Development of a Surveillance System for Methicillin-Resistant *Staphylococcus aureus* in German Hospitals •

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ORIGINAL ARTICLE

Development of a Surveillance System for Methicillin-Resistant *Staphylococcus aureus* in German Hospitals

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OBJECTIVE. To determine the appropriate method to calculate the rate of methicillin-resistant *Staphylococcus aureus* (MRSA) infection and colonization (hereafter, MRSA rates) for interhospital comparisons, such that the large number of patients who are already MRSA positive on admission is taken into account.

DESIGN. A prospective, multicenter, hospital-based surveillance of MRSA-positive case patients from January through December 2004.

SETTING. Data from 31 hospitals participating in the German national nosocomial infections surveillance system (KISS) were recorded during routine surveillance by the infection control team at each hospital.

RESULTS. Data for 4,215 MRSA-positive case patients were evaluated. From this data, the following values were calculated. The median incidence density was 0.71 MRSA-positive case patients per 1,000 patient-days, and the median nosocomial incidence density was 0.27 patients with nosocomial MRSA infection or colonization per 1,000 patient-days (95% CI, 0.18-0.34). The median average daily MRSA burden was 1.13 MRSA patient-days per 100 patient-days (95% CI, 0.86-1.51), with the average daily MRSA burden defined as the total number of MRSA patient-days divided by the total number of patient-days times 100. The median MRSA-days–associated nosocomial MRSA infection and colonization rate, which describes the MRSA infection risk for other patients in hospitals housing large numbers of MRSA-positive patients and/or many patients who were MRSA positive on admission, was 23.1 cases of nosocomial MRSA infection and colonization per 1,000 MRSA patient-days (95% CI, 17.4-28.6). The values were also calculated for various MRSA screening levels.

CONCLUSIONS. The MRSA-days–associated nosocomial MRSA rate allows investigators to assess the extent of MRSA colonization and infection at each hospital, taking into account cases that have been imported from other hospitals, as well as from the community. This information provides an appropriate incentive for hospitals to introduce further infection control measures.

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The problems of multidrug-resistant pathogens are well-known worldwide.[1-3] Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most important of these pathogens. Numerous studies have reported the burden of MRSA in hospitals: life-threatening and adverse effects for patients, on the one hand, and cost-intensive measures for hospitals, on the other hand.[4-9]

Tiemersma et al.[10] have shown significant increases in MRSA as a proportion of total isolates in European countries between 1999 and 2002, primarily in Belgium, Germany, Ireland, The Netherlands, and the United Kingdom. Therefore, it is absolutely necessary that further efforts be applied to control this problem.

For healthcare facilities, surveillance is an important and approved method to assess the incidence of infection due to multidrug-resistant bacteria and to improve infection control measures, if necessary. Although the numbers of MRSA-positive patients in hospitals have been recorded, up to this point no surveillance method allowing calculation of the rate of MRSA infection and colonization (hereafter, MRSA rate) has gained acceptance as a valid method for interhospital comparisons.

Surely, one reason for this is that, until now, no method of calculating MRSA rates has taken sufficient account of the large number of patients who are already MRSA positive on admission to allow a fair comparison. Therefore, a method should be developed that takes this into account. For this reason, we invited the hospitals of the German nosocomial infections surveillance system (KISS) to provide data for MRSA surveillance, too. The purpose of this study was to use the data provided by the new component of the German national infection surveillance system—MRSA-KISS—and to develop more appropriate measures of MRSA prevalence as an incentive for hospitals to introduce further infection control measures.[11]

From the Institute of Medical Microbiology and Hospital Epidemiology, Medical School Hannover (I.F.C., P.G.), the Institute of Hygiene and Environmental Medicine, Charité-University Medicine, Free University and Humboldt University Berlin (D.S., H.R.), and the German National Reference Center for Surveillance of Nosocomial Infections (I.F.C., D.S., H.R., P.G.), Germany.

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TABLE 1. Measures Used to Determine the Prevalence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Colonization and Infection in the 31 Study Hospitals

Measure	Value
Total no. of MRSA-positive case patients	4,215
Total no. of patient-days	5,930,946
Total no. of MRSA patient-days	80,287
Mean no. of MRSA patient-days per MRSA-positive case patient	19.05
Median incidence density, MRSA-positive case patients per 1,000 patient-days	0.71
Median nosocomial incidence density, MRSA case patients per 1,000 patient-days (95% CI)	0.27 (0.18-0.34)
Median average daily MRSA burden, no. of MRSA patient-days per 100 patient-days (95% CI)	1.13 (0.86-1.51)
Median MRSA-days–associated nosocomial MRSA rate, no. of nosocomial MRSA case patients per 1,000 MRSA patient-days (95% CI)	23.1 (17.4-28.6)

NOTE. CI, confidence interval; nosocomial MRSA case patient, patient with nosocomial MRSA infection or colonization.

METHODS

Surveillance Protocol

A surveillance protocol was developed and sent to the hospitals. According to the protocol, the hospitals were asked to include data on all MRSA-positive patients, indicating whether the patients were infected or colonized and whether the patients were MRSA-positive on admission or had acquired MRSA nosocomially. In addition, the number of patient-days, MRSA patient-days, patients, and nares cultures performed were to be recorded for the entire hospital.

The following definitions were used in this protocol. MRSA-positive case patients included all hospitalized patients from whom MRSA was isolated from clinical samples or from screening cultures during their stay as well as hospitalized patients with known clinical evidence of MRSA infection or colonization. Every hospital stay for an MRSA-positive case patient was recorded as a separate case of MRSA infection or colonization, no matter how many times the patient was known to have been admitted previously. Patients whose clinical diagnostic specimens or screening culture samples yielded 1 or more isolates of MRSA were classified as having MRSA colonization. Patients who had clinical signs and symptoms of infection and who had provided a sample identified as MRSA positive from a corresponding culture were classified as having MRSA infection. In case of doubt, the decision about whether the patient actually had an MRSA infection was made by the treating physician.

MRSA infection or colonization was considered nosocomial if the positive clinical specimen or screening culture sample was obtained more than 48 hours after the patient's admission to the hospital and no previous culture result positive for MRSA was available. All remaining cases of MRSA infection or colonization were identified at admission and defined as imported. A case was defined as eradicated if MRSA could not be detected in a series of 3 control samples from a patient's previously MRSA-positive sites (eg, samples from the nares and throat obtained on 3 consecutive days) and no appropriate antimicrobial therapy was given during this testing period.[12] The number of MRSA patient-days was calculated as the number of patient-days with MRSA infection or colonization, extending from the diagnosis or detection of MRSA infection or colonization until either patient discharge or termination of isolation measures because MRSA infection or colonization was judged to have been eradicated. To assess the extent of the screening regime in each hospital, the total number of nares cultures performed was recorded (1 culture per patient; multiple cultures of samples from the same patient were excluded).

Data Recording

The surveillance period lasted from January 1 to December 31, 2004. The infection control teams in each hospital prospectively surveyed every MRSA-positive case patient and collected data according to the protocol. Data on the number of patient-days and the number of patients were derived from the hospitals' administration systems. After the end of 2004, the data were sent to the surveillance center.

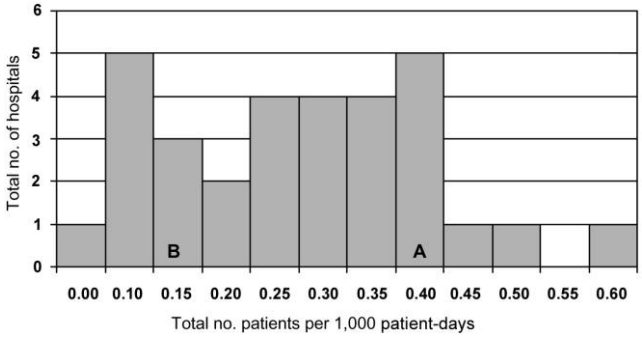

FIGURE 1. Distribution of the incidence density of patients with nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection or colonization for 31 study hospitals. Example hospitals A and B discussed in the text are labeled.

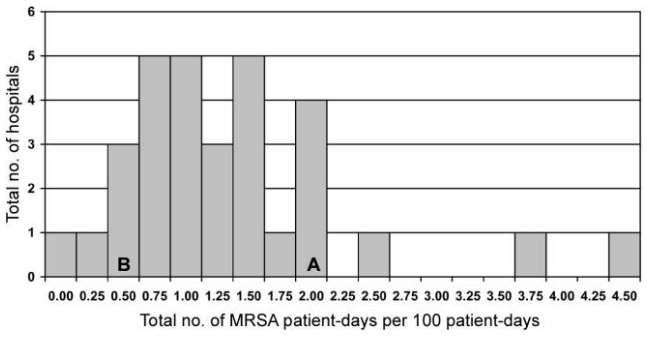

FIGURE 2. Distribution of average daily methicillin-resistant *Staphylococcus aureus* (MRSA) burden for 31 study hospitals. Example hospitals A and B discussed in the text are labeled.

Data Analysis

To calculate MRSA rates, denominator data included the total number of patient-days and the total number of MRSA patient-days per year for each hospital. The overall incidence rate of MRSA infection or colonization was calculated by dividing the total number of MRSA-positive case patients at a hospital during the year by the total number of patient-days at that hospital times 1,000. The incidence rate of nosocomial MRSA infection or colonization was calculated the same way but using the total number of patients with nosocomial MRSA infection or colonization (hereafter, nosocomial MRSA case patients).

Analogous to the established surveillance method in intensive care units (ICUs), we calculated the MRSA rates as follows.[13] The average daily MRSA burden was calculated to assess the influence of the total number of MRSA-positive patients on the ward[14]; this value was determined by dividing the total number of MRSA patient-days by the total number of patient-days times 100. To measure the strength of association between the average daily MRSA burden and the number of nosocomial MRSA case patients per 1,000 patient-days, we calculated the Spearman rank correlation coefficient. The MRSA-days–associated nosocomial MRSA rate was calculated to assess the MRSA infection risk for other patients in a hospital housing large numbers of MRSA-positive patients and/or many patients who were MRSA-positive on admission. This rate was determined by dividing the total number of nosocomial MRSA case patients by the total number of MRSA patient-days times 1,000.

To stratify the data according to screening policies in each hospital, the number of nares cultures performed per 1,000 patient-days was calculated and MRSA rates were calculated according to various screening categories.

RESULTS

Thirty-one hospitals were able to send all data according to the protocol. The participating hospitals are spread all over Germany and vary in size. Among the study hospitals, there were 5 hospitals with fewer than 300 beds, 13 hospitals with 300-600 beds, and 13 hospitals with more than 600 beds.

Data were analyzed from 4,215 MRSA-positive case patients who accounted for 80,287 MRSA patient-days (part of a larger population of 660,042 patients who accounted for 5,930,946 patient-days) (Table 1). Of the total number of MRSA-positive case patients, 2,786 (66.1%) were colonized with MRSA, and 1,429 (33.9%) had MRSA infection. Of these cases of infection and colonization, 2,616 (62.1%) were imported and 1,599 (37.9%) were nosocomial. However, the incidence of nosocomial MRSA infection and colonization was largely heterogeneous among the hospitals. Figure 1 shows the distribution of the incidence density of nosocomial MRSA case patients and Figure 2 shows the average daily MRSA burden for all participating hospitals.

There was a strong positive correlation between the incidence density of nosocomial MRSA case patients in a hospital and that hospital's average daily MRSA burden (correlation coefficient $r = 0.81$; $P < .0001$) (Figure 3). Therefore, we attempted to control for the influence of the average daily MRSA burden by using MRSA patient-days as the denominator. This new rate was called the MRSA-days–associated nosocomial MRSA rate. The median value for this rate was 23.1 cases per 1,000 MRSA patient-days (95% CI, 17.4-28.6).

Figure 4 shows the distribution of the MRSA-days–associated nosocomial MRSA rates of the individual hospitals, and Figure 5 gives an overview of the distribution of the MRSA-days–associated nosocomial MRSA rates according to the average daily MRSA burden of the individual hospitals.

A comparison of the Figures 1, 2, and 4 illustrates the effect of risk adjustment more fully by allowing the comparison of various values related to the prevalence of MRSA in hospitals

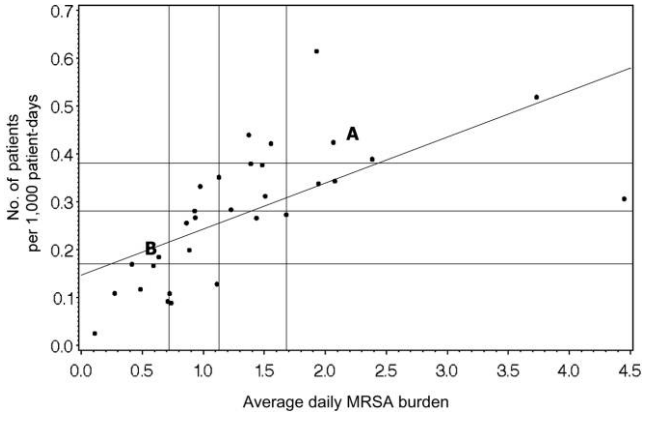

FIGURE 3. Incidence density of patients with nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection or colonization for 31 study hospitals. Median values, with 25th and 75th percentiles, are indicated with vertical and horizontal lines. Example hospitals A and B discussed in the text are labeled. The average daily MRSA burden was calculated by dividing the total number of MRSA patient-days by the total number of patient-days times 100. *Diagonal line,* trend line.

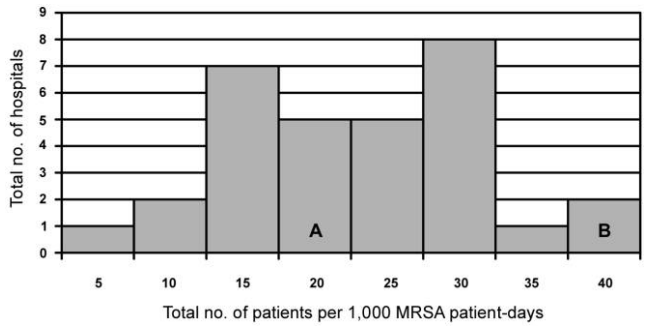

FIGURE 4. Distribution of methicillin-resistant *Staphylococcus aureus* (MRSA)-days–associated nosocomial MRSA rates for 31 study hospitals. Example hospitals A and B discussed in the text are labeled. For details about the MRSA-days–associated nosocomial MRSA rate, see Data Analysis, in Methods.

A and B. The incidence density of nosocomial MRSA case patients in hospital A, a value that uses the number of patient-days as the denominator, was twice as high as the median for the other hospitals. However, hospital A had a very high average daily MRSA burden, probably because of a large number of imported cases of MRSA infection and colonization. When the incidence of MRSA infection and colonization is being assessed, use of MRSA patient-days as the denominator helps to take this high average daily MRSA burden into account. The MRSA-days–associated nosocomial MRSA rate at hospital A was slightly lower than the median. For hospital B, on the other hand, the MRSA-days–associated nosocomial MRSA rate was very high and the average daily MRSA burden was very low. This may indicate a problem in the management of MRSA-positive patients, and this problem would not be recognized if investigators were using only the incidence of MRSA-positive case patients to compare the hospitals.

However, a hospital can increase the recognized daily number of MRSA-positive case patients by collecting many MRSA screening samples. Therefore, the number of screening samples collected should also be considered, for instance, by stratification. In Table 2, the nares cultures are accurately stratified according to median values for different measures and MRSA rates are presented according to these different MRSA screening categories.

DISCUSSION

Established MRSA surveillance systems (eg, the European Antimicrobial Resistance Surveillance System) only provide information on the proportional occurrence of MRSA infection and colonization. They do not allow any assessment of the actual burden of disease. For the first time, we are representing data collected from a large number of patients treated in German hospitals. Furthermore, surveillance of nosocomial infections with appropriate feedback to healthcare personnel has been proven to be effective in reducing nosocomial infection rates.[15] Ongoing surveillance of antimicrobial resistance in hospitals can also be an appropriate intervention to decrease resistance rates. However, a method of analysis must be applied that simultaneously motivates better compliance with the guidelines for controlling the spread of resistance.

Various methods were used in the past to assess the incidence of MRSA infection and colonization. Most of these methods are inappropriate because of their substantial disadvantages. Table 3 shows these different methods with their advantages and disadvantages. The first 3 methods listed there are most common, but the use of different denominators in these methods complicates national and international comparison.[2,16-25] The method described in the present study (ie, calculation of the MRSA-days–associated nosocomial MRSA rate) is very similar to the method described by Jarvis et al.[13] for taking account of device utilization in ICUs when assessing the nosocomial infection rates in ICUs. By including MRSA patient-days in the calculations, our surveillance method takes into consideration the average daily MRSA burden in every hospital. Every MRSA patient-day entails the risk of concomitantly hospitalized patients acquiring nosocomial MRSA colonization or infection. For this reason, MRSA patient-days can be regarded as analogous to device utilization–days in the National Nosocomial Infections Surveillance (NNIS) System for ICUs.

With our method, hospitals with high or low rates of nosocomial MRSA infection or colonization and those with high or low average daily MRSA burdens can be easily identified, and prevention control measures can be reviewed. The MRSA-days–associated nosocomial MRSA rate and the average daily MRSA burden should be examined together, and this information should help infection control practitioners to identify and address possible problems. For instance, a hospital with a low average daily MRSA burden and a high MRSA-days–associated nosocomial MRSA rate has a

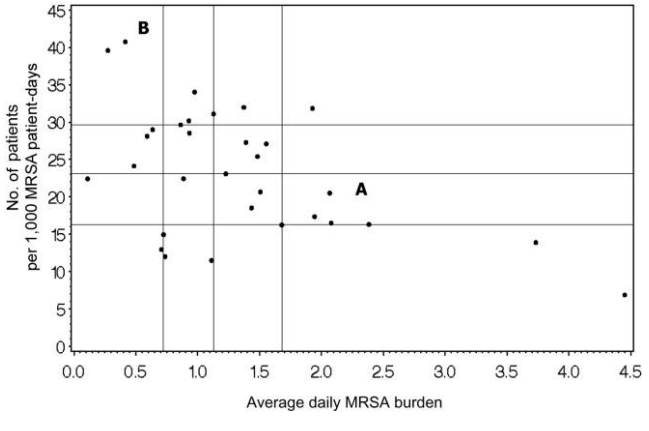

FIGURE 5. MRSA-days–associated nosocomial MRSA rate for 31 study hospitals. Median values, with 25th and 75th percentiles, are indicated with vertical and horizontal lines. Example hospitals A and B discussed in the text are labeled. For details about the MRSA-days–associated nosocomial MRSA rate, see Data Analysis in Methods.

TABLE 2. Measures Used to Determine the Prevalence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) in 31 Study Hospitals With Different Distinctive Screening Policies, Stratified by the Extent of Nares Culture Surveillance

Measure	Value, by median no. of nares cultures per 1,000 patient-days			
	⩽2 (n = 14)	>2 and ⩽4 (n = 7)	>4 and ⩽10 (n = 7)	>10 (n = 3)
Total no. of MRSA-positive case patients	1,165	537	1,468	1,045
Total no. of patient-days	2,621,324	747,542	1,693,495	868,585
Total no. of MRSA patient-days	20,043	8,370	24,511	26,363
Mean no. of MRSA patient-days per MRSA-positive case patient	17.20	17.45	16.70	25.22
Median incidence density, MRSA-positive case patients per 1,000 patient-days	0.45	0.63	0.67	1.073
Median nosocomial incidence density, MRSA case patients per 1,000 patient-days	0.19	0.32	0.29	0.29
Median daily MRSA burden, no. of MRSA patient-days per 100 patient-days	0.76	1.25	1.45	3.04
Median MRSA-days–associated nosocomial MRSA rate, no. of nosocomial MRSA case patients per 1,000 MRSA patient-days	25.3	25.2	20.2	13.8

NOTE. Nosocomial MRSA case patient, patient with nosocomial MRSA infection or colonization.

problem managing MRSA-positive patients. This hospital should intensify its infection prevention measures. On the other hand, a hospital with a high average daily MRSA burden (reflecting a large number of imported MRSA cases) and a low MRSA-days–associated nosocomial MRSA rate shows good management of MRSA-positive patients (see hospitals A and B in Figures 1 -5).

The average daily MRSA burden is a concept that is reasonably easy to understand and is descriptive in nature. Other authors have used the term "colonization pressure" to describe this concept.[14,26-28]

An important prerequisite for MRSA surveillance is correct identification of the pathogen responsible for the infections in each hospital. Validation testing was performed with an MRSA ST80 clone that was used for external quality control by the European Antibiotic Resistance Surveillance System (EARSS) in 2004. Of the laboratories of the MRSA-KISS hospitals, including those of the hospitals participating in this study, 98.2% performed a correct identification of this clone in 2005. It can be assumed that the testing methods of different laboratories do not have any influence on the validity of our data regarding MRSA rates.

However, for the method described it is not only essential to identify MRSA-positive patients accurately—MRSA patient-days must be identified accurately as well. Recording the required data can be done with little effort. If MRSA is detected in a culture of a sample from a hospitalized patient, the patient should be isolated in a private room in accordance with the German national MRSA guidelines. Additionally, other patients with whom the MRSA-positive patient has had contact should be examined with the help of screening cultures. Under these recommendations, every hospital has an interest in terminating the isolation measures as quickly as possible. Hence, they regularly collect control samples from MRSA-positive patients to determine whether those patients' MRSA infection or colonization has been eradicated according to the national MRSA guidelines. In the meantime, many hospitals have established alert systems for recognizing MRSA-positive patients when they are readmitted.[29] With the help of the hospital information systems, every admission and discharge date for each patient can be recorded for surveillance investigators. Given these measures, the recording of MRSA patient-days is easy in most hospitals. The MRSA-KISS module was introduced 3 years ago. Meanwhile, 101 participating hospitals have submitted their data for 2005, which proves that the module (ie, the surveillance method) is very well accepted. This supports the conclusion that the method is accessible as well as feasible.

The correct assessment of screening policies at hospital admission (eg, screening only in ICU vs screening extended to patients with risk factors for MRSA carriage hospitalized in non-ICU wards) in each hospital is important but difficult to evaluate. Screening for MRSA carriage was mainly performed using nares cultures. These cultures were not used for other diagnostic clinical investigations. Therefore, recording the number of nares cultures (documented per patient) seems to be a good method for identifying the actual screening policies of hospitals.

The results of the methods for assessing the incidence of MRSA infection and colonization show great differences when stratified according to various screening categories and display this dependency as a result of different screening levels. Hence, it is very important to record the number of nares cultures for the correct assessment of screening policies in each hospital.

CONCLUSIONS

This newly developed method for assessing MRSA rates allows investigators to assess the extent of MRSA infection and colonization in each individual hospital in a way that correctly accounts for cases imported from other hospitals and from

TABLE 3. Comparison of Different Methods for Assessing the Incidence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection and Colonization and Their Usage in the Literature

Method and example studies	Advantage(s)	Disadvantage(s)
MRSA isolates as a percentage of all *S. aureus* isolates[2,16,22,24]	Uses minimal laboratory resources	Yields no information concerning the expression of the average daily MRSA burden for the hospital (in terms of infection, colonization, and/or imported or nosocomial cases); inaccurate description (great dependence of the number of microbiological examinations, kind of specimen)
Incidence of MRSA-positive case patients per 1,000 patient-days[18,20,22-25]	Yields data on new MRSA-positive case patients	Data on patient-days for the denominator have to be obtained (but are easy to get) from hospital administration; provides little motivation to act because problems can be attributed to the imported MRSA case patients
Incidence of nosocomial MRSA case patients per 1,000 patient-days[17,19,22]	Yields data on incidence of MRSA-positive case patients	Each case has to be evaluated to determine whether it is nosocomial; defining nosocomial cases in samples obtained >48 hours after admission is not quite appropriate for all case patients if there is no general screening on admission; the average daily MRSA burden has to be considered because large numbers of imported cases increase risk
MRSA-days–associated nosocomial MRSA rate	Consideration of the average daily MRSA burden	Recording of the number of MRSA patient-days is required; without extensive screening, there can be no complete survey of the average daily MRSA burden
MRSA-days–associated nosocomial MRSA rate with stratification according to the extent of screening	Provides a complete survey of the average daily MRSA burden at each hospital, if all patients are screened	Performance of nares cultures (documented for each patient) is required

NOTE. Nosocomial MRSA case patient, patient with nosocomial MRSA infection or colonization. For details about the MRSA-days–associated nosocomial MRSA rate, see Data Analysis, in Methods.

the community. This information provides an incentive for hospitals to introduce further infection control measures, such as screening methods.

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