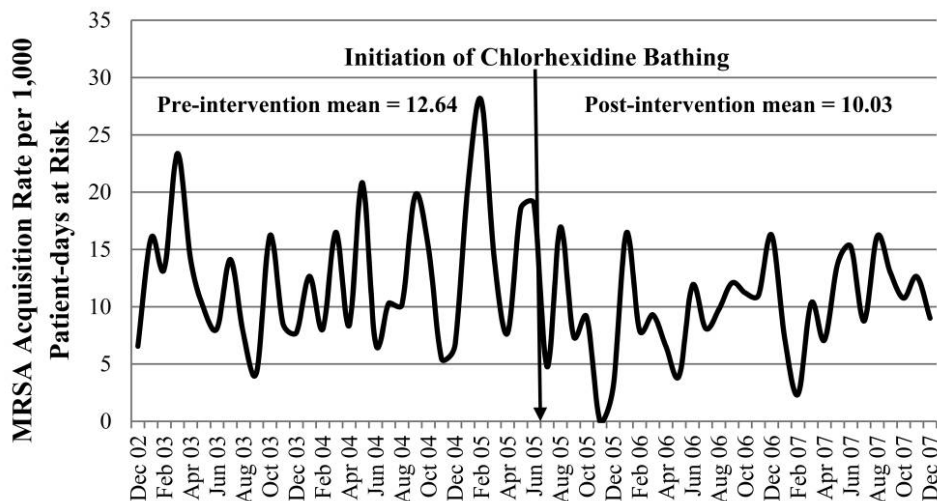


FIGURE 1. Unadjusted rates of methicillin-resistant *Staphylococcus aureus* (MRSA) acquisition per 1,000 patient-days at risk for the intervention intensive care unit.

autocorrelation were assessed for each model using Durbin-Watson statistic and Box-Ljung  $Q(k)$  test, respectively. Because autocorrelation was present in the control ICU, an autoregressive moving average model was created for the primary outcome; an autoregressive part and a moving average part were included in this model. Because the hypothesis of the study is that overall colonization pressure should decrease as a result of the intervention, an instrumental variable “adjusted colonization pressure” was created to account for variation in colonization pressure attributable to changes over time in the proportion of patients already colonized at the time of ICU admission. This is expressed as

$$X_{\text{adj.pressure,t}} \equiv X_{\text{pressure,t}} - \hat{\pi} \cdot D_t,$$

where  $D_t$  is the binary variable for the intervention. The Andrews-Ploberger test for a break in mean at an unknown date<sup>22</sup> was performed to determine the month with the maximal change in mean MRSA transmission rate in both units. All analysis was conducted in EViews 6 (IHS Global). The Wilcoxon rank-sum test was used to examine differences between medians. This study was approved by the Washington University Human Research Protection Office.

## RESULTS

During the study periods mentioned above, data were collected for a total of 53,526 patient-days, 35,124 from the intervention ICU and 18,402 from the control ICU (Table 1). There was higher use of central lines and ventilators in the intervention ICU than in the control ICU as well as a higher monthly proportion of patients receiving enteral feeds and having tracheostomies. MRSA colonization at admission to the ICU was higher in the control ICU (median proportion of patients with MRSA colonization at admission, 0.24 vs

0.17 per month;  $P < .001$ ). No other interventions were implemented during the periods of study that substantively affected *S. aureus* acquisition and/or infection rates.

The intervention unit had a 20.68% decrease in MRSA acquisition after institution of the chlorhexidine bathing protocol in June 2005 (12.64 cases per 1,000 patient-days at risk before intervention vs 10.03 cases per 1,000 patient-days at risk after intervention;  $\beta$ ,  $-2.62$  [95% confidence interval (CI),  $-5.19$  to  $-0.04$ ];  $P = .046$ ; Table 2; Figure 1). The reduction in MRSA acquisition was similar when intervention compliance (measured by antiseptic soap bottles used per patient-day) was used in the model (data not shown). There was no significant change in MRSA acquisition in the control ICU after June 2005 (10.97 cases per 1,000 patient-days at risk before June 2005 vs 11.33 cases per 1,000 patient-days at risk after June 2005;  $\beta$ ,  $-11.10$  [95% CI,  $-37.40$  to  $15.19$ ];  $P = .40$ ). To account for changes in MRSA prevalence at the time of ICU admission, adjusted MRSA colonization pressure was included in the final model (Table 2). Other factors, such as the proportion of ICU patients with decubitus ulcers or the monthly central venous catheter device utilization ratio, were not significant in the multivariable model. By the Andrews-Ploberger test, July 2005 was the month in the intervention unit with the maximal change in MRSA acquisition (1 month after the intervention started).

Using June 2005 as the breakpoint for analysis in both units, there was a 41.37% decrease in MRSA infection in the intervention ICU (1.96 infections per 1,000 ICU-days before the intervention vs 1.15 infections per 1,000 ICU-days after the intervention). There was no significant change in the prevalence of MRSA infection in the control ICU (2.19 infections per 1,000 ICU-days before June 2005 vs 1.05 infections per 1,000 ICU-days after June 2005;  $\beta$ ,  $-1.51$  [95% CI,

TABLE 3. Comparison of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection Rates in the Intervention Intensive Care Unit (ICU), 2002–2007, and Control ICU, 2005–2007

| Variable   | Intervention (surgical) ICU <sup>a</sup> | <i>P</i> | Control (medical) ICU  | <i>P</i> |
|--|--|----------|------------------------|----------|
| Crude rate per 1,000 ICU-days                    |  |          |                        |          |
| Before intervention                              | 1.96                                     |          | 2.19                   |          |
| After intervention                               | 1.15                                     |          | 1.05                   |          |
| Change, %  | –41.37                                   |          | –51.95                 |          |
| Time series model, $\beta$ (95% CI) <sup>b</sup> |  |          |                        |          |
| Intervention                                     | –0.90 (–1.40 to –0.40)                   | .001     | –1.51 (–4.01 to 1.00)  | .228     |
| Adjusted MRSA colonization pressure              | 10.78 (5.41–16.15)                       | <.001    | 1.37 (–1.76 to 4.51)   | .377     |
| AR(1)  | ...                                      |          | –0.57 (–0.91 to –0.24) | .002     |
| AR(2)  | ...                                      |          | –0.38 (–0.69 to –0.07) | .018     |
| MA(5)  | –0.36 (–0.62 to –0.11)                   | .005     | ...                    |          |
| MA(9)  | –0.30 (–0.53 to –0.08)                   | .009     | ...                    |          |
| MA(10)   | –0.31 (–0.57 to –0.06)                   | .017     | ...                    |          |
| MA(12)   | ...                                      |          | –0.93 (–1.00 to –0.86) | <.001    |
| Constant   | –0.13 (–1.33 to 1.06)                    | .822     | 2.32 (–0.18 to 4.82)   | .068     |
| Model parameters                                 |  |          |                        |          |
| Adjusted R <sup>2</sup>                          | 0.42                                     |          | 0.70                   |          |
| Durbin-Watson statistic                          | 2.12                                     |          | 2.37                   |          |
| Q(4)   | ...                                      | .24      | ...                    | .28      |
| Q(8)   | ...                                      | .66      | ...                    | .54      |
| Q(12)  | ...                                      | .90      | ...                    | .40      |

NOTE. The inclusion of autoregressive (AR) and moving average (MA) terms in the model addressed serial correlation seen, as evidenced by the Durbin-Watson statistic and the Box-Ljung  $Q(k)$  tests of the unadjusted model. AR(1), AR variable 1; AR(2), AR variable 2; CI, confidence interval; MA(5), MA variable 5; MA(9), MA variable 9; MA(10), MA variable 10; MA(12), MA variable 12.

<sup>a</sup> Models are based on all available data for the surgical ICU (61 months, 2002–2007) and medical ICU (24 months, 2005–2007).

<sup>b</sup> In the multivariate time series model,  $\beta$  indicates the magnitude and the direction of the variable in the model, whereas the *P* value and 95% CI indicate the precision and significance of the variable within the model.

–4.01 to 1.00]; *P* = .228; Table 3). There was a 20.78% decrease in all *S. aureus* acquisition in the intervention ICU from 2002 to 2007 (19.73 cases per 1,000 patient-days at risk before the intervention vs 15.63 cases per 1,000 patient-days at risk after the intervention;  $\beta$ , –4.1 [95% CI, –7.25 to –0.95; *P* = .012; Table 4). There was no change in *S. aureus* acquisition from 2005 to 2007 in the control ICU (19.21 cases per 1,000 patient-days at risk before June 2005 vs 15.33 cases per 1,000 patient-days at risk after June 2005;  $\beta$ , –6.75 [95% CI, –20.75 to 7.26]; *P* = .334). ICU-acquired *S. aureus* infection rates also decreased by 34.31% in the intervention ICU (2.71 *S. aureus* infections per 1,000 ICU-days before the intervention vs 1.78 *S. aureus* infections per 1,000 ICU-days after the intervention; Table 5), but not in the control ICU (2.19 *S. aureus* infections per 1,000 ICU-days before June 2005 vs 1.98 *S. aureus* infections per 1,000 ICU-days after June 2005;  $\beta$ , 1.58 [95% CI, –1.31 to 4.47]; *P* = .273).

## DISCUSSION

Institution of daily chlorhexidine bathing in a surgical ICU resulted in a decrease in the acquisition of and infections with *S. aureus*, including MRSA. This effect persisted even when accounting for temporal changes in *S. aureus* and MRSA colonization pressure at admission to the ICU and other pa-

tient risk factors. There was no significant decrease in *S. aureus* and MRSA acquisition or infections during an overlapping time frame in the control ICU, which did not implement chlorhexidine bathing.

The use of time-series analysis allows for evaluation of the impact of an intervention while controlling for issues related to changes in *S. aureus* and MRSA colonization pressure among newly admitted patients, differences in patient comorbidities and severity of illness, and seasonality. This is important because external trends in MRSA prevalence at admission to the ICU can affect subsequent changes in observed rates of *S. aureus* transmission and infection, independent of a particular intervention. The use of an instrumental variable, adjusted colonization pressure, to account for the changes in the *S. aureus* and MRSA colonization pressure present at ICU admission is novel.

Additional evidence supporting causality includes our finding that the maximal change in the MRSA monthly acquisition rate (as measured by the Andrews-Ploberger test) coincided with the implementation of chlorhexidine bathing in the intervention unit, whereas no change was seen during the same time frame in a control unit that was within the same hospital but did not use chlorhexidine bathing. This supports our findings and reduces the risk that observed decreases in



TABLE 4. Time Series Models for *Staphylococcus aureus* Acquisition Rates in the Intervention Intensive Care Unit (ICU), 2002–2007, and Control ICU, 2005–2007

| Variable  | Intervention (surgical) ICU <sup>a</sup> | <i>P</i> | Control (medical) ICU   | <i>P</i> |
|---|--|----------|-------------------------|----------|
| Crude rate per 1000 patient-days at risk <sup>b</sup> |  |          |                         |          |
| Before intervention                                   | 19.73                                    |          | 19.21                   |          |
| After intervention                                    | 15.63                                    |          | 15.33                   |          |
| Change, %   | –20.78                                   |          | –20.18                  |          |
| Time series model, $\beta$ (95% CI) <sup>c</sup>      |  |          |                         |          |
| Intervention  | –4.10 (–7.25 to –0.95)                   | .012     | –6.75 (–20.75 to 7.26)  | .334     |
| Adjusted <i>S. aureus</i> colonization pressure       | 49.13 (26.21–72.04)                      | .000     | 25.96 (–15.38 to 67.31) | .210     |
| AR(1)   | ...                                      |          | 0.24 (–0.13 to 0.61)    | .191     |
| MA(4)   | ...                                      |          | –0.38 (–0.74 to –0.02)  | .039     |
| Constant  | 2.40 (–5.99 to 10.79)                    | .569     | 12.50 (–9.77 to 34.76)  | .261     |
| Model parameters                                      |  |          |                         |          |
| Adjusted R <sup>2</sup>                               | 0.28                                     |          | 0.10                    |          |
| Durbin-Watson statistic                               | 1.90                                     |          | 1.99                    |          |
| Q(4)  | ...                                      | .83      | ...                     | .81      |
| Q(8)  | ...                                      | .87      | ...                     | .87      |
| Q(12)   | ...                                      | .87      | ...                     | .88      |

NOTE. The inclusion of autoregressive (AR) and moving average (MA) terms in the model addressed serial correlation seen, as evidenced by the Durbin-Watson statistic and the Box-Ljung  $Q(k)$  tests of the unadjusted model. AR(1), AR variable 1; CI, confidence interval; MA(4), MA variable 4.

<sup>a</sup> Models are based on all available data for the surgical ICU (61 months, 2002–2007) and medical ICU (24 months, 2005–2007).

<sup>b</sup> See “Methods” for definition of patient-days at risk.

<sup>c</sup> In the multivariate time series model,  $\beta$  indicates the magnitude and the direction of the variable in the model, whereas the *P* value and 95% CI indicate the precision and significance of the variable within the model.

*S. aureus* and MRSA acquisition and infection rates in the ICU using chlorhexidine were attributable to seasonal variation or other unmeasured confounders. Even when examined in the time period from 2005 to 2007 for both units, the reduction in MRSA acquisition was still significant in the intervention unit (data not shown).

These results expand on previous studies<sup>12,13</sup> that demonstrated that decolonization of *S. aureus* carriers identified by active microbiologic surveillance using brief (7-day) periods of daily chlorhexidine baths significantly decreased rates of MRSA in an ICU. Ridenour et al<sup>13</sup> reported a 52% decreased rate of MRSA acquisition in the ICU, and Fraser et al<sup>12</sup> demonstrated a 47% decrease in *S. aureus* colonization incidence and 63% decreased incidence in total *S. aureus*-related hospital-acquired infections. However, these studies did not take into account the impact of routine chlorhexidine bathing for all patients over a longer period of time, which could have an independent and potentially additive effect on *S. aureus* carriage and acquisition. Several studies have examined the effect of daily chlorhexidine bathing on ICU patients and have reported decreases in the rates of healthcare-associated infection<sup>10,16,18,23</sup> and the transmission of VRE.<sup>9,10</sup> Milstone et al<sup>24</sup> found decreased incidence in bacteremia in pediatric ICUs in per-protocol analysis, but similar rates of *S. aureus* bacteremia, very possibly attributable to very small numbers of positive cultures. Huang et al<sup>15</sup> found comparable significant decreases in MRSA-positive clinical cultures (37%, compared

with 41% seen in our study) after the institution of universal decolonization with daily chlorhexidine baths and nasal mupirocin. None of the studies were able to demonstrate decreased MRSA transmission.

Few studies<sup>8,11,17</sup> have used time-series methodology to evaluate the impact of daily chlorhexidine bathing on MRSA in ICUs. The use of time-series methodology allowed us to address secular trends in colonization pressure, which might otherwise bias our findings. Climo et al<sup>8</sup> reported a multicenter study using time-series analysis to evaluate daily bathing with chlorhexidine and reported a 32% decrease in MRSA acquisition but no difference in MRSA bacteremia. The decrease in reported MRSA acquisition was comparable to that seen in our study. However, we also noted a 41.4% decrease in all MRSA infections in the ICU using chlorhexidine bathing. The difference might be explained by accounting for incoming colonization pressure in our model. In a smaller study, Gould et al<sup>17</sup> evaluated daily chlorhexidine bathing as one of multiple simultaneous interventions and found an 11.4% decrease in MRSA in their ICU and nonsignificant decreases in MRSA bacteremia. However, because chlorhexidine bathing was only one of multiple interventions adopted (which included active surveillance culturing and contact isolation of colonized and infected patients), the effect of chlorhexidine bathing alone could not be determined.

Our study had some limitations. Although the use of time-series methodologies and a concurrent control ICU addresses

TABLE 5. Time Series Models for *Staphylococcus aureus* Infection Rates in the Intervention Intensive Care Unit (ICU) (2002–2007) and Control ICU (2005–2007)

| Variable   | Intervention (surgical) ICU <sup>a</sup> | <i>P</i> | Control (medical) ICU  | <i>P</i> |
|--|--|----------|------------------------|----------|
| Crude rate per 1,000 ICU-days                    |  |          |                        |          |
| Before intervention                              | 2.71                                     |          | 2.19                   |          |
| After intervention                               | 1.78                                     |          | 1.98                   |          |
| Change, %  | –34.31                                   |          | –9.37                  |          |
| Time series model, $\beta$ (95% CI) <sup>b</sup> |  |          |                        |          |
| Intervention                                     | –0.87 (–1.25 to –0.49)                   | <.001    | 1.58 (–1.31 to 4.47)   | .273     |
| Adjusted <i>S. aureus</i> colonization pressure  | 11.35 (6.86–15.84)                       | <.001    | 11.17 (6.39–15.95)     | <.001    |
| AR(1)  | ...                                      |          | –0.40 (–0.77 to –0.04) | .032     |
| AR(2)  | ...                                      |          | –0.36 (–0.73 to 0.01)  | .059     |
| MA(1)  | –0.21 (–0.46 to 0.03)                    | .083     | ...                    |          |
| MA(5)  | –0.33 (–0.57 to –0.09)                   | .008     | ...                    |          |
| MA(6)  | –0.44 (–0.70 to –0.18)                   | .001     | ...                    |          |
| MA(7)  | ...                                      |          | –0.91 (–0.99 to –0.83) | <.001    |
| Constant   | –1.37 (–3.04 to 0.31)                    | .107     | –3.63 (–7.40 to 0.14)  | .059     |
| Model parameters                                 |  |          |                        |          |
| Adjusted R <sup>2</sup>                          | 0.35                                     |          | 0.46                   |          |
| Durbin-Watson statistic                          | 2.09                                     |          | 1.87                   |          |
| Q(4)   | ...                                      | .14      | ...                    | .22      |
| Q(8)   | ...                                      | .66      | ...                    | .18      |
| Q(12)  | ...                                      | .71      | ...                    | .28      |

NOTE. The inclusion of autoregressive (AR) and moving average (MA) terms in the model addressed serial correlation seen, as evidenced by the Durbin-Watson statistic and the Box-Ljung  $Q(k)$  tests of the unadjusted model. AR(1), AR variable 1; AR(2), AR variable 2; CI, confidence interval; MA(1), MA variable 1; MA(5), MA variable 5; MA(6), MA variable 6; MA(7), MA variable 7.

<sup>a</sup> Models are based on all available data for the surgical ICU (61 months, 2002–2007) and medical ICU (24 months, 2005–2007).

<sup>b</sup> In the multivariate time series model,  $\beta$  indicates the magnitude and the direction of the variable in the model, whereas the *P* value and 95% CI indicate the precision and significance of the variable within the model.

many potential confounders, this was not a randomized controlled trial, and we cannot completely exclude the impact of other unmeasured confounders or temporal trends on the outcome. We did not evaluate length of stay (LOS) or mortality using these data; there would be additional confounding factors and/or interventions impacting LOS and mortality that would need to be included in the model. A future dedicated study could be performed to look at the impact of chlorhexidine bathing on those outcomes. We did not evaluate the MRSA strains in this study for the chlorhexidine resistance loci (ie, *qacA/B*). Future studies will be needed to determine whether widespread use of chlorhexidine for patient bathing will select for chlorhexidine tolerance in *S. aureus* and MRSA within healthcare settings and the community.

Our findings support the routine use of daily chlorhexidine baths to decrease rates of *S. aureus* transmission and infection in ICU settings. Chlorhexidine bathing is an inexpensive and relatively simple measure to adopt. Additional studies are needed to evaluate the effect of chlorhexidine bathing in non-tertiary care centers as well as in noncritical care settings to define the role of routine chlorhexidine bathing in healthcare and to evaluate for the development of resistance to chlor-

hexidine and/or potential adverse events that might occur with more widespread use of this topical antiseptic.

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ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to David K. Warren, MD, MPH, Washington University School of Medicine, Campus Box 8051, 660 South Euclid Avenue, St. Louis, MO 63110 (dwarren@dom.wustl.edu).

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