ORIGINAL ARTICLE

Universal vs Risk Factor Screening for Methicillin-Resistant *Staphylococcus aureus* in a Large Multicenter Tertiary Care Facility in Canada

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OBJECTIVE. To assess the clinical effectiveness of a universal screening program compared with a risk factor–based program in reducing the rates of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) among admitted patients at the Ottawa Hospital.

DESIGN. Quasi-experimental study.

SETTING. Ottawa Hospital, a multicenter tertiary care facility with 3 main campuses, approximately 47,000 admissions per year, and 1,200 beds.

METHODS. From January 1, 2006 through December 31, 2007 (24 months), admitted patients underwent risk factor–based MRSA screening. From January 1, 2008 through August 31, 2009 (20 months), all patients admitted underwent universal MRSA screening. To measure the effectiveness of this intervention, segmented regression modeling was used to examine monthly nosocomial MRSA incidence rates per 100,000 patient-days before and during the intervention period. To assess secular trends, nosocomial *Clostridium difficile* infection, mupirocin prescriptions, and regional MRSA rates were investigated as controls.

RESULTS. The nosocomial MRSA incidence rate was 46.79 cases per 100,000 patient-days, with no significant differences before and after intervention. The MRSA detection rate per 1,000 admissions increased from 9.8 during risk factor–based screening to 26.2 during universal screening. A total of 644 new nosocomial MRSA cases were observed in 1,448,488 patient-days, 323 during risk factor–based screening and 321 during universal screening. Secular trends in *C. difficile* infection rates and mupirocin prescriptions remained stable after the intervention whereas population-level MRSA rates decreased.

CONCLUSION. At Ottawa Hospital, the introduction of universal MRSA admission screening did not significantly affect the rates of nosocomial MRSA compared with risk factor–based screening.

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Infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) are associated with higher hospital readmission rates, poorer prognosis, and increased mortality compared with infections caused by susceptible strains.[1–6] Healthcare organizations have been challenged with implementing effective infection control strategies to reduce the risk of nosocomial MRSA transmission. The emergence of community MRSA compounds this challenge.[7] Because 85%–90% of patients with MRSA are asymptomatic carriers who can serve as a silent reservoir for further transmission,[8] screening patients for MRSA on admission to the hospital using rapid detection methods has the potential to identify asymptomatic carriers early, thereby allowing timely implementation of infection control measures.[9,10]

There is conflicting evidence regarding which admission screening approach is most clinically effective in reducing nosocomial MRSA transmission and infection.[11–20] Whereas risk factor–based screening applies to select patients with certain risk factors for MRSA, universal screening applies to all patients. A recent systematic review demonstrated that there is insufficient evidence to support or refute the utility of universal screening.[21] Our objective was to assess the clinical effectiveness of using a hospital-wide universal MRSA admission screening compared with risk factor–based screening for reducing nosocomial MRSA transmission.

METHODS

Study Design and Setting

This was a quasi-experimental study conducted at the Ottawa Hospital, a large multicenter tertiary care facility. There are approximately 47,000 admissions per year and approximately

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1,200 medical, surgical, obstetrical, critical care, mental health, and rehabilitation beds.[22]

This study took place during 2 periods. From January 1, 2006 through December 31, 2007 (24 months), patients were screened for MRSA through a standard risk factor–based approach if 1 or more of the following signs were identified at the time of admission: previous hospitalization in the past 6 months, direct transfer from another healthcare facility, or history of MRSA colonization or infection. From January 1, 2008 through August 31, 2009 (20 months), all admitted patients (excluding newborns) underwent universal MRSA screening.

Throughout both phases, all patients with MRSA from a screening or clinical specimen were placed on contact precautions in a private room with dedicated patient care equipment for the duration of their hospitalization and for subsequent admissions. In addition to hand hygiene upon room entry and exit, all staff were required to wear gloves and gowns to enter the room. Decolonization was not routinely performed.

Data Collection

The data required for this analysis were obtained from the Ottawa Hospital Data Warehouse, a relational database that links clinical, laboratory, and administrative data using common identification keys. Data were collected at monthly intervals in order to improve rate stability at each data point.

Primary Outcome

The primary outcome of interest was the nosocomial MRSA incidence rate, calculated as the total number of newly identified nosocomial MRSA patients per 100,000 patient-days. This included patients identified through screening swabs or clinical specimens obtained more than 48 hours after admission, excluding patients previously known to be colonized or infected with MRSA.[23] At our institution, only a minority of nosocomial MRSA patients are identified through clinical specimens.[24]

Secondary Outcomes

Throughout both study periods infection control measures, with the exception of screening, remained constant. However, other events external to the intervention could have potentially impacted the nosocomial MRSA rates. Both internal and external control groups were included in order to control for potential threats to validity.

The incidence of nosocomial *Clostridium difficile* infection (CDI) was used as the internal comparison group because hand hygiene adherence, environmental cleaning practices, and adherence to isolation protocols on nosocomial MRSA were expected to lead to a corresponding impact on nosocomial CDI incidence rates. Thus, any decrease in nosocomial MRSA incidence rates, in the face of constant or increased nosocomial CDI incidence rates, was more likely attributable to the screening intervention. A nosocomial CDI case was defined as any patient with onset of diarrhea 72 hours or more after admission and laboratory confirmation by a positive toxin assay result for *C. difficile*.

MRSA decolonization therapy may theoretically reduce the in-hospital reservoir of MRSA. Data were collected on the number of inpatients who received mupirocin, a topical antibiotic that is standard therapy for MRSA decolonization. Because MRSA decolonization is not routinely performed, this remains the predominant indication for mupirocin use in our inpatient setting. A decrease in nosocomial MRSA incidence at the Ottawa Hospital while mupirocin incidence rates remained constant would be more likely attributable to the screening intervention than to decolonization practices.

To account for the population prevalence of MRSA in the community, regional MRSA rates (ie, the incidence of MRSA in the region per 100,000 population) were used as the external comparison. The Ottawa Hospital is the sole adult tertiary care center within the Champlain Local Health Integration Network, a health region spanning approximately 18,000 square kilometers with a population of 1.2 million.[25] Hospital and private laboratories in the Champlain health region submitted MRSA isolates and basic epidemiologic data on a voluntary basis to the Microbiology Division of the Ottawa Hospital. Each patient was attributed to only 1 positive MRSA test (always the first 1 detected). The regional rates were calculated as all newly identified MRSA-positive cases in the Champlain health region per 100,000 population. A decrease in nosocomial MRSA incidence at the Ottawa Hospital while regional MRSA incidence remained constant or increased would be more likely attributable to the screening intervention than external factors.

Demographic and Clinical Characteristics

Data extracted from the Ottawa Hospital Data Warehouse for all inpatients included demographic information such as sex, age, campus of admission, admission date, discharge date, total days in the intensive care unit, number of acute care inpatient-days, number of patients in the hospital per day (patient-days), mortality rate, and the Charlson Comorbidity Index.[26]

Laboratory Methods

Screening swab specimens were obtained from the nares and rectum of each patient, as well as from any open skin lesions (up to a maximum of 2 sites) and catheter exit sites, where applicable. Swabs were inoculated into selective broths, incubated overnight, and tested using a commercial real-time polymerase chain reaction assay. The polymerase chain reaction test has a negative predictive value of 98%; however, with a lower positive predictive value of 65%, broth samples positive by polymerase chain reaction undergo culture confirmation.[24] Those patients who tested positive by polymerase chain reaction but whose culture results were negative were considered to be false-positives and had their contact precautions discontinued. Results were generally available within 24 hours of specimen collection.

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Statistical Analysis

All statistical analyses were conducted using SAS, version 9.1 (SAS Institute). Proportions and percentages were used to display the frequency of all categorical variables. Medians and interquartile ranges were used to display the distribution of continuous variables. Where specified, rates were calculated based on incident cases per 100,000 patient-days.

Controlling for seasonality, a pattern in the data that may be due to seasonal trends or fluctuations, requires at least 12 data points before and 12 after the intervention collected at equally spaced intervals.[27,28] A total of 44 time points (24 preintervention and 20 postintervention) were used and the presence of a seasonal effect was examined using the Dickey-Fuller unit root test and residual plots.[27] Residual plots and the Durbin-Watson statistic were used to examine the presence of serial autocorrelation. When significant autocorrelation was detected, this was accounted for in the analysis by including the autocorrelation parameter in the segmented regression model. To account for a possible delayed effect of the intervention, all patients screened within the first month of the intervention were excluded from the analyses. Overdispersion, described as extravariability arising from events that may not be considered independent, is often a result of uncontrolled experimental conditions.[29] A dispersion parameter was introduced into the relationship between the variance and the mean to account for any overdispersion in the model. The dispersion parameter was estimated using both the deviance and Pearson χ^2 statistic divided by the degrees of freedom.

Segmented regression analysis of interrupted time series data was chosen because it is able to estimate dynamic changes in various processes and outcomes following intervention intended to change the MRSA transmission rate, while controlling for secular changes that may have occurred in the absence of the intervention. Segmented regression controls for preintervention trends, estimates the size of the intervention effect at different time points, and evaluates changes in trends over time.[27] Four regression models were constructed to investigate the primary outcome of interest (nosocomial MRSA rates) and 3 secondary outcomes (nosocomial CDI rates, mupirocin prescription rate, regional MRSA rates). Ethics approval was obtained from the Ottawa Hospital Research Ethics Board (ID: 2008620-01H).

RESULTS

Description of the Ottawa Hospital Population

From January 1, 2006 through August 31, 2009, the Ottawa Hospital admitted 147,975 patients. Approximately 57% of the inpatient hospital population was female, with a median (interquartile range) age of 57.0 (37.0–72.0) years. The median (interquartile range) hospitalization was 3.0 (2.0–7.0) days, and 6,820 patients (4.6%) were admitted to the intensive care unit during their encounter. A total of 6,118 inpatients (4.1%) died during their hospitalization. There were no clinically significant differences in the hospital population in the pre- and postintervention periods (Table 1).

Description of Nosocomial MRSA Within the Ottawa Hospital

During the study period, there was a total of 644 newly identified nosocomial MRSA cases, 323 cases in the preintervention period and 321 in the postintervention period, for an incidence rate of 41.8 per 100,000 patient-days and 47.5 per 100,000 patient-days, respectively (Table 2). MRSA bacteremia occurred in 28 patients, 14 in each study period, for an incidence rate of 1.8 per 100,000 patient-days in the preintervention period and 2.1 per 100,000 patient-days in the postintervention period. The graphical presentation of pre- and postintervention nosocomial MRSA rates per 100,000 patient-days in Figure 1 shows near-identical pre- and postintervention trends.

In the preintervention period under risk factor–based screening, 29.2% (22,271/76,273) of admitted patients were screened within 48 hours of admission compared with 83.9% (51,815/61,782) of admitted patients in the postintervention period using universal screening. Of 76,273 patients screened during the preintervention phase, 745 (1.0%) were positive for MRSA (both previously known and newly identified). Of the 61,782 patients screened during the postintervention phase, 1,621 (2.6%) were MRSA positive. This resulted in a detection rate of 9.8 per 1,000 admitted patients before intervention and 26.2 per 1,000 admitted patients after intervention. The number of newly identified MRSA cases on admission increased from 132 (1.73 per 1,000 admissions) to 273 (4.42 per 1,000 admissions).

Statistical tests investigating the effects of seasonality were not significant. However, negative autocorrelation was detected in the rates of mupirocin prescriptions ($P = .020$) and positive autocorrelation was detected in the regional rate of MRSA ($P = .001$) and were therefore adjusted for in the final analysis. Overdispersion was also accounted for in all models because this is a more conservative approach to account for any variability that may have occurred owing to uncontrolled factors.

Segmented Regression Modeling

Table 3 displays the results from the segmented regression modeling. There was no significant change in the monthly rate of nosocomial MRSA from the preintervention to the postintervention phases. At baseline there were 46.79 MRSA cases detected per 100,000 patient-days (Model 1). The preintervention time trend was stable and not significantly different from 0 over the 24 months before the intervention. Immediately following the intervention, there was a nonsignificant decrease in the number of MRSA cases detected through universal screening (1.11 cases per 100,000 patient-days). Over the 20 months of the universal screening, there was a nonsignificant decrease in the monthly rate of MRSA transmission by 0.21 cases per 100,000 patient-days.

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TABLE 1. Demographic and Clinical Characteristics of Patients Admitted to Ottawa Hospital January 1, 2006–August 31, 2009

Characteristic	Total (n = 147,975)	Preintervention risk-factor screening (January 1, 2006–December 31, 2007) (n = 76,273)	Postintervention universal screening (January 1, 2008–August 31, 2009) (n = 61,782)
Demographic			
Female sex, no. (%)	85,077 (57.5)	43,958 (57.6)	39,064 (63.2)
Age, median (IQR), y	57.0 (37.0–72.0)	57.0 (37.0–72.0)	57.0 (37.0–72.0)
Campus, no. (%)			
General	69,097 (46.7)	35,722 (46.8)	31,715 (46.6)
Civic	58,608 (39.6)	29,821 (39.1)	27,356 (40.2)
Heart Institute	20,270 (13.7)	10,730 (14.1)	8,996 (13.2)
Clinical			
Length of stay, median (IQR), d	3.0 (2.0–7.0)	3.0 (2.0–7.0)	3.0 (2.0–8.0)
ICU days, no. (%)	6,820 (4.6)	3,612 (4.7)	3,028 (4.4)
Acute care days, median (IQR)	3.0 (2.0–7.0)	3.0 (2.0–7.0)	3.0 (2.0–7.0)
Crude mortality, no. (%)	6,118 (4.1)	3,166 (4.2)	2,797 (4.5)
Charlson Comorbidity Index, no. (%)			
0	81,472 (55.1)	41,917 (55.0)	37,600 (55.2)
1–2	33,964 (23.0)	17,367 (22.8)	15,715 (23.1)
3–4	14,572 (9.9)	7,496 (9.8)	6,727 (9.9)
≥5	17,967 (12.0)	9,493 (12.4)	8,025 (11.8)

NOTE. Pre- and postintervention totals will not add to total because January 2008 was excluded from intervention months to allow for an integration period. ICU, intensive care unit; IQR, interquartile range.

TABLE 2. Summary of Nosocomial MRSA Cases at the Ottawa Hospital Before and After Implementation of Universal Screening

	Preintervention risk factor screening (January 1, 2006–December 31, 2007)	Postintervention universal screening (January 1, 2008–August 31, 2009)	Total
Nosocomial MRSA cases	323	321	644
Nosocomial MRSA rate	41.8 / 100,000 patient-days	47.5 / 100,000 patient-days	
MRSA bacteremia cases	14	14	28
MRSA bacteremia rate	1.8 / 100,000 patient-days	2.1 / 100,000 patient-days	
No. of patient-days	773,072	675,416	1,448,488

NOTE. Data excludes newborns. MRSA, methicillin-resistant *Staphylococcus aureus.*

Model 2 indicates a baseline nosocomial CDI rate of 41.01 cases per 100,000 patient-days. Significant decreases in the rates of nosocomial CDI were recorded in the risk factor–screening phase ($P = .026$). There were no significant changes immediately following the intervention or during the post-intervention period. This model suggests that there were no significant secular trends detected that would differentially influence nosocomial CDI or MRSA transmission.

Model 3 indicates a baseline rate of 76.22 mupirocin prescriptions per 100,000 patient-days. There were no significant changes in the prescription rate in the preintervention phase, immediately following the intervention, or in the post-intervention phase. This model suggests that the rates of mupirocin prescriptions were stable over time and unlikely to affect the MRSA reservoir.

Model 4 displays a baseline regional MRSA rate of 7.39 per 100,000 patient-days. The results suggest a small increasing trend in monthly rates before the intervention ($P = .017$) and a small decreasing trend in monthly rates after the intervention ($P = .004$). These results suggest that despite a population-level

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decrease in the regional MRSA rates, this trend was not mirrored in nosocomial MRSA rates in the Ottawa Hospital.

DISCUSSION

We found that universal MRSA admission screening improved the detection of MRSA by almost 3-fold compared with risk factor–based screening. Despite improved detection, universal screening was not more effective in reducing nosocomial MRSA transmission in our hospital. The strength of this study is the use of internal controls to address potential threats to internal validity by means of competing measures (eg, improved hand hygiene, environmental cleaning, decolonization). Furthermore, we observed a decrease in regional MRSA rates that was not mirrored in our nosocomial rates, further strengthening the validity of our results. The reasons for this decrease are not clear because there was no regionwide intervention introduced during this period. However, similar decreases were noted in other health regions during this period.[30,31]

Several factors may explain why universal screening did not prove beneficial in our patient population. Adherence to infection control practices is difficult to enforce and measure, and changes in adherence may alter the impact of the intervention. Although we attempted to account for this by using an internal control group, it is possible that the effects were more noticeable within the MRSA rates than the CDI rates. Additionally, other studies have suggested that universal screening may be beneficial only in the setting of high MRSA prevalence.[13,32–35] Our MRSA prevalence was moderately low (2.6% of admitted patients) compared with prevalence rates in other studies that range from 1.7% to 10%.[16,20,36–39] This may have lessened the effects of the intervention. Finally, our adherence to universal screening averaged approximately 84% and we are unable to determine whether a higher adherence to admission screening would have altered our results. Nonetheless, our adherence rate is comparable with that of other studies[12,16,17,20,37] and we believe it is a realistic reflection of hospital function.

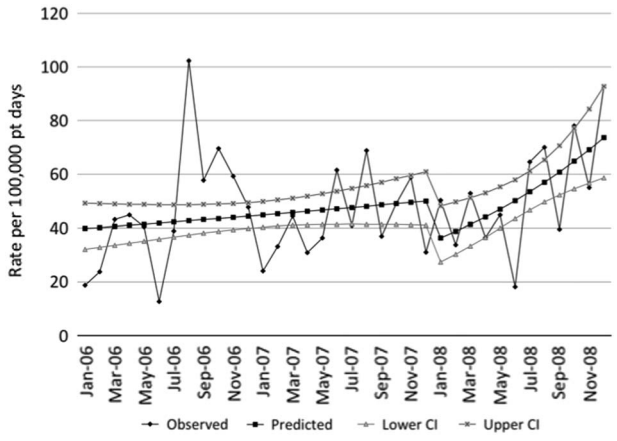

FIGURE 1. Rates of nosocomial methicillin-resistant *Staphylococcus aureus* before and after intervention, per 100,000 patient-days (pt days), January 1, 2006–August 31, 2009.

To the best of our knowledge, this is the first study to compare the clinical effectiveness of a hospital-wide universal MRSA screening intervention in reducing the nosocomial transmission of MRSA compared with risk factor–based screening using robust data and analytical techniques to control for confounding and secular trends.[21] Two previously published studies suggest that universal screening may reduce the incidence of MRSA infections compared with targeted screening, although this difference was significant in only 1 study.[16,20] Although the development of MRSA infection is an important health outcome, it represents only a small proportion of patients who acquire MRSA during their hospital stay.[40] Such patients serve as a reservoir for further MRSA transmission and are at considerable risk for subsequent MRSA infections after hospital discharge.[41] We chose MRSA transmission rates as our primary outcome measure to provide a more direct assessment of the impact of universal screening on nosocomial MRSA acquisition and the associated reservoir.

Because the results from this study indicated that universal admission screening for MRSA was not clinically effective in reducing nosocomial transmission, our universal screening program was discontinued. We analyzed the data from our universal screening program to develop a prediction rule for MRSA carriage. Since 2010, only high-risk patients as determined

TABLE 3. Segmented Regression Analyses Modeling Baseline Rates, Intervention-Specific and Secular Changes Over Time for MRSA Rates, and 3 Secondary Outcomes of CDI Rates, Mupirocin Prescription Rates, and Regional MRSA Rates

	Model 1		Model 2		Model 3		Model 4	
	MRSA rates		CDI rates		Mupirocin prescription rates		Regional MRSA rates	
Variable	Rate	*P* value	Rate	*P* value	Rate	*P* value	Rate	*P* value
Baseline rate per 100,000	46.79	<.001	41.01	<.001	76.22	<.001	7.39	<.001
Change in preintervention rate (24-month risk factor screening period)	0.40	.482	−0.95	.026	0.70	.155	0.10	.017
Change in pre-post rate (immediate rate difference)	−1.11	.923	12.52	.142	3.93	.694	0.83	.316
Change in postintervention rate (20-month universal screening period)	−0.21	.826	0.24	.753	−0.78	.331	−0.20	.004

NOTE. CDI, *Clostridium difficile* infection; MRSA, methicillin-resistant *Staphylococcus aureus.*

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by the prediction rule are screened for MRSA on admission (ie, patients admitted through the emergency department, direct transfers from another institution, admissions to an intensive care unit, and admissions to the rehabilitation center).

Although every effort was made to follow sound epidemiologic principles in the design and analysis of this study, some limitations were noted. First, as discussed above, we did not achieve 100% adherence to universal screening. Second, we used a composite measure of nosocomial MRSA including both surveillance swabs and clinical specimens obtained more than 48 hours after admission; as a result we cannot accurately quantify the contribution of each individual approach in case detection. Additionally, we did not conduct discharge surveillance cultures and therefore may have missed some nosocomial cases. Finally, reporting of regional MRSA data was voluntary and incomplete because data were missing from 1 of the 22 area hospitals for the final 2 months of the study period. This is unlikely to have a significant impact on the overall regional rates or to affect the primary outcome of this analysis.

In conclusion, these findings provide further evidence that hospital-wide universal MRSA admission screening is not clinically effective in reducing the nosocomial transmission of MRSA.[20,38,42–45] Although MRSA control measures continue to be the subject of much debate, the rates of nosocomial transmission and infection have decreased at the same time as the implementation of local and national control programs.[13,15,30,46] With increasing evidence that decolonization is an important component of MRSA control,[44,47,48] universal decolonization has been proposed owing to its simplicity and the avoidance of screening cultures.[48] However, the emergence of resistance is predictable with indiscriminate antimicrobial use and may circumvent any long-term benefits of universal decolonization.[48–50] These results have directly informed practice at the Ottawa Hospital and have been used to develop a prediction rule to enhance a risk factor–based screening approach to improve the identification of patients at high risk for MRSA on admission.

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