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The Attributable Costs of Enterococcal Bloodstream Infections in a Non-Surgical Hospital Cohort

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Abstract

Background—Vancomycin-resistant enterococcal (VRE) bloodstream infections (BSI) are associated with increased morbidity and mortality.

Objective—To determine the attributable costs of vancomycin-sensitive (VSE) and VRE BSI and the independent impact of vancomycin-resistance on hospital costs.

Methods—A retrospective cohort study was conducted of 21,154 non-surgical patients admitted to an academic medical center between 2002 and 2003. Using administrative data, attributable hospital costs (inflation adjusted to $2007) and length of stay were estimated with multivariate generalized least squares (GLS) models and propensity score matched-pairs.

Results—The cohort included 182 VSE and 94 VRE BSI cases. After adjustment for demographics, comorbidities, procedures, non-enterococcal BSI, and early mortality, the attributable costs of VSE BSI were $2,250 (95% confidence interval [CI], $1,758–$2,880) in the standard GLS model and $2,023 (95% CI, $1,588–$2,575) in the propensity-score weighted GLS model and the attributable costs of VRE BSI were $4,479 (95% CI, $3,500–$5,732) in the standard GLS model and $4,036 (95% CI, $3,170–$5,140) in the propensity-score weighted GLS model. The median of the difference in costs between matched-pairs was $5,282 ($2,042–$8,043) for VSE BSI and $9,949 (95% CI, $1,579–$24,693) for VRE BSI. The attributable costs of vancomycin-resistance were $1,713 (95% CI, $1,338–$2,192) in the standard GLS model and $1,546 (95% CI, $1,214–$1,968) in the propensity-score weighted GLS model. Attributable length of stay ranged from 1.1–2.2 days for VSE BSI and 2.2–3.5 days for VRE BSI cases.

Conclusions—VSE and VRE BSI were independently associated with hospital costs and length of stay. Vancomycin-resistance was associated with increased costs.

Keywords

Bloodstream infections; Enterococcal; Costs

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INTRODUCTION

Vancomycin-resistant enterococcal (VRE) bloodstream infections (BSI) are associated with increased morbidity, mortality, and costs [1–4]. Rates of vancomycin resistance among enterococcal isolates, which are among the most common pathogens associated with nosocomial BSI [5], have increased substantially during the past decade [6]. The pooled mean rate in 2003 of vancomycin resistance among intensive care unit patients with enterococcal infections was 28.5%, as reported to the Centers for Disease Control and Prevention's National Nosocomial Infections Surveillance System [6]. Although the incidence of VRE pathogens is higher in intensive care unit patients, infections are also common among patients treated in noncritical care units. Since infection control measures to prevent transmission of VRE BSI are effective but resource-intensive [7], accurate estimates of the attributable cost of enterococcal BSI infections are necessary to assess the cost-effectiveness of prevention strategies.

Despite the increasing prevalence of VRE in US hospitals, the financial burden of enterococcal pathogens has not been adequately explored [8]. We are aware of only two published studies that estimate the hospital costs associated with VRE BSI [1, 4]. However, neither study adequately controlled for underlying severity of illness or hospital procedures that may affect the cost of care, which may have resulted in biased cost estimates. In addition, there are limited cost data regarding the independent impact of acquiring a vancomycin-resistance phenotype. Estimation of the independent effects of a resistance trait or phenotype (e.g., vancomycin-resistance) requires a control group of patients infected with a susceptible organism (e.g., vancomycin-sensitive), rather than a control group of uninfected patients [8, 9]. The conclusions drawn from prior studies that compared vancomycin-sensitive and resistant infections were limited by small sample size and/or inadequate adjustment for potential confounding by underlying comorbidities [9, 10]. The purpose of our study was to estimate the attributable costs and length of stay of VSE and VRE BSI in a non-surgical hospital cohort using administrative data and three reproducible analytical methods. We also sought to determine the independent impact of vancomycin-resistance on hospital costs.

METHODS

Study design

Non-surgical patients admitted to Barnes-Jewish Hospital (BJH) from January 2002 through December 2003 for > 48 hours were included in the study. Surgical patients were excluded from the analysis because the distribution of costs was very different for patients with operating room costs compared with other hospitalized patients. Data on demographics, inpatient mortality, microbiology results, and *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis and procedure codes were obtained from the hospital Medical Informatics database. ICD-9-CM diagnosis codes were collected for all admissions within the previous two years. ICD-9-CM procedure codes were collected for the current admission only. Comorbidity and procedure variables were created from ICD-9-CM codes using guidance from the Healthcare Cost and Utilization Project (HCUP) Clinical Classifications Software [11]. The presence of a central venous catheter was defined by ICD-9-CM codes assigned within six months prior to enterococcal BSI infection for cases and six months prior to hospital discharge for uninfected controls, with the assumption that central venous catheters inserted after diagnosis of infection were used for therapeutic purposes and that these costs needed to be captured in the costs of the infection.

Enterococcal BSI cases were identified by positive blood cultures during hospital admission. The first episode of enterococcal BSI was analyzed. In the event of a polymicrobial BSI

with both VSE and VRE organisms, the patient was classified as having a VRE BSI. Patients without any history of BSI served as the comparison group. For non-cases with multiple admissions during the study period, one admission per patient was randomly selected for analysis.

Hospital cost data (from the hospital payer perspective) were obtained from the BJH cost accounting database (Trendstar; McKesson Corp, Alpharetta, Georgia). The departmental cost for each charge code assigned during hospitalization was calculated as the proportion of total departmental charges accounted for by the charge code multiplied by the department's actual cost components. Departmental costs were summed to calculate total hospital costs for each admission and were inflation adjusted to 2007 US dollars according to the medical care component of the Consumer Price Index (accessed at http://www.bls.gov/).

Statistical analyses

Patient characteristics were compared with the Student's t, χ^2 or Fisher's exact test. Crude costs and hospital length of stay were compared with the Mann-Whitney U test. Three methods were used to estimate total hospital costs and hospital length of stay associated with VSE and VRE BSI, controlling for the variation of other factors significantly associated with expenditures: standard regression adjustment, propensity-score weighted regression adjustment, and matched pairs.

Standard GLS Model

A generalized least squares (GLS) regression model was fit with total cost as the dependent variable; total cost was natural log-transformed because of the highly skewed distribution of costs. The multivariate GLS model was developed using backward stepwise regression, including all variables associated with the natural logarithm of cost in the bivariate analysis ($p \leq 0.05$) or biologic plausibility. Variables that applied to < 10 patients were excluded from the analysis. A "feasible GLS estimator" was used to weight the observations to account for heteroskedasticity [12]. Since the GLS model used the natural logarithm of costs as the dependent variable, an intermediate regression was performed to predict costs. Each coefficient obtained in the GLS model represented the mean difference in the natural logarithm of costs between individuals with and without that variable, assuming all other predictors of costs remained constant. The attributable costs were calculated by solving the regression equation separately for each variable of interest (i.e., VSE BSI, VRE BSI, and vancomycin-resistance). Specifically, each coefficient was multiplied by the proportion of patients with that particular covariate and added to the constant, with the exception of non-enterococcal BSI. This exclusion allowed the adjusted costs of the uninfected control group to represent the "average" patient without non-enterococcal BSI. All independent variables were checked for collinearity. Models were checked for functional form misspecification using Ramsey's regression specification error test and for heteroskedasticity using the Breusch-Pagan test [12]. In order to assess the impact of vancomycin-resistance, a second standard GLS model was fit with enterococcal BSI and vancomycin-resistance as the primary independent variables. Attributable hospital length of stay was calculated using this final model with the natural logarithm of length of stay as the dependent variable.

Propensity-score Weighted GLS Model

A GLS regression model adjusted for propensity score inverse weighting was also used to estimate attributable costs [13, 14]. The predicted probabilities for development of enterococcal BSI (i.e., VSE and/or VRE BSI) were obtained from a multivariate logistic regression model with all variables with $p < 0.20$ in bivariate analysis. Each case was weighted by the inverse of the propensity score and each control was weighted by the inverse of 1 minus the propensity score [13, 14]. The final regression model included the primary independent

variables (i.e,, enterococcal BSI and vancomycin-resistance) as well as all covariates that were unbalanced in at least one quintile of the propensity score. A second propensity-score weighted GLS model was also fit with enterococcal BSI and vancomycin-resistance as the primary independent variables. Attributable hospital length of stay was calculated using this final model with the natural logarithm of length of stay as the dependent variable.

Propensity Score Matched-Pairs

Propensity score matched-pairs analyses were used to estimate the attributable costs and attributable length of stay of VSE and VRE BSI. The predicted probabilities for development of VSE and VRE BSI were obtained from separate multivariate logistic regression models with all biologically plausible variables associated with VSE BSI in the bivariate analysis ($p < 0.20$). VSE BSI cases were matched 1:1 to uninfected controls based on their propensity to develop VSE BSI and VRE BSI cases were matched 1:1 to uninfected controls based on their propensity to develop VRE BSI, using the nearest neighbor method within calipers of 0.25 standard deviations [15, 16]. Cases without a suitable control were excluded from the analyses. Matched and unmatched cases were compared using the χ^2 or Fisher's exact test, with Bonferroni correction. Due to highly skewed cost data, attributable costs and attributable length of stay were presented as the median value of the difference in costs and length of stay, respectively, between matched-pairs and compared with the Wilcoxon signed-rank test. Confidence intervals were calculated based on the binomial distribution.

Statistical analyses were performed using SPSS version 15.0 (SPSS Inc, Chicago, IL) and Stata version 9.2 (Stata Corp, College Station, TX). Approval for this study was obtained from the Washington University Human Research Protection Office.

RESULTS

During the 2-year study period, 21,154 non-surgical patients were admitted to BJH for > 48 hours (Table 1). Of 276 (1%) patients identified with an enterococcal BSI, there were 94 (34%) VRE BSI cases and 182 (66%) VSE BSI cases. Enterococcal BSI occurred significantly more often in patients with ICD-9-CM comorbidity codes for congestive heart failure, acute renal failure, *Clostridium difficile* diarrhea, and urinary tract infection and ICD-9-CM procedure codes for bone marrow transplant, mechanical ventilation, hemodialysis, cancer chemotherapy, and placement of a central venous catheter (excluding catheters placed to administer antibiotics for enterococcal BSI). Patients with an enterococcal BSI were more likely to have been in an intensive care unit (VRE BSI, 41 (44%) and VSE BSI, 62 (34%)) vs. no enterococcal BSI, 3,330 (16%); $p < 0.001$ for both) and were more likely to die in the hospital (VRE BSI 30 (32%) and VSE BSI 31 (17%) vs. no enterococcal BSI, 845 (4%); $p < 0.001$ for both).

Crude costs and hospital length of stay are presented in Table 2. Patients with VRE BSI had significantly higher total crude median costs compared to those with VSE BSI ($p < 0.001$) and those without BSI ($p < 0.001$). Median departmental costs were significantly higher for patients with VSE BSI compared to patients without BSI, as well as patients with VRE BSI compared to patients without BSI ($p < 0.001$ for all). The crude median costs attributable to VSE BSI were $12,557 and $33,768 for VRE BSI. The median hospital length of stay was significantly longer for patients with VRE BSI (14.6 days) and VSE BSI (10.0 days) compared to patients without enterococcal BSI (4.0 days; $p < 0.001$ for both). The crude increases in length of hospital stay were 6.0 days for VSE BSI and 10.6 days for VRE BSI ($p < .001$ for both).

Standard and Propensity-score Weighted GLS Models

Both VRE and VSE BSI were independent predictors of hospital costs ($p < 0.001$) in the standard and propensity-score weighted GLS model after controlling for significant cost predictors, including demographics, underlying comorbidities, procedures, non-enterococcal BSI, and early mortality. After these adjustments, non-enterococcal BSI was also associated with significantly increased costs ($p < 0.001$). The standard and propensity-score weighted GLS models had adjusted coefficients of determination (R^2) of 0.42 and 0.38, respectively, indicating that approximately 40% of the variation in costs was explained by the models.

The attributable cost estimates from the GLS models are presented in Table 3. In the standard GLS model, the adjusted costs of VSE BSI were $2,250 (95% CI, $1,758–$2,880) and the adjusted costs of VRE BSI were $4,479 (95% CI, $3,500–$5,732). In the propensity-score weighted GLS model, the adjusted costs of VSE BSI were $2,023 (95% CI, $1,588–$2,575) and the adjusted costs of VRE BSI were $4,036 (95% CI, $3,170–$5,140). In the alternative models with enterococcal BSI and vancomycin-resistance as the primary independent variables, vancomycin-resistance was an independent predictor of hospital costs ($p = 0.001$). The attributable costs of vancomycin-resistance ranged from $1,713 (95% CI, $1,338–$2,192) with the standard GLS model to $1,546 (95% CI, $1,214–$1,968) with the propensity-score weighted GLS model.

Table 3 also presents the attributable length of stay estimates. In the standard GLS model, the attributable length of stay of VSE BSI was 1.2 days (95% CI, 0.9–1.5) and the attributable length of stay of VRE BSI was 2.3 days (95% CI, 1.8–2.8). In the propensity-score weighted GLS model, the attributable length of stay of VSE BSI was 1.1 days (95% CI, 0.9–1.4) and the attributable length of stay of VRE BSI was 2.2 days (95% CI,1.7–2.7). The standard and propensity-score weighted GLS models had adjusted coefficients of determination (R^2) of 0.35 and 0.33, respectively, indicating that approximately 34% of the variation in hospital length of stay was explained by the models.

Propensity Score Matched-Pairs

Based on the predicted probabilities of developing VSE BSI and VRE BSI, 179 (98%) VSE BSI cases were successfully matched with uninfected controls and 88 (94%) VRE BSI cases were successfully matched with uninfected controls. Three VSE BSI cases and six VRE BSI cases were excluded from the analyses due to the absence of a suitable nearest-neighbor control. All covariates were balanced between matched and unmatched cases, adjusting for multiple comparisons. While there were no significant differences in median costs between unmatched and matched VSE cases ($23,013 vs. $20,076; $p = 0.417$), median costs were significantly higher for the six unmatched VRE cases compared to matched VRE cases ($182,763 vs. $40,140; $p = 0.029$).

The difference in total costs between the matched VSE BSI case and control pairs was $5,282 (median) and the difference in total costs between the matched VRE BSI case and control pairs was $9,949 (median) (Table 3). The median values for the difference in the hospital length of stay for the matched pairs were equal to 2.2 days for VSE BSI, and 3.5 days for VRE BSI ($p < .001$ for both, Wilcoxon signed-rank test).

DISCUSSION

In this retrospective cohort of non-surgical patients admitted to a university-affiliated tertiary care hospital, we used administrative data and readily reproducible methodology to estimate the attributable costs of enterococcal BSI and vancomycin-resistance. VSE and VRE BSI were independently associated with significantly increased hospital costs after adjustment for other cost predictors, including demographics, underlying comorbidities,

procedures, non-enterococcal BSI, and early mortality. In addition, we determined that vancomycin-resistance was independently associated with increased hospital expenditures. This is the first study, to our knowledge, to report that vancomycin-resistance among enterococcal BSI is independently associated with increased costs. In this era of increasing antimicrobial resistance, accurate estimates of the financial burden associated with nosocomial infections are important for cost-effectiveness evaluations of prevention strategies.

Since patients with infection often have more severe underlying diseases that are independently predictive of adverse outcomes and increased costs, adjustment for underlying severity of illness is essential for accurate cost estimation [8]. In our cohort, patients who developed enterococcal BSI were much more likely to have risk factors for developing a BSI, including diabetes, congestive heart failure, cancer, and bone marrow transplant. Given that the large differences in observed covariates between patients with and without enterococcal BSI could lead to biased estimates of costs, we used three different analytical methods to adjust for the variation of factors significantly associated with expenditures. In this cohort, we calculated the crude median attributable costs of VRE BSI to be $33,768. After adjustment for an extensive number of comorbidities and procedures that were associated with hospital expenditures, the VRE BSI cost estimates were $4,479 in the standard GLS model and $4,036 in the propensity-score weighted GLS model. The cost estimate generated by the propensity score matched-pairs method ($9,949) was more than twice as large as the GLS model estimates, despite the exclusion of 6 (6%) VRE BSI cases with significantly higher median costs than the 88 (94%) VRE BSI cases included in the analysis. The disparity between the cost estimates generated by the GLS models and the matched-pairs may be due, in part, to different control groups. Whereas the control group in the GLS models was the “average” uninfected patient because we used the mean of all covariates (except non-enterococcal BSI) to calculate attributable costs, the control group in the matched-pairs analysis was limited to a more severely ill subset of patients. Since patients with enterococcal BSI tend to be sicker than the “average” patient, the results of the matched-pairs analysis suggest that VRE in sicker patients is associated with approximately $10,000 in additional hospital costs. The matched-pairs design is an effective method for eliminating bias, but the reduction in sample size reduces the precision of cost estimates. This provides justification for the propensity-score weighted GLS model, which allows for analysis of the full cohort with the advantages of propensity score-adjustment to reduce confounding.

Published cost estimates associated with VRE are limited with varying results, due in part to variability in study designs, case definitions, control groups, sample sizes, and adjustment for confounders. Stosor et al. [4] reported that patients with VRE BSI had crude mean hospitalization costs $27,000 higher than the crude mean costs of patients with VSE BSI. Song et al. [1] estimated the excess difference in median costs between hospital patients with VRE BSI and without BSI to be $77,558. Song and colleagues [1] calculated median costs using pairs matched by age, year of admission, days of hospitalization prior to the diagnosis of BSI, principal diagnosis and primary procedure (by ICD-9-CM codes), and the All Patient Refined-Diagnosis Related Groups (APR-DRGs), however, a number of important cost drivers also associated with infection were not included in the analysis. Additional cost estimates from studies involving other VRE infections (i.e., colonization or infection at sites other than the bloodstream) range from $8,936 to $38,669 [9, 10, 17–19].

In both the standard and propensity-score weighted GLS models, vancomycin-resistance was a highly significant independent predictor of hospital costs, indicating that expenditures for BSI with resistant enterococci were significantly higher than expenditures for BSI with sensitive enterococci. The attributable costs of vancomycin-resistance were $1,713 in the

standard GLS model and $1,546 in the propensity-score weighted GLS model. Of four published studies that used multivariate methods to estimate the costs of vancomycin resistance [1, 9, 10, 17], only two studies attempted to assess the independent financial impact of the acquisition of a resistance determinant [9, 10]. Pelz et al. [10] did not find a significant difference between the median costs of 117 ICU patients with VSE ($21,914) and VRE ($33,251) infections of the urine, wound, abscess, or blood (including catheter colonization). However, the null result is likely due to small sample size (12 VRE cases, 22 VSE cases). Kaye et al. [9] reported that vancomycin-resistance was a significant predictor of increased costs among patients with enterococcal wound infection, with an attributable cost of $8,936. Our estimates were substantially lower than the estimate by Kaye et al. [9], which may be related to our exclusion of surgical patients from the study population due to a markedly higher distribution of costs for patients with operating room costs compared to other hospitalized patients. It is also possible that the attributable costs of vancomycin-resistance vary by infection site.

Our finding that vancomycin-resistance was independently associated with increased hospital costs has a few possible explanations. In our cohort, room and board costs made up the highest percentage of total crude costs, accounting for approximately half of total crude costs regardless of BSI infection status. The positive correlation between the incremental increases in crude room and board costs (VRE BSI, $20,213 vs. VSE BSI, $10,127 vs. no BSI, $3,976) and crude length of stay (VRE BSI, 14.6 days vs. VSE BSI, 10.0 days vs. no BSI, 4.0 days) indicates that length of stay was the major driver of increased costs. Pharmacy costs were the second largest contributor to total crude costs, making up 18%, 15%, and 8% of the total costs for VRE BSI cases, VSE BSI cases, and control uninfected patients, respectively. Antibiotic resistance frequently leads to a delay in the administration of appropriate antimicrobial therapy, which may be associated with adverse outcomes [1, 2, 8, 20–24]. In addition, appropriate antimicrobial agents for treatment of VRE cost significantly more per day than antimicrobials typically used to treat VSE BSI [8].

Recent increases in rates of antibiotic resistant-infections [6] highlight the need to standardize the methods for cost studies of nosocomial infections. The use of readily available administrative data is advantageous because it is relatively inexpensive to obtain and is available at all hospitals in the U.S., facilitating the analysis of large cohorts [25]. Our study of 21,154 hospital inpatients has excellent power, and provides results that are generalizable to university-affiliated tertiary care hospitals in the US. It is important to note that our data were restricted to one institution. We created comorbidity and procedure variables from ICD-9-CM code data using the Healthcare Cost and Utilization Project (HCUP) Clinical Classifications Software [11] as a guide, a standardized process that can improve comparability of cost estimates across studies. Compared to medical record data, comorbidities are undercoded by administrative data [25]. Nevertheless, studies comparing diagnoses and procedures reported in administrative data compared with medical records and self-reporting have found good levels of agreement [26]. Furthermore, comorbidity adjustment using diagnoses identified via claims data does not markedly differ from comorbidity adjustment using diagnoses identified in medical records [26–28].

The significantly higher hospital costs of VRE BSI that we identified in this study suggest that effective control of vancomycin-resistant pathogens would result in cost savings. Recent empiric evidence-based guidelines for the prevention of VRE transmission recommend active surveillance cultures to identify the reservoir for spread and the Centers for Disease Control and Prevention's long-recommended contact precautions to decrease transmission [7]. Other prevention strategies include healthcare personnel education, hand hygiene, judicious antimicrobial-use policies, and enhanced environmental cleaning [7, 29, 30]. Our estimates of

the cost of vancomycin resistance can also be used to help assess the cost-effectiveness of interventions to reduce transmission of resistant organisms in hospital settings.

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Table 1

Characteristics of the Cohort (N=21,154)

Characteristic	VRE BSI (n=94)	VSE BSI (n=182)	No VRE or VSE BSI (n=20,878)	*p* (VRE BSI vs. VSE BSI)	*p* (VRE BSI vs. No VRE or VSE BSI)	*p* (VSE BSI vs. NoVRE or VSE BSI)
Age, median (range), y	58.3 (20.9–88.0)	65.4 (18.1–98.2)	60.1 (14.0–106.2)	.005	< .001	.004
Female sex	48 (51.1)	102 (56.0)	11,154 (53.4)	NS	NS	NS
Black race	42 (44.7)	84 (46.2)	7,485 (35.9)	NS	NS	.004
Acute cerebrovascular disease	4 (4.3)	9 (4.9)	1,037 (5.0)	NS	NS	NS
Acute myocardial infarction	10 (10.6)	9 (4.9)	1,308 (6.3)	NS	NS	NS
Atrial fibrillation	15 (16.0)	39 (21.5)	2,603 (12.5)	NS	NS	NS
Congestive heart failure, nonhypertensive	28 (29.8)	66 (36.5)	4,354 (20.9)	NS	.034	< .001
Pulmonary embolism and pulmonary hypertension	8 (8.5)	25 (13.8)	1,128 (5.4)	NS	NS	< .001
Chronic obstructive pulmonary disease	20 (21.3)	34 (18.8)	3,012 (14.4)	NS	NS	NS
Pneumonia	20 (21.3)	20 (11.0)	1,692 (8.1)	.021	< .001	NS
Asthma	6 (6.4)	13 (7.2)	1,390 (6.7)	NS	NS	NS
Diabetes without complications	19 (20.2)	51 (28.2)	4,316 (20.7)	NS	NS	.015
Diabetes with complications	12 (12.8)	29 (16.0)	1,564 (7.5)	NS	NS	< .001
Acute renal failure	37 (39.4)	46 (25.3)	2,091 (10.0)	.016	< .001	< .001
Liver disease	14 (14.9)	16 (8.8)	1,547 (7.4)	NS	.006	NS
Clostridium difficile diarrhea	19 (20.2)	24 (13.2)	433 (2.1)	NS	< .001	< .001
Urinary tract infection	29 (30.9)	57 (31.3)	3,383 (16.2)	NS	< .001	< .001
Non-enterococcal BSI[a]	54 (57.4)	76 (41.8)	728 (3.5)	.013	< .001	< .001
Central venous catheter[b]	61 (64.9)	89 (48.9)	2,677 (12.8)	.011	< .001	< .001
Hemodialysis	15 (16.0)	12 (6.6)	588 (2.8)	.013	< .001	.002
Mechanical ventilation	27 (28.7)	36 (19.8)	1,145 (5.5)	NS	< .001	< .001
Abdominal paracentesis	10 (10.6)	6 (3.3)	439 (2.1)	.013	< .001	NS
Bone marrow transplant	9 (9.6)	14 (7.7)	213 (1.0)	NS	< .001	< .001
Cancer chemotherapy	15 (16.0)	20 (11.0)	599 (2.9)	NS	< .001	< .001

NOTE. Data are given as number (percentage) of patients unless otherwise indicated. VRE indicates Vancomycin-resistant enterococcus; VSE, Vancomycin-sensitive enterococcus; BSI, Bloodstream infection; NS, non-significant.

[a]Defined as ≥ 1 positive blood culture of a non-enterococcal pathogen or ≥ 2 blood cultures with potential skin contaminants (e.g., coagulase-negative Staphylococci, Micrococcus sp., etc.).

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[b] Inserted before the onset of enterococcal BSI in case patients.

Table 2

Crude Median Costs and Length of Stay of Patients With and Without Enterococcal Bloodstream Infection (BSI)

Outcomes	VRE BSI[a,b] (n=94)	VSE BSI[a,b] (n=182)	No BSI[c] (n=20,150)
Hospital length of stay, days	14.6 (7.3 – 28.3)	10.0 (4.9 – 17.6)	4.0 (2.9 – 6.2)
Departmental costs, $US 2007			
Room and board	$20,213 (7,209 – 45,610)	$10,127 (5,829 – 21,212)	$3,976 (2,793 – 6,456)
Pharmacy	$7,430 (3,095 – 20,241)	$3,205 (1,397 – 6,925)	$669 (339 – 1,339)
Laboratory	$4,143 (1,804 – 10,569)	$1,989 (1,172 – 4,716)	$628 (375 – 1,103)
Radiology	$1,942 (940 – 4,591)	$1,222 (501 – 2,053)	$554 (125 – 1,197)
Respiratory therapy	$412 (0 – 1,510)	$130 (0 – 719)	$0 (0 – 152)
Physical therapy	$172 (0 – 448)	$114 (0 – 370)	$0 (0 – 175)
Other[d]	$3,710 (1,907 – 7,061)	$2,193 (1,380 – 3,636)	$1,140 (656 – 2,245)
Total costs	$42,106 (16,310 – 93,870)	$20,895 (11,263 – 41,879)	$8,192 (5,615 – 13,495)

NOTE. Data are given as median (interquartile range). VRE indicates Vancomycin-resistant enterococcus; VSE, Vancomycin-sensitive enterococcus; BSI, Bloodstream infection.

[a] $p < 0.001$ for all comparisons vs. uninfected control group.

[b] $p < 0.001$ for all comparisons of VRE BSI vs. VSE BSI cases, with the exceptions of respiratory costs ($p = 0.015$) and physical therapy costs ($p = 0.205$).

[c] Defined as patients without enterococcal or non-enterococcal BSI.

[d] Defined as costs not allocated to room and board, pharmacy, laboratory, radiology, respiratory therapy, or physical therapy departments.

Table 3

Attributable Costs and Length of Stay of VSE and VRE Bloodstream Infections

	Costs (US$) (95% CI)		Length of stay (days) (95% CI)	
Statistical Method	**VRE BSI**	**VSE BSI**	**VRE BSI**	**VSE BSI**
GLS regression model, mean	$4,479 (3,500 – 5,732)	$2,250 (1,758 – 2,880)	2.3 (1.8 – 2.8)	1.2 (0.9 – 1.5)
GLS regression model with IPW, mean[a]	$4,036 (3,170 – 5,140)	$2,023 (1,588 – 2,575)	2.2 (1.7 – 2.7)	1.1 (0.9 – 1.4)
Matched-pairs, median[a,b]	$9,949 (1,579 – 24,693)	$5,282 (2,042 – 8,043)	3.5 (2.1 – 7.3)	2.2 (1.0 – 3.5)

NOTE. VRE indicates Vancomycin-resistant enterococcus; VSE, Vancomycin-sensitive enterococcus; BSI, Bloodstream infection.

[a]The variables in the logistic regression model to create the propensity score for development of VSE or VRE BSI include demographic variables [age (5-year age intervals), non-Caucasian race, gender], medical conditions [pneumonia, aspiration pneumonitis, chronic obstructive pulmonary disease and bronchiectasis, non-hypertensive congestive heart failure, pulmonary heart disease, coronary atherosclerosis, cardiac dysrhythmias not including atrial fibrillation, hypertension with complications and secondary hypertension, heart valve disorders, cardiac arrest and ventricular fibrillation, atrial fibrillation, atrial flutter, conduction disorders, peri-, endo-, and myocarditis, hyperlipidemia, diabetes mellitus without complications, diabetes mellitus with complications, chronic renal failure, acute renal failure, solid tumor malignancy, leukemia, Non-Hodgkin's lymphoma, multiple myeloma, HIV infection, *Clostridium difficile* diarrhea, urinary tract infection, infective arthritis and osteomyelitis, rheumatoid arthritis, agranulocytosis (neutropenia), peritonitis and intestinal abscess, Graft vs. Host disease, chronic ulcer of the skin, deficiency and other anemias, hypovolemia, later complications following transplant of whole organ, complications of transplant and reattached limbs, depression, methicillin-sensitive Staphylococcus aureus infection (prior to VSE/VRE BSI), methicillin-resistant Staphylococcus aureus infection (prior to VSE/VRE BSI), sensitive gram negative rods infection (prior to VSE/VRE BSI), resistant gram negative rods infection (prior to VSE/VRE BSI), non-enterococcal, non- Staphylococcus aureus, or non-gram negative rods BSI (prior to VSE/VRE BSI)], and procedures [hemodialysis, mechanical ventilation >96 hours during admission, mechanical ventilation <96 hours during admission, gastrostomy (temporary and permanent), bone marrow transplant, cancer chemotherapy, central venous catheter inserted within six months (of VSE/VRE BSI for cases and discharge date for uninfected controls)].

[b]Data are the median values of the difference between case-control pairs and corresponding 95% confidence intervals are based on the binomial distribution.