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Improving the Assessment of Vancomycin-Resistant Enterococci by Routine Screening


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(See the editorial commentary by Talbot, on pages 314–7, and the article by Huang et al., on pages 330–8.)

Background. As infection with vancomycin-resistant enterococci (VRE) increases in hospitals, knowledge about VRE reservoirs and improved accuracy of epidemiologic measures are needed. Many assessments underestimate incidence by including prevalent carriers in at-risk populations. Routine surveillance cultures can substantially improve prevalence and incidence estimates, and assessing the range of improvement across diverse units is important.

Methods. We performed a retrospective cohort study using accurate at-risk populations to evaluate the range of benefit of admission and weekly surveillance cultures in detecting unrecognized VRE in 14 patient-care units.

Results. We assessed 165 unit-months. The admission prevalence of VRE was 2.2%–27.2%, with admission surveillance providing 2.2–17-fold increased detection. Medical units were significantly more likely to admit VRE carriers than were surgical units. Monthly incidence was 0.8%–9.7%, with weekly surveillance providing 3.3–15.4-fold increased detection. The common practice of reporting incidence using the total number of patients, rather than patients at risk, underestimated incidence by one-third. Overall, routine surveillance prevented the misclassification of 43.0% (unit range, 0%–85.7%) of “incident” carriers on the basis of clinical cultures alone and increased VRE precaution days by 2.4-fold (unit range, 2.0–2.6-fold).

Conclusions. Routine surveillance markedly increases the detection of VRE, despite variability across patient-care units. Correct denominators prevent the substantial underestimation of incidence.

Vancomycin-resistant enterococci (VRE) are the third most common cause of health-care–associated infections, despite the fact that they are generally considered to be indolent pathogens [1]. Among immunosuppressed or critically ill patients, enterococcal infections are often severe [2]. Recent data from the Centers for Disease Control and Prevention (CDC) [3, 4] showed that 29% of enterococcal infections in intensive care unit (ICU) settings are caused by vancomycin-resistant isolates [3, 4]. This increase in vancomycin resistance in enterococci is much steeper than that in oxacillin resistance seen in Staphylococcus aureus, and it appears to be unabated by current in-
fection control measures. In addition, clinical VRE isolates resistant to newer agents, such as linezolid [5, 6], have been reported.

In contrast to European nations, where vancomycin-related antibiotics were used in animal feed and led to VRE infection in humans because of meat consumption, the emergence and spread of VRE in the United States is almost exclusively attributable to health-care–associated transmission [7]. Because VRE have spread rapidly and extensively within and between health-care facilities [8–10], more aggressive measures, such as routine screening cultures to identify and isolate VRE carriers, have been used to prevent further transmission. Because VRE has become endemic in increasing numbers of US health-care facilities, the accurate assessment of VRE during nonoutbreak settings is needed to inform interventions targeting transmission.

Single-center studies instituting screening cultures for VRE in nonoutbreak settings have found a high prevalence of asymptomatic carriage at the time of admission [11–13]. However, multicenter assessments of diverse units are still needed. In addition, a better appreciation of intra- or interunit month-to-month variation in monthly prevalence and incidence measures would be valuable, given that accounting for these expected fluctuations is essential for the accurate assessment of infection control interventions. In addition, incorrect denominators for VRE incidence, such as total patient days or total admissions that include prevalent carriers in the denominator, are widely used [14–19]. For incidence measures, patients already known to carry VRE should not be included in the denominator, because they are no longer eligible to acquire VRE.

We conducted a multicenter retrospective study to describe the range of benefit of routine screening for VRE in diverse patient-care units in US academic medical centers. We sought to evaluate variations in the size of the VRE reservoir among these centers, the impact of surveillance on improving estimates of incidence and prevalence across different units, the correlation between measures based on clinical cultures alone (compared with those where surveillance is added), the magnitude of error associated with including VRE carriers in incidence denominators, and whether certain units are more likely to detect high numbers of VRE carriers with surveillance efforts. We further evaluated the impact of surveillance on lead time until the institution of contact precautions and the duration of VRE positivity.

METHODS

Description of Participating Patient-Care Units

Participating hospitals were from 4 US academic medical centers that routinely obtained rectal surveillance cultures for VRE in 14 adult patient-care units as part of infection control initiatives. All centers participated in the CDC Epicenters Program and included Brigham and Women’s Hospital (Boston, MA), Johns Hopkins Medical Institutions (Baltimore, MD), Northwestern Memorial Hospital (Chicago, IL), and University of Iowa Hospitals and Clinics (Iowa City, IA). The study was approved by the institutional review boards of the CDC and all participating centers.

Each center provided retrospective data for ∼1 year between 1 January 2002 and 31 August 2004. Outside of active surveillance cultures, there was no change in infection control practices and no other special infection control programs to reduce VRE during the study period. All admission and discharge dates of patients admitted to the 14 units were collected, along with dates and sites of all positive VRE clinical cultures and all surveillance cultures (positive and negative results). In addition, the date of the most recent institutional VRE-positive culture before the unit study period was provided for VRE-positive patients. VRE cultures were processed by each institution’s microbiology laboratory on the basis of growth in the presence of 6 µg/mL vancomycin, in accordance with Clinical and Laboratory Standards Institute guidelines. Finally, each center completed a detailed questionnaire on hospital and unit characteristics and VRE surveillance policies. One center (University of Iowa Hospitals and Clinics) performed both culture and polymerase chain reaction testing on all rectal specimens. Positive results from either test were accepted for analysis.

Data Analysis

Measuring prevalence and incidence adjusting for at-risk populations. Univariate descriptions were provided for unit characteristics. Percentage compliance with surveillance was calculated on the basis of rectal cultures sent within 1 calendar day of the admission or weekly surveillance day. Monthly prevalence (the number of patients in the unit ever known to be VRE-positive before or during that month/total patients in the unit that month), monthly prevalence density (prevalence numerator/total monthly person-days), monthly admission prevalence (the number of patients in the unit ever known to be VRE-positive before or within 2 calendar days of admission/total monthly admissions), monthly incidence (the number of patients newly detected to be VRE-positive/number of patients at risk for new VRE detection), and monthly incidence density (incidence numerator/number of person-days at risk for new VRE detection) were calculated monthly for each unit, along with unit-specific means and SDs. Incident carriers were defined as patients with newly detected VRE (colonization or infection) occurring at least 2 days after admission through 2 days after unit discharge in persons without prior institutional cultures positive for VRE. Unit-specific summary measures were calculated as the mean of monthly measures for a single patient-care unit.

Because studies of infection control interventions are often based on changes in monthly epidemiologic measures across
Table 1. Characteristics of participating patient-care units.

<table>
<thead>
<tr>
<th>Unit type</th>
<th>Beds, no.</th>
<th>LOS, median, days</th>
<th>Monthly admissions, mean no.</th>
<th>Study period, months</th>
<th>Admissions, total no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompromised units</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone-marrow transplant</td>
<td>14</td>
<td>15</td>
<td>16.8</td>
<td>12</td>
<td>202</td>
</tr>
<tr>
<td>Hematology-oncology</td>
<td>20</td>
<td>5</td>
<td>71.0</td>
<td>12</td>
<td>852</td>
</tr>
<tr>
<td>Transplant</td>
<td>16</td>
<td>5</td>
<td>76.3</td>
<td>12</td>
<td>915</td>
</tr>
<tr>
<td>Hematology–bone-marrow transplant</td>
<td>30</td>
<td>6</td>
<td>65.0</td>
<td>9</td>
<td>585</td>
</tr>
<tr>
<td>Medical units</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical ICU</td>
<td>10</td>
<td>3</td>
<td>59.3</td>
<td>12</td>
<td>712</td>
</tr>
<tr>
<td>Medical ICU</td>
<td>16</td>
<td>3</td>
<td>86.6</td>
<td>12</td>
<td>1039</td>
</tr>
<tr>
<td>Cardiac ICU</td>
<td>10</td>
<td>2</td>
<td>73.6</td>
<td>12</td>
<td>883</td>
</tr>
<tr>
<td>Surgical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical ICU</td>
<td>10</td>
<td>2</td>
<td>72.0</td>
<td>12</td>
<td>864</td>
</tr>
<tr>
<td>Burn ICU</td>
<td>16</td>
<td>6</td>
<td>45.9</td>
<td>12</td>
<td>551</td>
</tr>
<tr>
<td>Burn/trauma ICU</td>
<td>10</td>
<td>2</td>
<td>58.8</td>
<td>12</td>
<td>706</td>
</tr>
<tr>
<td>Cardiac surgery ICU</td>
<td>10</td>
<td>2</td>
<td>56.4</td>
<td>12</td>
<td>677</td>
</tr>
<tr>
<td>Cardiac surgery ICU</td>
<td>10</td>
<td>2</td>
<td>66.3</td>
<td>12</td>
<td>796</td>
</tr>
<tr>
<td>Neurosurgery ICU</td>
<td>10</td>
<td>2</td>
<td>75.9</td>
<td>12</td>
<td>911</td>
</tr>
<tr>
<td>Thoracic surgery ICU</td>
<td>10</td>
<td>2.5</td>
<td>39.0</td>
<td>12</td>
<td>468</td>
</tr>
</tbody>
</table>

**NOTE.** ICU, intensive care unit; LOS, length of stay.

Time, we evaluated the intra- and interunit stability of these measures. Intraunit month-to-month variability was described by SDs of a unit’s monthly measures. Interunit differences in epidemiologic measures were evaluated using 1-way analysis of variance (ANOVA) tests that accounted for intraunit variability. Summary statistics across all units were reported as the mean and range of unit-specific summary measures. All epidemiologic measures were based on both clinical and surveillance cultures, unless otherwise stated.

**Evaluating the impact of surveillance on estimates of prevalence and incidence.** We compared monthly incidence and prevalence measures with and without the inclusion of surveillance culture data using paired t tests and tests of correlation. Patients with a positive VRE culture (clinical or surveillance) before or within 2 calendar days of admission to the unit were excluded from comparisons of incidence measures with and without surveillance data. We also determined the proportion of imported VRE that would have been attributed to hospital-associated acquisition when only clinical cultures were considered. Finally, we assessed the linear change in monthly incidence over the course of the study period using mixed models accounting for clustering within units.

**Assessing types of patient-care units associated with elevated incidence and prevalence.** We used multivariate analyses to evaluate predictors of monthly admission prevalence and monthly incidence. In particular, we evaluated whether the type of unit (medical or surgical, immunocompromised or nonimmunocompromised) or monthly compliance with admission screening was associated with monthly admission prevalence and whether the type of unit, monthly admission rate, monthly admission prevalence, or the number of unit beds was associated with the monthly incidence of VRE. For ease of interpretation, we used a priori binary outcomes of monthly VRE admission prevalence >10% and monthly incidence of VRE >5%. Dichotomous variables associated with the outcome at \( \alpha < 0.2 \) in bivariate analyses (\( \chi^2 \) tests) were entered into generalized linear mixed models (PROC GLIMMIX in SAS version 9.1; SAS Institute), along with any continuous variables. Final models were determined using stepwise backward selection at \( \alpha = 0.05 \), and all models accounted for clustering within patient-care units.

**Assessing the impact of using incidence denominators adjusted for at-risk populations.** We assessed the effect of counting prevalent carriers in incidence density denominators. We compared incidence density, which excluded patient-days of patients already harboring VRE from the denominator (1000 patient-days at risk for new VRE detection) with incidence density denominators of 1000 total patient-days. Comparisons were made graphically and by performing 2-tailed paired t tests of monthly measures.

**Assessing the impact of surveillance on infection control precautions.** Lead time was defined as the number of unit precaution days attributable to VRE surveillance cultures. This was determined by selecting persons who were newly detected to have VRE by a surveillance culture and summing the number of unit-days within the study period that occurred between the surveillance culture date and any subsequent VRE-positive clinical culture. In the absence of a subsequent VRE-positive clinical
culture, all patient-care days within the study period were counted as added precaution days.

**Assessing the persistence of VRE carriage.** We estimated the persistence of VRE carriage by evaluating the proportion of patients previously known to harbor VRE who still harbored VRE at the time of admission. We plotted the likelihood of positivity according to the time since their last positive institutional culture.

**RESULTS**

**Description of participating patient-care units.** We evaluated a total of 165 unit-months from 7 surgical ICUs, 3 medical ICUs and 4 non-ICUs caring for immunocompromised patients (table 1). Overall, 8266 patients were admitted 11,236 times to the 14 units over the course of the study period, accounting for 60,884 patient-days. Of all patients, 39.2% were at least 65 years old, and 56.2% were male.

VRE screening policies are described in table 2. Overall compliance was 82% with admission rectal cultures and 83% with weekly cultures. All centers had policies for contact precautions and private rooms for VRE carriers. Two units preemptively placed patients on contact precautions while admission VRE screen results were pending.

**Impact of routine surveillance.** Average monthly prevalence and incidence estimates derived from both clinical and surveillance cultures are shown in table 3. VRE surveillance cultures significantly increased the detection of VRE carriers for all epidemiologic measures. The detection of imported VRE increased 3.3-fold (unit range, 2.2–17.0-fold) with screening admission cultures, and estimated VRE incidence increased 6.1-fold (unit range, 3.3–15.4-fold) with weekly surveillance cultures. Overall, prevalence increased 3.1-fold (unit range, 2.2–13.5-fold). Fold increases differed slightly from the calculations shown in table 3, which reports rounded estimates. Among all ICUs, VRE incidence decreased monthly by 0.22% (P = .004). Similarly, VRE incidence density decreased monthly by 0.34 cases/1000 patient-days at risk (P = .02).

**Monthly variation in VRE prevalence and incidence.** There was substantial variability within and between the units in their monthly incidence and prevalence of VRE carriage (table 3). The addition of surveillance culture data revealed a greater variation in all measures than was seen when only clinical cultures were used. SDs (table 3) were ≥30% of mean monthly VRE prevalence in one-half the units and ≥50% of mean monthly VRE incidence in all units. Because the Poisson distribution is often used to model predictors of VRE incidence, we assessed the distribution criterion that the variance (the square of the SD) approximates the mean of incidence estimates. In the 14 units, the variance was 11–69-fold greater than the mean monthly incidence. Nevertheless, even when accounting for the large intraunit variation, the interunit variation resulted in significant differences among units for incidence (F = 5.6; P<.0001, ANOVA), incidence density (F = 3.5; P<.0001), prevalence (F = 29.7; P<.0001), prevalence density

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**Table 2. Vancomycin-resistant enterococci (VRE) surveillance policies by patient-care unit.**

<table>
<thead>
<tr>
<th>Unit type</th>
<th>Admission screen</th>
<th>Weekly screen</th>
<th>Screen if VRE positive</th>
<th>Screen if on precautions</th>
<th>Precautions pending screen results</th>
<th>Screening compliance, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical unit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>91</td>
</tr>
<tr>
<td>Medical ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>84</td>
</tr>
<tr>
<td>Cardiac ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>93</td>
</tr>
<tr>
<td>Bone-marrow transplant</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>58</td>
</tr>
<tr>
<td>Hematology-oncology</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>72</td>
</tr>
<tr>
<td>Transplant</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>59</td>
</tr>
<tr>
<td>Hematology–bone-marrow transplant</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>89</td>
</tr>
<tr>
<td>Surgical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>85</td>
</tr>
<tr>
<td>Burn ICU</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>89</td>
</tr>
<tr>
<td>Burn/Trauma ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>69</td>
</tr>
<tr>
<td>Cardiac surgery ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>88</td>
</tr>
<tr>
<td>Cardiac surgery ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>94</td>
</tr>
<tr>
<td>Neurosurgery ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>80</td>
</tr>
<tr>
<td>Thoracic surgery ICU</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>91</td>
</tr>
</tbody>
</table>

**NOTE.** ICU, intensive care unit; N, no; Y, yes.

a Assesses whether rectal cultures were sent for patients already known to harbor VRE or already placed on contact precautions because of the presence of other antibiotic-resistant organisms.

b Percentage of ICU admissions with surveillance rectal cultures sent at the time of admission.
Table 3. Average monthly incidence and prevalence measures across all patient-care units.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Excluding surveillance</th>
<th>Including surveillance</th>
<th>Added detection with surveillance, % (unit range)</th>
<th>(P^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate, % (unit range)</td>
<td>Unit SDa</td>
<td>Estimate, % (unit range)</td>
<td>Unit SDa</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission prevalence</td>
<td>3.9 (0.1–9.2)</td>
<td>0.5–6.4</td>
<td>13.1 (2.2–27.2)</td>
<td>1.5–11.1</td>
</tr>
<tr>
<td>Prevalence</td>
<td>6.2 (0.3–13.6)</td>
<td>0.9–7.5</td>
<td>19.2 (4.5–39.2)</td>
<td>2.8–13.7</td>
</tr>
<tr>
<td>Prevalence densityc</td>
<td>1.0 (0.1–2.4)</td>
<td>0.2–0.6</td>
<td>3.3 (1.2–6.3)</td>
<td>0.5–1.4</td>
</tr>
<tr>
<td>Incidence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence</td>
<td>0.7 (0–1.9)</td>
<td>0–2.8</td>
<td>4.0 (0.8–9.7)</td>
<td>1.3–8.2</td>
</tr>
<tr>
<td>Incidence densityd</td>
<td>1.2 (0–3.7)</td>
<td>0–3.6</td>
<td>7.9 (2.5–13.2)</td>
<td>2.3–11.9</td>
</tr>
</tbody>
</table>

\(a\) Calculated across all monthly estimates from a given unit. The range across all units is provided.

\(b\) Paired 2-tailed \(t\) test comparing monthly unit estimates, which include and exclude surveillance culture data.

\(c\) Per 1000 patient-days.

\(d\) Per 1000 patient-days at risk for newly detected vancomycin-resistant enterococci.

\((F = 32.0; \ P < .0001)\), and admission prevalence \((F = 27.6; \ P < .0001)\).

**Impact of surveillance on reducing the misclassification of incident cases.** Admission surveillance cultures prevented the misclassification of imported carriers as incident ones. Admission rectal cultures identified an additional 826 patients carrying VRE at the time of admission. Of these 826 patients, 43 (5.2%; unit range, 0%–18.4%) would have had their VRE erroneously attributed to hospital acquisition if classification was based on clinical cultures alone. From another vantage point, these 43 prevalent carriers represented a 43.0% (unit range, 0%–85.7%) misclassification among the 100 “incident” carriers if classification was based on clinical cultures alone.

**Correlation of prevalence and incidence measures with and without surveillance data.** Although monthly prevalence and incidence measures based on clinical cultures significantly underestimated values obtained by both clinical and surveillance cultures, these measures were often correlated. Correlation coefficients for monthly measures with and without surveillance cultures were as follows: admission prevalence, 0.73; prevalence, 0.76; prevalence density, 0.66; incidence, 0.55; and incidence density, 0.46.

**Types of patient-care units associated with elevated incidence and prevalence.** In bivariate analyses of dichotomous variables, medical (vs. surgical) units \((P < .0001)\) and those for immunocompromised patients \((P < .0001)\) were associated with a monthly admission prevalence >10%, and surgical (vs. medical) units \((P = .0002)\) and those for immunocompromised patients \((P = .03)\) were associated with a monthly VRE incidence >5%. In multivariate models controlling for clustering by patient-care unit, we found that medical units had a 34.1-fold increased odds (95% confidence interval \([CI\), 2.0–574.8\]) of having a monthly VRE admission prevalence >10%, compared with surgical units. Compliance with monthly admission cultures was not associated with monthly admission prevalence across the range of compliance seen in this study. The only predictor of monthly VRE incidence >5% was an elevated VRE admission prevalence (odds ratio, 1.1 for each percentage increase \([95\% CI, 1.0–1.1]\)). Monthly admission rates, unit size, and type of unit were not found to be predictive of elevated monthly VRE incidence.

**Impact of using incidence denominators adjusted for at-risk populations.** In evaluating the mean monthly VRE in-

![Figure 1](image-url)  
**Figure 1.** Graph depicting the divergence of vancomycin-resistant enterococci (VRE) incidence density estimates when comparing measures using total patient-days with patient-days at risk denominators. Denominators using patient-days at risk limit patient-days to those belonging to patients in whom VRE has yet to be found (those eligible to become a carrier). The upper line represents the hypothetical case in which the 2 measures give identical results. The lower line is a regression line based on monthly data from the 14 units \((P < .0001)\). The lines increasingly diverge as VRE incidence density increases.
cidence density, use of total patient-day denominators underestimated incidence density by an average of 29.6% (5.6 vs. 7.9 cases/1000 patient-days at risk; \( P < .0001 \)). Similar to paired \( t \) test results, linear regression analysis found that incidence density based on total patient-day denominators underestimated incidence density by 32.9%, compared with using patient-days at risk. Figure 1 shows linear regression results, with progressive divergence between incidence density using days at risk versus total patient-days as denominators as incidence density increases. Similar discrepancies were observed for measures of mean monthly incidence when excluding versus including prevalent carriers from the denominator (4.0% of patients at risk vs. 3.3% of total patients; \( P < .0001 \)).

Impact of surveillance on infection control precautions. Of the 60,884 unit patient-days studied, 12,605 (20.7%) were spent in contact isolation because of VRE. In the absence of surveillance cultures, 5313 contact isolation days would have been implemented because of VRE-positive clinical cultures obtained before and during the study period. Therefore, admission and weekly surveillance cultures resulted in 7292 additional days (655 persons) of unit contact precautions, an increase of 137.2%. Among the 85 patients initially identified by surveillance cultures who had subsequent VRE-positive clinical cultures, the average lead time was 11.0 unit patient-days (range, 7.2–16.4 unit patient-days). Only 13.0% of patients identified through surveillance cultures had a subsequent clinical culture positive for VRE during their unit stay. These patients accounted for only one-eighth (12.4%) of the lead time gained by surveillance cultures. When surveillance data were ignored, there was an average of 32.2 precaution days per unit month. Surveillance cultures added an average of 44.2 (range, 29.3–83.7) additional precaution days per unit month. Additional precautions days that occurred after transfer to other unit areas or hospital readmission to a nonparticipating unit were not included.

Persistence of VRE carriage. Duration of carriage was evaluated among patients with an institutional VRE-positive culture before admission to the unit (\( n = 671 \)). Figure 2 depicts the likelihood of a positive unit admission surveillance culture for VRE, based on the time since the last known positive VRE culture. The majority of patients (76.4%; 301/394) admitted within 60 days of their last positive VRE culture tested positive for VRE. Among patients admitted >300 days since their last positive VRE culture, 15.9% (20/126) were still positive for VRE on screening surveillance cultures.

DISCUSSION

We have shown that clinical cultures detect only a small fraction of the VRE reservoir in high-risk patient-care units of tertiary-care centers and that these cultures can be misleading in the absence of routine admission and weekly rectal cultures. In evaluating a range of ICUs and units caring for immunocompromised patients, we found that clinical cultures detected only 30% of the VRE reservoir and 18% of incident carriers, compared with carriers identified by both clinical and surveillance
cultures. Routine surveillance resulted in the implementation of contact precautions an average of 11 days earlier than they would have been on the basis of clinical cultures alone. Surveillance cultures more than doubled the number of precaution days in study units, which suggests that infection control precautions based solely on clinical cultures may be insufficient to prevent transmission. Furthermore, approximately one-half of the “incident” carriers identified by clinical cultures alone were, in fact, imported. This substantial misclassification may lead to labor-intensive and costly evaluations of pseudo-outbreaks.

Compared with the results of a similar study of methicillin-resistant Staphylococcus aureus (MRSA) presented in this issue of the Journal of Infectious Diseases [20], the reservoir of VRE identified by clinical cultures alone was one-half that of MRSA, with seemingly negligible (<1%) transmission. However, when routine admission and weekly cultures were obtained with high compliance, the mean monthly incidence and prevalence were nearly identical for these 2 organisms. That VRE is more likely to produce asymptomatic carriage and transmission further emphasizes the need for routine surveillance, particularly in populations where the excess morbidity [21–24], mortality [25, 26], and cost [21] attributable to this pathogen are well known. Notably, high compliance active surveillance with resultant contact precautions significantly reduced the health-care-associated transmission of VRE over time.

Compared with surgical units, medical units admitted a significantly higher percentage of patients who harbored VRE; these results were similar to those for MRSA. In fact, medical units were 30 times more likely than surgical units to have >10% of patients harboring VRE at the time of admission. Not surprisingly, elevated admission prevalence was significantly associated with transmission, which suggests that strategies for detection should be coupled with efforts to maximize compliance with isolation precautions. We did not detect an increased risk of VRE transmission in surgical units, in contrast to our findings for MRSA.

All monthly measures of incidence and prevalence varied substantially, even during the nonoutbreak, or endemic, conditions of the present study. SDs were often >30% of monthly prevalence and >50% of monthly incidence. Such fluctuations are not unexpected and can be explained by the transmissibility of VRE in small units that admit varying numbers of patients importing VRE. Nevertheless, the magnitude of these variations makes it difficult to assess VRE trends accurately. Meaningful conclusions about a potential VRE outbreak or the success of interventions aimed at controlling the spread of VRE require monitoring of prevalence and incidence over a long period of time and statistical expertise to adjust for large amplitude variation and clustering of carriers within hospital units.

Importantly, comprehensive knowledge about the VRE reservoir enabled us to calculate appropriate incidence denominators that included only persons eligible to acquire colonization (i.e., those not already colonized). In the present study, 19% of all patients admitted to study units already harbored VRE. The commonly used denominator of total patients or total patient-days underestimated VRE incidence by one-third, which could result in erroneous conclusions for hospital infection control programs or research studies.

The present study had several limitations. First, the complete identification of imported VRE carriers was limited by a lack of knowledge about the VRE cultures from prior institutions, imperfect compliance with VRE surveillance cultures, and imperfect sensitivity of rectal cultures [27, 28]. Nevertheless, overall compliance with rectal cultures was >80%, and rectal surveillance greatly improved prevalence estimates and reduced the misclassification of incident VRE carriers. These results are likely to reflect the expected improvement based on usual knowledge known to most institutions. In fact, the value of surveillance cultures may be underestimated, given that they were performed only at the time of admission and weekly thereafter, although it is not known whether more-frequent sampling would be cost-effective. In addition, we did not collect or perform any genetic typing of VRE strains to support whether isolates were imported or were acquired from circulating strains in a study unit. Finally, the large benefit of routine surveillance cultures in improving VRE incidence and prevalence may reflect the fact that our study population was limited to high-risk patients in ICUs and units for immunocompromised patients in academic medical centers.

In summary, routine admission and weekly rectal cultures for VRE obtained from patients in ICUs and units for immunocompromised patients markedly improved the detection and accurate assessment of VRE carriage. By detecting large numbers of asymptomatic carriers, surveillance cultures substantially improved estimates of the VRE reservoir and advanced the initiation of contact precautions, resulting in consistently reduced monthly transmission over the course of a 12-month period. Admission surveillance prevented the misclassification of imported cases as incident ones, and weekly surveillance increased the identification of hospital-associated cases. Furthermore, added detection through surveillance enabled the calculation of appropriate denominators for incidence—a necessity for accurate assessments of intervention effects. Routine surveillance also unmasked a large variation in monthly values. Understanding and accounting for this variation is critical to the accurate assessment of containment strategies. Routine surveillance for VRE provides numerous advantages for hospitals that are attempting to contain this pathogen. Costs of routine surveillance and contact precautions must be weighed against the risks of transmission and subsequent in-
fectious sequelae after carriage in individual patient-care units and medical institutions.

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References