Automated Alerts Coupled with Antimicrobial Stewardship Intervention Lead to Decreases in Length of Stay in Patients with Gram-Negative Bacteremia

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ORIGINAL ARTICLE

Automated Alerts Coupled with Antimicrobial Stewardship Intervention Lead to Decreases in Length of Stay in Patients with Gram-Negative Bacteremia

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OBJECTIVE. To assess the impact of active alerting of positive blood culture data coupled with stewardship intervention on time to appropriate therapy, length of stay, and mortality in patients with gram-negative bacteremia.

DESIGN. Quasi-experimental retrospective cohort study in patients with gram-negative bacteremia at the Detroit Medical Center from 2009 to 2011.

SETTING. Three hospitals (1 community, 2 academic) with active antimicrobial stewardship programs within the Detroit Medical Center.

PATIENTS. All patients with monomicrobial gram-negative bacteremia during the study period.

INTERVENTION. Active alerting of positive blood culture data coupled with stewardship intervention (2010–2011) compared with patients who received no formalized stewardship intervention (2009).

RESULTS. Active alerting and intervention led to a decreased time to appropriate therapy (8 [interquartile range (IQR), 2–24] vs 14 [IQR, 2–35] hours; $P = .014$) in patients with gram-negative bacteremia. After controlling for differences between groups, being in the intervention arm was associated with an independent reduction in length of stay (odds ratio [OR], 0.73 [95% confidence interval (CI), 0.62–0.86]), correlating to a median attributable decrease in length of stay of 2.2 days. Additionally, multivariate modeling of patients who were not on appropriate antimicrobial therapy at the time of initial culture positivity showed that patients in the intervention group had a significant reduction in both length of stay (OR, 0.76 [95% CI, 0.66–0.86]) and infection-related mortality (OR, 0.24 [95% CI, 0.08–0.76]).

CONCLUSIONS. Active alerting coupled with stewardship intervention in patients with gram-negative bacteremia positively impacted time to appropriate therapy, length of stay, and mortality and should be a target of antimicrobial stewardship programs.

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The primary focus of antimicrobial stewardship programs is to optimize outcomes in patients with infections through effective antimicrobial therapy.[1] Electronic data capture systems have the ability to greatly enhance stewardship programs via communication of real-time, important data to stewardship personnel and other healthcare professionals.

One way that alerts have the potential to optimize patient outcomes is by improving the time to appropriate therapy for patients with gram-negative bacteremia. Time to appropriate therapy is one of the most important modifiable risk factors for mortality in patients with gram-negative bacteremia.[2,3] Among patients with septic shock, every hour of delay in appropriate therapy decreases survival rates by 7.6%.[4]

With the rise in multidrug-resistant gram-negative bacteria—including multidrug-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Acinetobacter baumannii*, and extended-spectrum β-lactamase-producing and carbapenem-resistant enterobacteriaceae—interventions by stewardship team members as soon as culture results become available or are updated have the potential to significantly improve the time to appropriate therapy and patient outcomes.

The primary objective of this analysis was to analyze the

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impact of active alerting coupled with intervention by stewardship pharmacists on the time to appropriate therapy among patients with gram-negative bacteremia. Secondary objectives included determining the impact of the alerting process on length of stay and the incidence of infection-related and 30-day mortality.

METHODS

Study Setting and Design

This retrospective cohort study was performed at 3 hospitals, including 1,100 beds (Detroit Receiving Hospital, Harper University Hospital, and Sinai-Grace Hospital) within the Detroit Medical Center. Each hospital had an antimicrobial stewardship program during the entire study period, with the daily activities led by a stewardship pharmacist. The Detroit Medical Center has a central microbiology laboratory, which analyzed all study specimens. In April 2010, the Detroit Medical Center implemented clinical decision support software (TheraDoc) with alerting capabilities for infection control and antimicrobial stewardship purposes. This study was approved by the institutional review boards of the Detroit Medical Center and Wayne State University.

Patient Selection

Nonintervention group patients consisted of patients with gram-negative bacteremia in the calendar year 2009, before implementation of TheraDoc (Figure 1). At this time, there was no uniform real-time method by which the stewardship pharmacists were alerted to patients with positive blood cultures for gram-negative bacilli or to updates of preliminary culture results (eg, when a gram-negative bacilli is updated to nonlactose fermenter, oxidase negative). Stewardship activities during this time frame were largely limited to prospective audit and feedback driven by daily antibiotic reports. Intervention group patients consisted of patients with gram-negative bacteremia from November 2010 to July 2011. During this time period, antimicrobial stewardship pharmacists at each site received automated pages to their pager when blood cultures became positive for gram-negative bacilli and when results were updated. The pages were received during normal work hours (Monday–Friday, 0800–1700 hours). When alerted, stewardship pharmacists analyzed pertinent parts of the medical record of the patients, including past medical history, recent antimicrobial exposures, presenting symptoms, hospital location, and history of multidrug-resistant pathogens. Afterward, the stewardship pharmacists contacted the physician of record and recommended, when appropriate, changes to the antimicrobial regimen, including implementation of antimicrobials to provide or enhance gram-negative coverage, including multidrug-resistant pathogens, and de-escalation of antimicrobial therapy. When culture results were updated off shift and/or on weekends, the results were automatically e-mailed to the pharmacist, who reviewed them upon returning to work. While unit clerks received notification from the microbiology laboratory when cultures initially turned positive for gram-negative bacilli, there was no formal process for getting that information to treating physicians. Additionally, there were no notifications when culture reports were updated as described above. Patients were excluded from the study if they had a polymicrobial bacteremia or infection at any site that warranted

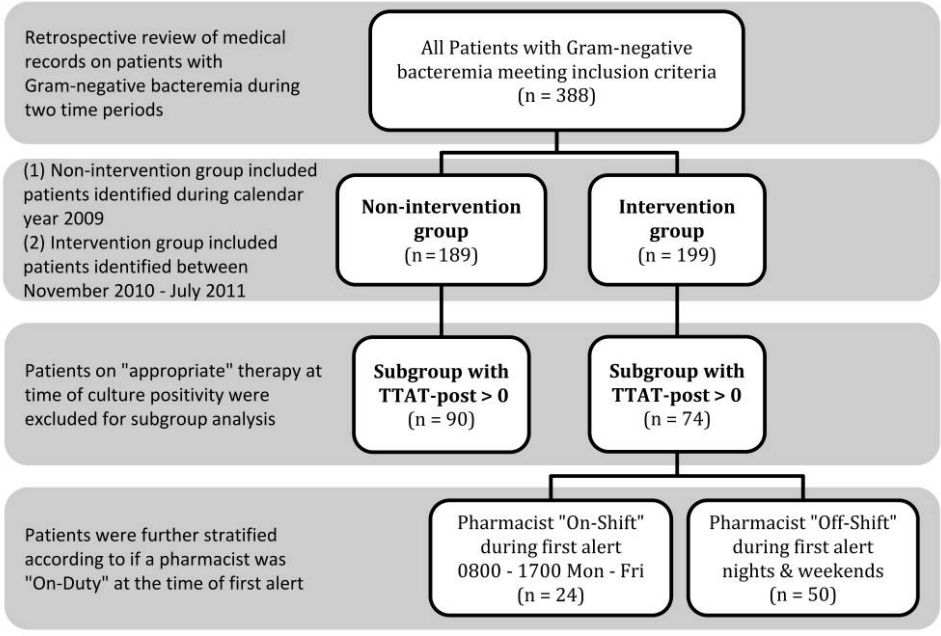

FIGURE 1. Description of the study population. TTAT, time to appropriate therapy.

gram-positive or antifungal therapy. Patients were excluded if they died or were discharged prior to the blood culture becoming initially positive.

Baseline Prescribing Characteristics at the Detroit Medical Center

The Detroit Medical Center has a centralized antimicrobial stewardship committee that develops empiric therapy recommendations for commonly encountered disease states (eg, urinary tract infection, community-acquired pneumonia, hospital-acquired pneumonia/healthcare-associated pneumonia/ventilator-associated pneumonia), and these recommendations are detailed to prescribers via educational sessions. Empiric therapy, in accordance with these guidelines, is promoted through order sets. However, prescribers are ultimately free to select any nonrestricted antimicrobial for a given disease state. Restricted antimicrobials with extended gram-negative activity (ie, carbapenems, tigecycline, colistimethate sodium) require approval by the infectious diseases or antimicrobial stewardship team. Baseline rates of resistance to workhorse agents used as gram-negative therapies (ie, ceftriaxone in *Escherichia coli* and *Klebsiella pneumoniae*, cefepime in *P. aeruginosa*) are roughly 20% throughout the Detroit Medical Center.

Study Measures and Definitions

Two different measures of time to appropriate therapy were analyzed. Time to appropriate therapy 1 (TTAT-pre) was defined as the time from when the culture was drawn to the time that the patient received an antimicrobial with in vitro activity against the causative organism. Time to appropriate therapy 2 (TTAT-post) was defined as the time from when the culture initially was reported as positive for gram-negative bacilli until the time that the patient received an antimicrobial with in vitro activity against the causative organism. For the purposes of this analysis, therapy was considered appropriate if it had in vitro activity against pathogens, regardless of whether the dose was optimized.

Length of stay was defined as length of stay following the onset of gram-negative bacteremia, after excluding patients who died in the hospital. Infection-related mortality was defined as mortality occurring among patients for whom the physician of record stated in the medical record that infection was the reason for death.

Subgroup Analyses

Two a priori subgroup analyses were performed. The first analyzed outcome measures among patients who were not on appropriate empiric therapy at the time that the blood culture first became positive for gram-negative bacilli (in these patients, TTAT-post was greater than 0). The second analyzed patients in the intervention group with TTAT-post greater than 0 and analyzed outcome measures as a function of whether stewardship pharmacists were on shift (Monday–Friday, 0800–1700 hours) or off shift (all other times; Figure 1).

Statistics and Analysis

All analyses were performed using SAS software (ver. 9.3; SAS Institute). Bivariate analyses were conducted using a Student *t* test or Wilcoxon rank sum test for continuous variables and a Fisher exact or χ^2 test for dichotomous variables. Percentages displayed are the valid percent, which indicates the percent excluding the missing data from the denominator, unless otherwise stated. If there was a significant association between the intervention and an outcome in bivariate analysis, multivariate modeling was performed to determine the independent impact of the intervention on the outcome. Multivariate modeling was conducted using logistic regression for mortality and linear regression for length of stay. The inverse log

TABLE 1. Bacteremia Pathogens

	Overall (n = 412)	Nonintervention group (n = 202)	Intervention group (n = 210)	P
Escherichia coli	168 (41)	71 (35)	97 (46)	.03
Klebsiella pneumoniae	70 (17)	37 (18)	33 (16)	.51
Pseudomonas aeruginosa	28 (7)	13 (6)	15 (7)	.92
Enterobacter cloacae	20 (5)	13 (6)	7 (3)	.21
Proteus mirabilis	26 (6)	9 (4)	17 (8)	.006
Acinetobacter baumannii	19 (5)	13 (6)	6 (3)	.10
Morganella morganii	6 (1)	3 (1)	3 (1)	1.0
Citrobacter spp.	4 (1)	1 (1)	3 (1)	.62
Serratia spp.	14 (3)	8 (4)	6 (3)	.59
Bacteroides spp.	18 (4)	13 (6)	5 (2)	.05
Other[a]	39 (9)	21 (10)	18 (9)	.64

NOTE. Data are no. (%).

[a] Includes *Enterobacter* spp., *Prevotella* spp., *Klebsiella oxytoca*, *Neisseria meningitidis*, *Acinetobacter* spp., *Achromobacter* spp., *Pantoea* spp., *Stenotrophomonas maltophilia*, *Salmonella* spp., and *Proteus* spp.

TABLE 2. Baseline Demographics of Study Patients

	Nonintervention group (n = 189)	Intervention group (n = 199)	P
Age, mean ± SD, years	61.6 ± 19.1	62.7 ± 17.2	.57
Sex, female	105 (56)	91 (46)	.05
Race, African American	157 (83)	171 (86)	.64
Chronic kidney disease	46 (24)	93 (47)	<.001
Chronic obstructive pulmonary disease	30 (16)	56 (28)	.004
Hemodialysis	21 (11)	22 (11)	.99
Diabetes	58 (15)	71 (18)	.30
Neutropenia	8 (4)	3 (2)	.11
Pitt bacteremia score	2 (1–3)	2 (0–3)	.98
Charlson score	4 (1–6)	6 (4–9)	<.001
ICU stay at time of onset of bacteremia	71 (38)	52 (26)	.02
Source of bacteremia			
Urine	80 (42)	107 (54)	.04
Catheter related	23 (12)	22 (11)	.86
Pneumonia	31 (16)	16 (8)	.01
Intra-abdominal	25 (13)	21 (11)	.51
Other	30 (15)	33 (16)	1.0

NOTE. Data are no. (%), unless otherwise indicated. ICU, intensive care unit; SD, standard deviation.

value (reported as odds ratios [ORs]) was calculated for β coefficients of variables included in the model for length of stay. Variables were considered for model inclusion if P = .10 in bivariate analysis, comparing the intervention with the nonintervention group. If a covariate affected the β coefficient of a variable in the model by more than 10%, then the confounding variable was left in the model. Two-sided $P < .05$ was considered statistically significant.

RESULTS

Overview of the Cohort

A total of 388 patients were included, with a mean age of 62.2 years. Fifty-one percent were female, and 85% were African American. Thirty-two percent of patients were in the intensive care unit at the time of bacteremia. Urine (48%) was the primary source of infection. The most common causative pathogens were *E. coli* (41%), *K. pneumoniae* (17%), and *P. aeruginosa* (7%; Table 1).

There were 189 intervention group patients and 199 nonintervention group patients. Patients in the nonintervention group were more likely to be female, be located in the intensive care unit at the time of bacteremia, and have a pulmonary source of bacteremia. Patients in the nonintervention group were less likely to have chronic kidney disease, chronic obstructive pulmonary disease, and a urinary source of bacteremia. Nonintervention group patients were less likely to have *E. coli* as a bacteremia pathogen (Table 2).

Outcome Measures

Patients in the intervention group had significantly lower median (8 [interquartile range (IQR), 2–24] vs 14 [IQR, 2–35] hours; P = .014) TTAT-pre values than did patients in the nonintervention group (Table 3). Similarly, median (0 [IQR, 0–0] vs 0 [IQR, 0–10] hours; P = .024) TTAT-post values were lower in the intervention group. Patients in the intervention group had a significantly lower median length of stay following onset of the gram-negative bacteremia (7 [IQR, 4–12] vs 8 [IQR, 6–17.5] days; $P < .001$). There was no significant difference between duration of bacteremia, fever, leukocytosis, infection-related mortality, or all-cause 30-day mortality between the groups.

In multivariate analysis, after controlling for intensive care unit status, urinary source, sex, Charlson score, and causative pathogen, being in the intervention arm was associated with a significant reduction in length of stay from onset of bacteremia (0.73-fold reduction [95% confidence interval (CI), 0.62–0.86]; median attributable decrease in length of stay of 2.2 days per patient). The intervention had no significant association with infection-related mortality (OR, 0.67 [95% CI, 0.32–1.37]).

Subgroup of Patients Who Were Not on Appropriate Therapy at the Time of Initial Culture Positivity (TTAT-Post Greater than 0)

A total of 164 (42%) of patients were not on appropriate therapy at the time that the blood culture first was reported as positive for gram-negative bacilli, with 74 (45%) in the intervention group and 90 (55%) in the nonintervention group. Baseline characteristics of these 2 groups were similar except that patients in the intervention group had a higher frequency of chronic kidney disease (46% vs 25%; P = .006), median Charlson score (6 [IQR, 4–8] vs 5 [IQR, 2–6]; P = .002), and a higher incidence of bacteremia secondary to a urinary source (52% vs 37%; P = .04).

TABLE 3. Time to Appropriate Therapy and Clinical Outcomes

	Nonintervention group (n = 189)	Intervention group (n = 199)	P
TTAT-pre, hours	14 (2–35)	8 (2–24)	.01
TTAT-post, hours	0 (0–10)	0 (0–5)	.02
Length of stay[a]	8 (6–17.5)	7 (4–12)	<.001
Fever	1 (1–3)	2 (1–3)	.25
Leukocytosis	3 (1–8)	3 (2–7)	.95
Bacteremia	1 (1–2)	1 (1–1)	.15
Infection-related mortality	26 (14)	22 (11)	.42
30-day mortality	33 (17)	38 (19)	.68

NOTE. Data are median no. of days (interquartile range), unless otherwise indicated. TTAT, time to appropriate therapy.

[a] Following onset of bacteremia, excluding in-hospital deaths.

In this subgroup, patients in the intervention group had a significantly lower median TTAT-pre (27 [IQR, 20–49] vs 32.5 [IQR, 24–73] hours; P = .03) but no reduction in median TTA2 (8 [IQR, 3–31] vs 11 [IQR, 5–44] hours; P = .09) compared with patients in the nonintervention group. Median length of stay following the onset of gram-negative bacteremia was significantly lower in the intervention arm (8 [IQR, 6–13] vs 10 [IQR, 6–22] days; P = .047). There were no differences in duration of fever, bacteremia, leukocytosis, or 30-day mortality. There was also no difference in infection-related mortality (18% vs 9%; P = .13; Table 4).

In order to further evaluate the association between being in the intervention group and length of stay and infection-related mortality, multivariate analyses were performed. After controlling for Charlson score and urinary source, patients in the intervention group had a significant reduction in both length of stay following the onset of bacteremia (OR, 0.76 [95% CI, 0.66–0.86]) and infection-related mortality (OR, 0.24 [95% CI, 0.08–0.76]).

Effect of Stewardship Pharmacists Being on Shift on Outcomes of Patients Who Were Not on Appropriate Therapy at the Time Initial Culture Positivity Was Reported

Of the 74 intervention group patients who were not on appropriate therapy at the time of initial culture positivity, 24 (32%) had cultures become positive when the stewardship pharmacist was on shift, while 50 (68%) became positive when pharmacists were off shift. Baseline characteristics of the 2 patient groups were similar except that patients whose blood cultures turned positive when the pharmacist was off shift had a higher incidence of chronic kidney disease (56% vs 25%; P = .01).

Patients with initial culture positivity reported when the stewardship pharmacists were on shift had a significantly decreased median TTAT-pre (24 [IQR, 18.5–27.5] vs 29 [IQR, 22–57] hours; P = .03) and TTAT-post (3.5 [IQR, 2–5.5] vs 13 [IQR, 5–41] hours; P = .003) compared with patients whose culture became positive off shift. There was no difference in length of stay, duration of bacteremia, or leukocytosis. In bivariate analysis, there was a significant decrease in 30-day mortality (4% vs 24%; P = .05) but no significant decrease in infection-related mortality (0% vs 14%; P = .06). In multivariate analysis, after controlling for Charlson and Pitt bacteremia scores, there was no longer a significant association between stewardship pharmacists being on shift and 30-day mortality (OR, 0.36 [95% CI, 0.03–4.37]).

In order to confirm the role of the intervention in on-shift outcomes, an additional analysis was performed among nonintervention group patients, comparing patients cared for during periods when stewardship pharmacists were on shift to patients cared for when stewardship pharmacists were off shift. There was no difference in TTAT-post among patients whose cultures initially became positive off shift (n = 67) or on shift (n = 23; median TTAT-post of 11 [IQR, 5–46] vs 9 [IQR, 4–44] hours; P = .64).

DISCUSSION

This comprehensive analysis demonstrates the impact of a real-time automated alerting system coupled with response and intervention by an antimicrobial stewardship pharmacist on the management and outcomes of patients with gram-negative bacteremia. In all analyses performed, there were clinically and statistically significant decreases in the time to effective antimicrobial therapy, as measured by both TTAT-pre and TTAT-post. Even more striking was the reduction in length of stay among patients who were cared for when the automated alerting system was in place.

The impact of the alerting system was particularly notable among patients who were not on effective empiric therapy when the culture first was reported to be positive for gram-negative bacilli (ie, TTAT-post greater than 0). In these patients, through rapid initiation of effective antimicrobial therapy, implementation of an alerting system coupled with intervention by a stewardship pharmacist resulted in decreased length of stay and infection-related mortality. Among patients in the intervention group who were not on effective

TABLE 4. Subgroup Analyses

	Outcomes of subgroup with TTAT-post greater than 0 minutes			Intervention group patients with TTAT-post greater than 0		
	Nonintervention group (n = 90)	Intervention group (n = 74)	P	Pharmacist off shift (n = 50)	Pharmacist on shift (n = 24)	P
TTAT-pre, hours	32.5 (24–73)	27 (20–49)	.03	29 (22–57)	24 (18.5–27.5)	.03
TTAT-post, hours	11 (5–44)	8 (3–31)	.09	13 (5–41)	3.5 (2–5.5)	.003
Length of stay[a]	10 (6–22)	8 (6–13)	.047	8 (5–13)	8 (6–13)	.97
Fever	1 (0–3)	2 (1–3)	.53	1 (0–2)	2 (2–3)	.05
Leukocytosis	4 (1–9)	4 (2–8)	.91	4 (1–8)	5 (2–11.5)	.28
Bacteremia	1 (1–2)	1 (1–2)	.92	1 (1–2)	1 (1–2.5)	.78
Infection-related mortality	16 (18)	7 (9)	.13	7 (14)	0 (0)	.06
30-day mortality	18 (20)	13 (18)	.69	12 (24)	1 (4)	.05

NOTE. Data are median no. of days (interquartile range), unless otherwise indicated. TTAT, time to appropriate therapy.
[a] Following onset of bacteremia, excluding in-hospital deaths.

antimicrobial therapy at the time of initial blood culture positivity, TTAT-pre and TTAT-post were reduced by 5.5 and 3 hours, respectively, compared with the baseline group, and length of stay following the onset of bacteremia was reduced by 2.4 days after controlling for differences between the group. Furthermore, when controlling for differences between groups, the intervention was associated with a 416% reduction in infection-related mortality.

During the intervention period, the altering system was acted on only in real time if the culture became positive or was updated when the stewardship team was on shift. Thus, if blood culture positivity occurred when a stewardship pharmacist was off shift, there was often a delay before the stewardship pharmacist responded to the alert (up to 15 hours during the week and 63 hours during the weekend). A subgroup analysis comparing care during the intervention period when stewardship pharmacists were on shift to when stewardship pharmacists were off shift demonstrated a statistically significant median decrease in TTAT-post of almost 10 hours. This is also clinically meaningful, since 30-day mortality was reduced almost 3-fold when stewardship pharmacists were on shift during the intervention period. Although the reduction in 30-day mortality failed to reach statistical significance, the study was not sufficiently powered to adequately address this subgroup. In the nonintervention group, there was no significant difference between TTAT-post in patients whose blood cultures initially became positive when pharmacists were on or off shift, indicating that the impact of the intervention was due to the coupling of the alerting system with having a stewardship pharmacist available to immediately act on results. However, it is important to note that outcomes being worse during off shift periods were likely multifactorial in nature and might not have been adequately controlled for in this analysis. These findings are in accordance with those by Holtzman et al,[5] who reported that the implementation of peptide nucleic acid fluorescence in situ hybridization for rapid identification of coagulase-negative staphylococci in the absence of antimicrobial stewardship intervention did not impact on the duration of vancomycin usage or length of stay.

These data are also consistent with recently published data examining the impact of integration of rapid pathogen identification (via Matrix-assisted laser desorption ionization time of flight [MALDI-TOF]) coupled with stewardship-based interventions on management of gram-negative bacteremia.[6] Among patients who were not on active therapy at the time of initial culture positivity (ie, TTAT-post greater than 0), the authors reported a significant decrease in time to initiation of an active agent in the intervention group. The time to appropriate therapy in the intervention group in our analysis was almost identical to the time previously reported (39 and 36.5 hours, respectively). Interestingly, the prior study also reported significant decreases in both total length of stay and length of stay following the onset of bacteremia. When taken together, these data highlight the impact that real-time information, such as that provided by electronic data capture systems, coupled with active stewardship interventions can have on time to appropriate therapy and length of stay. The current study demonstrates that the time to appropriate therapy and clinical outcomes of bacteremic patients can be significantly impacted even if rapid diagnostics, such as MALDI-TOF, are not available.

This study has several limitations that warrant discussion. The study design was not a randomized controlled study but a quasi-experimental before/after study. Once we had the capability to utilize the alerting system, withholding the system from clinical use in some patients was not considered because of the known importance of time to appropriate therapy on patient outcomes. This type of limitation will continue to be a common characteristic of system-level stewardship studies, since withholding technology and interventions that improve patients' safety in order to conduct controlled studies is not ethical. Second, our institution has TheraDoc, an electronic capture data system that allows real-time information to be automatically sent to stewardship personnel. While such data platforms might not be available in

all institutions, these results are still generalizable to other institutions. Similar mechanisms, such as direct communications between a microbiological technician and the stewardship team, should afford similar opportunities to optimize care by reducing delays in effective antimicrobial therapy. This has been demonstrated previously. Bauer et al[7] were able to decrease the time to optimal therapy, length of stay, and ultimately costs in patients with *Staphylococcus aureus* bacteremia by having stewardship personnel contacted by the microbiology laboratory when culture updates were available. Wong et al[8] reported that antibiotics were able to be discontinued more rapidly when coagulase-negative staphylococci were isolated in blood cultures when stewardship personnel were directly contacted by the microbiology lab.

The use of infection-related mortality in infectious diseases literature is controversial, and cases of death are often multifactorial. Thus, infection-related mortality estimates might not be completely accurate. Also, this retrospective analysis was underpowered to show statistical significance for some clinically important outcomes, most notably the impact of the on-shift status of stewardship pharmacists on clinical outcomes. Furthermore, this study did not analyze the impact of the intervention on the duration and total antibiotic days of broad-spectrum agents during the study period. It is imperative that broad-spectrum empiric antimicrobial therapy is coupled with equally aggressive de-escalation and duration of therapy processes in order to limit the emergence of antimicrobial resistance. Finally, we did not analyze costs associated with this intervention. The cost effectiveness of stewardship interventions has been described in previous literature;[6,9-11] however, future analyses should determine the cost effectiveness of implementing an automated alerting system and providing resources to keep stewardship pharmacists on shift 24 hours a day and 7 days a week.

This study demonstrates the value and impact of the implementation of an automated alerting system coupled with rapid response by antimicrobial stewardship pharmacists on the outcomes of patients with gram-negative bacteremia. As antimicrobial resistance continues to emerge and spread and as hospitals are increasingly measured on quality of care, a strong case can be made for implementation of an automated alerting system to provide real-time data to stewardship pharmacists and/or physicians. Furthermore, the coupling of this type of alerting system with the provision of on-shift stewardship pharmacists 24 hours a day and 7 days a week to review, interpret, and act upon data should be analyzed from clinical and cost effectiveness perspectives.

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