Background: The objective of this study is to determine the costs per hospital admission of screening intensive care unit patients for methicillin-resistant Staphylococcus aureus (MRSA) and isolating those who are colonized.

Methods: Data on the costs of the intervention come from the Minneapolis Veterans Affairs Medical Center, a 279-bed teaching hospital and outpatient facility. A microcosting approach is used to determine the intervention costs for 3 different laboratory testing protocols. The costs of caring for MRSA-infected patients come from the experience of 241 Minneapolis Veterans Affairs Medical Center patients with MRSA infections in 2004 through 2006. The effectiveness of the intervention comes from the extant literature. To capture the effect of screening on reducing transmission of MRSA to other patients and its effect on costs, a Markov simulation model was employed.

Results: The intervention was cost saving compared with no intervention for all 3 laboratory processes evaluated and for all of the 1-way sensitivity analyses considered.

Conclusion: Because of the high cost of caring for a MRSA patient, interventions that reduce the spread of infections—such as screening intensive care unit patients upon admission studied here—are likely to pay for themselves.

Key Words: Methicillin-resistant Staphylococcus aureus; MRSA; screening; costs.

Methicillin-resistant Staphylococcus aureus (MRSA) infections have become increasingly prevalent in the United States. In 1992, MRSA accounted for 36% of S. aureus isolates in US intensive care units (ICUs) but rose to 64% by 2003. By 2006, the prevalence was estimated at 46% in US health care facilities (34 infections and 12 colonizations per 1,000 inpatients). MRSA infections are associated with increased morbidity and mortality and cost more to treat than methicillin-susceptible S. aureus (MSSA) infections.

In a companion study to this one, the median cost of a hospital episode at the Minneapolis Veterans Affairs Medical Center (MVAMC) for patients with MRSA infections was found to be over twice as great as for patients with MSSA infections.

Aggressive interventions to screen patients and decolonize MRSA-positive cases are standard approaches in some European countries, but, in the United States, less aggressive interventions are used. The Government Accountability Office surveyed 14 US hospitals in 2007 regarding infection control activities and found that 11 tested all ICU patients for MRSA upon admission, but only 3 tested all hospital patients. All of these hospitals isolated the colonized patients, but only a few attempted decolonization. Review of published studies on the effectiveness of these programs found varying degrees of effectiveness, with some producing a reduction in infections as high as 75% but others producing no change at all. Not all of these studies, however, were relevant because not all investigated the same intervention that was used in our study. Thus, the limited number of comparable studies also limited the range of effectiveness results that could be applied in the present study.

The objective of the present study was to determine the cost per hospital admission of what appears to be the typical MRSA intervention used in the United States—screening all ICU patients for MRSA and
imposing isolation precautions on the colonized ones—compared with no intervention. A Markov model was developed and used to capture the feedback effect that the reduction of MRSA infections has on transmission of the disease hospital wide and therefore on the cost of an average hospital admission. Compared with studies that use a fixed reduction in MRSA patients per time period to adjust the costs for the effects of the intervention,6,14 a Markov model has the advantage that it also captures the effect of a reduction in MRSA patients on subsequent costs through reduced transmission of the disease. The model uses probabilities associated with transitioning from one disease state to another (in this case for patients admitted to the MVAMC) and the likelihood of becoming colonized or infected with MRSA to simulate the systemic effect of the intervention on the cost per hospital admission compared with the cost per admission without the intervention.

The Markov model was parameterized using data on (1) the costs of the screening intervention taken from the experience of the MVAMC, (2) the costs of treating MRSA-infected patients at the MVAMC using data from a companion study,8 (3) the effectiveness of the intervention using the findings of the Huang et al15 study of routine screening of ICU patients, and (4) starting and transition probabilities taken from the literature. Screening costs were calculated for 3 alternative nasal swab laboratory testing protocols: (1) nonselective culture media (henceforth, standard culture), (2) selective media (chromogenic agar), and (3) polymerase chain reaction (PCR). These tests are progressively more costly and could also be increasingly effective because the results are available after progressively smaller time intervals. Because significant differences in the effectiveness of these tests do not appear in the literature, however, no incremental cost-effectiveness analysis was possible. Instead, our Markov model calculated the increase in effectiveness that would be necessary to cover the additional costs of the 2 more costly screening approaches, compared with the standard culture test.

**METHODS**

**Markov model simulation**

The Markov model used here is based on Garber.16 Five Markov states were specified: (1) no MRSA infection or colonization, (2) MRSA colonization, (3) MRSA infection, (4) discharge, and (5) death, the latter 2 being the absorbing states. The MRSA infection state was modeled as 2 sequential states (MRSA infection 1 and MRSA infection 2), with MRSA infection 1 being a temporary state simply representing the first day of MRSA infection. This artificial distinction between the first and subsequent days of an MRSA infection was made to facilitate counting the number of additional MRSA infection cases with the TreeAge Pro software program (TreeAge Software, Inc, Williamstown, MA) and does not affect the generalizability of the results. The Markov cycle was modeled as a hospital day, and the program was run over a maximum of 365 days. Figure 1 shows the Markov states and the permitted transitions as indicated by the arrows.

**Costs of the intervention**

The costs of nasal swabbing, laboratory testing, and contact isolation precautions are based on the experience of MVAMC, a 279-bed teaching hospital and outpatient facility built in 1987, during 2005 and 2006. To identify appropriate cost components, personnel from the MVAMC’s laboratory, infection control, supply staff, and accounting office were consulted. The analysis was conducted from the perspective of the hospital, so no indirect costs were included.

The costs of the intervention were calculated on an annual basis as described below, divided by the number of patients admitted to MVAMC in a year, and entered into the Markov model as a one-time-only initial cost. This number represents the expected costs of the intervention itself, per hospital patient admitted.

The cost of nasal swabs and laboratory testing were estimated for the 3 alternative screening tests: standard culture, chromogenic agar, and PCR. A microcosting approach was used to determine the cost per screening test with the main components being the laboratory supplies, the technician’s time in conducting the test,
the nurse’s time to collect the sample, and the costs of the dedicated capital equipment for the PCR test. Specifically, for the PCR test, the cost of the $25,000 SmartCycler (Eurogentec, Belgium) processing instrument was included at an annual cost of $5,000 because of the machine’s 5-year warranty. For all tests, the number of screens per ICU patient was assumed to be 1.5, a conservatively high assumption given that the average ICU length of stay was only 3.2 days.

The cost of patient isolation included (1) the infection barrier materials (gown, gloves, and mask), (2) the time required by the staff to don them, and (3) the cost of equipment dedicated to each individual infected patient. The costs of isolation carts were also included, based on the assumption that 3 additional carts would be needed if a hospital with the characteristics of MVAMC adopted this ICU screening program anew. Isolation costs per day were calculated assuming that an isolation patient would receive 37 staff visits per day.

The additional isolation costs generated by the intervention would come from the colonized patients because infected cases already would have been detected without the intervention. To capture this effect, isolation costs per MRSA patient-day at the MVAMC also were applied to the MRSA infection cases. It was, however, not clear whether the MVAMC expenditure data had already captured these costs. Therefore, to account for possible double counting, the cost analysis was performed alternatively with and without these costs.

Cost of treating MRSA-infected patients

Per diem costs of caring for MRSA-infected patients were taken from the experience of patients served by MVAMC. Medical records were reviewed for all MVAMC patients with S aureus isolates from January 1, 2004, through June 30, 2006, to find cases of illness attributable to S aureus. Illnesses were categorized according to National Nosocomial Infections Surveillance System definitions. Cases with more than 1 manifestation during the first episode of disease (eg, cystitis and pyelonephritis) were categorized by the most severe one, and patients with multiple episodes of S aureus disease were enrolled only for the first one. The institutional review boards of the MVAMC, University of Minnesota, and Minnesota Department of Health approved this study.

The average length of stay and per diem costs of the hospital patients with MRSA infections were calculated from the experience of a portion of the patients of the companion study using costs recorded by the VA Decision Support System (DSS). DSS is a detailed itemized costing system used by the VA nationally and is known for its ability to determine actual costs associated with care. Whereas the companion study estimated the cost of a 6-month period and included nonhospital costs, the cost estimates used in present study included only the hospital costs of those 241 patients with a hospitalization occurring during the first 3 weeks of a primary MRSA infection. Per diem costs were found by dividing total hospital costs for persons with MRSA infections by the number of patient-days. The MRSA patients averaged $1,620.69 per diem during the period 2004 to 2006, with an average length of stay of 39.0 days. (This length of stay for MRSA-infected patients matched the one found in the Nulen et al [2008] study almost exactly.) A person who was uninfected or simply colonized with MRSA was assumed to have per diem costs of $2,553, which is the average cost of a patient-day in MVAMC and to have an average length of stay of 5.9 days, both numbers based on total VA experience in fiscal year 2005. The higher cost and lower length of stay of the non-MRSA patients reflects the fact that most VA admissions are for acute care procedures that are costly but for which the patient is discharged relatively quickly.

Effectiveness of the intervention

Again, the goal of the study was to estimate the change in costs per hospital admission that is generated by the intervention. Any cost savings from this intervention would be derived from its effectiveness in reducing MRSA infections throughout the hospital. In a recent review of the effectiveness literature, a study by Huang et al was found to be among the better studies. Huang et al found that this same intervention of screening ICU admission for MRSA and subsequent isolation of patients identified as colonized or infected with MRSA was effective in reducing MRSA bacteremia infections throughout the hospital. Because bacteremia is such a common form of MRSA infection, the reduction in the incidence of bacteremia infections was used as a proxy for the effectiveness of the intervention in reducing all MRSA infections.

Specifically, Huang et al found that screening ICU patients for MRSA and isolating colonized cases resulted in a 67% reduction in hospital-wide, hospital-acquired bacteremia incidence over 16 months of the intervention. Two transition in the Markov model from the present study determine the overall probability of infection, namely, moving from no MRSA colonization to MRSA colonization and moving from MRSA colonization to MRSA infection. To achieve a 67% reduction in infections, it was determined that (1) a 64% reduction in the probability of transitioning from no MRSA infection or colonization to MRSA colonization and (2) a 64% reduction in the probability of transitioning from MRSA colonization to MRSA infection.
Starting and transition probabilities

Starting and transition probabilities for the Markov simulation also were identified by a systematic review of the literature. A bibliographic database maintained at the Minnesota Department of Health containing over 900 articles on MRSA infections and colonizations was searched by 2 epidemiologists and a physician. Once candidate studies containing the same parameter were identified, the team evaluated them on a number of quality dimensions, and the best study was chosen by consensus. In cases of ties, the parameters were averaged.

Daily probabilities of transition to MRSA colonization and to MRSA infection were approximated by dividing the percent of patients making these transitions by the length of stay and then converting the rate to a probability. The daily probabilities of remaining in the same state were calculated as 1 minus the sum of all the transition probabilities from that state. The daily probabilities of transitioning from an MRSA infection state back to MRSA colonization were calculated by dividing 1 by the average length of stay minus the average duration of illness and again converting to a probability. The probabilities of discharge were determined by the lengths of stay identified in our companion study \(^8\) and adjusted for probability of dying, as determined by the literature. The various probabilities and literature sources are cited in Table 1.

Starting probabilities were assumed to be 5.15% colonized and 2.75% infected. The probability of a patient being colonized upon admission is based on the average of data from 5 articles.\(^{20,21,28-31}\) The probability of a patient being infected upon admission was based on data from Ridenour et al\(^{25}\) describing rates of ICU infection upon admission and applying the ratio of infection in the ICU to the entire hospital, based on the ratio of colonization between them.
RESULTS

Cost results

The total annual costs of screening ICU patients at the MVAMC appear in Table 2 and were $126,788 for the standard culture, $135,906 for chromogenic agar, and $192,709 for PCR. The total annual costs of isolating the colonized cases who are identified by the intervention appear in Table 3 and were $56,908. The expected cost of the intervention per patient is the sum of these 2 annual amounts divided by the 8,266 patients discharged from the MVAMC in fiscal year 2005. Thus, the expected costs of the intervention per admitted hospital patient were $22.22 for standard culture, $23.33 for chromogenic agar, and $30.20 for PCR.

Table 4 presents the cost savings per admission achieved with this intervention. For the base case, the results suggest that each patient admitted is expected to cost $18,051 without the intervention but $17,567 with the intervention that uses the standard culture test. This is because, although the screening of ICU patients (and isolation of colonized patients) cost an additional $22.22 per admission, for every admission about 0.0321 MRSA infections were avoided with the intervention, resulting in a net savings of $484 per admission. For the chromogenic agar and PCR tests, the savings were similar at $483 and $476 per admission, respectively. Table 4 confirms that the cost reductions are based on a 67% reduction in MRSA infections, from 0.0480 to 0.0159 per admission, attributable to the intervention.

Sensitivity analysis

Table 4 also presents the sensitivity analyses. First, the base case used an additional cost of $55.75 per day for isolating an MRSA-infected patient. This would represent double counting if the VA DSS had already included these costs in their estimates. Omitting these
costs did not change the level of savings appreciably. Second, in the base case, it was assumed that 5.15% of admissions were colonized with MRSA. Reducing or increasing that level by 50% also did not change the cost-saving conclusion. Third, in the base case, the intervention was assumed to result in a 67% reduction in hospital MRSA infections. If that level were reduced to 33%, the model still shows that the intervention is cost saving but by less than half as much as the base case. Indeed, if the intervention generated only a 6% decrease in the number of MRSA infections, it would have generated sufficient savings to exactly cover the cost of the screening program; or, if the 67% effectiveness level were reinstated, the screening intervention would have to cost $506 or more per admission in order not to be cost saving. The overwhelming strength of these results using a deterministic approach obviates the need for further analysis using a stochastic (Monte Carlo) approach.

Chromogenic agar is virtually as cost saving as standard culture. PCR would need to be only 1% more effective to be as cost saving as the culture test, given its additional costs.

DISCUSSION

The present study found that, when the cost of the intervention is netted against the cost reduction from reduced MRSA infection treatment costs, screening of ICU patients produces a net cost savings to the hospital. This is true for all 3 alternative nasal screening tests: standard culture, chromogenic agar, and PCR. It should be kept in mind that there is a dearth of data on the precise outcome measures of nasal screening. Additional studies on the effectiveness of screening in decreasing infections would be useful. We used estimates from the Huang et al study because it represented the best existing American study of an intervention like ours.15 Our study suggested that screening would be cost saving even if the intervention were only half as effective as was found in the Huang et al study. Indeed, given our model and parameters, the hospital-wide level of effectiveness could decrease by a factor of almost 10 and still be cost saving.
Studies of MRSA screening in other countries have found evidence of cost savings or cost-effectiveness, but the specific studies differ widely in their methods, interventions, and approaches. Moreover, the health care systems of the countries in which these studies are set differ dramatically from the system in the United States and have different cost levels and different prices. For these reasons, the applicability of these findings to the United States is questionable.

A recent US study by Lee et al investigated the cost-effectiveness of screening with a “single culture of an anterior nares specimen” and isolation, but applied to all hospital admissions, instead of just the more vulnerable ICU admissions. Using a similar Markov simulation approach but assuming only 5.1 additional hospital-days for a MRSA infection instead of the 33.1 days we found in our study, the authors estimated that this intervention cost approximately $6,000 per quality adjusted life-year saved. In the present study, the central question was to estimate the cost per admission of the intervention for ICU patients only when the feedback reduction in costs from fewer transmitted MRSA infections was taken into account. Because the intervention was found to be cost saving because of its effect on reducing the MRSA infections in the hospital, screening ICU patients also would have been cost saving per quality adjusted life-year gained. Thus, although screening both ICU patients and all patients is cost-effective, screening ICU patients appears to pay for itself.

Although the present study uses the experience of the VA, it does represent American experience. The VA may be atypical for a number of reasons. First, the VA engages in aggressive price negotiations that would interject a conservative bias into the results. That is, the cost savings generated by the screening intervention may have been even greater if the resources used had been evaluated at non-VA unit prices. Second, the VA serves a population with a high proportion of underlying health conditions, which would likely increase the costs of treating an infection during a hospital stay and therefore increase the cost savings associated with an intervention that avoided these infections. The sensitivity analysis, however, suggested that none of these characteristics are likely to change the conclusion that the intervention is cost saving. Finally, because the study focused on the net costs of the intervention, a number of other benefits—the increased quality of life of persons who remain uninfected and the deaths avoided—are not included in this study. If these benefits were measured and included in a full-fledged cost-benefit study, they would no doubt reinforce the conclusion that screening ICU patients upon admission is cost saving.

The debate continues among hospitals and rolls over into public forums as we as a nation struggle to control the infections that are associated with provision of health care, including MRSA infections in hospitals. This study presents evidence of the cost savings from implementing a program that targets the ICU population but that has an effect that is hospital wide. Although we find that this program pays for itself through the MRSA infections prevented, it is important that hospitals also consider how this type of program fits into their overall institutional, infection-prevention programs and realize that this intervention is only one of many alternative interventions that are designed to prevent health care-associated infections. This study focuses on the cost of this one intervention compared to without the intervention and does not further examine the cost-effectiveness of this program relative to other infection-prevention programs. Consideration of other programs is important because MRSA represents only one of many pathogens causing infections in hospitals. An approach to infection prevention that decreases central line infections or ventilator-associated pneumonia would also decrease infections because of MRSA as well as other pathogens causing those infections. We owe it to the patients to continue to assess and improve our preventive strategies.

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