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ORIGINAL RESEARCH

Infectious Disease

Descriptive epidemiology and outcomes of emergency department visits with complicated urinary tract infections in the United States, 2016–2018

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Abstract

Objective: There are >1 million emergency department visits and 100,000 admissions with urinary tract infection (UTI) annually in the United States. A fraction of total UTI volume, complicated (cUTI) costs the health care system over $3.5 billion per year. We evaluated the contemporary annual burden of emergency department (ED) visits with cUTI.

Methods: We conducted a cross-sectional multicenter study within the National Emergency Department database, a 20% stratified sample of all US hospital-based EDs, 2016–2018, to explore characteristics of visits with a cUTI. We compared cUTI as the principal (PD) versus secondary diagnosis (non-PD). We applied survey methods to develop national estimates.

Results: Among 2,379,448 ED cUTI visits (44.8% PD), 40.1% were female (45.1% PD; 36.9% non-PD) and 62.2% were ≥ 65 years (52.5% PD; 70.2% non-PD). Mean Charlson score was 2.3 (3.0 PD; 2.1 non-PD); end-stage renal disease prevalence was 2.3% (1.4% PD; 3.0% non-PD). Whereas pyelonephritis occurred in ~10% of both groups, severe sepsis (7.2% vs 2.0%) and septic shock (7.1% vs 1.8%) were ~4 times more prevalent among those with cUTI-non-PD than cUTI-PD. Overall, two thirds of all visits ended in hospitalization (44.9% PD; 85.5% non-PD). Despite similar numbers of visits, the annual national ED bill for cUTI rose from $2.8 billion in 2016 to $3.2 billion in 2018.

Conclusion: There were over 2 million ED visits with cUTI in 2016–2018. Although <10% met criteria for severe sepsis/septic shock, ~two thirds were admitted. The aggregate cost for cUTI visits rose by 15% without a substantial increase in volume.

KEYWORDS
complicated UTI, costs, emergency department, hospitalization, UTI

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1 | INTRODUCTION

1.1 | Background

Urinary tract infection (UTI) remains one of the most frequent diagnoses in US hospitals. In the early 2000s there were over 1 million annual emergency department visits related to UTIs along with over 100,000 inpatient admissions for this condition.[1] A decade later, UTI was responsible for ~400,000 hospitalizations, a 4-fold increase over that time period.[2] Even this staggering number is likely an underestimate of the full burden of UTI, because it fails to account for admissions where the UTI was either incidental to another condition or led to a more serious complication such as sepsis.[2] Despite excluding more severely ill patients with UTI, the annual aggregate hospital costs for these admissions in 2010 were over $2.8 billion. To develop a more comprehensive and up-to-date snapshot of the impact of UTI on health care use, particularly given the growth and aging of the US population, we identified nearly 3 million US hospitalizations involving these infections in 2018, costing in aggregate over $45 billion.[3]

Rising rates of antimicrobial resistance (AMR) have complicated the clinical approach to UTI. Because AMR as an etiology distinguishes complicated from uncomplicated infections, the increase in AMR increases the potential for an uncomplicated UTI to transform into a complicated one (cUTI), making clinical approaches to treatment more challenging.[4,5] Indeed, though still a minority of all UTI admissions, cUTIs incur much higher costs than uncomplicated cases.[3] At the same time, some investigators estimate that one fifth of all cUTI-related admissions may be avoidable.[6] They postulate that, if adequate antimicrobial coverage were available orally, these patients could potentially be treated outside the hospital, thus eliminating the need for hospitalizations and the attendant concerns regarding hospital-acquired complications and unnecessary expenditures.

1.2 | Importance

Because the vast majority of all UTI admissions originate in the ED, the ED is an important locus where admission decisions may be amenable to modification. However, no modification is possible without first understanding the population and practices as they exist today.

1.3 | Goals of this investigation

To get a better view of cUTI in the ED, we set out to characterize the current volume, characteristics, and outcomes of those ED visits in the United States stratified by whether they were seen specifically for cUTI (ie, principal diagnosis, PD) or whether cUTI was secondary to another reason for the presentation (ie, secondary diagnosis, non-PD). We specifically examined their demographic, baseline clinical, and hospital characteristics, as well as processes of care in the ED and such outcomes as discharge disposition and charges and costs, both per patient and aggregate annual across ED visits overall.

The Bottom Line

The authors undertake a retrospective analysis of the multicenter cohort National Emergency Department Sample database, looking specifically at the role of complicated urinary tract infection (cUTI) as a primary or secondary diagnosis. The cUTI, whether clothed as a primary or secondary diagnosis, is shown as a major entity to be reckoned with, with respect to the health care of many patients and the economic burden imposed on the health care system. This paper has done a remarkable job in categorizing cUTI as a major player in the emergency department and points to further research for better management and cost management.

2 | METHODS

2.1 | Ethics statement

Because this study used publicly available fully deidentified data, we did not seek ethics review, per US 45 CFR 46.101(b)4.[7]

2.2 | Study design and patient population

We conducted a multicenter cross-sectional study of patients with cUTI presenting to EDs in acute care hospitals in the United States. Because we were interested in the total annual burden of ED visits with cUTI in the United States, we erred on the side of sensitivity and thus did not exclude any visits that our algorithm identified as having this condition. To quantify the prevalence of resistant pathogens, we used their corresponding *International Classification of Diseases, Tenth Revision* (ICD-10) codes (Table S1).

2.3 | Definition of complicated UTI

Our case identification approach relied on an ICD-10 algorithm (Table 1).[3,4] Namely, cUTI was defined as co-occurrence of at least 1 ICD-10 code from group B plus **at least** 1 **ICD-10 code from group D** or **from group E**.

2.4 | Data source

The data for the study derived from the Agency for Healthcare Research and Quality's National Emergency Department Sample (NEDS) database. The NEDS was created to enable analyses of ED usage patterns and support stakeholders in their decision-making regarding this locus of care delivery.[8] The NEDS contains over 30 million ED visits annually from nearly 1000 hospitals located in 36 US states and District of Columbia, and approximates a 20%

TABLE 1 cUTI identification algorithm[a]

	Description	ICD-10
Group A	Infection and inflammatory reaction due to indwelling urinary catheter	T83.511X, N39
Group B	Acute pyelonephritis	N10
Pyelonephritis	Chronic pyelonephritis	N11.0, N11.1
	Unspecified pyelonephritis	N12
	Pyeloureteritis cystica	N28.85, N30
Group C	Insertion of indwelling urinary catheter	0T9B70Z
Urinary catheter		0T9B80Z
		0T2BX0Z
	Replacement of indwelling urinary catheter	3E1K78Z
	Irrigation of indwelling urinary catheter	3E1K88Z
	Fitting and adjustment of urinary devices	Z46.6
	Attention to other artificial opening of urinary tract	Z43.6
Group D	Vesicoureteral reflux	N13.7
Urinary tract obstruction or other abnormality	Nephrolithiasis or ureteric calculi	N20
	Obstructive defect of renal pelvis and ureter	Q62.3
	Urinary obstruction	N13.9
	Prostate hyperplasia	N40
	Bladder neck obstruction	N32.0
	Hydronephrosis	N13.0, N13.1, N13.2 N13.3
	Retention of urine	R33, R39.14
	Ureteral strictures and fistulas	N35, N36
Group E Immunocompromised	Encounter for chemotherapy and immunotherapy for neoplastic conditions	Z51.1
	Personal history of irradiation	Z92.3
	Organ or tissue replaced by transplant	Z94

[a]CAUTI, Any group A OR (At least 1 group B + At least 1 group C); cUTI, (At least 1 group B + At least 1 group D) OR (At least 1 group B + At least 1 group E).
CAUTI, catheter-associated UTI; cUTI, complicated urinary tract infection; ICD-10, *International Classification of Diseases, Tenth Revision*.

stratified sample of all US hospital-based EDs.[8] We applied complex survey methods to develop national and regional estimates for cUTI visits.

The unit of analysis in this database is a discharge and not a patient. Thus, it is not feasible to distinguish repeat presentations from index ones for any single patient. In the current manuscript, we use the terms "visit," "presentation," and "discharge" interchangeably.

2.5 | Exposure and outcomes

Primary exposure of interest was whether or not the ED visit was **for** (cUTI-PD) or **with** (cUTI-non-PD) a cUTI. The outcomes examined were ED discharge destination and ED costs per visit and as an annual aggregate.

2.6 | Statistical analyses

We examined demographic, clinical, and hospital characteristics of the individual visits, as well as their ED outcomes. We report continuous variables as means with SD and categorical variables as percentages based on complex survey methods that weight strata provided by NEDS (sample statistical code can be found online at www.hcup-us.ahrq.gov/tech_assist/tutorials.jsp). We further provide medians and interquartile ranges (IQR) for select variables based on observed encounters but *without* using weighted strata. Consequently, the median and IQR results do not reflect national estimates but do reflect the observed sample. We compared characteristics and outcomes of those with cUTI as PD (cUTI-PD) versus cUTI as non-PD (cUTI-non-PD). Although $P < 0.05$ represents statistical significance, we note that owing to large numbers, statistical significance may not equate to clinically meaningful differences. All analyses were done using Stata/MP 15.1 for Windows software (StataCorp LLC, College Station, TX).

3 | RESULTS

There were a total of 2,379,448 cUTI ED visits in the United States, divided evenly across the 3 years examined (Table 2). Among these

TABLE 2 Baseline characteristics

	cUTI all		cUTI-PD		cUTI-non-PD		
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	*P* value
Total Ns	*2,379,448*		*1,067,833*	*44.88%*	*1,311,615*	*55.12%*	
Year							
2016	787,595	33.10%	357,482	33.48%	430,113	32.79%	0.1466
2017	803,965	33.79%	356,806	33.41%	447,158	34.09%	
2018	787,889	33.11%	353,545	33.11%	434,343	33.12%	
Age group							
18 to 44	338,672	14.23%	231,192	21.65%	107,480	8.19%	<0.001
45 to 64	560,039	23.54%	276,297	25.87%	283,742	21.63%	
65 to 84	1,044,432	43.89%	403,005	37.74%	641,427	48.90%	
85+	436,305	18.34%	157,339	14.73%	278,966	21.27%	
Mean (SD) age, years	66.86	18.28	62.49	19.78	70.42	16.09	<0.001
Gender							
Female	965,436	40.57%	481,184	45.06%	484,252	36.92%	<0.001
End-stage renal disease	54,649	2.30%	14,775	1.38%	39,874	3.04%	<0.001
Weekend admission	640,238	26.91%	297,025	27.82%	343,213	26.17%	<0.001
Charlson Comorbidity Score	2.3	2.5	1.5	3.0	2.1	2.7	<0.001
Hospital urban/academic status							
Metro non-teaching	637,548	26.79%	302,305	28.31%	335,244	25.56%	<0.001
Metro teaching	1,455,402	61.17%	608,645	57.00%	846,757	64.56%	
Non-metropolitan	286,498	12.04%	156,884	14.69%	129,614	9.88%	
Region							
Northeast	443,992	18.66%	181,764	17.02%	262,228	19.99%	<0.001
Midwest	507,451	21.33%	229,134	21.46%	278,317	21.22%	
South	948,349	39.86%	448,080	41.96%	500,269	38.14%	
West	479,656	20.16%	208,855	19.56%	270,801	20.65%	

cUTI, complicated urinary tract infection; cUTI-non-PD, cUTI secondary diagnosis; cUTI-PD, cUTI principal diagnosis.

1,067,833 (44.8%) had cUTI as the principal reason for presentation. The cUTI-PD group was younger (mean ± SD age 62.5 ± 19.8 vs 70.4 ± 16.1 years, $P < 0.001$) and had a higher proportion of females (45.1% vs 36.9%, $P < 0.001$) than the group with cUTI-non-PD. Although end-stage renal disease was rare, it was more than twice more common in the cUTI-non-PD (3.0%) than cUTI-PD (1.4%) group, $P < 0.001$. The mean Charlson comorbidity score mirrored this relationship (cUTI-non-PD 2.1 ± 2.7; cUTI-PD 1.5 ± 3.0, $P < 0.001$). In both groups, over 50% of all cUTI visits occurred in metropolitan teaching institutions, with 40% located in the Southern US census region. There was slightly more seasonal variation in visits with cUTI-PD (6.4% in February to 8.1% in July and August) than cUTI-non-PD (6.7% in February to 7.6% in August, Figure 1).

Diagnoses and procedures performed in the ED are listed in Table 3. Renal ultrasound, though rare overall, was nevertheless 4 times more common in the cUTI-PD than cUTI-non-PD group. Similarly, catheter-associated UTI was twice as likely in cUTI-PD as in cUTI-non-PD. In contrast, diagnoses of severe sepsis (7.2% vs 2.0%, $P < 0.001$) and septic shock (7.1% vs 1.8%, $P < 0.001$) were nearly 4 times more prevalent among those with cUTI-non-PD than cUTI-PD (Table 3). Though slightly more common in the setting of cUTI-PD, pyelonephritis was present in ~1 in 10 visits in both groups. AMR codes were rare in both groups.

ED visits with cUTI-non-PD ended in a hospitalization in 85.5% of the cases, nearly twice the rate for cUTI-PD (44.9%, $P < 0.001$, Table 4). In contrast, routine discharges home with no further services were nearly 5 times as prevalent in the cUTI-PD (50.7%) as in the cUTI-non-PD group (11.4%, $P < 0.001$). Hospital mortality was low in both groups, though tripled in the cUTI-non-PD (0.03%) versus that in the cUTI-PD (0.01%). Median ED charges in the observed sample were higher in the cUTI-PD group ($3477 [IQR $1992, $7055]) than in the cUTI-non-PD group ($2732 [IQR $1863, $5303]). In aggregate, the annual national bills for cUTI ED visits ranged from $2.8 billion in 2016 to $3.2 billion in 2018, a 15% increase (Figure 2). This rise occurred despite the volumes in the 2 years being virtually the same.

TABLE 3 Diagnoses and procedures in the ED

	cUTI all		cUTI-PD		cUTI-non-PD		
	N	%	N	%	N	%	*P* value
Total Ns	*2,379,448*		*1,067,833*		*1,311,615*		
Renal ultrasound	20,376	0.86%	15,511	1.45%	4,865	0.37%	<0.001
Severe sepsis	115,988	4.87%	21,205	1.99%	94,784	7.23%	<0.001
Septic shock	112,358	4.72%	19,584	1.83%	92,774	7.07%	<0.001
Pyelonephritis	262,105	11.02%	123,061	11.52%	139,044	10.60%	<0.001
CAUTI	386,219	16.23%	254,545	23.84%	131,674	10.04%	<0.001
Altered mental status[a]	29,458	1.24%	9,791	0.92%	19,667	1.50%	< 0.001
Pathogen							
ESBL	28,634	1.20%	10,812	1.01%	17,823	1.36%	<0.001
CR	216	0.01%	112	0.01%	104	0.01%	0.6468
Any beta-lactam R	3,565	0.15%	1,508	0.14%	2,057	0.16%	0.1739
FQ-R	8,822	0.37%	3,819	0.36%	5,003	0.38%	0.1815
FQ-R AND CR	25	0.05%	16	0.00%	9	0.00%	0.3335
MDRO	26,213	1.10%	12,447	1.17%	13,766	1.05%	<0.001

CAUTI, catheter-associated urinary tract infection; CR, carbapenem resistant; cUTI, complicated urinary tract infection; cUTI-non-PD, cUTI secondary diagnosis; cUTI-PD, cUTI principal diagnosis ED, emergency department; ESBL, extended spectrum beta-lactamase; FQ-R, fluoroquinolone resistant; MDRO, multidrug resistant.

[a] *International Classification of Diseases*, *Tenth Revision* code R41.82.

TABLE 4 ED outcomes

	cUTI		cUTI-PD		cUTI-non-PD		
	N/Mean/ Median[a]	%/SD/IQR	N/Mean/ Median[a]	%/SD/IQR	N/Mean/ Median[a]	%/SD/IQR	*P* value
Total Ns	*2,379,448*		*1,067,833*		*1,311,615*		
Discharge destination from ED							
Admitted to this hospital	1,599,764	67.23%	478,979	44.86%	1,120,785	85.45%	<0.001
Died	512	0.02%	62	0.01%	450	0.03%	
Routine	691,707	29.07%	541,700	50.73%	150,007	11.44%	
Transfer to short-term hospital	35,671	1.50%	20,937	1.96%	14,698	1.12%	
Transfer to other type facility	30,293	1.27%	14,920	1.40%	15,373	1.17%	
Home health care	13,164	0.55%	5,610	0.53%	7,554	0.58%	
Against medical advice	6,024	0.25%	4,146	0.39%	1,879	0.14%	
Unknown	2,311	0.10%	1,443	0.14%	869	0.07%	
ED charges[b], $							
Mean (SD)	4,890.41	6,534.39	5,747.48	6,945.96	4,130.64	6,039.08	<0.001
95% CI	4721.24; 5059.58		5547.47; 5947.49		3979.65; 4281.63		
Median (IQR)[a]	2,981	1,863; 5,303	3,477	1,992; 7,055	2,732	1,863; 5,303	<0.001

cUTI, complicated urinary tract infection; cUTI-non-PD, cUTI secondary diagnosis; cUTI-PD, cUTI principal diagnosis; ED, emergency department; IQR, interquartile range.

[a] The median values represent estimates for the non-weighted sample only.

[b] Total charges missing for ~20% of the population.

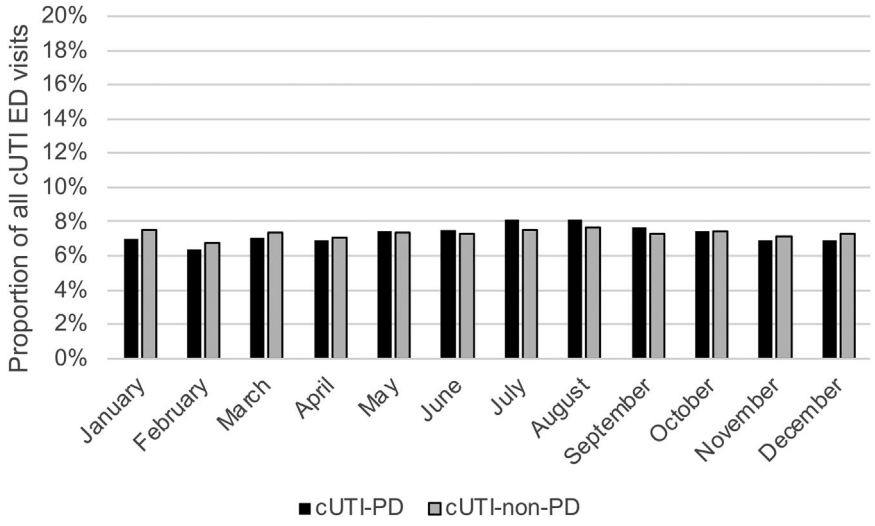
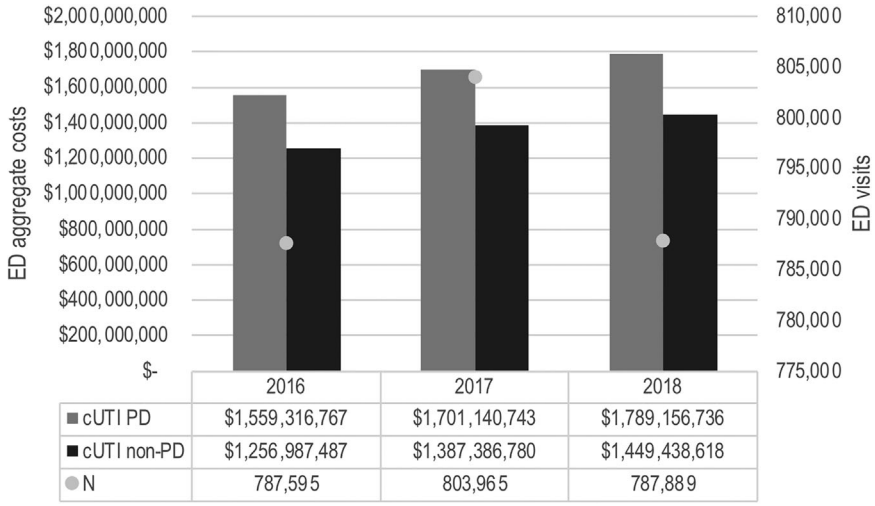


FIGURE 1 Seasonal variation in cUTI ED visits[a].
[a]Values missing in 13% cUTI-PD and 12% cUTI-non-PD. cUTI, complicated urinary tract infection; cUTI-non-PD, cUTI secondary diagnosis; cUTI-PD, principal diagnosis; ED, emergency department



	2016	2017	2018
cUTI PD	$1,559,316,767	$1,701,140,743	$1,789,156,736
cUTI non-PD	$1,256,987,487	$1,387,386,780	$1,449,438,618
N	787,595	803,965	787,889

FIGURE 2 Annual cUTI ED visits and aggregate costs. cUTI, complicated urinary tract infection; cUTI-non-PD, cUTI secondary diagnosis; cUTI-PD, principal diagnosis; ED, emergency department; N, number of ED visits

3.1 | Limitations

Our study, although large and highly generalizable, has a number of limitations. Because our case definition relied on administrative coding, there may be misclassification. Although our algorithm to identify cUTI has not been clinically validated, our numbers generally comport with other studies, particularly allowing for different times and sample frames. To the best of our knowledge, no study to date has addressed coding practices in the setting of cUTI. Thus, misclassification from this perspective remains a concern. Another possible source of misclassification is that at least some of the cUTI-PD patients may have presented with a secondary complication, such as, for example, a fall, or an altered mental status, but were still coded as cUTI as the principal reason for the visit. Such misclassification would mean we have underestimated the severity of acute illness in the group with cUTI-PD thus overstating the potential for avoidable hospitalizations. Another important limitation is our inability to differentiate between initial and repeat visits. However, given the aim of the study, this did not preclude us from estimating the full burden of ED presentations with cUTI. Finally, we did not attempt to calculate the attributable burden from cUTI as a secondary diagnosis in the current study. Therefore, though it surely likely contributes to the burden of both ED and admissions, cUTI-non-PD is responsible for only a part of this burden.

4 | DISCUSSION

In this large multicenter study, we have demonstrated that in years 2016–2018 US EDs evaluated nearly 2.5 million visits with cUTI, of which almost half were specifically *for* cUTI. Although seasonal swings in ED presentations in both groups were narrow, those in cUTI-PD directionally comported with the reported spikes in UTI during warm months.[9,10] Though the cUTI-PD group had a lower burden of both chronic and acute conditions than cUTI-non-PD, nearly half of the former group nevertheless required a hospital admission. Moreover, hospitalization rates in both groups were substantial, despite a low prevalence of such severe conditions as severe sepsis and septic shock, or pyelonephritis. Although the ED charges associated with cUTI-PD

were higher than for cUTI-non-PD, neither number reflects the costs incurred for subsequent hospitalizations among those who required admission. Furthermore, the costs for both are 4–5 times higher than the cost of an average ED visit in the United States.[11] Overall, given the nearly identical total numbers of visits in 2016 and 2018, the 15% rise in the annual charges for all cUTI ED visits within the same time period cannot be explained by volume alone. Likewise, if ED costs for cUTI had been on pace with inflationary trends in medical care, the aggregate bill in 2018 would have been $2.9 million instead of the observed $3.2 billion. Although this is consistent with reports of general price increases for ED services, the reasons for such steep rise in the charges for ED visits with cUTI require further investigation.[12]

In 2018, total ED visits in the United States exceeded 143 million.[11] Numbering over 3.6 million, UTIs were the seventh most common reason for being seen in the ED.[13] Thus, in the same year, complicated UTIs, which in the NEDS data numbered 787,889, comprised 22% of all UTI in the ED, and accounted for 1 out of every 200 ED visits overall. Moreover, in that year the average rate of hospital admissions from the ED across all presenting conditions was 14%.[11] This means that cUTI visits were nearly 5 times more likely to result in an acute hospitalization and cUTI-non-PD specifically 6 times more so. The prevalence of older age, coexisting comorbidities, as well as higher severity of acute illness in the cUTI-non-PD group are some of the plausible reasons for their high admission rate. The same cannot be said for cUTI-PD, who, presumably, present to the ED *for* their specific infection. Because this group has a significantly lower age and burden of chronic illness than cUTI-non-PD patients, it is unclear what specific circumstances push almost half of them to require admission. It may be that the conditions making their UTI "complicated," for example, potential for AMR or immunocompromised status, make clinicians reluctant to discharge these patients. On the one hand, this may be a limitation of the administrative data, which do not provide the level of detail available to the clinician at the bedside, thus leaving the actual cause of hospitalization ambiguous. Alternatively, this may reflect the paucity of adequate outpatient treatments for at least a subgroup of these patients, in particular those who may have failed prior attempts at outpatient treatment and who, therefore, face a higher risk for an AMR infection. Although in the absence of better data on reasons for admission, this remains a conjecture, it is reasonable to hypothesize that ready access to current antibiograms would be helpful in making treatment and admission decisions.

The current burden of ED visits with cUTI has not been well described. Sammon et al. examined the NEDS database from over a decade before our study's sample frame to explore ED visits with any UTI diagnosis.[14] The study reported a total volume of 10.8 million UTI visits with an accompanying 16.7% rate of hospitalization. Similarly, Caterino and colleagues reported 25.4 million adult ED UTI visits in the 2001–2008 National Hospital Ambulatory Medical Care Survey, ED component.[15] Among these patients, one fifth5 were 65 years of age or older, and ~10% were >85 years old. Both studies, however, included both uncomplicated and complicated UTI visits, as opposed to ours, which was limited to the latter. Consequently, these proportions contrast with our findings, where the >65-year-old population represented 44% and >85, 18%, of all cUTIs, which implies that our algorithm successfully excluded uncomplicated infections. Another reason that we observed a higher proportion of patient in the oldest subgroups is undoubtedly the graying of the US population.[16]

Why is it important to distinguish cUTI from its uncomplicated counterpart and to understand the former's burden? By definition, cUTI is a better reflection of the current impact of AMR on this condition, as many cUTI definitions include this factor. This characteristic alone makes it more likely for patients with cUTI than an uncomplicated UTI to require an admission for broader-spectrum antimicrobials which currently may only be available in the intravenous form. Furthermore, the sheer volume of these infections demands a more granular understanding of its implications for hospital policies in general and for allocation of resources specifically. Indeed, if future studies confirm that a substantial proportion of cUTI admissions occurs because of the lack of adequate oral antimicrobials, such data would have real-world applications for both manufacturers and regulators. Along the same lines, the fact that over half of all patients who present to the ED specifically for the treatment of their cUTI end up discharged, yet their ED visits in aggregate incur an estimated nearly $1 billion in costs annually, begs the question whether the costly setting of the ED is the best locus of health care delivery for this population of patients. On the other hand, given easy availability and already existing pathways for ED evaluation, it may be that the current setup is indeed cost effective. Without further study, however, it is impossible to make an informed policy decision with regard to this matter. Our study is a step in building an evidence platform for understanding how to streamline care for these patients.

In summary, we have estimated the contemporary volume of ED visits associated with cUTIs in the United States, stratified by whether this infection was the principal reason for the visit or incidental to it. The patient population is large and resource intensive. One important finding is that the aggregate ED charges for cUTI visits skyrocketed between 2016 and 2018, well out of proportion to either increases in the volume of visits or to the background rate of inflation. Another finding with potential policy implications is that only a small proportion of visits where cUTI is either primary or incidental reason for presenting carries a concurrent diagnosis of a serious infection, such as severe sepsis or septic shock or pyelonephritis, and that the relatively high hospital admission rates in both groups are ostensibly much higher than the prevalence of these conditions would imply. This finding requires further exploration in data that contain granular clinical variables. Finally, the near-$1-billion aggregate annual price tag for the ED visits that end in discharge requires further examination of possible less costly alternatives for delivery of care to this population of patients.

CONFLICTS OF INTEREST

Marya D. Zilberberg is a consultant to Spero Therapeutics. Her employer, EviMed Research Group, LLC, has received research grant support from Spero Therapeutics. Brian H. Nathanson's employer, OptiStatim, LLC, has received support from EviMed Research Group, LLC. Kate Sulham was an employee of and stockholder in Spero Therapeutics during the conduct of this study. She currently serves as a

consultant to Spero. Andrew F. Shorr is a consultant to and has received research grant support from Spero Therapeutics. Marya D. Zilberberg and Andrew F. Shorr have received grant support and/or have served as consultants to Merck, Melinta, Tetraphase, Pfizer, Astellas, Shionogi, The Medicines Company, Lungpacer, and Theravance.

AUTHOR CONTRIBUTIONS

Marya D. Zilberberg, Kate Sulham, and Andrew F. Shorr contributed substantially to the study design, data interpretation, and the writing of the manuscript. Brian H. Nathanson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. He contributed substantially to the study design, data analysis, and the writing of the manuscript. No persons other than the authors participated in the study or the writing of the manuscript.

DATA AVAILABILITY STATEMENT

This is a public data set available for purchase through the Agency for Healthcare Research and Quality HCUP (Healthcare Utilization Project) division.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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