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ORIGINAL ARTICLE

Surveillance for Vancomycin-Resistant Enterococci: Type, Rates, Costs, and Implications

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OBJECTIVE. To evaluate 2 active surveillance strategies for detection of enteric vancomycin-resistant enterococci (VRE) in an intensive care unit (ICU).

DESIGN. Thirty-month prospective observational study.

SETTING. ICU at a university-affiliated referral center.

PATIENTS. All patients with an ICU stay of 24 hours or more were eligible for the study.

INTERVENTION. Clinical active surveillance (CAS), involving culture of a rectal swab specimen for detection of VRE, was performed on admission, weekly while the patient was in the ICU, and at discharge. Laboratory-based active surveillance (LAS), involving culture of a stool specimen for detection of VRE, was performed on stool samples submitted for *Clostridium difficile* toxin detection.

RESULTS. Enteric colonization with VRE was detected in 309 (17%) of 1,872 patients. The CAS method initially detected 280 (91%) of the 309 patients colonized with VRE, compared with 25 patients (8%) detected by LAS; colonization in 4 patients (1%) was initially detected by analysis of other clinical specimens. Most patients with colonization (76%) would have gone undetected by LAS alone, whereas use of the CAS method exclusively would have missed only 3 patients (1%) who were colonized. CAS cost $1,913 per month, or $57,395 for the 30-month study period. Cost savings of CAS from preventing cases of VRE colonization and bacteremia were estimated to range from $56,258 to $303,334 per month.

CONCLUSIONS. A patient-based CAS strategy for detection of enteric colonization with VRE was superior to LAS. In this high-risk setting, CAS appeared to be the most efficient and cost-effective surveillance method. The modest costs of CAS were offset by the averted costs associated with the prevention of VRE colonization and bacteremia.

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Infections caused by multidrug-resistant organisms are associated with increased morbidity and mortality,[1-11] prolonged hospital stays, and excess costs.[9,12-14] Adverse effects of infection with multidrug-resistant organisms lead not only to higher healthcare costs but also to higher societal costs in terms of decreased productivity and quality of life for patients and their families.[15] Because enteric colonization with vancomycin-resistant enterococci (VRE) is an important risk factor for VRE infection, prevention of colonization through identification of others who are colonized, followed by implementation of measures to control the spread of VRE after their identification, seem imperative.[9,16-19]

Existing guidelines recommend that healthcare facilities develop and implement a plan to prevent and control the spread of VRE.[9,20] However, definitive recommendations regarding methods of surveillance have not been determined. Although the costs of surveillance for enteric VRE have only begun to be described,[5,21,22] the attributable costs to the healthcare system associated with VRE bacteremia alone may justify surveillance and control programs.[5,7,8,13,23,24] Identification of VRE-colonized patients and implementation of contact isolation have been shown to be cost-effective and may reduce VRE-related morbidity and mortality in populations at high-risk for VRE acquisition.[5,6,23,25-28]

A variety of active and passive surveillance methods have been used for detection of enteric VRE.[5,15,22,24,29-34] A few studies have compared active surveillance methods but were unable to conclude which method was superior.[31,32,34] The objectives of this study were to compare the performance of 2 active surveillance strategies for detection of enteric VRE and to describe the associated costs and implications of these strategies.

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TABLE 1. Demographic and Clinical Characteristics of 1,872 Intensive Care Unit Patients by Vancomycin-Resistant Enterococci (VRE) Colonization Status

Variable	Colonization status of patients		
	VRE prevalent[a] (n = 182)	VRE incident (n = 127)	VRE negative (n = 1,563)
Categorical			
White race	109 (60.0)	73 (57.5)	867 (55.5)
Male sex	74 (40.7)	59 (46.5)	761 (48.7)
Bacteremia, by causal pathogen			
MRSA	14 (7.7)	14 (11.0)	126 (8.1)
Pseudomonas aeruginosa	3 (1.6)	4 (3.1)	26 (1.7)
Clostridium difficile	8 (4.4)	15 (11.8)	70 (4.5)
Mortality	79 (43.4)	47 (37.0)	396 (25.3)
Continuous			
Age, y	62.3 ± 17.6	62.5 ± 15.9	58.9 ± 17.9
Duration of MICU stay, d[b]	7.5 ± 8.7	16.9 ± 18.5	5.5 ± 7.6
Duration of hospitalization, d[b]	23.2 ± 31.2	33.7 ± 27.8	14.7 ± 19.8
APACHE II score[c]	24.4 ± 7.5	23.9 ± 6.3	21.1 ± 8.2

NOTE. Data are no. (%) of patients or mean value ± SD. See Methods for definitions of colonization status. APACHE, Acute Physiology and Chronic Health Evaluation; MICU, medical intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] Four patients with VRE initially detected in culture of a nonsurveillance clinical isolate (ie, culture of sterile body fluid, performed as a component of routine clinical care) were categorized as having VRE identified through CAS.

[b] Defined as the time of admission through the time of discharge.

[c] From Knaus et al.[41]

METHODS

Setting and Patients

Eligible participants were all patients admitted from July 1, 1997, through December 31, 1999, to the 19-bed medical intensive care unit (ICU) at Barnes-Jewish Hospital (BJH), a 1,287-bed tertiary care facility in St. Louis, Missouri. Data on patients residing in the ICU for 24 hours or more were included; data from multiple admissions were combined if subsequent admissions occurred 30 days or less after the initial admission. Data from only the first admission were included in the analysis if subsequent admissions occurred more than 30 days after the initial admission. Patients were excluded if microbiological data were incomplete or the patients' medical records could not be reviewed. The research review committees at Saint Louis University (St. Louis) and Washington University Medical Center (St. Louis) approved this study.

Study Design and Definitions

Clinical active surveillance (CAS) for VRE was defined as prospective screening using rectal swab specimens. The CAS method was performed by clinical staff who procured specimens for detection of enteric VRE from all ICU patients at ICU admission, ICU discharge, and every 7 days if the ICU stay was 7 days or longer. Laboratory-based active surveillance (LAS) was defined as screening of clinical stool specimens for VRE that were originally collected for *Clostridium difficile* screening in accordance with hospital-wide policy established on October 1, 1996.[35] Patients with enteric VRE initially detected in culture of a nonsurveillance clinical isolate (ie, culture of sterile body fluid, performed as a component of routine clinical care) were categorized as having VRE identified through clinical specimens. Stool samples submitted by 12 patients for *C. difficile* testing at the time of admission were classified as CAS specimens. Patients with a stool specimen positive for *C. difficile* toxin by cytotoxicity assay (Bartels) were categorized as having *C. difficile*–associated diarrhea or colitis.

Patients with VRE detected by surveillance or clinical culture before or on admission to the ICU were classified as having a prevalent case of VRE colonization. Patients with enteric VRE acquired during ICU stay were characterized as having an incident case of VRE colonization. Patients with negative culture results from the time of admission through the time of discharge were classified as being VRE negative. The incidence density was calculated by dividing the number of patients with an incident case of VRE colonization by the number of inpatient-days in the ICU from either admission until discharge (for patients without VRE colonization) or from admission until the date of initial VRE detection (for patients with VRE colonization).

Data Collection

During the study period, differential infection control strategies were used for the scheduled rotation of antimicrobial therapy and gown use, as described elsewhere.[6,29] Cost data

TABLE 2. Costs Attributable to Clinical Active Surveillance (CAS) and Laboratory-Based Active Surveillance (LAS) Programs for Detection of Vancomycin-Resistant Enterococci

Cost variable	Unit cost	CAS costs over 30 mo (3,224 tests)[a]	LAS costs over 30 mo (562 tests)[b]
Labor costs			
Nursing time (6 min per specimen)	2.70	8,705	1,517
Laboratory technologists' time			
9.6 min per negative culture result	2.78	7,542	1,187
15.9 min per positive culture result	4.97	2,540	671
Supply costs			
Fixed negative surveillance test results	5.00	13,565	2,135
Fixed positive specimens	13.00	6,643	1,755
Processing costs			
Initial laboratory cost per culture	1.20	3,869	674
Extra laboratory cost per positive culture result	1.97	1,007	266
Stool collection cups	0.07	NA	40
Swabs	0.28	903	NA
Hand hygiene[c]	0.10	322	56
Gloves	0.07	226	39
Total cost per negative test result	12.13	…	…
Total cost per positive test result	24.29	…	…
Total cost of surveillance program	…	45,321	8,341
Total cost of surveillance program in 2003 US dollars	…	57,395	10,563
Monthly cost of surveillance program in 2003 US dollars	…	1,913	352
Cost of surveillance program per patient in 2003 US dollars[d]	…	30.66	5.64

NOTE. Costs are in 1997 US dollars, unless otherwise indicated. Costs in columns indicating totals have been rounded. See Methods for definitions of CAS and LAS. NA, not applicable.

[a] A total of 2,713 negative test results and 551 positive test results.

[b] A total of 427 negative test results and 135 positive test results.

[c] Comprised the cost of alcohol foam and of soap and water with paper towels.

[d] Of 1,872 patients who met the study criteria, 759 were excluded because they had a stay of less than 24 hours (748 patients) or had incomplete data (11 patients).

were harvested through the hospital laboratory information system and the hospital informatics system.[36]

Cost Data

Program costs were obtained from 2 clinical databases and 1 cost administrative database. Costs, rather than charges, were used because they represent the cost to the institution undertaking a surveillance program. The cost data were harvested in 1997 and 1998 US dollars, reflecting the value of the US dollar during the study period. The total costs of the surveillance program were converted to 2003 US dollars using the medical care component of the Consumer Price Index[37] and are reported in the text in 2003 US dollars.

Labor, supply, and processing costs were reported for cultures with positive results and cultures with negative results. Labor costs included estimated staff expenditures. The cost of the technologists' time to receive, process, finalize, and report the specimen was converted to dollars, using the mean salary of a technologist at BJH in 1997, and added into the final cost of the test. The amount of time spent for specimen procurement by healthcare personnel was estimated to be 6 minutes per specimen. The mean hourly wage, excluding fringe benefits, calculated for the staff collecting the specimens was $27.00 in 1998 (study midpoint). The combined costs for the performance of hand hygiene before and after each patient encounter was estimated to be $0.10. The supply costs included the fixed costs per test that did not vary with the volume of testing.

Estimated Cost Savings

Detection of VRE should lead to fewer cases of colonization and bacteremia and, therefore, lower costs of hospitalization. To estimate the cost savings associated with averted cases, transmission of VRE was varied between a predictive rate of 0.5 and 2 times the rate.[38] The proportion of VRE-colonized patients who became bacteremic in this study was 7.8%, slightly lower than the rates of up to 13.4% reported in 3 distinct oncology populations.[16,18,39] These differential rates were used to estimate the number of at-risk bacteremic patients. The excess cost of each case of VRE colonization was estimated using the values $3,065[25] and $9,970[40] (both in 2003 dollars) obtained from the literature. The excess healthcare cost of each case of VRE bacteremia was estimated as $17,143[8] and $36,380.[13]

TABLE 3. Clinical and Epidemiological Characteristics of Vancomycin-Resistant Enterococci (VRE) Colonization Among 1,872 Patients Over a 30-Month Surveillance Period

Variable	CAS and LAS	CAS	LAS	Surveillance at admission only
Cultures performed, no.				
Overall	3,786	2,684	575	1,734
Negative results	3,140	2,173	427	1,552
Positive results	646	511	148	182
Patients with VRE detected, no.				
Overall	309	306	75	182
Detected at admission	182	182	38	182
Detected during hospital stay	127	124	37	
Patients with no VRE detected, no.				
During hospital stay	0	3	234	127
At admission	0	0	144	0
Patients with bacteremia but no VRE detected, no.	0	0	9	10
Transmission dynamic of undetected VRE[a]				
0.50	−190.5	−186	160.5	Referent
2.00	−381	−372	321	Referent
Likelihood of colonized patient becoming bacteremic[a]				
0%	0	0	0	Referent
7.8%	−20	−19.5	17	Referent
13%	−33	−32.22	28	Referent

NOTE. See Methods for definitions of clinical active surveillance (CAS) and laboratory-based active surveillance (LAS).

[a] Number of patients colonized as a result of contact with a colonized patient. The value 7.8% is from Puzniak et al.[29]; the value 13% is from Leber et al.,[22] Mayhall et al.,[23] and Hachem et al.[24]

Statistical Analysis

SPSS statistical software, version 11.0 (SPSS), was used for all analyses. Descriptive analyses were performed, including analyses of frequencies, mean values, and median values.

RESULTS

Patients

Of 2,631 admitted patients, 1,872 (71%) met the study criteria; 748 patients (28%) with an ICU stay of less than 24 hours and 11 patients with incomplete or missing medical records were excluded. Demographic and clinical characteristics by VRE colonization status are reported in Table 1. The mean length of ICU stay (±SD) for the study cohort was 6.7 ± 9.3 days, although a prolonged mean duration of ICU stay (±SD) of 16.9 ± 18.5 days was observed for patients with incident enteric colonization with VRE. Few patients (less than 10%) had coexisting methicillin-resistant *Staphylococcus aureus* or *Pseudomonas aeruginosa* bacteremia. Overall crude mortality was 28% and was higher among patients with enteric VRE.

Surveillance

A total of 3,224 rectal swab specimens and 562 stool specimens were tested for VRE (Table 2). Patients who acquired VRE had approximately 1 more active screen culture performed (mean [±SD] of 0.97 ± 1.87 CAS cultures and 2.8 ± 1.5 CAS swab samples per patient), compared with patients colonized with enteric VRE on admission (mean [±SD] of 0.38 ± 0.91 CAS cultures and 1.8 ± 0.85 CAS swab specimens per patient) and patients who remained negative for VRE through discharge (mean [±SD] of 0.24 ± 0.74 CAS cultures and 1.6 ± 1.0 CAS swab specimens per patient). In total, 309 patients (17%) were VRE colonized; 182 (59%) had VRE detected on admission (prevalent cases), and 127 patients (41%) acquired VRE (incident cases) (Table 3).

Among VRE-colonized patients, VRE was initially detected in 280 (91%) by CAS, in 25 (8%) by LAS, and in 4 (1%) by analysis of clinical specimens. The incidence density of VRE was 12.7 cases of acquired VRE per 1,000 ICU patient-days. VRE in most (100 [79%]) of the 127 patients who acquired VRE was detected by CAS. The LAS method alone would have missed 234 cases of enteric colonization with VRE (76%), 144 (62%) of which were prevalent cases and 90 (38%) of which were incident cases. Three cases (1%) would not have been identified without LAS. A consistent pattern of VRE surveillance occurred (Figure). Approximately 20 LAS screening cultures per month were completed, compared with 116 CAS screening cultures per month. Screening on ad-

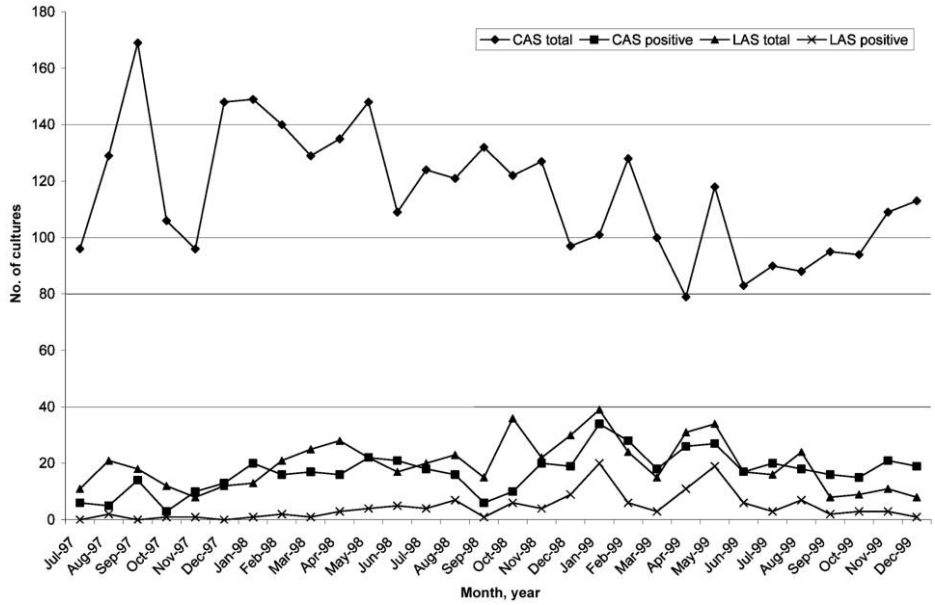

FIGURE. Comparison of clinical active surveillance (CAS) with laboratory-based active surveillance (LAS), by number of cultures performed and number of cultures with positive results, at Barnes-Jewish Hospital during a 30-month period. See Methods for definitions of CAS and LAS.

mission detected 59% of the patients in our sample who were colonized with VRE, and an additional 36 patients (12%) with colonization would have been detected by LAS at some point during the ICU stay. The percentage of patients from whom specimens were procured for CAS at admission was 93% (1,734 of 1,872 patients), whereas the percentage at discharge was 53% (984 patients). Forty-one percent of patients (766) had only one surveillance test performed, and among

TABLE 4. Characteristics of Surveillance Performed for 5 Patients for Whom Results of Cultures for Detection of Vancomycin-Resistant Enterococci Varied During Hospitalization

Patient, surveillance characteristic	Swab sample tested								
	Admission	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7	No. 8	Discharge
Patient 1									
Type	LAS	LAS	CAS	LAS	LAS	LAS	LAS	LAS	CAS
Test result	Positive	Negative	Negative	Negative	Negative	Positive	Positive	Positive	Positive
Date[a]	12/19	12/22	12/23	12/24	12/25	1/2	1/3	1/4	1/16
Patient 2									
Type	CAS	CAS	CAS	LAS	CAS	CAS	…	…	CAS
Result	Negative	Negative	Positive	Negative	Positive	Negative	…	…	Negative
Date[a]	1/11	1/15	2/2	2/6	2/7	2/25	…	…	2/26
Patient 3									
Type	CAS	LAS	CAS	LAS	LAS	CAS	CAS	…	CAS
Result	Negative	Negative	Negative	Negative	Positive	Positive	Negative	…	Negative
Date[a]	10/21	10/2	11/8	11/20	11/21	11/23	11/24	…	11/29
Patient 4									
Type	CAS	CAS	LAS	CAS	CAS	CAS	LAS	…	CAS
Result	Negative	Negative	Positive	Negative	Positive	Positive	Negative	…	Negative
Date[a]	2/3	2/10	2/15	2/17	2/23	2/25	3/3	…	3/4
Patient 5									
Type	CAS	CAS	CAS	CAS	CAS	…	…	…	CAS
Result	Negative	Negative	Negative	Positive	Negative	…	…	…	Negative
Date[a]	5/22	6/2	6/10	6/22	6/28	…	…	…	7/2

NOTE. See Methods for definitions of clinical active surveillance (CAS) and laboratory-based active surveillance (LAS).

[a] Date on which swab sample was collected.

TABLE 5. Estimated Cost Savings of Clinical Active Surveillance (CAS), Compared With Laboratory-Based Active Surveillance, During a 30-Month Period, According to Estimated Averted Cases of Vancomycin-Resistant Enterococci (VRE) Colonization and Associated Bacteremia

Variable	Cost savings associated with use of CAS, 2003 US$	
	During 30-mo study period	Per month
Incremental MICU colonization cost savings for levels of transmission (0.5-2) of undetected VRE		
Excess cost of colonization = $3,065[a]		
0.50	1,062,023	35,401
1.00	1,416,030	47,201
1.50	1,770,038	59,001
2.00	2,124,045	70,802
Excess cost of colonization = $9,970[b]		
0.50	3,454,605	115,154
1.00	4,606,140	153,538
1.50	5,757,675	191,923
2.00	6,909,210	230,307
Likelihood of colonized patient becoming bacteremic		
Increased cost of VRE bacteremia = $17,143[c]		
7.8%	625,720	20,857
13%	1,032,351	34,412
Increased cost of VRE bacteremia = $36,380[d]		
7.8%	1,327,870	44,262
13%	2,190,804	73,027

NOTE. We assumed a transmission rate of 1.00 (ie, that each case patient with VRE transmitted VRE to one other person). See Methods for definitions of clinical active surveillance (CAS) and laboratory-based active surveillance (LAS). MICU, medical intensive care unit.

[a] From Montecalvo et al.[40]

[b] From Puzniak et al.[25]

[c] From Carmelli et al.[13]

[d] From Stosor et al.[8]

the patients for whom a discharge surveillance test was not performed, 381 (43%) of 888 stayed in the ICU for less than 72 hours, and 242 (27%) of 888 died while in the ICU.

Atypical Test Results

Among patients who tested positive for enteric VRE, all but 20 (8%) of 237 patients for whom 2 or more tests were performed remained VRE positive throughout their ICU stay. Five patients (0.02%) displayed atypical results of cultures, with oscillations between negative and positive results for enteric colonization with VRE (Table 4). Nine patients who stayed in the ICU for less than 48 hours had an initial culture that was positive for VRE and a discharge culture that was negative for VRE. In addition, 6 patients with varying numbers of VRE-positive test results had a single surveillance test that was negative for enteric VRE at ICU discharge.

Programmatic Costs

The total cost estimated for both the CAS and LAS programs in 2003 dollars was $67,958 for 30 months. The LAS costs were $10,563, whereas the CAS costs were $57,395. These estimates include allocated and direct costs, which may vary among different institutions. Estimated monthly costs for VRE surveillance were $1,913 for CAS and $352 for LAS (Table 2). The cost was $30.66 per patient for CAS and $5.64 per patient for LAS. An additional 337 VRE cultures were performed subsequent to a culture that yielded enteric VRE. A 30-month cost savings of $10,367 would have been realized if VRE surveillance was terminated after a positive test result was documented. The associated costs of VRE surveillance would have been $1,568 per month for CAS ($25.12 per patient) if the cost of these 337 cultures was excluded.

Estimated Cost Savings

The CAS method requires the performance of 4.7 times more cultures than the LAS method (Table 3). The LAS method alone would not have identified 234 cases of VRE colonization, whereas the CAS method identified all but 3 cases of VRE colonization. Use of CAS would prevent 346.5-693 cases of VRE colonization, depending on the transmission dynamic

of VRE, and 36.5-60.22 cases of bacteremia. By applying excess cost estimates for colonization and bacteremia, adjusted to 2003 dollars,[40] and varying the VRE transmission rate, prevention of colonization by use of CAS would have an estimated cost savings ranging from $35,401 to $230,307 per month, relative to the cost associated with the LAS method (Table 5).[5,21,25] Assuming that 1 case patient with VRE transmits VRE to 1 other person and that, of those colonized with VRE, between 8% and 13% become VRE bacteremic, the estimated cost savings attributable to prevented bacteremia ranges from $20,857 to $73,027 per month.[8,13] Taken together, the total estimated cost savings associated with use of CAS ranges from $56,258 to $303,334 per month.

DISCUSSION

These data suggest that strategic CAS was superior to LAS for detecting enteric colonization with VRE in an ICU where VRE is endemic. The excess costs of surveillance were modest relative to the estimated averted costs of associated infections. Colonization in most (91%) of the VRE-colonized participants was initially identified by CAS, a method of surveillance that routinely surveys the population at risk, prospectively identifies acquired cases, and allows for the calculation of colonization pressure.[6,38] In contrast, the *C. difficile* specimen–associated LAS missed most cases of colonization (76%) in patients colonized with VRE.[31,32,34] We propose that the focused screening of submitted *C. difficile* specimens for VRE may be appropriate for institutions or units within institutions with historically low rates of VRE colonization and limited resources.[43] In such algorithms, if LAS determines an increase in the prevalence of VRE colonization, then endemicity may indicate a need for transition to a CAS method.

Overall, the total costs for the CAS program (estimated to be $1,913 monthly) were minimal, compared with the estimated averted excess costs attributable to preventing VRE colonization and bacteremia. The estimated cost savings of CAS attributable to preventing VRE colonization and bacteremia ranged from $56,258 to $303,334 per month. The large variation resulted from different assumptions about the VRE transmission rate, the likelihood of a colonized patient becoming bacteremic, and the increased hospital costs attributable to colonization and bacteremia. Despite the large variation, all cost-saving estimates greatly exceed the monthly costs of implementing CAS. Of note, the third-party payer and societal costs were likely significant and were not accounted for in the resources estimated herein. The additional benefits of placing patients in isolation to reducing transmission of other transmissible agents, such as extended-spectrum β-lactamase–producing bacteria, were not assessed.[42] Furthermore, because most VRE-colonized patients remained colonized with this pathogen, the incremental cost of the CAS and LAS methods would decrease if subsequent testing did not occur after the initial positive test result was available, for an estimated cost savings of $10,367.

We recognize the study limitation associated with decreased compliance with performing surveillance cultures at ICU discharge (53% of patients), which was low compared with the percentage of patients (93%) who had cultures performed at ICU admission; thus, incidence rates for enteric colonization with VRE were likely to be underestimated. In addition, cost-to-charge ratios were not calculated because of difficulties with estimating reimbursements received and because actual hospital costs are better indicators of economic costs.[44] Finally, placement of a patient in isolation occurred when a patient was culture positive for VRE, not at admission, limiting an evaluation of direct patient-to-patient transmission. Colonization pressure for this subset of patients has previously been used to estimate transmission likelihoods.[6] In summary, we propose that LAS can be used in a prevalence-based approach to enteric VRE surveillance in low-risk, low-incidence settings, whereas in high-risk settings, such as ICUs and other units with high colonization pressure for VRE, CAS surveillance seems most efficient and cost-effective.

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