



Original Contribution

Impact of an emergency medicine pharmacist on antibiotic dosing adjustment☆☆



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ABSTRACT

Objective: Overall medication-related errors in the emergency department (ED) are 13.5 times more likely to occur in the absence of an emergency medicine pharmacist (EMP). Although the effectiveness of pharmacist-driven renal dosing adjustment has been studied in the intensive care unit, data are lacking in the ED setting. The aim of our study was to evaluate the appropriateness of antibiotic dosing when an EMP is physically present in the ED compared to when absent.

Methods: This was a retrospective cohort study of patients treated in a level I trauma center with 75 adult and 12 pediatric beds and an annual census of 90 000 patients. The study period was from March 1 to September 30, 2014. An EMP was physically present in the ED from 11:00 to 01:30 and absent from 01:31 to 10:59. Male and female patients 18 years and older were considered for inclusion if cefazolin, cefepime, ciprofloxacin, piperacillin-tazobactam, or vancomycin was ordered. The primary outcome was the composite rate of correct antibiotic dose and frequency. Statistics included a multivariable logistic regression using age, sex, presence of EMP, and creatinine clearance as independent predictors of correct antibiotic use.

Results: A total 210 cases were randomly chosen for evaluation, half during times when EMPs were present and half when they were absent. There were 130 males (62%) with an overall mean age of 54 ± 18 years. Overall, 178 (85%) of 210 of the antibiotic orders were appropriate, with 95% appropriate when an EMP was present compared to 74% when an EMP was absent (odds ratio, 6.9; 95% confidence interval, 2.5–18.8). In a logistic regression model, antibiotic appropriateness was independently associated with the presence of the EMP and creatinine clearance.

Conclusion: Antibiotics that require renal and/or weight dosing adjustment are 6.5 times more likely to be appropriate in the ED when an EMP is present. Prevalence of antibiotic dosing error is related to both the presence of EMPs and the degree of renal impairment.

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1. Introduction

The role of the pharmacist within the emergency department (ED) was first documented in the 1970s and has since transitioned from basic inventory management to the provision of comprehensive clinical services [1]. Emergency medicine pharmacist (EMP) participation in cardiac arrest and trauma resuscitations, therapeutic formulary interchanges, provision of drug information responses, and dosing of medications is attributed with improving economic, humanistic, and clinical outcomes [2]. Thus, the American Society of Health-Systems

Pharmacists supports further clarification of the issue of hospital pharmacy department providing ED with the pharmacy services that are necessary for safe and effective patient care [3].

Frequent interruptions, in combination with the often overcrowded and fast-paced environment of the ED, make this setting prone to medication errors [4]. With an estimated 129.8 million patients treated in EDs annually, it is crucial that these errors be minimized to prevent further patient harm and unnecessary health care costs [5]. In a previous study, medication-related errors were 13.5 times less likely to occur when a pharmacist was present in the ED. This difference in errors represented significant issues such as medications given but not ordered, medications ordered and not given, incorrect rate of administration, and late administration of medications [6].

The effectiveness of pharmacist-driven renal dosing adjustment has been previously evaluated in intensive care units; however, on the subject of renal dosing, there is a paucity of literature within the ED setting [7,8]. To our knowledge, this study is the first to quantify the impact

☆ The authors report no conflicts of interest in this study.

☆☆ KD conceived the study, designed the trial, and obtained the data. SW managed the data, provided statistical advice, and analyzed the data. KD, SR, PS, AE, and SW provided oversight to the study design and data collection and drafted the manuscript. All authors contributed substantially to its revision. KD takes responsibility for the manuscript as a whole.

of a clinical pharmacist on optimization of antibiotic dosage adjustment within the ED. The aim of our study is to evaluate the appropriateness of antibiotic dosing which requires renal and/or weight adjustment when a pharmacist is physically present in the ED compared to when absent. Our hypothesis was that the presence of EMPs led to more appropriate antibiotic renal/weight dosing adjustment.

2. Methods

2.1. Study design and setting

We conducted a retrospective cohort study of patients treated in an academic level I trauma center with 75 adult and 12 pediatric bed over a 7-month period from March 1 to September 30, 2014. The hospital has residencies in all major fields that rotate through the ED, a program for mid-level providers and is a certified stroke center. Emergency medicine pharmacists were physically present in the ED from 11:00 to 01:30 and responsible for prospective verification of all antibiotic orders. When absent (01:31–10:59), antibiotic orders were verified remotely by a pharmacist located outside the ED. The ED has an annual census of approximately 90 000 patients. Computerized physician order entry was used during the study period and had been in use for approximately 4 years at the time of study initiation. All medications ordered through computerized physician order entry require verification by a pharmacist but are not automatically verified at the time of use. Nurses may override the verification function and obtain medications from automatic dispensing systems before pharmacist review.

2.2. Patient selection

Before the initiation of the study, a retrospective evaluation over the previous 3-month period of all antibiotics used in our ED was used to identify the most commonly ordered antibiotics which required renal and/or weight adjustment. Cefazolin, cefepime, ciprofloxacin, piperacillin-tazobactam, and vancomycin were selected based on the frequency of orders. Male and female patients 18 years and older were considered for inclusion if any of these antibiotics were ordered during the study period. Patients were excluded if younger than 18 years, pregnant, incarcerated, missing data required for calculation of creatinine clearance (CrCl), or the antibiotic was ordered as a take home prescription for outpatient use. In addition, patients were excluded if they received “once then discontinue” orders, with the exception of vancomycin due to the high occurrence of loading doses ordered within the ED. Random selection was done using izmm.com/random.pl which was accessed on February 1st, 2015, to provide a random table of patients for inclusion.

2.3. Methods of measurement

The study compared appropriateness of antibiotic dose adjustments for decreased renal function and/or weight between times when an EMP was present in the ED vs times when orders were verified remotely by a pharmacist located outside the ED. Height, weight, and serum creatinine (SCr) values available at the time of order validation were used to assess appropriateness of antibiotic dosage and frequency of administration. For the purpose of this study, all creatinine clearance values were calculated using the standard Cockcroft-Gault formula: $\text{CrCl (mL/min)} = [(140 - \text{age}) \times \text{IBW}] / (\text{SCr} \times 72) (\times 0.85 \text{ if female})$. Serum creatinine was rounded up to 1 mg/dL if an individual was 65 years of age or older per institutional protocol. Ideal body weight (IBW) was used for calculation of CrCl unless an individual's total body weight (TBW) was less than IBW. In this circumstance, TBW was used. An adjusted body weight was used for the calculation of CrCl and vancomycin dosing for individuals with a TBW greater than 130% of IBW. An institutional renal dosing protocol allows pharmacists to automatically adjust the dosage and frequency of several medications,

including the antibiotics within this study, for patients with renal impairment without physician approval.

2.4. Outcome measures

The primary outcome was the rate of correct antibiotic dose and frequency for the presumed diagnosis compared when an EMP is present in the ED vs when absent. *Appropriateness* was defined as compliance with institutional renal dosing guidelines. Secondary outcomes included the percentage of appropriate orders stratified by antibiotic agent and incidence of errors related to dose, frequency, or both. In addition, the investigators evaluated if an EMP's presence had the potential to improve the time to antibiotic order verification and time to administration.

Investigation review board approval was obtained from the University of New Mexico Health Sciences Center before initiation of the study.

2.5. Data collection and processing

2.5.1. Data collected

Data were extracted from Cerner PharmNet and Cerner PowerChart and included age, race, sex, height, weight, SCr, time SCr was obtained, antibiotic dosage and frequency verified, presumed indication for antibiotic use, time antibiotic was ordered by physician, time order was verified by a pharmacist, and time antibiotic was administered to the patient. Cerner Power Chart will calculate glomerular filtration rate, and most providers are aware; however, the calculated value may differ from true CrCl as the program does not round SCr up to 1 mg/dL for elderly patients. Prepopulated antibiotic orders exist but fail to incorporate loading doses, individual patient weight, or CrCl. Therefore, traditional standardized orders such as vancomycin 1 g every 12 hours may precipitate dosing error if not ordered carefully.

2.5.2. Data analysis

Continuous data were analyzed using a 2-tailed Student *t* test. Statistical analyses of discrete variables were performed by the χ^2 test. Factors associated with appropriate dosage adjustment were evaluated via a multivariable logistic regression using appropriateness of antibiotic dosing (both frequency and dose) as the main outcome variable. A priori, it was decided to include age, sex, presence of the EMP, and creatinine clearance as predictor variables. A Hosmer-Lemeshow statistic was used to determine goodness of fit.

An a priori power analysis was performed assuming a prevalence of medication errors based on a prior study in ED in which there was a greater than 20% difference in groups based on the presence of ED pharmacists [6]. Assuming 80% power to detect a difference of 20% between the 2 study groups in percentage of appropriate orders, approximately 85 patients were required to be enrolled in each arm for a total inclusion of 170 patients.

3. Results

There were a total of 3163 of the selected antibiotic orders verified within the 7-month study period. Of 500 randomly selected orders considered for inclusion, 105 orders were verified when an EMP was absent from ED and met inclusion criteria. Orders verified when an EMP was present were then considered for inclusion from remainder of the 500 orders until a total of 105 met inclusion criteria. Eighty-five orders were excluded based on exclusion criteria leaving a total of 415. Of these, 105 were from times when EMPs were absent. To match the groups, 105 of the orders verified when an EMP was present were randomly selected for inclusion to match sample sizes between study arms (Figure).

Both groups were compared on demographics. There were a total of 130 males (62%) and 80 females (38%); more males were included in the EMP present group (72 [69%] vs 58 [55%]; odds ratio [OR], 1.8; 95%

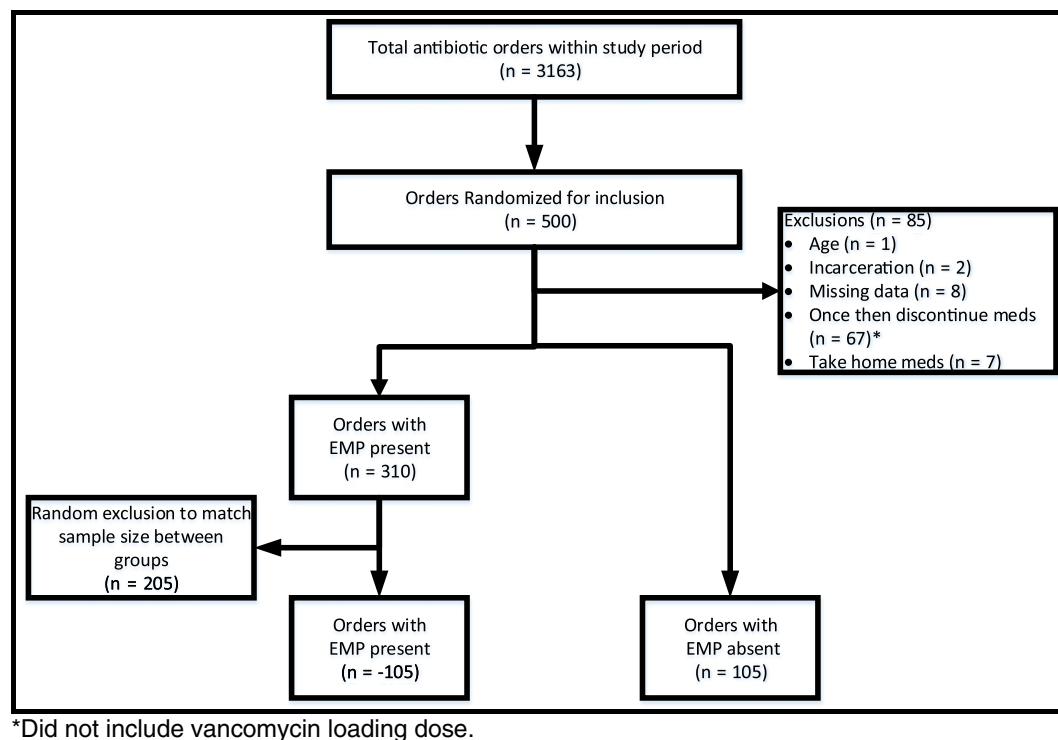


Figure. Study flow chart. *Did not include vancomycin loading dose.

confidence interval [CI], 1.0–3.1). Fifty-six percent were white; 10%, Hispanic; 16%, American Indian; and 18%, other. Mean age in both EMP absent and EMP present arms was 54 ± 18 years. Mean CrCl overall was 85 mL/min, 79 mL/min when an EMP was absent, and 91 mL/min with an EMP present (P , nonsignificant). There were no statistically significant differences in ethnicity, antibiotic verified, or presumed diagnosis between groups (Table 1).

Table 1
Demographics

	EMP absent	EMP present	Difference (95% CI)
n	105	105	
Age (y), mean $\pm$ SD	54 $\pm$ 20	54 $\pm$ 17	NS
Sex (% male)	58 (55)	72 (69)	1.8 (1.0–3.1)
Body mass index (kg/m ²)	28 $\pm$ 10	28 $\pm$ 8	NS
Creatinine clearance (mL/min)	79 $\pm$ 55	91 $\pm$ 62	NS
Race/ethnicity, n (%)			NS
Hispanic	10 (10)	10 (10)	
White	56 (53)	62 (59)	
American Indian	18 (17)	16 (15)	
Other	21 (20)	17 (16.5)	
Antibiotic, n (%)			NS
Vancomycin	48 (46)	49 (47)	
Piperacillin/tazobactam	43 (41)	37 (35)	
Ciprofloxacin	8 (8)	11 (11)	
Cefepime	3 (3)	3 (3)	
Cefazolin	3 (3)	5 (5)	
Diagnosis, n (%)			NS
Undifferentiated sepsis	33 (31)	33 (31)	
Respiratory	23 (22)	26 (25)	
Urinary	5 (5)	3 (3)	
SSTI	23 (22)	25 (24)	
Intraabdominal	20 (19)	15 (14)	
Central nervous system	1 (1)	2 (2)	
Osteomyelitis	0 (0)	1 (1)	

Abbreviations: SSTI, skin and soft tissue infection; NS, nonsignificant.

In comparing outcomes between the 2 groups, antibiotic orders were more appropriate when EMPs were present (OR, 6.9; 95% CI, 2.5–18.8). Overall, more errors were associated with an incorrect dose compared to incorrect frequency. A total of 32 inappropriate antibiotic orders were identified between both groups. Nineteen (19.6%) of 97 vancomycin, 10 (12.5%) of 80 piperacillin/tazobactam, 2 (33.3%) of 6 cefepime, and 1 (5.3%) of 19 ciprofloxacin orders were considered inappropriate. Overall, the mean time to order verification and antibiotic administration were 12 and 60 minutes, respectively. Mean time to order verification was 9 minutes when an EMP was present compared to 15 minutes when absent (P , nonsignificant). (See Table 2.)

Antibiotic appropriateness in relationship to the presence or absence of EMPs and either stage of renal failure or specific drug used was evaluated. The differences between the 2 groups was most marked when the patient was in stage 4/5 renal failure (difference, 45%; 95% CI, 14–65) or when the antibiotic chosen was vancomycin (difference, 23%; 95% CI, 7–38) or piperacillin/tazobactam (difference, 23%; 95% CI, 9–38).

After adjusting for age, sex, and CrCl, antibiotic orders were 6.5 times more likely to be dosed appropriately when an EMP was present. With each increase in CrCl of 10 mL/min, there was an increase in the odds of appropriate management in the presence of EMPs by 17% (adjusted OR, 1.17; 95% CI, 1.1–1.25) (Table 3).

Table 2
Study outcomes by treatment group

	EMP absent	EMP present	OR (95% CI)
n	105	105	
Primary outcome			
Order appropriate, n (%)	78 (74)	100 (95)	6.9 (2.5–18.8)
Secondary outcomes			
Dose appropriate, n (%)	85 (81)	101 (96)	6.0 (2.0–18.1)
Frequency appropriate, n (%)	96 (91)	104 (99)	9.8 (1.2–78.4)
Time to verification (min $\pm$ SD)	15 $\pm$ 19	9 $\pm$ 9	NS
Time to administration (min $\pm$ SD)	60 $\pm$ 55	60 $\pm$ 58	NS

Table 3
Logistic regression analysis

	β	SE of β	Adjusted OR (95% CI)	P
Age (increase of 10 y)	−0.03	0.14	0.99 (0.84–1.12)	.8
Male sex	0.12	0.43	1.13 (0.49–2.62)	.77
CrCl (increase of 10 mL/min)	0.16	0.06	1.17 (1.1–1.25)	.01
Presence of ED pharmacist	−1.9	0.5	6.5 (2.3–18.0)	<.01

4. Study limitations

We recognize that several limitations exist within our study. This was a single-center, retrospective study, and therefore, results may not be generalizable to other EDs or institutions with 24-hour EMP coverage. At our institution, EMPs are present from 11:00 to 01:30, which allowed for a unique opportunity to evaluate antibiotic dosing during times when an EMP was present and absent. During the 9.5 hours EMPs are absent, ED medication orders are verified by a centrally located pharmacist responsible for multiple floor units. There is the possibility that orders placed and verified during this time may be influenced by provider or pharmacist fatigue.

Less experienced medical residents beginning their inaugural rotations during the months of July and August may have increased the frequency of incorrect antibiotic orders within this period. Appropriate randomization of patients allowed for a distribution of patients throughout the 6-month study period in an attempt to minimize any potential differences in prescribing patterns or pharmacist staffing schedules.

Clinical judgment of individual patient cases may have influenced dosing when CrCl values were on the lower or upper limit of dosing thresholds. There were few antibiotic orders included in this study that required a coinvestigator to determine appropriateness. In these circumstances, the coinvestigator was blinded as to whether the order was verified by an EMP and only received objective laboratory and demographic information required for determination of appropriate dosing.

Data in this study were collected retrospectively, and antibiotic administration times relied upon the accurateness of charting. Thus, there was a potential for inaccurate antibiotic administration times based on nurse charting. Finally, inappropriate antibiotic dosing may result in suboptimal microbial eradication or supratherapeutic serum levels resulting in toxicity; however, we did not assess the occurrence of these adverse outcomes secondary to dosing errors.

Pharmacists do not administer medications within our institution, and therefore, timeliness is dependent upon nonpharmacy staff administration. During times of ED overcrowding, medication administration may be delayed due to the overwhelming patient burden placed on nursing personnel [13,14].

5. Discussion

Medication-related errors occur frequently in the ED. A prospective observational study by Patanwala et al [9] discovered at least 1 medication error in 59.4% of patients assessed during the study period. Furthermore, more than one-third of study patients experienced an error that reached them. Implementation of pharmacy services in the ED may help intercept these errors and prevent further patient harm [10].

Previous studies have reported that pharmacist-driven renal dosing adjustment was associated with improved cost savings, decreased intensive care unit length of stay, and fewer adverse events [7,8]; however, neither of these studies were conducted in an ED setting. Because our site has availability of EMPs 14.5 hours a day, we were able to compare orders verified when EMPs were present to times when absent.

Sex was the only significant difference in our baseline demographics between study groups; however, this was corrected for in our

multivariable model. We are not able to determine why more males presented during times when EMPs were present.

Our findings indicate significant improvement in the appropriateness of antibiotic dosing and frequency of administration when EMPs were present in the ED. The difference in appropriateness was reflected more in utilization of the correct dose compared to the correct frequency. One potential explanation of this finding is the inclusion of vancomycin loading doses, in which the frequency was automatically considered appropriate if ordered as once then discontinued.

In a multivariable logistic regression, when corrected for age and sex, both CrCl and presence of an EMP affected the appropriateness of antibiotic usage. Antibiotics orders verified when an EMP was present were 6.5 times more likely to be correct when an EMP was absent. This compares to a previous study at our institution in which times without on-site ED pharmacist presence led to a 13.5-fold increase in various medication-related errors [6]. In a study by Kane-Gill et al [15], critically ill patients with kidney injury were 16 times more likely to experience an adverse event. It is essential that clinicians maintain awareness of antibiotics that require dosage adjustment to prevent such adverse events in those with renal impairment. Our study demonstrates the presence of an EMP led to fewer antibiotic dosing errors and provides further rationale for implementation of clinical pharmacy services in the ED.

The primary antibiotics that required correction by our pharmacists were cefepime, vancomycin, piperacillin/tazobactam, and ciprofloxacin. Although cefepime was the antibiotic agent associated with the greatest prevalence of error, it was ordered the most infrequent and, therefore, more susceptible to a larger percentage of dosing error. We found the greatest variance in appropriate antibiotic usage with vancomycin and piperacillin/tazobactam when comparing whether an EMP was present. These medications should prompt a focused approach by pharmacists to ensure appropriate usage, especially in patients with evidence of renal dysfunction.

Vancomycin is frequently administered in the ED to provide empiric coverage against methicillin-resistant *Staphylococcus aureus*. Current Infectious Diseases Society of America guidelines recommend the use of appropriate weight-based dosing regimens to optimize pharmacodynamic parameters and reduce bacterial resistance [11]. In a retrospective cohort study of 4656 patients who received vancomycin in the ED, 70.6% of patients were considered to be underdosed [12]. Dosing error was more prevalent as body weight increased. Our findings were consistent in that multiple vancomycin orders in the EMP absent group were found to be underdosed when “conventional dosing” (eg, 1000 mg administered every 12 hours) was instituted.

6. Conclusion

Antibiotics that require renal and/or weight adjustment are 6.5 times more likely to be dosed appropriately when a pharmacist is present in the ED. These differences were amplified as the degree of renal impairment increased. Presence of a pharmacist in the ED was not associated with faster times to order verification or antibiotic administration. Clinicians must remain cognizant of antibiotics that require dosage adjustment, especially in elderly patients or those with evidence of renal dysfunction.

References

- [1] Elenbaas RM, Waeckerle JF, McNabney WK. The clinical pharmacist in emergency medicine. *Am J Hosp Pharm* 1977;34:843–6.
- [2] Cohen V, Jellinek SP, Hatch A, et al. Effect of clinical pharmacists on care in the emergency department: a systematic review. *Am J Health Syst Pharm* 2009;66(15):1353–61.
- [3] American Society of Health-System Pharmacists Council on Pharmacy Practice. ASHP statement on pharmacy services to the emergency department. *Am J Health Syst Pharm* 2008;65:2380–3.

- [4] The future of emergency care in the United States. National Academy of Sciences; 2016 [Available at: <http://www.iom.edu/CMS/3809/16107/35007.aspx> (accessed August 8, 2014)].
- [5] National Hospital Ambulatory Medical Care Survey. Emergency department summary tables; 2010 [Available at: http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2010_ed_web_tables.pdf (accessed September 2, 2014)].
- [6] Ernst AA, Weiss SJ, Sullivan 4th A, et al. On-site pharmacists in the ED improve medical errors. *Am J Emerg Med* 2012;30(5):717–25.
- [7] Jiang SP, Zhu ZY, Wu XL, et al. Effectiveness of pharmacist dosing adjustment for critically ill patients receiving continuous renal replacement therapy: a comparative study. *Ther Clin Risk Manag* 2014;10:405–12.
- [8] Jiang SP, Zhu ZY, Ma KF, et al. Impact of pharmacist antimicrobial dosing adjustments in septic patients on continuous renal replacement therapy in an intensive care unit. *Scand J Infect Dis* 2013;45(12):891–9.
- [9] Patanwala AE, Warholak TL, Sanders AB, et al. A prospective observational study of medication errors in a tertiary care emergency department. *Ann Emerg Med* 2010;55(6):522–6.
- [10] Patanwala AE, Sanders AB, Thomas MC, et al. A prospective, multicenter study of pharmacist activities resulting in medication error interception in the emergency department. *Ann Emerg Med* 2012;59(5):369–73.
- [11] 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. *Clin Infect Dis* 2011;52(3):e18–55.
- [12] Fuller BM, Mohr N, Skrupky L, et al. Emergency department vancomycin use: dosing practices and associated outcomes. *J Emerg Med* 2013;44(5):910–8.
- [13] Pines JM, Localio AR, Hollander JE, et al. The impact of emergency department crowding measures on time to antibiotics for patients with community-acquired pneumonia. *Ann Emerg Med* 2007;50(5):510–6.
- [14] Fee C, Weber EJ, Maak CA, et al. Effect of emergency department crowding on time to antibiotics in patients admitted with community-acquired pneumonia. *Ann Emerg Med* 2007;50(5):501–9, 509.e1.
- [15] Kane-Gill SL, Kirisci L, Verrico MM, Rothschild JM. Analysis of risk factors for adverse drug events in critically ill patients. *Crit Care Med* 2012;40:823–8.