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MAJOR ARTICLE

Leveraging Antimicrobial Stewardship in the Emergency Department to Improve the Quality of Urinary Tract Infection Management and Outcomes

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Background. The complex and fast-paced emergency department (ED) practice setting presents unique challenges that demand a tailored approach to antimicrobial stewardship. In this article, we describe the strategies applied by 1 institution's antimicrobial stewardship program (ASP) that were successful in improving prescribing practices and outcomes for urinary tract infection (UTI) in the ED.

Methods. Core strategies included pre-implementation research characterizing the patient population, antimicrobial resistance patterns, prescribing behavior, and morbidity related to infection; collaboration across multiple disciplines; development and implementation of a UTI treatment algorithm; education to increase awareness of the algorithm and the background and rationale supporting it; audit and feedback; and early evaluation of post-implementation outcomes.

Results. We observed a rapid change in prescribing post-implementation with increased empiric nitrofurantoin use and reduced cephalosporin use ($P < .05$). Our elevation of nitrofurantoin to firstline status was supported by our post-implementation analysis showing that its use was independently associated with reduced 30-day return visits (adjusted odds ratio, 0.547; 95% confidence interval, 0.312–0.960). Furthermore, despite a shift to a higher risk population and a corresponding decrease in antimicrobial susceptibility rates post-implementation, the preferential use of nitrofurantoin did not result in higher bug-drug mismatches while 30-day return visits to the ED remained stable.

Conclusions. We demonstrate that an outcomes-based ASP can impart meaningful change to knowledge and attitudes affecting prescribing practices in the ED. The success of our program may be used by other institutions as support for ASP expansion to the ED.

Keywords. antimicrobial stewardship; emergency department; urinary tract infection.

The positive impact of antimicrobial stewardship programs (ASPs) in the inpatient setting has been well described [1]. By comparison, there remains a dearth of literature pertaining to the successful implementation of ASP strategies in the emergency department (ED), due in part to unique barriers characteristic of the ED practice environment. High rates of patient turnover, decreased continuity of care due to variability in practitioners, and therapeutic decisions made in the absence of meaningful microbiologic data are notable challenges faced by ED clinicians when prescribing antibiotics [2–4]. Furthermore, the increasing emergence of antimicrobial resistance presents a significant challenge for ED clinicians to balance prompt initiation of effective empiric antibiotic therapy without overprescribing broad-spectrum agents [2, 4]. Notwithstanding these barriers, the ED is in a unique position to influence antimicrobial prescribing across the entire continuum of care.

Urinary tract infection (UTI) is a leading cause of infection among patients presented to the ED, accounting for nearly 2 million visits in females of all ages and 160 000 visits in males age 65 years and older in the United States [5]. Among those discharged with an antibiotic for outpatient treatment, up to 30% required postdischarge interventions primarily due to pathogen nonsusceptibility [6, 7]. On the other hand, unnecessary urine collection in asymptomatic patients, poor urine collection technique, and discrepancies in urinalysis interpretations contribute to a large portion of unnecessary antibiotic prescriptions [8].

In 2013, May and colleagues published a call to action for antimicrobial stewardship in the ED, underscoring the important role that ED clinicians play in promoting the judicious use of antimicrobials as well as the need for research to determine which antimicrobial stewardship strategies are most appropriate for implementation in the ED setting [3]. We hypothesized

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that expanding ASP services to the ED would improve prescribing practices and outcomes by targeting empiric treatment of symptomatic UTIs in a diverse population through a multifaceted intervention. Our multifaceted interventions included the following: pre-implementation research characterizing the patient population, antimicrobial resistance patterns, prescribing behavior, and morbidity related to infection; collaboration across multiple disciplines; development and implementation of a UTI treatment algorithm; education to increase awareness of the algorithm and the background and rationale supporting it; audit and feedback; and early post-implementation evaluation.

METHODS

Setting

Our institution is a 650-bed community teaching hospital located in California. The 50-bed ED has an annual census of approximately 70 000 patient visits. We have had a well-established ASP in the inpatient setting for more than 2 decades. The ASP team is comprised of 2 infectious diseases physicians, 2 infectious diseases pharmacists and a postgraduate year 2 pharmacy resident, clinical laboratory microbiologists, and infection control and prevention personnel. The positive impact of our ASP on reducing antimicrobial resistance rates and improving patient outcomes in the inpatient setting has been described in a number of publications [9–11]. ASP interventions had not been implemented in the ED before the present study.

Intervention

Pre-implementation review of antimicrobial prescribing and outcomes for patients treated for UTI in the ED revealed substantial opportunity for improvement [6, 12]. We therefore assembled a multidisciplinary working group comprised of the ASP team plus ED pharmacists and physicians to develop a best practice UTI empiric antimicrobial treatment algorithm for patients discharged directly from the ED. Antimicrobial therapy recommendations contained within the algorithm were based upon national and professional society guidelines, primary literature and findings from our background research characterizing the patient population, antimicrobial resistance patterns, prescribing behavior, and morbidity related to infection, as reported previously [2, 4, 6, 12–27]. Several features of our algorithm are noteworthy. The scope of the algorithm is broad but not all encompassing. The need to modify antibiotic selection by incorporating infection history, previous culture results, antimicrobial exposure, and source control is highlighted in the algorithm and was emphasized during education. This was in line with our ED clinicians' desire to work with a tool that provided guidance for a broad range of patients but also allowed autonomy in decision-making.

Because of our high *Escherichia coli* resistance rates to all oral antibiotics except nitrofurantoin (Table 1) and the variety of uropathogens isolated in a subset of patients to which nitrofurantoin activity was unreliable, we recommended that urine culture and sensitivity testing be performed for all patients with symptomatic UTI (but discouraged collection among patients lacking signs and/or symptoms). Nitrofurantoin was recommended as the agent of choice for all eligible patients with lower UTIs not involving the renal parenchyma or abscesses; among patients with pyelonephritis or signs of systemic infection, our recommendation was a 5-day course of levofloxacin (750 mg/d). High-quality evidence of efficacy in this setting and favorable pharmacokinetic properties were the main drivers of this recommendation [23, 28, 29]. Furthermore, *E. coli* fluoroquinolone susceptibility rates were higher among patients diagnosed with pyelonephritis and stable for discharge (87%). For males, in whom prostate involvement is almost always a concern, our antibiogram showed agents with good prostate penetration (ie, sulfamethoxazole-trimethoprim and fluoroquinolones) to have unreliable activity against common uropathogens [12]. With marginally higher susceptibility, we promoted sulfamethoxazole-trimethoprim over fluoroquinolones and suggested fosfomycin as an alternative. This latter recommendation was based on local surveillance data demonstrating impressive activity against multidrug-resitant (MDR) uropathogens and a number of case reports and pharmacokinetic analyses in this setting [13, 16, 19]. However, a thorough discussion of the risks and benefits with the patient is needed when the drug is considered given its relative high cost as well as reports of high incidence of gastrointestinal intolerance with prolonged treatment [30]. For female patients with lower UTIs in whom nitrofurantoin was deemed unsuitable (CrCl < 30 mL/min, allergy, etc.), we offered cefuroxime as an alternative based on institutional susceptibility data from testing a sample of Gram-negative uropathogens (n = 57) collected from patients in the ED against cefuroxime and cefpodoxime (Etest, Biomerieux, Durham, NC). All isolates tested were susceptible to cefpodoxime. Cefuroxime susceptibility rates were 92%, 100%, and 100% *E. coli*, *Klebsiella pneumoniae,* and *Proteus mirabilis,* respectively. The relatively high retail price and limited local availability of cefpodoxime rendered cefuroxime a more practical alternative. To compensate for low bioavailability (37%) and moderate plasma protein binding (50%) [25], we

Table 1. *Escherichia coli* Urinary Susceptibility Rates in the Pre-implementation and Post-implementation Cohorts (95% Confidence Interval)[a]

	Pre-implementation Cohort (n = 81)	Post-implementation Cohort (n = 101)	*P* Value
Cefazolin[b]	73 (62–82)	59 (48–68)	.043
Ceftriaxone	94 (83–97)	83 (74–90)	.028
Ciprofloxacin	78 (67–86)	66 (56–75)	.090
Sulfamethoxazole-trimethoprim	67 (55–77)	60 (50–70)	.383
Nitrofurantoin	99 (93–100)	96 (90–99)	.383

[a]Calculated using the Clopper-Pearson method.

[b]Susceptibility breakpoint ≤16 mg/L cultures from patients with uncomplicated cystitis; ≤2 mg/L all other patient cultures [32].

suggested utilizing a cefuroxime dose of 500 mg twice daily. This higher dose has been used extensively for respiratory and skin infections, demonstrating favorable tolerability and safety [25].

To promote knowledge of and adherence to the algorithm, we performed a multifaceted implementation strategy consisting of 3 core components:

Algorithm Dissemination

The algorithm was distributed as a quick reference pocket card and also made available on the hospital's intranet that could be readily downloaded to personalized computer devices. Hard copies of the algorithm were posted in ED clinician work areas and nursing stations.

Educational Campaign

To improve knowledge of UTI treatment, increase awareness of the algorithm, and encourage its use, ASP members presented the algorithm and relevant background information at monthly ED multidisciplinary meetings, clinical pharmacy forums, and grand rounds. Trainees received targeted education from ED and infectious diseases clinicians during their rotations. We also communicated our initial findings in medical staff newsletters and in peer-reviewed infectious diseases and emergency medicine journals [6, 12].

Considering the high rates of *E. coli* resistance to trimethoprim-sulfamethoxazole and fluoroquinolones, leaving only beta-lactams and nitrofuratoin as oral options, the high use of cephalexin (45%) in our pre-implementation cohort was not unexpected. However, the 19.5% rate of cephalexin-bug mismatches seen in our pre-implementation analysis [6] underscored the need for a reappraisal of its positioning for UTI treatment in our ED. Critical to the success of our ASP intervention was educating prescribers with the consistent message to consider nitrofurantoin as firstline therapy in eligible patients, as supported by our ED-specific antibiograms, literature review, and initial outcomes data [6, 12, 14, 15, 17, 20, 24, 27, 28]. Rather than establishing formulary restrictions, we focused on dispelling myths that were prevalent among our clinicians pertaining to appropriate candidates for nitrofurantoin. In particular, the lowering of the nitrofurantoin renal function cutoff to a creatinine clearance of 30 mL/min in the updated American Geriatrics Society Beers Criteria was not well known among many of our ED prescribers.

Audit and Feedback

During the 3-month intervention period, we performed biweekly review of cases to evaluate antibiotic prescribing practices. ASP members provided feedback to ED clinicians by phone and in person. Importantly, the ED clinical pharmacists were key frontline personnel, furnishing real-time, 1-to-1 guidance to prescribers for patient-specific algorithm application.

Study Design

We performed a retrospective pre-/post-implementation analysis comparing treatment and outcomes during 12 months before and 3 months after implementation of the algorithm. The pre- and post-implementation cohorts consisted of patients who presented to the ED with a primary or secondary UTI diagnosis by ICD-9/10 codes and who were discharged directly from the ED between July 2015 through June 2016 and March 2017 through May 2017, respectively. A random sample representing approximately 10% of the population of interest was selected for the baseline cohort, whereas the post-implementation cohort consisted of all eligible consecutive patients. Different methods were used for selection of the pre- and post-implementation cohorts to allow for early evaluation of unintended consequences, to motivate continued use of the algorithm among clinicians, and to keep pace with rapidly evolving resistance. Patients with an incomplete medical record and those who refused evaluation and/or treatment were excluded. Relevant demographic, laboratory, microbiology, and clinical data were extracted from the electronic medical record using a structured data collection form and entered into Research Electronic Data Capture, Vanderbilt University (REDCap), an electronic data capture tool hosted at the University of Southern California [31]. Uncomplicated UTI was defined as per the Infectious Diseases Society/European Society of Microbiology and Infectious Diseases (IDSA/ESCMID) guidelines [28]. Symptomatic presentation was classified as UTI-specific (dysuria, urgency, frequency, flank/back pain) or -nonspecific (nausea/vomiting, abdominal pain, subjective fevers/chills, acutely altered mental status, fall, anorexia, dizziness, and new or worsening incontinence). Patients with neither UTI-specific nor UTI-nonspecific symptoms were classified as asymptomatic. The coprimary outcomes of interest were bug-drug mismatches and return visits to the ED within 30 days in the 2 cohorts.

Statistical Analysis

Descriptive statistics were used to characterize the pre- and post-implementation cohorts. Categorical variables were compared between cohorts using Pearson's chi-square test or the Fisher exact test. Continuous variables were compared using the Student t test or Mann-Whitney U test, as appropriate. A multivariable logistic regression analysis was conducted in the post-implementation cohort to identify variables independently associated with 30-day return ED visits. Variables associated with this outcome at a P value <.1 in bivariate analyses and/or with biological plausibility were entered into the model simultaneously and removed in a backward, stepwise fashion, being retained in the model if the adjusted P value was <.05. Model fit was assessed with Hosmer-Lemeshow goodness of fit, with nonsignificant results ($P > .05$) deemed acceptable. All analysis was performed using SPSS Statistics, version 24.0 (IBM Corp., Armonk, NY). A 2-tailed P value <.05 was considered significant.

RESULTS

Four hundred one and 351 patients were included in the pre- and post-implementation cohorts, respectively. Tables 2 and 3 compare the patient and infection characteristics of the pre- and post-intervention study cohorts. When comparing the cohorts, a significantly higher proportion of the post-implementation group had risk factors for UTI (recurrent UTI 13% vs 27%, $P < .001$; obstructive uropathy 6% vs 13%, $P < .001$), prior health care or antibiotic exposures (26% vs 34%, $P = .021$; 15% vs 22%, $P = .017$, respectively), prior infection or colonization with a MDR pathogen (2% vs 7%, $P = .001$), altered mental status at presentation (2% vs 8%, $P < .001$), concomitant non–urinary tract infections (7% vs 12%, $P = .006$), and more diverse uropathogen distribution as well as more ESBL-producing *E. coli* (5% vs 15%, $P = .010$) and more *K. pneumoniae* (5% vs 15%, $P = .005$) (Tables 2 and 3). It is notable that a subset of patients in the pre- and post-intervention cohorts were asymptomatic

Table 2. Pre-implementation and Post-implementation Cohort Patient Characteristics

Characteristic	Pre-implementation (n = 401)	Post-implementation (n = 351)	*P* Value[a]
Median age (IQR), y	47 (30–71)	53 (31–74)	.089
Age ≥65 y, n (%)	110 (27.4)	118 (33.6)	.066
Male gender, n (%)	55 (13.7)	57 (16.2)	.332
Nursing home residence, n (%)	13 (3.2)	18 (5.1)	.194
Pregnancy, n (%)	8 (2.0)	9 (2.6)	.631
Comorbidities, n (%)			
Cardiovascular disease[a]	81 (20.2)	120 (34.2)	<.001
Diabetes mellitus	57 (14.2)	65 (18.6)	.110
Chronic lung disease[b]	11 (2.7)	39 (11.1)	<.001
Psychiatric disorder	59 (14.7)	63 (17.9)	.230
≥3 comorbidities	20 (5.0)	76 (21.7)	<.001
UTI risk factors, n (%)			
Recurrent UTI[c]	51 (12.7)	95 (27.1)	<.001
Obstructive uropathy	22 (5.5)	46 (13.1)	<.001
Urinary catheter[d]	12 (3.0)	30 (8.5)	.001
Antimicrobial resistance risk factors, n (%)			
Antibiotics within 3 mo	60 (15.0)	76 (21.7)	.017
Hospitalization within 6 mo[e]	44 (11.0)	46 (13.1)	.369
Health care exposure within 6 mo[f]	105 (26.2)	119 (33.9)	.021
History of infection or colonization with MDR pathogen	7 (1.7)	24 (6.8)	.001

Abbreviations: IQR, interquartile range; MDR, multidrug-resistant; UTI, urinary tract infection.

[a]Cardiovascular disease included coronary artery disease, prior myocardial infarction, stroke or transient ischemic attack, peripheral artery disease.

[b]Chronic lung disease included asthma, chronic obstructive pulmonary disease, interstitial lung disease, idiopathic pulmonary fibrosis, cystic fibrosis, and sarcoidosis.

[c]Recurrent UTI was defined as ≥2 episodes in 6 months or ≥3 episodes in 12 months.

[d]Urinary catheter ≥48 hours within 7 days.

[e]≥48 hours.

[f]Skill-nursing facility residence, ambulatory infusion therapy, chronic hemodialysis, home wound care, emergency department visit.

Table 3. Pre-implementation and Post-implementation Cohort Infection Characteristics

Characteristic	Pre-implementation	Post-implementation	*P* Value
Symptoms, n (%)	(n = 401)	(n = 351)	
Dysuria	90 (22.4)	84 (23.9)	.629
Frequency/urgency	50 (12.5)	43 (12.3)	.928
Suprapubic discomfort	44 (11.0)	34 (9.7)	.564
Flank/back pain	123 (30.7)	78 (22.2)	.009
Acutely altered mental status	9 (2.2)	28 (8.0)	<.001
Symptom classification, n (%)			
UTI-specific +/- nonspecific symptoms[a]	207 (51.6)	158 (45.0)	.071
Nonspecific symptoms only[b]	143 (35.7)	162 (46.2)	.003
Asymptomatic	51 (12.7)	31 (8.8)	.088
UTI classification, n (%)	(n = 401)	(n = 351)	
Uncomplicated cystitis[c]	54 (13.5)	60 (17.1)	.166
Pyelonephritis	51 (12.7)	36 (10.3)	.292
Vital signs/laboratory values, n (%)	(n = 401)	(n = 351)	
Temperature > 38°C	18 (4.5)	13 (3.7)	.589
Heart rate > 100	75 (18.7)	74 (21.1)	.414
SBP < 100 mmHg	34 (8.5)	16 (4.6)	.031
WBC > 12 000/mL	67 (16.7)	62 (17.7)	.729
SIRS criteria positive	42 (10.5)	35 (10.0)	.821
Estimated creatinine clearance, n (%)	(n = 326)	(n = 306)	
CrCl > 60 mL/min	196 (60.1)	171 (55.9)	.280
CrCl = 30–60 mL/min	103 (31.6)	110 (35.9)	.247
CrCl < 30 mL/min[d]	27 (8.3)	27 (8.8)	.808
	(n = 401)	(n = 351)	
Concomitant infection, n (%)	26 (6.5)	43 (12.3)	.006
Positive blood culture	5 (1.2)	3 (0.9)	.730
Urine culture result, n (%)	(n = 320)	(n = 313)	
Positive[e]	146 (45.6)	141 (44.8)	.884
No growth	51 (15.9)	58 (18.4)	.388
Contaminated[f]	123 (38.4)	114 (36.2)	.600
Polymicrobial	9/146 (6.2)	18/141 (12.8)	.055
Uropathogen, n (%)	(n = 155)	(n = 159)	
Escherichia coli	111 (71.6)	101 (63.5)	.126
ESBL - producing	5/111 (4.5)	15/101 (14.9)	.010
Klebsiella spp.	8 (5.2)	24 (15.1)	.005
Proteus mirabilis	1 (0.6)	5 (3.1)	.214
Pseudomonas aeruginosa	3 (1.9)	4 (2.5)	1.00
Enterococcus spp.	8 (5.2)	9 (5.7)	1.00

Abbreviations: CrCl, creatinine clearance calculated using the Cockcroft-Gault equation; ESBL, extended-spectrum beta-lactamases; SBP, systolic blood pressure; SIRS, systemic inflammatory response syndrome; UTI, urinary tract infection; WBC, white blood cell count.

[a]UTI-specific symptoms: dysuria, urgency, frequency, flank/back pain.

[b]Nonspecific symptoms: nausea/vomiting, abdominal pain, subjective fevers/chills, acutely altered mental status, fall, anorexia, dizziness, and new or worsening incontinence.

[c]Uncomplicated cystitis: symptomatic UTI in nonpregnant females under 50 years of age with no significant medical conditions, no urinary tract abnormalities, and no history of recurrent UTI [28].

[d]Includes patients receiving chronic hemodialysis.

[e]Uropathogen colony counts $\geq 10^3$ colony-forming units/mL on voided or catheter specimen.

[f]Three or more organisms on voided or catheter specimen.

(12.7% vs 8.8%, respectively), emphasizing the need to intensify ASP efforts toward reducing use of antibiotics in this subgroup (Table 3).

As shown in Table 1, *E. coli* susceptibility rates were low for all commonly prescribed oral agents (ciprofloxacin, sulfamethoxazole-trimethoprim, cephalosporins using cefazolin as a surrogate [32]) in both cohorts (59%–78%) except for nitrofurantoin (96%–99%). Furthermore, all susceptibility rates trended lower in the post-implementation cohort, and the decrease was statistically significant for cefazolin and ceftriaxone (73% vs 59%, $P = .043$; 94% vs 83%, $P = .028$, respectively). Of concern, 36% of urine cultures were deemed contaminated by standard criteria in the post-implementation cohort, which was unchanged from pre-implementation (Table 3).

Prescriptions for nitrofurantoin increased from 16% to 43% ($P < .001$), whereas cephalexin prescriptions decreased from 45% to 10% ($P < .001$). Notably, all *E. coli* isolates from patients discharged on nitrofurantoin were susceptible. A total of 9 patients discharged on nitrofurantoin (18%) had bug-drug mismatches, compared with 25 (28%) discharged on other agents ($P = .177$). Pathogens involved in the nitrofurantoin mismatches were those with known intrinsic resistance (*P. mirabilis, Pseudomonas aeruginosa, Serratia marcescens*) as well as *K. pneumoniae*.

Despite several factors previously reported to be associated with 30-day return visits (in the pre-implementation cohort) [6] being more prevalent in the post-implementation cohort (ie, obstructive uropathy and health care exposure), both cohorts had similar UTI-related 30-day return visits of 9% (Table 4). Specifically with the post-implementation cohort, we observed an overall trend toward fewer return visits among patients discharged with nitrofurantoin compared with alternative antibiotics (15% vs 23%, $P = .062$). Notably, this difference was largely driven by significantly fewer return visits specifically for a UTI-related reason among patients discharged with nitrofurantoin compared with alternatives (2% vs 7%, $P = .001$). In the subgroup of patients with a positive urine culture (n = 141), those discharged on nitrofurantoin also had significantly fewer return visits overall (14% vs 29%, $P = .041$) and significantly fewer return visits for a UTI-related reason (4% vs 16%, $P = .032$).

Patient characteristics were well balanced between those discharged on nitrofurantoin compared with alternatives in the post-implementation cohort, with the exception of male gender and obstructive uropathy, which were both associated with 30-day return visits and were more common in patients discharged on alternative antibiotics. Nonetheless, on multivariable analysis, nitrofurantoin prescription was found to be independently associated with a decreased odds of 30-day return visits in the post-implementation cohort (adjusted odds ratio, 0.547; 95% confidence interval, 0.312–0.960; $P = .035$) (Table 5).

Three patients returned to the ED secondary to possible adverse antibiotic effects. One patient discharged on levofloxacin returned with symptoms of tendonitis, and a second patient developed a rash after receiving ceftriaxone in the ED. The final patient returned with complaints of diarrhea; stool testing was negative for *Clostridium difficile* toxins, and the treating physician attributed the diarrhea to nitrofurantoin (Naranjo score 5—probable adverse drug reaction) [33].

A total of 110 patients with an estimated CrCl of 30–60 mL/min were included in the post-implementation cohort, of whom 51 (46%) received a prescription for nitrofurantoin. Return visits were similar among nitrofurantoin patients stratified by renal function level (CrCl > 60 mL/min 19% vs CrCl 30–60 mL/min 18%, $P = .196$). By contrast, 29% of patients discharged on an alternative antibiotic who had a CrCl 30–60 mL/min returned to the ED within 30 days ($P = .169$).

Of note, 1 alarming finding of our post-implementation analysis was that despite education, a number of patients with systemic signs of infection or CrCl <30 mL/min were prescribed nitrofurantoin (n = 12 and 8, respectively). This was uncovered during an early audit of prescribing, which prompted us to educate our prescribers on appropriate candidates for nitrofurantoin.

DISCUSSION

Previous studies describing ASP interventions in the ED have been limited in scope to uncomplicated UTIs and consequently focused on a lower-risk patient population than that seen in our study [18, 21, 22, 34, 35]. In contrast, we sought to address the needs of our diverse ED population comprised of patients with varying levels of comorbidity and index infection severity. Notably, our susceptibility rates were alarming and reflective of the escalating crisis of antimicrobial resistance. Despite these challenges, our ED ASP intervention was associated with

Table 4. Outcomes in the Pre-implementation and Post-implementation Cohorts

	Pre-implementation Cohort	Post-implementation Cohort	OR (95% CI)	*P* Value
Bug-drug mismatch	(n = 146)	(n = 141)	0.741 (0.441–1.245)	.257
	45 (30.8)	35 (24.8)		
30-d return visits	(n = 401)	(n = 351)		
All-cause	59 (14.7)	70 (19.9)	1.444 (0.987–2.113)	.058
UTI-related return visit	35 (8.7)	30 (8.5)	0.977 (0.587–1.628)	.930

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 5. Multivariable Analysis for 30-Day Return Visits in the Post-implementation Cohort

	OR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Age ≥ 65 y	1.311 (0.762–2.255)	.327	____	____
Male gender	1.933 (1.018–3.667)	.041	____	____
Health care exposure within 6 mo	1.878 (1.101–3.203)	.020	2.014 (1.171–3.465)	.011
Temperature > 38°C	2.625 (0.831–8.287)	.089	____	____
Obstructive uropathy	1.945 (0.974–3.885)	.056	____	____
Nitrofurantoin discharge prescription	0.593 (0.342–1.030)	.062	0.547 (0.312–0.960)	.035

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

positive changes in prescribing practices, most notably a substantial increase in use of nitrofurantoin, an agent with excellent in vitro activity against *E. coli* and minimal potential for ecological collateral damage. Our positioning of nitrofurantoin as a firstline agent in eligible patients was supported by our early post-implementation analysis showing that its use was independently associated with reduced 30-day return visits to the ED. Furthermore, despite a shift to a higher-risk population and a corresponding decrease in antimicrobial susceptibility rates, bug-drug mismatches and 30-day return visits remained stable.

Rather than using conventional educational messaging that emphasizes the public health threat of antimicrobial resistance, which has been shown to have modest effects on motivating practice change [36], we instead focused on emphasizing opportunities to improve outcomes in our own patient population. We believe that our study contributes to the growing body of literature showing that the most convincing data to motivate change in practice are those measured at the institutional level, beginning with characterizing the target patient population, antimicrobial resistance patterns, and prescribing behavior and, finally, measuring outcomes related to infection [7, 9, 11, 21, 22, 34]. Although we did not quantify how often our algorithm was used to guide prescribing, feedback and requests for clarification in reference to the algorithm from ED clinicians suggest that it was being considered or utilized for the care of patients with UTI. Importantly, the substantial changes we observed in prescribing practices in a relatively short period of time support the effectiveness of our interventions, though the exact contribution of each component of the multifaceted approach is not clear. It is reasonable to expect that a multifaceted approach is likely more effective than any singular approach as clinicians with different training backgrounds and practice approaches respond differently to varied intervention types.

Our study was designed to reflect the real-world setting. However, we recognize that the results may not be generalizable to other EDs in distinct geographic areas or serving a different patient population by age, comorbid conditions, or risk factors for resistance. Thus, algorithm development will need to be institution specific, taking into account multiple factors. Furthermore, the distinction between uncomplicated and complicated UTI varies considerably across guidelines and studies [4, 21, 27, 28, 34]. We expanded the pool of patients eligible for nitrofurantoin beyond the definition of uncomplicated lower UTI suggested in the Infectious Diseases Society of America/European Society of Clinical Microbiology and Infectious Diseases consensus guidelines [28] to include postmenopausal females, the elderly, those with diabetes or other comorbidities, and those with moderately reduced renal function. This approach is in line with the more recent guidelines from the European Association of Urology in which infection classification is based upon severity (ie, systemic signs and symptoms) and the presence of uncorrectable structural urinary tract abnormalities [27]. Although accumulating evidence, including results of the present study, suggests that nitrofurantoin is both safe and effective in higher-risk patients with lower urinary tract infection [20, 24, 37–39], the continued controversy around this issue underscores the need for prospective randomized controlled trials.

The tools we used to achieve our objectives were simple and inexpensive (pocket cards, intranet web image, posters), but the multistep process took time and a concerted effort from a multidisciplinary team, which may not be feasible in institutions with more limited human resources. We were fortunate to have the full support of our ED colleagues from the inception of the program, which facilitated close collaboration and was absolutely essential in ensuring that our strategies could be successfully implemented in the complex ED setting. Our study attests to the value of investing human resources in ASP interventions and supports guidelines that emphasize the importance of gaining broad stakeholder buy-in [1].

Our study had several limitations. Our ASP did not comprehensively address all infections encountered in the ED or patients with urosepsis requiring subsequent inpatient admission. Although we emphasized that the algorithm was targeted to symptomatic UTI only and that treatment of asymptomatic bacteriuria is, with few exceptions, of no benefit, a subset of patients in both cohorts were asymptomatic, albeit at a lower proportion following our educational campaign. These findings underscore the need to intensify our future ASP efforts toward reducing unnecessary antibiotic use in this subgroup. In addition, it should be noted that our study was not designed to determine the prevalence or management of asymptomatic bacteriuria, and it is possible that a higher proportion of patients in the post-implementation period were not given a diagnosis of UTI and were instead followed up closely without antibiotic

treatment. These patients would not have been captured in our analysis as we used ICD coding to identify study patients.

The relatively high rate of urine culture specimen contamination seen in our pre-implementation cohort was troubling. We sought to address this problem through targeted patient education by the nursing staff. However, contamination rates remained unchanged in the post-implementation cohort, suggesting that competing priorities may have resulted in failure to deliver instruction on proper urine collection consistently. Our plan moving forward is to work with ED nursing staff to create illustrated patient instruction pamphlets and posters that would be applicable across multiple languages and display them in patient bathrooms, modeling after the success demonstrated in a large urban Australian ED [40].

CONCLUSIONS

We demonstrate that an outcomes-based approach to ASP can impart meaningful change to knowledge and attitudes affecting prescribing behavior in the ED. The success demonstrated here may be used as support to other institutions attempting to gain buy-in and secure human resources for ASP expansion to the ED. Importantly, results from our post-implementation analysis reinforce the need to incorporate ASP efforts as part of a continuous quality improvement process.

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