MAJOR ARTICLE

Impact of Infectious Disease Consultation on Quality of Care, Mortality, and Length of Stay in *Staphylococcus aureus* Bacteremia: Results From a Large Multicenter Cohort Study

Anthony D. Bai,[1] Adrienne Showler,[2] Lisa Burry,[3,4] Marilyn Steinberg,[3] Daniel R. Ricciuto,[2,5] Tania Fernandes,[6] Anna Chiu,[6] Sumit Raybardhan,[7] Michelle Science,[8] Eshan Fernando,[2] George Tomlinson,[2,9] Chaim M. Bell,[2,3,10] and Andrew M. Morris[2,3,9]

[1]Faculty of Medicine, University of Ottawa, [2]Department of Medicine, University of Toronto, [3]Mount Sinai Hospital, Toronto, [4]Leslie Dan Faculty of Pharmacy, University of Toronto, [5]Lakeridge Health, Oshawa, [6]Trillium Health Partners, Mississauga, [7]North York General Hospital, [8]Hospital for Sick Children, [9]University Health Network, and [10]Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada

Background. We assessed the impact of infectious disease (ID) consultation on management and outcome in patients with *Staphylococcus aureus* bacteremia (SAB).

Methods. A retrospective cohort study examined consecutive SAB patients from 6 academic and community hospitals between 2007 and 2010. Quality measures of management including echocardiography, repeat blood culture, removal of infectious foci, and antibiotic therapy were compared between ID consultation (IDC) and no ID consultation (NIDC) groups. A competing risk model with propensity score adjustment was used to compare in-hospital mortality and time to discharge.

Results. Of 847 SAB patients, 506 (60%) patients received an ID consultation and 341 (40%) patients did not. Echocardiography was done for 371 (73%) IDC and 191 (56%) NIDC patients ($P < .0001$) in hospital. Blood cultures were repeated within 2–4 days of bacteremia in 207 (41%) IDC and 107 (31%) NIDC patients ($P = .0058$). The infectious foci removal rate was not statistically different between the 2 groups. For empiric therapy, 474 (94%) IDC and 297 (87%) NIDC patients received appropriate antibiotics ($P = .0013$). For patients who finished the planned course of antibiotics, 285 of 422 (68%) IDC and 141 of 262 (54%) NIDC patients received the appropriate duration of antibiotic therapy ($P = .0004$). In hospital, 204 (24%) patients died: 104 of 506 (21%) IDC and 100 of 341 (29%) NIDC patients. Matched by propensity score, ID consultation had a subdistribution hazard ratio of 0.72 (95% confidence interval [CI], .52–.99; $P = .0451$) for in-hospital mortality and 1.28 (95% CI, 1.06–1.56; $P = .0109$) for being discharged alive.

Conclusions. ID consultation is associated with better adherence to quality measures, reduced in-hospital mortality, and earlier discharge in patients with SAB.

Keywords. bacteremia; *Staphylococcus aureus*; infectious disease consultation; mortality; quality of care.

Staphylococcus aureus bacteremia (SAB) is a leading bloodstream infection with 10%–30% mortality [1–5]. Based on published guidelines and observational studies, SAB management standards include repeat blood culture, echocardiography, removal of infectious foci, and early empiric antibiotic therapy, as well as intravenous antibiotic therapy of ≥14 days for uncomplicated bacteremia and ≥28 days for complicated bacteremia [6–11].

The value of specialist involvement on management and outcome of many medical conditions including acute kidney injury, myocardial infarction, congestive heart failure, and chronic obstructive pulmonary disease is well established [12–15]. Likewise, infectious disease (ID) specialists may be useful in guiding SAB

Received 30 October 2014; accepted 3 February 2015; electronically published 20 February 2015.

Correspondence: Andrew M. Morris, MD, SM, Mount Sinai Hospital, 600 University Ave, Rm 415, Toronto, ON M5G 1X5, Canada (amorris@mtsinai.on.ca).

Clinical Infectious Diseases® 2015;60(10):1451–61

DOI: 10.1093/cid/civ120

management. ID consultation is associated with adherence to the aforementioned management standards [1, 16–24]. In some studies, ID consultation did not significantly decrease mortality after adjusting for other variables [1, 4, 6, 22, 25]. In other studies, ID specialist consultation improved survival [16–21, 23, 24, 26–28]. However, the most recent review described the current evidence on ID consultation as low quality [29]. First, these studies were conducted at single tertiary academic centers and most had relatively small sample sizes, making their results less generalizable [16–21, 23, 24, 26–28]. Second, although the allocation of ID consultation may be biased, no study adjusted for all measurable covariates that may affect assignment of ID consultation and reported a significant impact of ID consultation on mortality. Last, no study examined length of stay (LOS) in hospital while accounting for death in hospital as a competing event.

We conducted a retrospective cohort study to assess the impact of ID specialist consultation on in-hospital mortality, LOS, and quality of care in patients with SAB using multivariable modeling and matched propensity score analysis.

METHODS

Study Design

We conducted a retrospective cohort study at 6 acute care academic and community hospitals in the Greater Toronto Area, which accounted for a total of 2968 acute care beds and 145 000 annual patient admissions. Consecutive patients were included in the analysis from 1 April 2007 to 31 March 2010. Research ethics board approval was obtained from each institution.

Patient records were included if the patient had at least 1 positive blood culture for *S. aureus* as identified in microbiology computerized database at all 6 sites, where all selected patient files were analyzed. Identification of *S. aureus* and antimicrobial susceptibility testing of blood culture were based on Clinical and Laboratory Standards Institute guidelines [30].

Patients <18 years of age were excluded from analysis. Additionally, patients were excluded from analysis if any of the following occurred within 2 days of blood culture: death, discharge to another institution, left against medical advice, or deemed palliative (specifically not undergoing any investigation or medical therapy). The threshold of 2 days was chosen because >90% of blood culture returned a positive *S. aureus* result within 2 days and it allowed adequate time for ID consultation [1].

Data Collection

Data were obtained from patients' electronic and paper medical records at each site and entered into a standardized case report form. Collected data included patient demographics, comorbidities, microbiological data, antibiotic treatment, investigations, removal of infectious foci, and clinical outcomes.

Patient Characteristics and SAB Clinical Characteristics

Infection acquisition was deemed nosocomial, healthcare-associated, or community-acquired based on standard definitions [31]. Patients were assumed to have community-acquired infection unless proven otherwise.

High- and intermediate-risk cardiac conditions were defined according to American Heart Association guidelines for infective endocarditis [32]. Immune suppression was defined as high-dose corticosteroid (>10 mg prednisone or equivalent), human immunodeficiency virus/AIDS, chemotherapy within last 6 weeks, neutropenia within 72 hours of bacteremia, or transplantation requiring immunosuppressive therapy.

Renal insufficiency was defined as serum creatinine level >177 μmol/L within 24 hours of bacteremia. Early infectious foci were defined as documented foci preceding or within 2 days of blood culture collection, whereas late infectious foci were defined as documented foci after 2 days following blood culture collection. Endocarditis was adjudicated using the modified Duke criteria [33].

Uncomplicated SAB was defined as no deep tissue infection, no metastatic infection, and no endocarditis [6, 7, 19]. Complicated SAB was defined as endocarditis, deep tissue infection, or metastatic infection [6, 7, 19].

Quality Measures of Management

For antibiotic therapy to be considered appropriate, it had to be administered intravenously. For methicillin-susceptible *S. aureus* (MSSA), appropriate antibiotics included β-lactams (cloxacillin, nafcillin, cefazolin, piperacillin-tazobactam, ticarcillin-clavulanate, amoxicillin-clavulanate, and penicillin if susceptible), quinupristin-dalfopristin, daptomycin, and vancomycin. For methicillin-resistant *S. aureus* (MRSA), appropriate antibiotics included vancomycin, quinupristin-dalfopristin, and daptomycin. Duration of antibiotic was calculated from start of appropriate antibiotic closest to blood culture collection date. For patients who were discharged alive, the planned treatment stop date was considered the last day of appropriate antibiotics.

Empiric therapy was defined as any appropriate antibiotic started within 3 days of blood culture collection. The threshold of 3 days was chosen, because >90% of blood culture reported susceptibility as MSSA or MRSA within 3 days. Definitive antibiotic therapy was defined as any appropriate antibiotic started or continued past 4 days since blood culture collection, allowing 1 day after susceptibility report to switch antibiotics.

Appropriate antibiotic duration was defined as ≥14 days for uncomplicated and ≥28 days for complicated SAB [6, 7, 19].

ID Consultation

At all sites, ID service consultation was available and optional. There were 29 consultants at 6 sites. All had full accreditation in ID from the Royal College of Physicians and Surgeons of

Canada. At 3 sites, the microbiology laboratory notified the ID service when blood culture was positive for *S. aureus*, and an ID consultation was offered to the most responsible physician as per departmental policy. However, these ID consultations were not mandatory. In all other sites, ID consultation was done based on request from the most responsible physician.

ID consultation was defined as a formal ID consultation documented in the patient chart within 7 days of blood culture collection or having an ID specialist as the most responsible physician.

Outcome

Primary outcome was in-hospital mortality within 90 days. All patient outcomes were followed until death in hospital or 90 days, whichever came first. LOS was calculated as time from blood culture collection to discharge or death in hospital.

Statistical Analysis

Comparison between ID consultation and no ID consultation groups were done with Wilcoxon rank-sum test for nonnormally distributed continuous variables and Fisher exact test for categorical variables.

A competing risk model was used to describe in-hospital mortality and time to discharge, where possible endpoints included alive in-hospital by day 90, deceased in-hospital, and discharged alive. Based on a cumulative incidence function, a subdistribution hazard ratio (sHR) was calculated using the Fine and Gray model [34]. In the univariate analysis, patient baseline characteristics and SAB clinical characteristics with the exception of variables beyond 2 days were considered potential predictors. All predictors with $P < .2$ on univariate analysis were included in the final multivariable Fine and Gray model along with ID consultation.

Propensity score for ID consultation was estimated using a logistic regression of all patient baseline characteristics and SAB clinical characteristics with the exception of variables beyond 2 days. Patients without ID consultation were matched in a 1:1 ratio to patients with ID consultation using nearest neighbor matching with specified caliper width of 0.55 times the standard deviation of the logit of propensity scores. The matched groups were compared with the Fine and Gray model in terms of in-hospital mortality and being discharged alive.

All reported confidence intervals (CIs) were 2-sided 95% intervals and all tests were 2-sided with a $P < .05$ significance level. All analyses were done with R version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

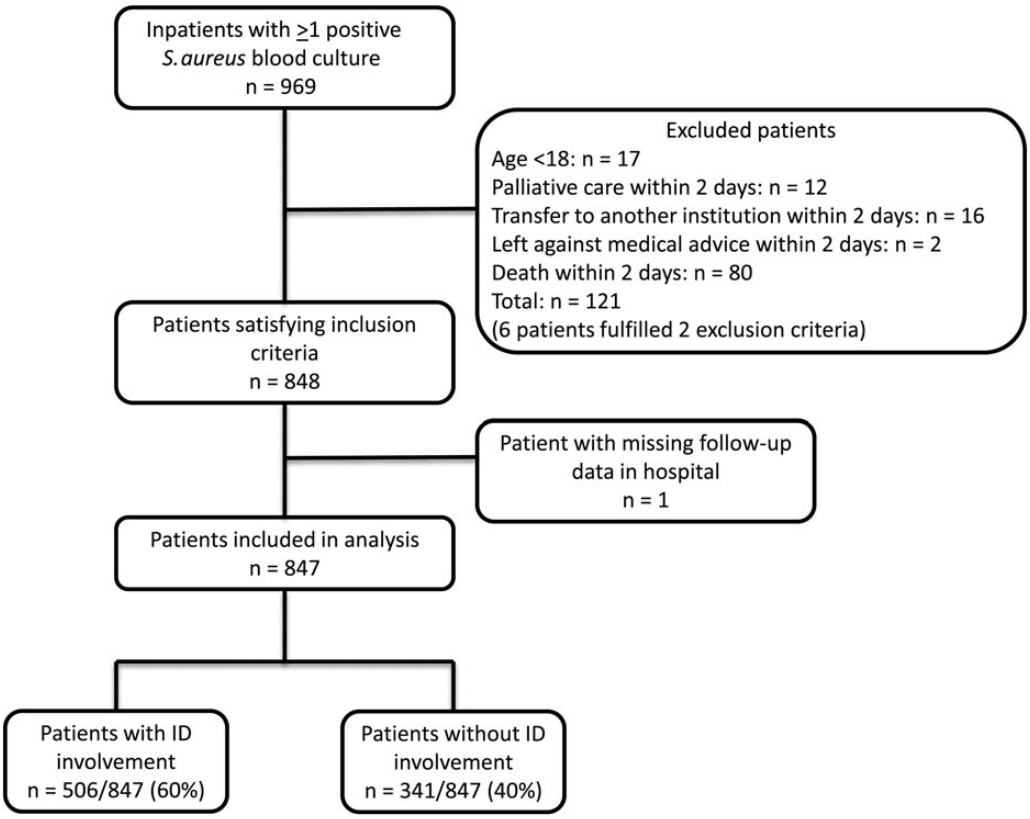

Figure 1. Flow diagram of patients included in the study. Abbreviation: ID, infectious disease.

Table 1. Patient Baseline and *Staphylococcus aureus* Bacteremia Characteristics

Characteristic	All Patients (N = 847)	ID Consultation (n = 506)	No ID Consultation (n = 341)	*P* Value of ID vs No ID Consultation
Age, median, y (IQR)	65.00 (51.50–78.00)	63.00 (51.00–76.00)	68.00 (52.00–80.00)	.0105
Age >65 y	414 (49)	235 (46)	179 (52)	.0926
Male	545 (64)	332 (66)	213 (62)	.3802
Hospital sites				<.0001
Site 1	121 (14)	52 (10)	69 (20)	
Site 2	82 (10)	66 (13)	16 (5)	
Site 3	227 (27)	115 (23)	112 (33)	
Site 4	173 (20)	123 (24)	50 (15)	
Site 5	127 (15)	86 (17)	41 (12)	
Site 6	117 (14)	64 (13)	53 (16)	
Admitting service				.0005
ICU	135 (16)	68 (13)	67 (20)	
Medical	518 (61)	301 (59)	217 (64)	
Surgical	194 (23)	137 (27)	57 (17)	
Healthcare setting				.0414
Community acquired	249 (29)	160 (32)	89 (26)	
Healthcare associated	311 (37)	191 (38)	120 (35)	
Nosocomial	287 (34)	155 (31)	132 (39)	
Intravenous drug use	42 (5)	23 (5)	19 (6)	.5213
Comorbidity				
High-risk cardiac condition	73 (9)	51 (10)	22 (6)	.0800
Intermediate-risk cardiac condition	18 (2)	12 (2)	6 (2)	.6327
Myocardial infarction	166 (20)	103 (20)	63 (18)	.5371
Congestive heart failure	171 (20)	96 (19)	75 (22)	.2956
Peripheral vascular disease	77 (9)	56 (11)	21 (6)	.0149
Chronic pulmonary disease	82 (10)	57 (11)	25 (7)	.0590
Connective tissue disease	31 (4)	22 (4)	9 (3)	.2627
Chronic kidney disease	189 (22)	101 (20)	88 (26)	.0528
Hemodialysis	95 (11)	55 (11)	40 (12)	.7394
Peritoneal dialysis	12 (1)	8 (2)	4 (1)	.7709
Diabetes	280 (33)	181 (36)	99 (29)	.0444
Malignancy	221 (26)	135 (27)	86 (25)	.6901
Liver cirrhosis	59 (7)	37 (7)	22 (6)	.6812
Immune suppression	178 (21)	110 (22)	68 (20)	.5482
MRSA	145 (17)	82 (16)	63 (18)	.4053
At presentation (within 24 h)				
Fever	531 (63)	323 (64)	208 (61)	.4258
Hypotensive shock	221 (26)	124 (25)	97 (28)	.2029
Renal insufficiency	190 (22)	106 (21)	84 (25)	.2091
Infectious foci/complication preceding or within 2 d of blood culture				
Intravascular catheter[a]	136 (16)	76 (15)	60 (18)	.3404
Skin and soft tissue	135 (16)	95 (19)	40 (12)	.0072
Respiratory	131 (15)	64 (13)	67 (20)	.0066
Bone and joint	88 (10)	74 (15)	14 (4)	<.0001
Abscess	42 (5)	33 (7)	9 (3)	.0099
Endocarditis	43 (5)	34 (7)	9 (3)	.0099
Urinary tract	60 (7)	26 (5)	34 (10)	.0091
Other foci[b]	80 (9)	59 (12)	21 (6)	.0081
Unknown foci	306 (36)	173 (34)	133 (39)	.1660
Embolic stroke	21 (2)	15 (3)	6 (2)	.3683
ICU admission within 72 h	158 (19)	105 (21)	53 (16)	.0593

Table 1 continued.

Characteristic	All Patients (N = 847)	ID Consultation (n = 506)	No ID Consultation (n = 341)	*P* Value of ID vs No ID Consultation
Mechanical ventilation within 7 d	181 (21)	94 (19)	87 (25)	.0168
Infectious foci/complication after 2 d of blood culture				
Intravascular catheter[a]	12 (1)	10 (2)	2 (1)	.1374
Skin and soft tissue	45 (5)	27 (5)	18 (5)	>.9999
Respiratory	29 (3)	16 (3)	13 (4)	.7008
Bone and joint	62 (7)	41 (8)	21 (6)	.3466
Abscess	40 (5)	30 (6)	10 (3)	.0478
Endocarditis	36 (4)	28 (6)	8 (2)	.0243
Urinary tract	2 (0.2)	1 (0.2)	1 (0.3)	>.9999
Other foci[b]	31 (4)	22 (4)	9 (3)	.2627
Embolic stroke	11 (1)	9 (2)	2 (1)	.2150

Data are presented as No. of patients (%) unless specified otherwise. Time points refer to time of culture collection as baseline.

Abbreviations: ICU, intensive care unit; ID, infectious disease; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] Intravascular catheter included central venous catheter and arterial line infection.

[b] Other foci included intra-abdominal infection, biliary tract infection, central nervous system infection, endovascular infection, mycotic aneurysm, cardiac device infection, and any other infectious foci that did not belong in the infectious foci categories.

RESULTS

General Cohort and ID Consultation

Of 969 patients with SAB, 847 patients were eligible for the study, including 506 (60%) patients in the ID consultation (IDC) group and 341 (40%) patients in the no ID consultation (NIDC) group (Figure 1). The proportion of ID consultation ranged from 43% to 80% for different sites. Within the IDC group, 476 (94%) patients had a formal ID consultation and 30 (6%) patients had an ID specialist as the most responsible physician. Of 506 ID consultations, 346 (68%) were done within 2 days of bacteremia. Of the 29 ID specialists, from ID certification to start of study, 9 (31%) had ≤5 years, 5 (17%) had 6–10 years, 5 (17%) had 11–15 years, 2 (7%) had 16–20 years, and 8 (28%) had >20 years of experience.

Patient baseline and SAB clinical characteristics are outlined in Table 1.

Quality Measures of Management

For IDC patients, ID recommendations are listed in Table 2.

Compared to NIDC patients, IDC patients were more likely to receive an echocardiogram, a repeat blood culture, appropriate empiric antibiotics, and longer duration of antibiotic therapy (Table 3). Ninety-two patients had both a transthoracic echocardiogram (TTE) and a transesophageal echocardiogram (TEE) in hospital. Of the 65 patients with both TTE and TEE where the TTE was negative, 12 (18%) patients had a positive TEE for signs of endocarditis.

Antibiotic choices for MSSA and MRSA patients are outlined in Tables 4 and 5, respectively.

In patients who were alive when their antibiotic therapy ended, 285 of 422 (68%) IDC and 141 of 262 (54%) NIDC patients received antibiotic therapy for an appropriate duration ($P = .0004$) (Supplementary Appendix Table 1). In 357 uncomplicated

Table 2. Infectious Disease Consultation Recommendations

Recommendations	No. (%) of 506 ID Consultation Cases
Removal of infectious foci	
Removal of intravascular device	96 (19)
Surgical/interventional source control drainage	115 (23)
Cardiovascular surgery consultation	24 (5)
Repeat blood culture in 2–4 d	204 (40)
Antibiotic therapy	
Use of β-lactam in MSSA bacteremia	324 (64)
≥14 d of antibiotic therapy in uncomplicated SAB	146 (29)
≥28 d of antibiotic therapy in complicated SAB	272 (54)
Echocardiography	
Transthoracic echocardiography	222 (44)
Transesophageal echocardiography	114 (23)
Imaging	
Head CT	14 (3)
Head MRI	7 (1)
Chest CT	43 (9)
Abdominal ultrasound	23 (5)
Abdominal CT	28 (6)

Abbreviations: CT, computed tomography; ID, infectious disease; MRI, magnetic resonance imaging; MSSA, methicillin-susceptible *Staphylococcus aureus*; SAB, *Staphylococcus aureus* bacteremia.

Table 3. Management of *Staphylococcus aureus* Bacteremia in Infectious Disease (ID) Consultation and No ID Consultation Groups

Procedure	All Patients (N = 847)	ID Consultation (n = 506)	No ID Consultation (n = 341)	*P* Value of ID vs No ID Consultation
Echocardiography				
Any echo in hospital	562 (66)	371 (73)	191 (56)	<.0001
TTE in hospital	536 (63)	350 (69)	186 (55)	<.0001
TEE in hospital	118 (14)	82 (16)	36 (11)	.0202
TTE and TEE in hospital	92 (11)	61 (12)	31 (9)	.1790
Repeat blood culture				
Repeat culture in 2–4 d	314 (37)	207 (41)	107 (31)	.0058
Repeat culture in hospital	531 (63)	334 (66)	197 (58)	.0168
Antibiotic treatment				
Appropriate empiric antibiotic therapy	771 (91)	474 (94)	297 (87)	.0013
Days to appropriate antibiotics, median (IQR)[a]	1.00 (0.00–2.00)	1.00 (0.00–2.00)	1.00 (0.00–2.00)	.8218
Days of appropriate antibiotics[a]	17.00 (11.00–32.00)	21.00 (14.00–36.00)	15.00 (8.00–27.25)	<.0001

Data are No. of patients (%) unless specified otherwise.

Abbreviations: ID, infectious disease; IQR, interquartile range; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram.

[a] Data available for 809 patients: 497 in the ID consultation group; 312 in the no ID consultation group.

bacteremia cases, 155 of 191 (81%) IDC and 98 of 166 (59%) NIDC patients received appropriate antibiotic therapy duration of ≥14 days ($P < .0001$). In 327 complicated bacteremia cases, 130 of 231 (56%) IDC and 43 of 96 (45%) NIDC patients received appropriate antibiotic therapy duration of ≥28 days ($P = .0681$).

In patients with central venous catheter (CVC) as an early infectious focus, 59 of 73 (81%) IDC and 49 of 57 (86%) NIDC patients had their catheters removed ($P = .4873$). In patients with bone or joint infection as an early infectious focus, 46 of 74 (62%) IDC and 6 of 14 (43%) NIDC patients had bone debridement or joint aspiration ($P = .2380$). In patients with an abscess as an early infectious focus, 25 of 33 (76%) IDC and 4 of 9 (44%) NIDC patients had their abscess drained ($P = .1067$).

Modeling In-Hospital Mortality and Discharge

In all patients, 204 (24%) patients died in hospital: 104 (21%) IDC and 100 (29%) NIDC patients. Seven patients (<1%) were discharged within 2 days of positive blood culture. None of these 7 patients died in follow-up postdischarge. For all patients, the median LOS was 17.00 days (interquartile range [IQR], 9.00–35.00 days): 16.00 days (IQR, 9.00–33.00 days) for IDC patients and 17.00 days (IQR, 9.00–36.00 days) for NIDC patients. Excluding patients who died in hospital, the median LOS was 16.00 days (IQR, 9.00–35.00 days) for IDC patients and 19.00 days (IQR, 10.00–46.00 days) for NIDC patients.

Relative to no ID consultation, the unadjusted sHR for ID consultation was 0.66 (95% CI, .50–.86; $P = .0025$) for in-hospital mortality and 1.36 (95% CI, 1.15–1.61; $P = .0003$) for being discharged alive (Figure 2).

Univariate analysis predicting in-hospital mortality is listed in Supplementary Appendix Table 2. Multivariable modeling of significant predictors for in-hospital mortality is listed in Supplementary Appendix Table 3. After adjusting for these predictors in the multivariable model, ID consultation had an sHR for in-hospital mortality of 0.68 (95% CI, .50–.93; $P = .0151$). Likewise, for predicting time to discharge, univariate analysis and multivariable modeling of significant predictors are listed in Supplementary Appendix Tables 4 and 5, respectively. After adjusting for these predictors in the multivariable model, ID consultation had an sHR for being discharged alive of 1.22 (95% CI, 1.01–1.48; $P = .0360$).

Propensity Score–Matched Analysis

Based on propensity score, 303 IDC patients were matched with 303 NIDC patients (Table 6). After matching, the maximum standardized difference of mean was <0.10, suggesting that the 2 groups were similar with respect to measured variables.

Comparing the 2 groups matched by propensity score, the sHR for ID consultation was 0.72 for in-hospital mortality (95% CI, .52–.99; $P = .0451$) and 1.28 for being discharged alive (95% CI, 1.06–1.56; $P = .0109$) (Supplementary Appendix Figure 1). For quality of care measures that apply to all SAB patients, IDC patients were more likely than NIDC patients to receive an echocardiogram, a repeat blood culture, appropriate empiric antibiotic therapy, and longer duration of antibiotic therapy in the propensity score–matched groups (Table 7).

Table 4. Antibiotic Choice for Patients With Methicillin-Susceptible *Staphylococcus aureus* in the Infectious Disease (ID) Consultation and No ID Consultation Groups

Antibiotic	MSSA (n = 702)		
	IDC (n = 424)	NIDC (n = 278)	*P* Value (IDC vs NIDC)
Empiric therapy			
No appropriate antibiotics	23 (5)	37 (13)	.0005
Cloxacillin	227 (54)	99 (36)	<.0001
Nafcillin	1 (0.2)	0 (0)	>.9999
Penicillin	1 (0.2)	0 (0)	>.9999
Piperacillin-tazobactam	78 (18)	56 (20)	.6236
Ticarcillin-clavulanate	0 (0)	0 (0)	NA
Amoxicillin-clavulanate	0 (0)	0 (0)	NA
Cefazolin	125 (29)	87 (31)	.6150
Meropenem	7 (2)	8 (3)	.2946
Imipenem	0 (0)	0 (0)	NA
Ertapenem	2 (0.5)	0 (0)	.5209
Vancomycin	300 (71)	172 (62)	.0170
Quinupristin-dalfopristin	0 (0)	0 (0)	NA
Daptomycin	0 (0)	0 (0)	NA
Definitive therapy			
Cloxacillin	269 (63)	121 (44)	<.0001
Nafcillin	0 (0)	0 (0)	NA
Penicillin	6 (1)	0 (0)	.0864
Piperacillin-tazobactam[a]	40 (9)	33 (12)	.3137
Ticarcillin-clavulanate	0 (0)	0 (0)	NA
Amoxicillin-clavulanate	0 (0)	0 (0)	NA
Cefazolin	95 (22)	89 (32)	.0050
Meropenem	10 (2)	9 (3)	.4857
Imipenem	2 (0.5)	0 (0)	.5209
Ertapenem	1 (0.2)	0 (0)	>.9999
Vancomycin[b]	62 (15)	49 (18)	.2920
Quinupristin-dalfopristin	0 (0)	0 (0)	NA
Daptomycin	0 (0)	0 (0)	NA

Data are presented as No. of patients (%) unless specified otherwise.

Abbreviations: IDC, infectious disease consultation group; MSSA, methicillin-susceptible *Staphylococcus aureus*; NA, not applicable; NIDC, no infectious disease consultation group.

[a] Thirty of 40 MSSA patients in the IDC group who received piperacillin-tazobactam as definitive therapy also received antistaphylococcal penicillin or cefazolin as definitive therapy; 26 of 33 MSSA patients in the NIDC group who received piperacillin-tazobactam as definitive therapy also received antistaphylococcal penicillin or cefazolin as definitive therapy.

[b] Thirty-seven of 62 MSSA patients in the IDC group who received vancomycin as definitive therapy also received antistaphylococcal penicillin or cefazolin as definitive therapy; 32 of 49 MSSA patients in the NIDC group who received vancomycin as definitive therapy also received antistaphylococcal penicillin or cefazolin as definitive therapy.

Table 5. Antibiotic Choice for Patients With Methicillin-Resistant *Staphylococcus aureus* in the Infectious Disease (ID) Consultation and No ID Consultation Groups

Antibiotic	MRSA (n = 145)		
	IDC (n = 82)	NIDC (n = 63)	*P* Value (IDC vs NIDC)
Empiric therapy			
No appropriate antibiotics	9 (11)	7 (11)	>.9999
Vancomycin	73 (89)	55 (87)	.7983
Quinupristin-dalfopristin	0 (0)	1 (2)	.4345
Daptomycin	0 (0)	0 (0)	NA
Definitive therapy			
Vancomycin	71 (87)	53 (84)	.8125
Quinupristin-dalfopristin	0 (0)	0 (0)	NA
Daptomycin	2 (2)	2 (3)	>.9999

Data are presented as No. of patients (%) unless specified otherwise.

Abbreviations: IDC, infectious disease consultation group; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not applicable; NIDC, no infectious disease consultation group.

DISCUSSION

In our multicenter cohort study, ID consultation was associated with a reduction of in-hospital mortality and increased likelihood of discharge on any given day reflecting shorter LOS, even after adjustment by multivariable modeling or propensity score–matched analysis. The borderline significant propensity score–matched analysis estimate was most likely due to a smaller sample size and consequently wider CI.

ID consultation was associated with increased adherence to quality of care measures including repeat blood culture, echocardiography, appropriate empiric antibiotic therapy, and duration of antibiotic therapy in our study. In past studies, these quality of care measures have independently or in combination

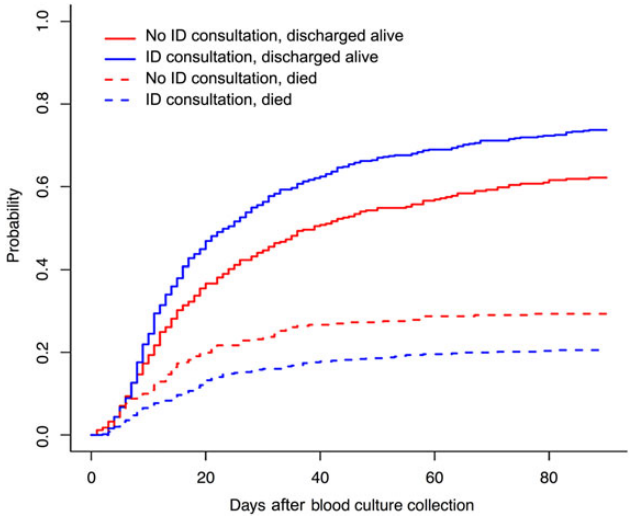

Figure 2. Unadjusted cumulative incidence curves for discharge and in-hospital mortality of patients in the infectious disease (ID) consultation group and patients in the no ID consultation group.

Table 6. Baseline Patient Characteristics and *Staphylococcus aureus* Bacteremia Clinical Characteristics Between Propensity Score–Matched Groups

Variable	ID Consultation (n = 303)	No ID Consultation (n = 303)	Standardized Difference of Mean	Variance Ratio
Age >65 y	144 (48)	156 (51)	0.07927	1.0016
Male sex	202 (67)	189 (62)	0.0898	1.0560
Hospital sites				
Site 1	45 (15)	52 (17)	0.0630	1.1242
Site 2	18 (6)	16 (5)	0.0287	0.8951
Site 3	89 (29)	95 (31)	0.0431	1.0375
Site 4	61 (20)	50 (17)	0.0940	0.8569
Site 5	48 (16)	40 (13)	0.0750	0.8595
Site 6	42 (14)	50 (17)	0.0736	1.1540
Admitting service				
ICU	50 (17)	55 (18)	0.0436	1.0783
Medical	191 (63)	193 (64)	0.0137	0.9924
Surgical	62 (20)	55 (18)	0.0586	0.9129
Healthcare setting				
Community acquired	94 (31)	82 (27)	0.0873	0.9224
Healthcare associated	107 (35)	105 (35)	0.0138	0.9913
Nosocomial	102 (34)	116 (38)	0.0964	1.0580
Intravenous drug use	14 (5)	17 (6)	0.0450	1.2017
Comorbidity				
High-risk cardiac condition	24 (8)	21 (7)	0.0378	0.8844
Intermediate-risk cardiac condition	7 (2)	6 (2)	0.0228	0.8600
Myocardial infarction	51 (17)	52 (17)	0.0088	1.0156
Congestive heart failure	57 (19)	67 (22)	0.0819	1.1277
Peripheral vascular disease	21 (7)	19 (6)	0.0266	0.9112
Chronic pulmonary disease	30 (10)	24 (8)	0.0695	0.8176
Connective tissue disease	9 (3)	9 (3)	0.0000	1.0000
Chronic kidney disease	60 (20)	69 (23)	0.0726	1.1074
Hemodialysis	32 (11)	36 (12)	0.0418	1.1084
Peritoneal dialysis	3 (1)	4 (1)	0.0309	1.3289
Diabetes	97 (32)	85 (28)	0.0865	0.9273
Malignancy	89 (29)	78 (26)	0.0813	0.9215
Liver cirrhosis	18 (6)	21 (7)	0.0404	1.1544
Immune suppression	65 (21)	67 (22)	0.0160	1.0221
MRSA	50 (17)	53 (17)	0.0264	1.0474
At presentation (within 24 h)				
Fever	192 (63)	188 (62)	0.0273	1.0145
Hypotensive shock	79 (26)	86 (28)	0.0520	1.0546
Renal insufficiency	64 (21)	69 (23)	0.0399	1.0556
Early SAB infectious foci preceding or within 2 d of blood culture				
Intravascular catheter	52 (17)	55 (18)	0.0260	1.0450
Skin and soft tissue	43 (14)	37 (12)	0.0585	0.8803
Respiratory	50 (17)	61 (20)	0.0940	1.1670
Bone and joint	19 (6)	14 (5)	0.0728	0.7498
Abscess	13 (4)	9 (3)	0.0706	0.7019
Endocarditis	14 (5)	9 (3)	0.0864	0.6540
Urinary tract	21 (7)	29 (10)	0.0961	1.3418
Other foci	29 (10)	21 (7)	0.0961	0.7453
Unknown foci	116 (38)	113 (37)	0.0204	0.9898
Embolic stroke within 2 d	9 (3)	6 (2)	0.0638	0.6735

Data are presented as No. of patients (%) unless specified otherwise.

Abbreviations: ICU, intensive care unit; ID, infectious disease; MRSA, methicillin-resistant *Staphylococcus aureus*; SAB, *Staphylococcus aureus* bacteremia.

Table 7. Management of *Staphylococcus aureus* Bacteremia in Propensity Score–Matched Infectious Disease (ID) Consultation and No ID Consultation Groups

Procedure	ID Consultation (n = 303)	No ID Consultation (n = 303)	*P* Value
Echocardiography			
Any echo in hospital	223 (74)	170 (56)	<.0001
TTE in hospital	210 (69)	165 (54)	.0002
TEE in hospital	51 (17)	32 (11)	.0330
TTE and TEE in hospital	38 (13)	27 (9)	.1889
Repeat blood culture			
Repeat culture in 2–4 d	124 (41)	94 (31)	.0140
Repeat culture in hospital	197 (65)	175 (58)	.0796
Antibiotics treatment			
Appropriate empiric antibiotic therapy	279 (92)	262 (86)	.0350
Time to appropriate antibiotics, d, median (IQR)[a]	1.00 (0.00–2.00)	1.00 (0.00–2.00)	.7582
Days of appropriate antibiotics[a]	22.00 (13.50–35.00)	14.00 (7.00–27.25)	<.0001

Data are presented as No. of patients (%) unless specified otherwise.

Abbreviations: ID, infectious disease; IQR, interquartile range; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram.

[a] Data available for 571 patients: 295 in the ID consultation group; 276 in the no ID consultation group.

been associated with better outcomes [6, 21, 35]. Improvement in outcome due to ID consultation is most likely multifactorial. It would be difficult to discern the effect of each ID consultation–resultant change in management on outcome due to relation of one management factor with other management, ID consultation, patient characteristics, survival time, and outcome. Similar speculation of the causal pathway from specialist involvement to changes in management to outcome has been described previously [12–15].

Our study showed ID consultation being associated with an approximately 30% decrease in in-hospital mortality, less than the estimate of 31%–82% in previous studies [16–21, 23, 24, 26–28]. This difference may be due to numerous reasons. First, we excluded patients who died within 2 days of blood culture. These patients with early death would be less likely to receive an ID consultation and thus increase the difference in mortality between IDC and NIDC patients. Besides our study, only 5 other studies excluded patients who died within ≥2 days of blood culture [19, 21, 23, 24, 28]. Second, our endpoint was in-hospital mortality, whereas other studies used different outcomes such as all-cause mortality and mortality at different time points [18–21, 23, 26, 27]. Third, the overall in-hospital mortality in our study was 24%, which was slightly higher than some studies [16–21, 23, 24, 27]. In contrast to these studies, the higher mortality in our study could be attributed to patients being older and inclusion of community centers. Still, our in-hospital mortality rate was very close to SAB case fatality in a Canadian study [5]. Last, our study included 847 patients, whereas the largest past study included 699 cases from 603 patients [26]. Our larger sample size increases the precision of our estimate.

Our study demonstrates that ID consultation is associated with increased likelihood of repeat blood culture, echocardiography, appropriate empiric antibiotic therapy, and longer duration of antibiotics. These findings were similar to other studies [1, 16–22, 24, 28]. Catheter removal in CVC infections was similar in IDC and NIDC groups, most likely due to it being a widely accepted standard in SAB management. Although not statistically significant, IDC patients had a slightly lower CVC removal rate compared to NIDC patients. Although we did not collect data on tunneled catheters, we speculate that IDC patients who did not have their catheters removed most likely had tunneled catheter where catheter salvage may be attempted, because 6 of 14 (43%) patients in the IDC group with CVC infection without catheter removal had ongoing hemodialysis or chemotherapy. In contrast, 1 of 7 (13%) patients with CVC infection in the NIDC group without catheter removal had ongoing hemodialysis or chemotherapy. Besides catheter removal, ID consultation increased the likelihood of removal of other infectious foci in our study. Unfortunately, penicillin allergy data were incomplete in our study, so we could not evaluate use of β-lactams for MSSA bacteremia as a quality of care measure. Also, we did not collect information on ID recommendation of penicillin skin testing and desensitization for patients with penicillin allergy.

In our multivariable modeling of in-hospital mortality, significant or borderline risk factors for mortality included older age; hospital sites; nosocomial healthcare setting; no intravenous drug use; chronic kidney disease; absence of fever, shock, endocarditis, respiratory infection, and embolic stroke; and no ID consultation. Besides hospital sites and ID consultation, the

aforementioned predictors were described as significant predictors of mortality in past studies [36–39].

This study has several strengths. To our knowledge, our study is the largest study examining the impact of ID consultation on SAB outcomes. The study was conducted across both academic and community hospitals, enhancing its generalizability. The relationship of ID consultation to in-hospital mortality was confirmed using 2 different approaches of multivariable modeling and propensity score–matched analysis, thereby yielding a more robust result. Last, unlike other studies, we used in-hospital mortality in a competing risk model as an outcome. In-hospital mortality was more likely to be affected by ID consultation and consequent change in management that all occurred in hospital. Following discharge from hospital, many factors such as follow-up and patient compliance with treatment may affect mortality. Therefore, mortality after hospital discharge may be less likely due to ID consultation that occurred in hospital. The competing risk model can assess and account for both in-hospital mortality and time to discharge, giving a comprehensive and clinically relevant interpretation of both outcomes [40].

This study also had several limitations. First, the study used data from a retrospective medical records review. However, rigorous and consistent data collection and verification ensured that our data were of high quality and nearly complete. Second, informal curbside ID specialist consultation was not documented in our database. If that were the case, the misclassification would make the 2 groups more similar and the results more conservative in our study. Third, selection bias could be present. ID consultation was most likely to be nonrandom and based on patients' clinical presentation and prognosis. However, ID consultation most likely selected for more severe disease and poorer prognosis, which decreased likelihood of finding a positive effect of ID consultation. To minimize this selection bias, we adjusted for patient and SAB baseline characteristics using multivariable modeling and propensity score matching in our analysis.

Our study adds to a growing body of evidence suggesting that ID consultation optimizes management and improves outcomes in SAB. However, a significant proportion of individuals do not receive ID consultation. A future challenge will be to ensure that all patients benefit from this expert advice and improved care. Considering ID consultation as an intervention, our study shows an unadjusted 8.8% absolute risk reduction of in-hospital mortality, which equates to a number needed to treat of roughly 11. This number needed to treat suggests substantial benefits from mandatory ID consultation, which could be implemented in hospital policies to enhance patient care. A prospective clinical trial is needed to study whether such policies would deliver the anticipated results based on our study and those previously published.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Acknowledgments. This project was performed in collaboration with the Toronto Antimicrobial Stewardship Corridor. We are indebted to Pamilla Cheema, Bin Chen, Karol Sitarski, Bruce Tugwood, Bonnie Chi Thieu, Mei Shi, and Rochelle Liem for their assistance with data collection and verification.

Financial support. The Mount Sinai Hospital Antimicrobial Stewardship Program was supported by an unrestricted educational grant from Pfizer Canada from 2010 to 2012, which partially supported the salary of a research coordinator (M. St.). A. D. B. is funded by a Mount Sinai Hospital Department of Medicine Summer Studentship Award. A. M. M. receives partial salary support for his antimicrobial stewardship activities from Mount Sinai Hospital and University Health Network. C. M. B. is supported by a CIHR/CPSI Chair in Patient Safety and Continuity of Care.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Jenkins TC, Price CS, Sabel AL, Mehler PS, Burman WJ. Impact of routine infectious diseases service consultation on the evaluation, management, and outcomes of *Staphylococcus aureus* bacteremia. Clin Infect Dis **2008**; 46:1000–8.
2. Wyllie DH, Crook DW, Peto TE. Mortality after *Staphylococcus aureus* bacteraemia in two hospitals in Oxfordshire, 1997–2003: cohort study. BMJ **2006**; 333:281.
3. Chang FY, MacDonald BB, Peacock JE Jr, et al. A prospective multicenter study of *Staphylococcus aureus* bacteremia: incidence of endocarditis, risk factors for mortality, and clinical impact of methicillin resistance. Medicine (Baltimore) **2003**; 82:322–32.
4. Kaech C, Elzi L, Sendi P, et al. Course and outcome of *Staphylococcus aureus* bacteraemia: a retrospective analysis of 308 episodes in a Swiss tertiary-care centre. Clin Microbiol Infect **2006**; 12:345–52.
5. Laupland KB, Ross T, Gregson DB. *Staphylococcus aureus* bloodstream infections: risk factors, outcomes, and the influence of methicillin resistance in Calgary, Canada, 2000–2006. J Infect Dis **2008**; 198:336–43.
6. Fowler VG Jr, Sanders LL, Sexton DJ, et al. Outcome of *Staphylococcus aureus* bacteremia according to compliance with recommendations of infectious diseases specialists: experience with 244 patients. Clin Infect Dis **1998**; 27:478–86.
7. Mermel LA, Farr BM, Sherertz RJ, et al. Guidelines for the management of intravascular catheter-related infections. Clin Infect Dis **2001**; 32:1249–72.
8. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis **2009**; 49:1–45.
9. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children: executive summary. Clin Infect Dis **2011**; 52:285–92.
10. Kim SH, Kim KH, Kim HB, et al. Outcome of vancomycin treatment in patients with methicillin-susceptible *Staphylococcus aureus* bacteremia. Antimicrob Agents Chemother **2008**; 52:192–7.

11. Schweizer ML, Furuno JP, Harris AD, et al. Comparative effectiveness of nafcillin or cefazolin versus vancomycin in methicillin-susceptible *Staphylococcus aureus* bacteremia. BMC Infect Dis **2011**; 11:279.
12. Harel Z, Wald R, Bargman JM, et al. Nephrologist follow-up improves all-cause mortality of severe acute kidney injury survivors. Kidney Int **2013**; 83:901–8.
13. Ayanian JZ, Landrum MB, Guadagnoli E, Gaccione P. Specialty of ambulatory care physicians and mortality among elderly patients after myocardial infarction. N Engl J Med **2002**; 347:1678–86.
14. Ezekowitz JA, van Walraven C, McAlister FA, Armstrong PW, Kaul P. Impact of specialist follow-up in outpatients with congestive heart failure. CMAJ **2005**; 172:189–94.
15. Sharma G, Kuo YF, Freeman JL, Zhang DD, Goodwin JS. Outpatient follow-up visit and 30-day emergency department visit and readmission in patients hospitalized for chronic obstructive pulmonary disease. Arch Intern Med **2010**; 170:1664–70.
16. Rieg S, Peyerl-Hoffmann G, de With K, et al. Mortality of *S. aureus* bacteremia and infectious diseases specialist consultation—a study of 521 patients in Germany. J Infect **2009**; 59:232–9.
17. Lahey T, Shah R, Gittzus J, Schwartzman J, Kirkland K. Infectious diseases consultation lowers mortality from *Staphylococcus aureus* bacteremia. Medicine (Baltimore) **2009**; 88:263–7.
18. Nagao M, Iinuma Y, Saito T, et al. Close cooperation between infectious disease physicians and attending physicians can result in better management and outcome for patients with *Staphylococcus aureus* bacteraemia. Clin Microbiol Infect **2010**; 16:1783–8.
19. Honda H, Krauss MJ, Jones JC, Olsen MA, Warren DK. The value of infectious diseases consultation in *Staphylococcus aureus* bacteremia. Am J Med **2010**; 123:631–7.
20. Choi SH, Cho SY, Park JH, Chung JW. Impact of infectious-disease specialist consultations on outcomes of *Staphylococcus aureus* bacteremia in a hospital with a low volume of patients with *S. aureus* bacteremia. J Infect **2011**; 62:181–5.
21. Robinson JO, Pozzi-Langhi S, Phillips M, et al. Formal infectious diseases consultation is associated with decreased mortality in *Staphylococcus aureus* bacteraemia. Eur J Clin Microbiol Infect Dis **2012**; 31:2421–8.
22. Pragman AA, Kuskowski MA, Abraham JM, Filice GA. Infectious disease consultation for *Staphylococcus aureus* bacteremia improves patient management and outcomes. Infect Dis Clin Pract (Baltim Md) **2012**; 20:261–7.
23. Forsblom E, Ruotsalainen E, Ollgren J, Jarvinen A. Telephone consultation cannot replace bedside infectious disease consultation in the management of *Staphylococcus aureus* bacteremia. Clin Infect Dis **2013**; 56:527–35.
24. Fries BL, Licitra C, Crespo A, et al. Infectious diseases consultation and the management of *Staphylococcus aureus* bacteremia. Clin Infect Dis **2014**; 58:598–9.
25. Mylotte JM, Tayara A. *Staphylococcus aureus* bacteremia: predictors of 30-day mortality in a large cohort. Clin Infect Dis **2000**; 31:1170–4.
26. Pastagia M, Kleinman LC, Lacerda de la Cruz EG, Jenkins SG. Predicting risk for death from MRSA bacteremia. Emerg Infect Dis **2012**; 18:1072–80.
27. Isobe M, Uejima E, Seki M, et al. Methicillin-resistant *Staphylococcus aureus* bacteremia at a university hospital in Japan. J Infect Chemother **2012**; 18:841–7.
28. Tissot F, Calandra T, Prod'hom G, et al. Mandatory infectious diseases consultation for MRSA bacteremia is associated with reduced mortality. J Infect **2014**; 69:226–34.
29. Holland TL, Arnold C, Fowler VG Jr. Clinical management of *Staphylococcus aureus* bacteremia: a review. JAMA **2014**; 312:1330–41.
30. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 17th ed. Wayne, PA: CLSI, **2007**.
31. Friedman ND, Kaye KS, Stout JE, et al. Health care–associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med **2002**; 137:791–7.
32. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation **2007**; 116:1736–54.
33. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis **2000**; 30:633–8.
34. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Amer Stat Assoc **1999**; 94:496–509.
35. Chong YP, Moon SM, Bang KM, et al. Treatment duration for uncomplicated *Staphylococcus aureus* bacteremia to prevent relapse: analysis of a prospective observational cohort study. Antimicrob Agents Chemother **2013**; 57:1150–6.
36. van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Paterson DL, Gosbell IB. Predictors of mortality in *Staphylococcus aureus* bacteremia. Clin Microbiol Rev **2012**; 25:362–86.
37. McClelland RS, Fowler VG Jr, Sanders LL, et al. *Staphylococcus aureus* bacteremia among elderly vs younger adult patients: comparison of clinical features and mortality. Arch Intern Med **1999**; 159:1244–7.
38. Ruotsalainen E, Sammalkorpi K, Laine J, et al. Clinical manifestations and outcome in *Staphylococcus aureus* endocarditis among injection drug users and nonaddicts: a prospective study of 74 patients. BMC Infect Dis **2006**; 6:137.
39. Fowler VG Jr, Olsen MK, Corey GR, et al. Clinical identifiers of complicated *Staphylococcus aureus* bacteremia. Arch Intern Med **2003**; 163:2066–72.
40. Brock GN, Barnes C, Ramirez JA, Myers J. How to handle mortality when investigating length of hospital stay and time to clinical stability. BMC Med Res Methodol **2011**; 11:144.