Epidemiology of Complicated Urinary Tract Infections (cUTIs) Presenting in Emergency Departments Across the United States (US)

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ABSTRACT

Background: Complicated urinary tract infection (cUTI) is a common emergency department (ED) diagnosis. Results of urine culture and antimicrobial susceptibility testing are usually not available for up to 48 hours after an ED visit; therefore, diagnosis and treatment decisions are empiric and based on symptoms, physical findings, and underlying risk of resistance. We sought to understand the epidemiology and incidence of resistance to commonly used oral antibiotics among patients presenting to US EDs with cUTI.

Methods: A retrospective multi-center study using data from the Premier Healthcare Database (2013-18) was performed. Inclusion criteria: (1) age ≥ 18 years, (2) primary cUTI ED/inpatient discharge diagnosis, (3) positive blood or urine culture between index ED service days -5 to +2. Transfers from acute care facilities were excluded. We examined rates of resistance to the following drugs/classes: 3rd generation cephalosporins, fluoroquinolones, trimethoprim/sulfamethoxazole, fosfomycin, and nitrofurantoin in patients presenting to the ED, stratified by those who were ultimately admitted as inpatients vs. not. Regional variation by US Census Division was examined.

Results: 187,789 patients met inclusion criteria; 119,668 (63.7%) were admitted to the hospital. 4.6% had positive cultures only with gram-positive bacteria; the remainder had at least one gram-negative pathogen. *E. coli* was the most common infecting pathogen, present in 72.1% of ED-only infections and 51.4% of those admitted. 44.7% and 58.4% of ED-only and admitted patients, respectively, were resistant to at least 1 of the 5 drugs/classes examined. We saw substantial regional variation; resistance to at least 3 of 5 drugs/classes across all patients ranged from 5.0% in West North Central region to 11.1% in East South Central region (national average: 9.1%).

Conclusion: Patients with cUTI infections presenting to EDs in the US are frequently resistant to many commonly used oral antibiotics, even in patients not admitted to the hospital. Local epidemiology and resistance should be considered when making empiric treatment decisions in the ED. New oral options for cUTI patients are needed to address the growing challenge of resistance.
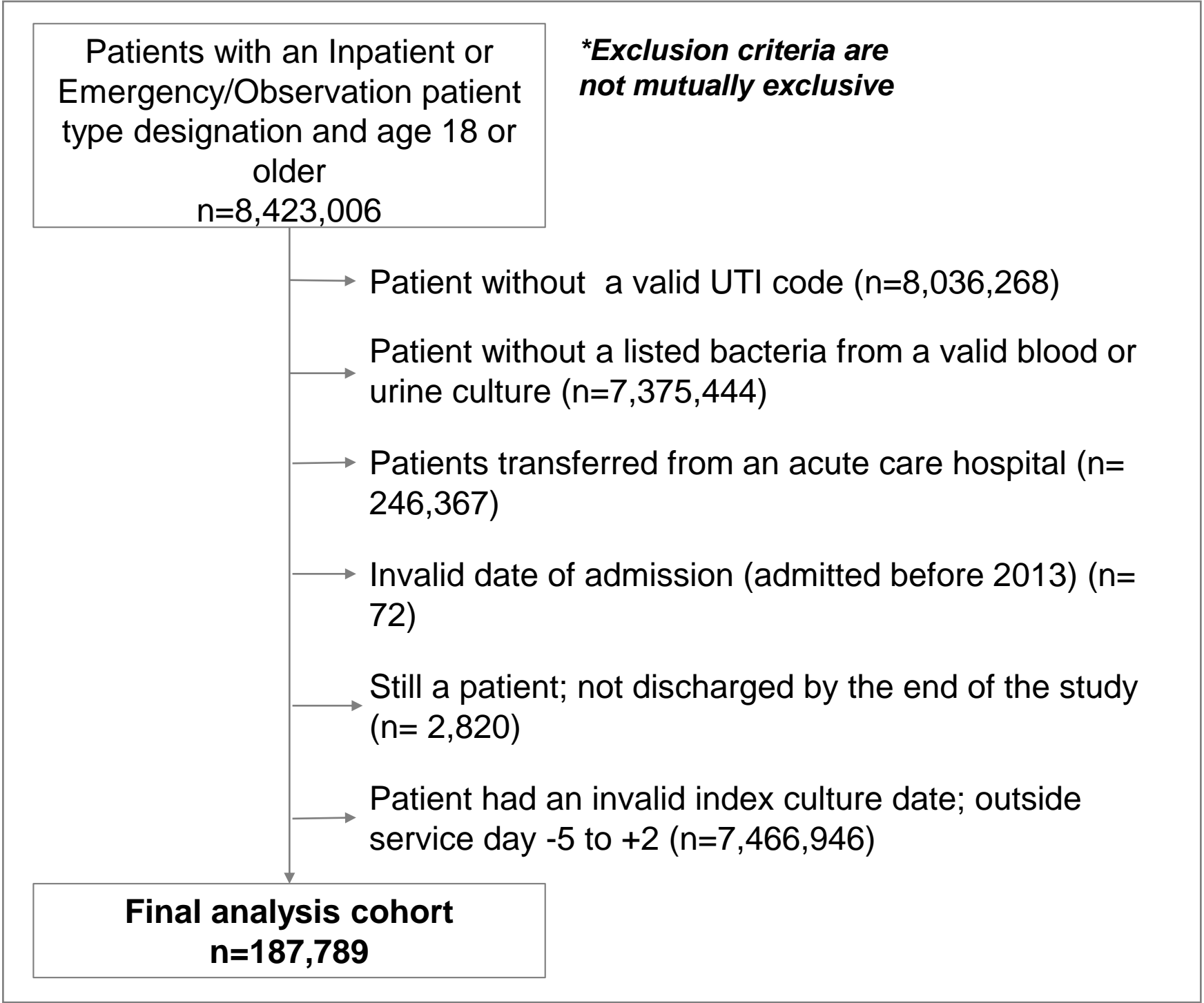
RESULTS

Figure 1: Cohort Attrition

Patients with an Inpatient or Emergency/Observation patient type designation and age 18 or older n=8,423,006

*Exclusion criteria are not mutually exclusive

→ Patient without a valid UTI code (n=8,036,268)
→ Patient without a listed bacteria from a valid blood or urine culture (n=7,375,444)
→ Patients transferred from an acute care hospital (n= 246,367)
→ Invalid date of admission (admitted before 2013) (n= 72)
→ Still a patient; not discharged by the end of the study (n= 2,820)
→ Patient had an invalid index culture date; outside service day -5 to +2 (n=7,466,946)

Final analysis cohort n=187,789

Table 1: Resistance Rates by Drug Class and Hospital Admission Status

	ED Only (n=68,121)	%	IPAT (n=119,668)	%	p-value
Presence of at least 1 organism that is resistant to the following:					
3rd Generation Cephalosporins	4,220	6.2%	15,979	13.4%	<0.001
Fluoroquinolones	12,570	18.5%	42,892	35.8%	<0.001
Trimethoprim-Sulfamethoxazole	16,070	23.6%	30,828	25.8%	<0.001
Nitrofurantoin	11,071	16.3%	30,211	25.3%	<0.001
Fosfomycin	10	0.0%	88	0.1%	<0.001
Most Resistant Organism; Resistant to the drugs above					
Resistant to 0 of the above antibiotics	37,675	55.3%	49,808	41.6%	
Resistant to 1 of the above antibiotics	20,790	30.5%	37,497	31.3%	<0.001
Resistant to 2 of the above antibiotics	6,457	9.5%	18,509	15.5%	
Resistant to 3+ of the above antibiotics	3,199	4.7%	13,854	11.6%	

ED; Emergency Department. IPAT; Inpatient

Table 2: Cross-Resistance Rates of *E. coli* by Drug Class and Hospital Admission Status

Emergency Only	C3-R	FQ-R	TMP/SMZ-R	NFT-R	FFM-R	Inpatient	C3-R	FQ-R	TMP/SMZ-R	NFT-R	FFM-R
C3-R		73.8%	57.1%	13.9%	0.1%	C3-R		86.5%	62.5%	14.5%	0.1%
FQ-R	22.3%		53.2%	8.4%	0.0%	FQ-R	30.3%		56.6%	10.6%	0.0%
TMP/SMZ-R	10.4%	32.1%		6.2%	0.0%	TMP/SMZ-R	23.9%	61.9%		9.3%	0.0%
NFT-R	20.3%	40.6%	49.4%		0.1%	NFT-R	32.6%	67.3%	54.2%		0.0%
FFM-R	66.7%	66.7%	100.0%	33.3%		FFM-R	70.0%	100.0%	90.0%	10.0%	

C3-R; 3rd-generation cephalosporin-resistant. FQ-R; fluoroquinolone-resistant. TMP-SMX-R; trimethoprim-sulfamethoxazole-resistant. NFT-R; nitrofurantoin-resistant. FFM-R; fosfomycin-resistant.

Table 3: Resistance Rates by US Census Division and Drug Class, All Patients;

	East North Central (n=16,729)	%	East South Central (n=2,787)	%	Middle Atlantic (n=5,744)	%	Mountain (n=1,768)	%	New England (n=2,586)	%	Pacific (n=9,368)	%	South Atlantic (n=15,979)	%	West North Central (n=2,496)	%	West South Central (n=10,664)	%
Presence of at least 1 organism that is resistant to the following:																		
3rd Generation Cephalosporins	4915	10.5%	1282	12.8%	2058	11.0%	498	14.8%	843	10.6%	2068	10.2%	5089	10.9%	548	6.4%	2898	11.5%
Fluoroquinolones	13593	29.1%	3458	34.4%	5542	29.5%	833	24.7%	2297	28.8%	5353	26.3%	14421	30.9%	2382	27.7%	7583	30.1%
Trimethoprim-Sulfamethoxazole	10311	22.0%	2577	25.6%	4979	26.5%	954	28.3%	1739	21.8%	5516	27.1%	11200	24.0%	1870	21.7%	7752	30.7%
Nitrofurantoin	10085	21.6%	2359	23.5%	4906	26.2%	530	15.7%	1750	21.9%	4058	20.0%	10452	22.4%	1531	17.8%	5611	22.2%
Fosfomycin	33	0.1%	0	0.0%	13	0.1%	1	0.1%	3	0.0%	1	0.0%	47	0.1%	0	0.0%	0	0.0%
Most Resistant Organism; Resistant to the drugs above																		
Resistant to 0 of the above antibiotics	22754	48.6%	4465	44.4%	8337	44.4%	1654	49.1%	3810	47.8%	9537	46.9%	21950	47.0%	4347	50.5%	10629	42.1%
Resistant to 1 of the above antibiotics	14232	30.4%	2912	29.0%	5865	31.3%	998	29.6%	2548	31.9%	6645	32.7%	13954	29.9%	2690	31.3%	8443	33.5%
Resistant to 2 of the above antibiotics	5723	12.2%	1564	15.6%	2589	13.8%	412	12.2%	917	11.5%	2488	12.2%	6399	13.7%	1138	13.2%	3736	14.8%
Resistant to 3 of the above antibiotics	4068	8.7%	1116	11.1%	1969	10.5%	305	9.1%	702	8.8%	1659	8.2%	4384	9.4%	428	5.0%	2422	9.6%

Each row in Table 3 is statistically significant (p<0.001) by US Census Division..

INTRODUCTION

- Complicated urinary tract infections (cUTIs) are one of the most common bacterial infections encountered in the health care setting.[1,2]
- cUTI are associated with substantial clinical and economic burden in both the in- and outpatient setting: Emergency Department (ED) visits for UTI are estimated to cost the US over $2 billion per year.[3]
- Oral antibiotics have long been a mainstay of treatment for cUTIs but use has been compromised by resistance to oral common used antibiotics.[4,5]
- In US hospitals, the percentages of *E. coli* in cUTIs identified as resistant to extended-spectrum cephalosporins, fluoroquinolones, trimethoprim/ sulfamethoxazole or classified as multidrug resistant (MDR), are increasing rapidly.[2]
- While much research has examined inpatient antibiotic resistance among cUTI patients, less is known about resistance in the ED.
- This study sought to quantify regional resistance rates among patients who present to the ED with a cUTI.

METHODS

- A retrospective multi-center analysis using data from the Premier Research Database (PHD) from 2013-18 was performed examining cUTI patients presenting to the ED; patients were classified as "ED only" (those who were discharged from the ED without an admission) and "Inpatient" (those who were admitted to the hospital).
- Inclusion criteria: Age ≥ 18 years, primary cUTI diagnosis, positive blood or urine culture between index ED/hospital days -5 to +2.
- Exclusion criteria: Patients transferred from other acute care facilities.
- Drug resistance was defined as resistant (R) or intermediate (I) susceptibility results. Individual hospitals were responsible for isolate testing; here, we report values as captured in the PHD.
- Counts and frequencies were used to characterize the patient population and resistance rates. The chi-square test was used to compare counts across categorical variables.
- All analyses were conducted using Stata/MP 15.1 for Windows (StataCorp LLC, College Station, TX).

CONCLUSIONS

- Patients with cUTI infections presenting to EDs in the US are frequently resistant to many commonly used oral antibiotics, even in patients not subsequently admitted to the hospital.
- Nearly all US Census Divisions exceed resistance thresholds cited for empiric use of trimethoprim/ sulfamethoxazole and fluoroquinolones for *uncomplicated* cystitis and pyelonephritis in women, though we examine a cUTI patient population in this analysis.
- Local epidemiology and resistance should be considered when making empiric treatment decisions in the ED.
- New oral options for cUTI patients are needed to address the growing challenge of resistance.

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