Evaluation of the impact of a pharmacist-run antimicrobial report in reducing delays in subsequent antibiotic administration in patients in the emergency department

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Purpose: To determine whether the implementation of a pharmacist-run, real-time electronic health record (EHR) antimicrobial report reduces the frequency of delays in subsequent antibiotic medication administration timing in patients in the emergency department (ED).

Methods: A single-center, retrospective, pre-and-post quasi-experimental study was conducted between July and December 2021 following the implementation of an antimicrobial EHR report of adult patients presenting to the ED who were continued on antibiotic therapy after receiving a one-time dose of an antibiotic in the ED. The primary objective was to determine the impact of the pharmacist-run, real-time EHR antibiotic dosing report in the ED on reducing the number of major delays in subsequent antibiotic administration times. A subanalysis of the primary outcome was performed to evaluate differences in major delays based on specific dosing intervals of 6, 8, and 12 hours.

Results: A total of 521 subsequent antibiotic dosing orders from 273 patient encounters were analyzed, with major delays in subsequent antibiotic dosing administration times identified in 20% of the intervention group compared to 27% of the control group ($P = 0.047$). Major delays were also significantly decreased in the intervention group compared to the control group for antibiotics dosed at 8-hour intervals (18% vs 32%; $P = 0.026$). No significant difference in delays was observed between the groups for antibiotics dosed at 6-hour intervals (18% vs 27%) or 12-hour intervals (29% vs 21%).

Conclusion: Implementing a real-time EHR antimicrobial report run by pharmacists in the ED was associated with significantly fewer major delays in subsequent antibiotic dosing following a first dose.

Keywords: antibiotic administration delays, boarding, emergency department, emergency medicine pharmacist, pharmacovigilance

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Antibiotics are among the most commonly prescribed medications in the emergency department (ED), and timely administration of these agents has been proven to be crucial.[1,2] The Surviving Sepsis Campaign (SSC) strongly suggests administration of antibiotics within 1 hour of diagnosis of sepsis or septic shock due to the association of each hour of delay with an increase in mortality.[3] A systematic review found that hospitalized patients with severe bacterial infections who experienced delays in appropriate antimicrobial therapy had a significantly higher mortality rate than those without delays.[4] While the SSC focuses heavily on time to first antibiotic dose, there is no mention of the importance of subsequent dosing. To date, few studies have evaluated the impact of antibiotic redosing delays on clinical outcomes such as mortality, length of stay, and mechanical ventilation. In a retrospective analysis of 1,075

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patients with severe sepsis or septic shock, 31% of patients had delayed administration of a second dose of antibiotics. The investigators identified an association of increased odds of delay with ED boarding and shorter dosing intervals, but delays were not associated with any increase in mortality.[5] Another retrospective analysis demonstrated significant delays in timing of the second dose of antibiotics in 33% of cases, and these delays were associated with increased mortality and a need for mechanical ventilation. The authors identified antibiotics with more frequent dosing (every 6 to 8 hours) and ED boarding at the time of the second dose as factors associated with delay.[6] Another study specifically evaluated the in-hospital mortality of patients admitted from the ED who received delayed second-dose antibiotic administration and the risk factors associated with these delays. Delays occurred in 21% of patients and were associated with increased odds of in-hospital mortality. ED boarding for more than 4 hours was identified as a risk factor for these delays.[7] A more recent retrospective study found no difference in the incidence of second-dose antibiotic delays in ED patients admitted with sepsis who had an ED length of stay of less than 6 hours (30.3%) compared to those with an ED length of stay of more than 6 hours (24.1%). In-hospital mortality was numerically higher, but not statistically significantly so, in patients with redosing delays compared to those without such delays (18.9% vs 8.8%).[8] While these studies reported conflicting results, each study found that delays in second-dose administration were common, especially in patients boarding in the ED.[5-8]

ED boarding is defined as a patient who is admitted or placed into an observation status but remains physically in the ED due to low or nonexistent availability of bed space. With ED boarding times becoming a rising concern, there is a need for continuity and standardization of care in antimicrobial redosing.[9] Data support negative clinical outcomes, such as in-hospital mortality, medication delays, medication errors, and increased lengths of stay, with increased ED boarding times.[10-14] A large retrospective study found increased odds of hospital mortality when antibiotic doses were delayed by 1.5 to 2 hours or by 2 to 2.5 hours in ED patients with suspected sepsis.[15] Although increased ED boarding times have been associated with major delays in subsequent antibiotic dosing, few strategies have been identified to combat such delays.

Clinical pharmacist presence and involvement in the ED has been shown not only to promote early and appropriate antimicrobial therapy, but also to decrease the time to administration of intravenous antibiotics for septic patients.[16-20] Recent data support the expansion of emergency medicine (EM) pharmacists' scope of practice to allow the reordering of continued antibiotic therapy for patients boarding in the ED as a means to decrease major delays in therapy, and this study also found a significantly lower incidence of in-hospital mortality following expansion of the pharmacist scope of practice.[21] Instead of expanding the scope of practice of pharmacists at our instution, we developed a real-time electronic health record (EHR) antibiotic dosing report to allow EM pharmacists to quickly identify and assess patients in need of subsequent antibiotic doses to prevent major delays in their care.

The primary objective of this study was to evaluate the ability of a pharmacist-run, real-time EHR antibiotic dosing report in the ED to reduce the number of major delays in subsequent antibiotic administration times.

KEY POINTS

- Delays in subsequent antibiotic administration times have been demonstrated to have negative clinical outcomes for emergency department (ED) patients, but there is no consensus on a strategy or protocol to combat such delays.
- A real-time electronic health record (EHR) antimicrobial report was developed to streamline pharmacovigilance in identifying patients in need of subsequent antibiotic doses.
- Implementation of a real-time EHR antimicrobial report in the emergency medicine pharmacist workflow is effective in reducing major delays in subsequent antibiotic administration and has the potential to correlate with better patient outcomes.

Methods

Study design. This study was conducted at an 803-bed tertiary care level 1 trauma and burn center that has approximately 65,000 ED patient visits per year, with an admission rate just over 30%. At the time of this study, the ED was consistently staffed 17 hours a day by EM pharmacists (day shift from 7:00 AM to 3:30 PM and evening shift from 2:00 PM to 12:00 AM), 7 days a week. This retrospective, quasi-experimental pre-and-post quality improvement project captured all adult patients in the ED who were continued on antibiotic therapy after receiving a one-time dose of an antibiotic in the ED. A real-time EHR antimicrobial report was developed with the assistance of the pharmacy analytics and outcomes team, with a go-live date of report utilization by all pharmacists covering in the ED of September 10, 2021. This was considered a real-time report as it captured any antimicrobial order immediately after it was placed and could be run at any time throughout the day by pharmacists. Epic (Epic Sysems, Verona, WI) was the EHR software system that was utilized by our institution and the platform in which this report was developed. This real-time report captured the following data for patients physically located in the ED: patient name and medical record number, chief complaint, room/bed number, service,

Figure 1. Real-time electronic health record–generated antimicrobial report.

Patient Name (MRN)	Chief Complaint	Room/Bed	Service	Order Name	Ordered Route	Frequency	Last Admin Date	Order Status	CrCl	Creatinine
	Wound Infection		Surg Vascular (SRV)	vancomycin (VANCOCIN) IVPB 1000 mg (premix)	Intravenous	Once	1:57 AM	Completed	132.6 mL/min	0.7 mg/dL
	Wound Infection		Surg Vascular (SRV)	cefepime (MAXIPIME) 2 g in sodium chloride 0.9 % (NS) 100 mL IVPB-connector bag	Intravenous	Once	12:17 AM	Completed	132.6 mL/min	0.7 mg/dL
	Wound Infection		Surg Vascular (SRV)	metroNIDAZOLE (FLAGYL) IVPB 500 mg	Intravenous	Once	12:27 AM	Completed	132.6 mL/min	0.7 mg/dL
	Alleged Sexual Assault		Psychiatry (PSY)	doxycycline (VIBRA-TABS) tablet/capsule 100 mg	Oral	2 times a day	8:25 AM	Dispensed		0.8 mg/dL
	Weakness		Emergency Medicine	cefTRIAXone (ROCEPHIN) 1 g in sodium chloride 0.9 % (NS) 100 mL IVPB-connector bag	Intravenous	Once	11:01 PM	Completed		0.7 mg/dL
	Shortness of Breath		Emergency Medicine	piperacillin-tazobactam (ZOSYN) IVPB (premix) 4.5 g	Intravenous	Once	7:53 AM	Completed		0.6 mg/dL
	Shortness of Breath		Emergency Medicine	vancomycin (VANCOCIN) IVPB 1000 mg (premix)	Intravenous	Once	7:37 AM	Completed		0.6 mg/dL
	Emesis		Emergency Medicine	cephalexin (KEFLEX) capsule 500 mg	Oral	Every 8 hours scheduled	6:56 AM	Dispensed		0.7 mg/dL

order name, order route, order frequency, administration date and time, order status, creatinine clearance (CL_{cr}) level if available, and serum creatinine level if available (Figure 1). The report was generated to include all antimicrobial doses ordered within the previous 24 hours for patients actively located in the ED, including one-time orders and scheduled regimens. At our institution, it is common practice in the ED for providers to place only a one-time order for an antibiotic while a patient undergoes further workup and their disposition is planned. This report was designed to optimize the pharmacist workflow to quickly identify patients in need of subsequent antibiotic doses.

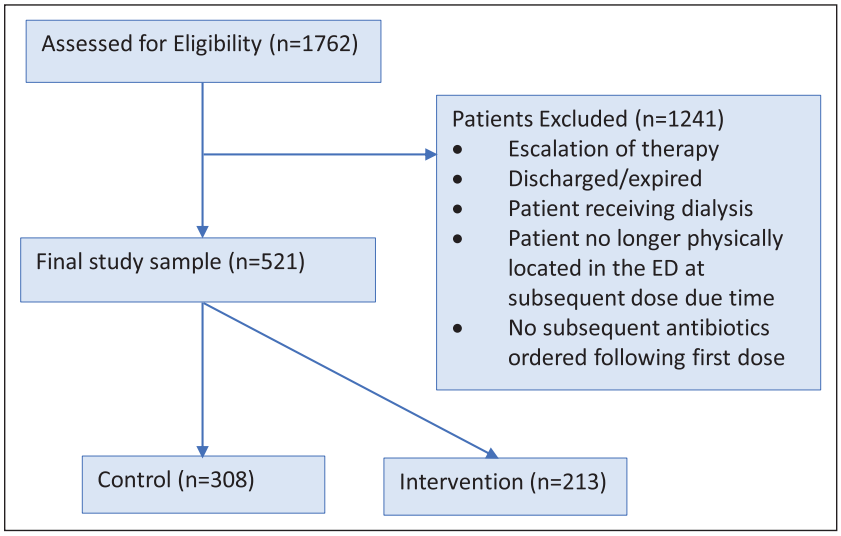
EM workflow implementation. The antimicrobial report was utilized only during the specified hours of EM pharmacist coverage each day. EM pharmacists and other cross-trained clinical pharmacists who cover in the ED were sent multiple communications regarding how to access and utilize the report appropriately via email before the go-live date. During their designated shift, the EM pharmacist was expected to run the report at least once. Because of variations in acuity and census in the ED, the specific time at which the report was run by each pharmacist was not standardized. Once the report was generated, renal function and the appropriateness of antibiotic selection and dosing were to be assessed for each patient using the functionality of this report. With the report, the EM pharmacist would then determine the appropriate timing of the next antibiotic dose based on renal function or whether changes to the regimen should be made (dose, frequency, or antibiotic agent). If the patient required a subsequent dose of their antibiotic(s) that had not yet been ordered by the provider or if the regimen needed to be adjusted based on renal function, the EM pharmacist would reach out to the provider, either via EHR chat function or in person, to ensure the next dose was ordered within the appropriate time window based on our hospital dosing interval protocol. The institutional antimicrobial dosing protocol is heavily focused on CL_{cr} and indication and is updated on a yearly basis to reflect the most up-to-date clinical recommendations by our antimicrobial stewardship team. Accordingly, providers are required to select the indication for antibiotic use when ordering initial doses. Following confirmation with the provider, an order would be placed by either the provider or EM pharmacist for subsequent antibiotic doses to be administered if continuation of therapy was deemed to be warranted.

In the ED at our institution, many commonly prescribed antibiotics are on an autoverify list and therefore are not reviewed by a pharmacist before administration. Thus, upon reviewing the antimicrobial report, it is expected that EM pharmacists also assess the appropriateness of the regimen selected based on any pertinent laboratory results or culture data, vital signs, and diagnostic imaging.

Study population. We included adult patients (18 years or older) who received a one-time dose of an antibiotic in the ED (Figure 2). Only intravenous antibiotics with a 4-, 6-, 8-, or 12-hour dosing interval were included. Additionally, we included the most commonly prescribed antibiotics in our ED: ampicillin, cefazolin, cefepime, ceftriaxone, meropenem, metronidazole, piperacillin/tazobactam, and ampicillin/sulbactam. Patients were excluded if antibiotics were not continued following administration of the first dose, if a patient died or was discharged after the initial dose, if antibiotic therapy was escalated from the initial regimen, if the patient was no longer physically located in the ED at the time their subsequent dose was due, or if the patient was on dialysis. We also excluded antibiotics that have pharmacokinetic dosing protocols with variable dosing and frequencies, such as vancomycin.

Data collection. Data were obtained retrospectively by chart review and analysis in our EHR system for all patients who received at least one dose of an antibiotic agent in the ED. A 2-month interval was selected for the preintervention period (July to August 2021) and the postintervention period (November to December 2021). If patients met the inclusion criteria, a pharmacist retrospectively reviewed all subsequent doses of antibiotics given based on EHR-recorded order verification and administration times to assess whether the antibiotic was administered within a 2-hour window

Figure 2. Consort diagram. ED indicates emergency department.



with respect to its appropriate interval. If antibiotic therapy was de-escalated, the subsequent dose with the new antibiotic was evaluated and assessed for major delays based on the frequency of the initial antibiotic. The primary outcome assessed whether our pharmacist-run, real-time EHR antibiotic report reduced the number of major delays in subsequent antibiotic administration times. Major delay was defined as an administsration time following the first dose outside of a 2-hour window with respect to the recommended dosing interval for each specific antibiotic, taking into account patient-specific factors. A subanalysis of the primary outcome was performed to evaluate differences in major delays based on specific dosing intervals of 6, 8, and 12 hours. Secondary outcomes evaluated included differences in major delays during times when there is no clinical pharmacist coverage in the ED. Other pertinent baseline characteristics were collected, including the ED length of stay, initial vitals, white blood cell count, mechanical ventilation, and vasopressor use while in the ED.

Data analysis. A χ^2 test was utilized to analyze categorical variables, and a *t* test was utilized to analyze continuous variables. Baseline characteristics were summarized with descriptive statistics using Excel (Microsoft Corporation, Redmond, WA). A *P* value of <0.05 was determined to be statistically significant for all data points.

Human subjects compliance. This project was deemed to be exempt by the institutional review board as it was a quality improvement project.

Results

A total of 521 subsequent antibiotic orders from 273 unique patient encounters were included in this study. Baseline characteristics were similar between the groups (Table 1). The mean age was 58 years in the intervention group and 60 years in the control group. Male patients made up 52% of the patient population in both groups. Patients who presented to the ED and received antibiotics on multiple occasions during this time period were evaluated independently for each patient encounter. The majority of patients received antibiotics with a 6- or 8-hour frequency after adjusting appropriately for renal function. An International Classification of Diseases, 10th Revision, Clinical Modification code for sepsis was found for approximately 10% of patients in both arms, and the most common indication for antibiotic use in both arms was infection with an unknown source, followed by intra-abdominal infection and skin and soft tissue infection (Table 2). Vasopressors were utilized in 8% of patients in both arms, and 5% of patients were mechanically ventilated. The mean ED length of stay was 22.4 hours in the intervention arm and 28.4 hours in the control arm.

When assessing the number of antibiotic orders that were redosed during the patient's stay in the ED, the intervention group had fewer overall orders (213) than the control group (308). The most common frequency of antibiotic administration for both groups was an 8-hour (43%) or 6-hour (40%) interval (Table 3). Each interval was determined utilizing patient-specific parameters including antibiotic indication and an established institutional renal dosing guideline.

Following the first dose of antibiotic administration in the ED, the freqiemcy of major delays in subsequent doses was significantly higher in the control group (27%) than in the intervention group (20%; *P* = 0.047) (Table 4). When assessing these delays based on specific frequency intervals, there were more delays in the control arm at 6 hours (27% vs 18%; *P* = 0.138) and 8 hours (32% vs 18%; *P* = 0.026) (Figure 3). In the time period where a clinical pharmacist was not covering the ED, there were major delays for 24% of redosed antibiotic administration times in the control arm compared to 15% in the intervention arm (*P* = 0.14) (Figure 4). No significant differences in major delays in administration were identified based on the timing of order placement and verification by a pharmacist.

Discussion

To our knowledge, this is the first study evaluating the impact of a real-time EHR antimicrobial report utilized by pharmacists on major delays in subsequent antibiotic dosing in the ED. Implementation of this report led to a statistically significant decrease in the number of major delays in subsequent antibiotic dose administration in the ED. Before the go-live of this report, ED pharmacists routinely

Table 1. Demographic Variables Per Patient Encounter

Variable[a]	Intervention group (N = 128)	Control group (N = 145)	*P* value
Age, mean (SD), years	58 (19)	60 (18)	0.364
Male sex	67 (52)	75 (52)	0.912
Serum creatinine, mean (SD), mg/dL[b]	1.19 (1.01)	1.41 (1.47)	0.154
White blood cell count <4,000/μL or >12,000/μL[b]	60 (47)	68 (47)	1
Temperature <36 °C or >38 °C[b]	15 (12)	16 (11)	1
Systolic blood pressure ≤100 mm Hg[b]	14 (11)	19 (13)	0.710
Diastolic blood pressure ≤60 mm Hg[b]	18 (14)	28 (19)	0.262
Heart rate >90 beats/min[b]	74 (58)	79 (54)	0.626
Lactate >18 mg/dL[b]	37 (29)	42 (29)	1
ICD-10 sepsis code	11 (9)	16 (11)	0.547
Vasopressor usage	10 (8)	11 (8)	1
Mechanical ventilation	7 (5)	7 (5)	1
ED LOS, mean (SD), hours	22.4 (11.1)	28.4 (12.8)	<0.05

Abbreviations: ED, emergency department; ICD-10, International Classification of Diseases, 10th Revision, Clinical Modification; LOS, length of stay.
[a]Data shown as No. (%) unless indicated otherwise.
[b]Initial reading of laboratory results or vital signs.

Table 2. Indication for Antibiotic Therapy

Diagnosis[a]	Intervention group (N = 128)	Control group (N = 145)	*P* value
Unknown source	24 (19)	36 (25)	0.244
Intra-abdominal infection	23 (18)	33 (23)	0.087
Skin and soft tissue infection	22 (17)	20 (14)	0.503
Urinary tract infection	7 (5)	14 (10)	0.256
Pneumonia	14 (11)	13 (9)	0.686
Other[b]	38 (30)	29 (20)	0.068

[a]Data shown as No. (%) unless indicated otherwise.
[b]Anaerobic infections, bloodstream infection, bone/joint infection, central nervous system infection, or neutropenic fever.

Table 3. Frequency of Subsequent Antibiotic Doses Ordered in the Emergency Department

Frequency of antibiotics ordered[a]	Intervention group (N = 213)	Control group (N = 308)	*P* value
4-hour interval	3 (1)	1 (0.3)	0.309
6-hour interval	94 (44)	117 (38)	0.174
8-hour interval	93 (44)	130 (42)	0.787
12-hour interval	21 (10)	58 (19)	0.006
24-hour interval	2 (1)	3 (1)	1

[a]Data shown as No. (%) unless indicated otherwise.

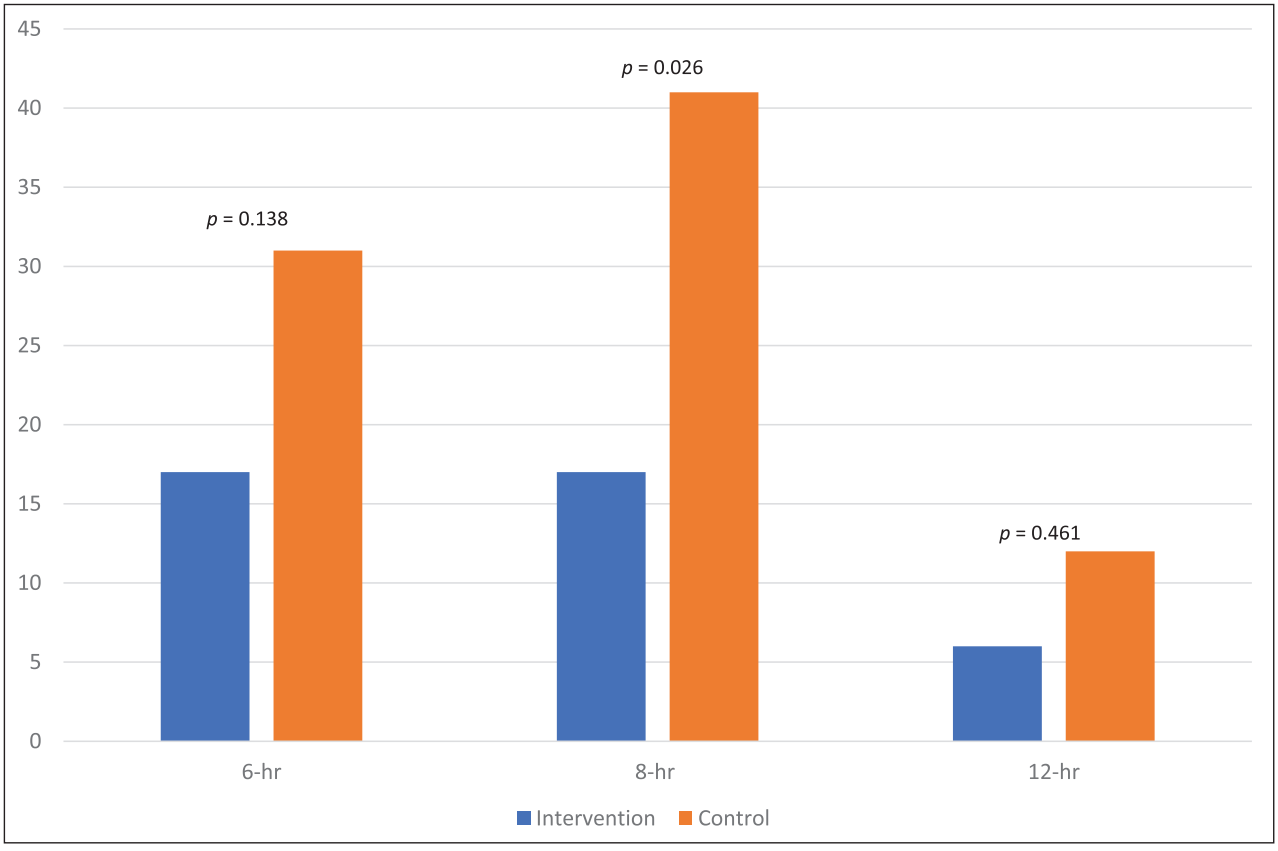
identified patients in need of subsequent antibiotic doses via standard profile review of each patient, which was often time consuming, with opportunities for redosing easily missed during busy times of the day. While somewhat reliable, this process was not streamlined and the variability of acuity in the ED during any given shift may have limited the ability of pharmacists to capture all patients in need of subsequent antibiotic doses in a timely manner. The standardization of this process and ease of use of the real-time EHR antimicrobial report to streamline pharmacovigilance likely led to a decrease in major delays in subsequent antibiotic dosing, although fluctuations in volume and acuity may have impacted the timing with which the report was run each shift. While our institution currently does not have 24-hour pharmacist coverage in the ED, we assessed the utility of this report to determine whether our impact on major delays in subsequent antibiotic dose administration would also be reflected in the 7-hour timespan when no clinical pharmacist is available to care for ED patients. We found a numerical

Table 4. Primary and Secondary Endpoints

Endpoints[a]	Intervention	Control	*P* value
Primary endpoints			
Major delays	42/213 (20)	84/308 (27)	0.047
6-hour frequency	17/94 (18)	31/116 (27)	0.138
8-hour frequency	17/93 (18)	41/130 (32)	0.026
12-hour frequency	6/21 (29)	12/58 (21)	0.461
Secondary endpoints			
Major delays during time period without pharmacist coverage (administration time)	12/79 (15)	27/113 (24)	0.14
Major delays during time period without pharmacist coverage (time ordered)	2/79 (3)	5/113 (4)	0.490

[a]Data shown as No. (%) unless indicated otherwise.

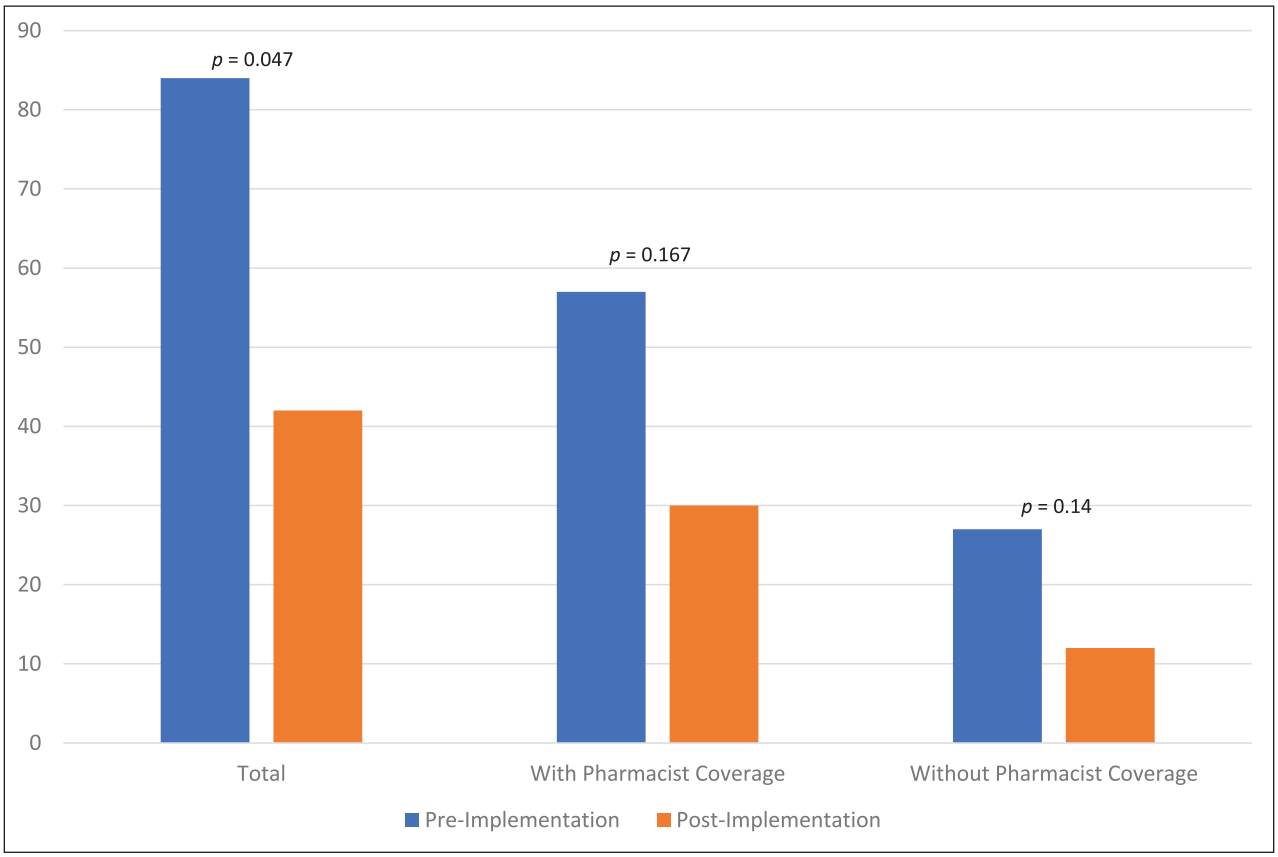
Figure 3. Major delays by frequency of antibiotic regimen.



decrease in delays in the intervention arm during this specified time period, although the decrease was not statistically significant. This is likely due to the evening ED pharmacist utilizing the report at the end of their shift to ensure that follow-up antibiotic doses are ordered, if warranted, during hours that are not covered by an EM pharmacist.

A reduction in the frequency of major delays for second-dose antibiotics, as well as a decreased incidence of in-hospital mortality, has previously been shown with the expansion of EM pharmacists' scope of practice.[20] While our study did not change the scope of our pharmacists' practice, we did implement a report to assist our pharmacists in quickly identifying patients in the ED receiving antibiotics who might require intervention. Our study

Figure 4. Major delays in subsequent antibiotic dosing by pharmacist coverage.



also demonstrates that this is a useful quality improvement approach if the scope of practice may not be changed or this may not be implemented at an institution promptly.

One study evaluating the time between administration of the first and second doses of an antibiotic and the frequency of delays among septic patients found that 33% of patients experienced major delays.[6] While our study did not assess only septic patients, the percentage of major delays found in our control arm was similar to that observed previously. The investigators also found an association between major delays in antibiotic dosing and increased in-hospital mortality, length of stay, and mechanical ventilation.[6] Although we did not evaluate these outcomes in our study, these data indicate the need for an intervention such as our real-time EHR antimicrobial report to most effectively provide consistent and detailed monitoring of such patients.

Limitations. This study had several limitations. First, this evaluation was retrospective in nature, was conducted at a single center with a relatively small sample size, and had short pre- and postintervention study periods of 2 months. Additionally, we were unable to document and track interventions in real time. Subsequent antibiotic doses may have been entered by providers without a pharmacist recommendation, and this ultimately could not be captured in our data. Before the implementation of this report, pharmacists working in the ED were actively performing chart review and assessing antibiotic dosing intervals to prevent delays in care and assist our providers in ordering subsequent doses, which may have positively skewed the control data. Because of the volume of antibiotic orders in our ED, we had to limit the scope of the data to the intravenous antibiotics that are most commonly prescribed and utilized in our ED and exclude any oral antibiotics. Vancomycin was not included in this analysis because of its pharmacokinetic dosing parameters, as mentioned previously, but is reportedly one of the most common antibiotics used in the ED. Patients who had therapy escalations from their initial antibiotic selection were also excluded from our study. Because of pharmacist awareness of the implementation of this report, there was strong potential for implicit bias as pharmacists could have been more vigilant overall during the study period, regardless of implementation of any reporting tool. Additionally, we did not collect data on the average times or magnitude of the delays in this study, which would have been a valuable contribution to the existing literature. Another limitation of this evaluation was that, once patients were no longer physically located in the ED, they were no longer pulled into the report; therefore, some additional patients may have had

delays in therapy once they were physically transferred to their respective admitting unit.

Conclusion

In summary, our study found that the implementation of a real-time EHR antimicrobial report in the ED utilized by EM clinical pharmacists was associated with fewer major delays in subsequent antibiotic dosing following a first dose. These findings contribute to the limited data on the importance of pharmacovigilance in the ED and have the potential to impact morbidity and mortality.

Disclosures

The authors have declared no potential conflicts of interest.

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