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Impact of empiric treatment failure on healthcare resource utilization and costs among females with uncomplicated urinary tract infections in a US-based Integrated Health Delivery Network

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Treatment failure after empiric antibiotic treatment in females with uUTI results in significant HCRU and cost burden during the uUTI episode and beyond

Introduction

- Treatment failure (TF) in uUTIs is associated with an increased risk of recurrence and increased costs and resource use[1,2]
- Limited data exist on the impact of TF on healthcare resource utilization (HCRU) and costs for empirically treated uUTIs[3]

Aim

- This study aimed to compare all-cause and uUTI-related HCRU and total healthcare costs in female patients with uUTIs, treated within a US Integrated Delivery Network (IDN), with and without TF

Methods

- Retrospective, observational cohort study using de-identified electronic health record (EHR) data from a US IDN[4] to assess female outpatients with uUTI aged ≥12 years between January 1, 2017–January 31, 2022
- Patients with TF (as defined below: "TF cohort") and without TF ("no-TF cohort") were identified
- All-cause and uUTI-related HCRU and costs up to 12 months post index (index date: the first ABX within ± 5 days of the uUTI diagnosis), including 0–90, 91–180, and 181–365 days, were captured by setting of care
  - HCRU costs were computed using Medicare Severity-Diagnosis Related Group codes (MS-DRG) to find relative value units (RVUs), with inpatient stay RVUs multiplied by $6000/RVU[5] and outpatient visits, labs, and imaging test RVUs multiplied by 33.90/RVU (2023 conversion factor)[6]
  - Prescription drug costs were computed using most recently available Medicare Part D drugs average spend per claim data, using the lowest weighted average cost for each matched generic name
- Key eligibility criteria are described in **Table 1**

Treatment failure definition: ≥1 of the following ≤28 days after the index date

- Prescription of a new oral ABX for uUTI, or second prescription of the same empirically prescribed oral ABX for uUTI
- Administration of an IV ABX treatment
- Primary diagnosis of UTI in an acute care setting (excluding index uUTI)

Table 1: **Key eligibility criteria**

Key inclusion criteria	Key exclusion criteria
• Females aged ≥12 years old on the index date with ≥1 uUTI diagnosis in an outpatient or emergency department (ED) setting after January 1, 2017 • ≥1 empiric prescription for nitrofurantoin (NTF), trimethoprim-sulfamethoxazole (SXT; separately or in combination), fluoroquinolones, fosfomycin, or β-lactams within ± 5 days of the uUTI diagnosis date • ≥12 months of EHR activity before and after the index date	• ABX susceptibility test results of the index uUTI diagnosis within 14 days prior to or on the index date • Evidence of a complicated UTI* ≤12 months prior to or on index date • Hospitalization ≤28 days prior to index date • Resident of a nursing home or long-term care facility ≤12 months prior to index date

Complicated UTI included: pregnancy; diagnosed with urological abnormalities, uncontrolled or complicated diabetes, or severe renal dysfunction; immunosuppressed or treated with immunosuppressive therapy; urological or nephrological procedures (e.g., catheter, surgery) within 28 days prior to or on index date; ureteral stent procedure during the baseline period; IV ABX within 28 days prior to or on index date.

- Propensity score matching (PSM) with 1-to-1 greedy nearest neighbor matching (caliper=0.2) without replacement was used to control for imbalances between the TF and no-TF cohorts. PSM variables included:
  - Age, Elixhauser comorbidity index, baseline healthcare costs, index year, baseline uUTI count, baseline hospitalizations, ED visits, uro-/nephro-logical procedure 29–365 days pre index, and diabetes

Results

- Of 28,460 patients with uUTI, 4330 (15.2%) experienced TF of empiric therapy
- Matched TF and no-TF patients (n=3957 patients per cohort) averaged 53 years old and were predominantly (>95%) White (**Table 2**)
- The TF cohort had higher mean index uUTI episode all-cause costs ($1369 vs $482; p<0.001) and uUTI-related costs ($392 vs $78; p<0.001) (**Figure 1**)
- All-cause and uUTI-related costs were significantly higher in the TF cohort versus the no-TF cohort across time intervals during the 12-month post-index period (**Figure 2**)

Figure 1: **Total mean costs during the index* uUTI episode**

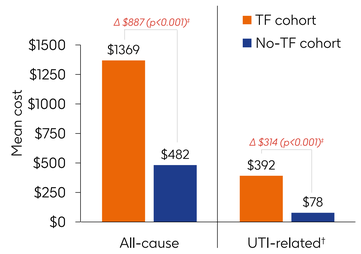

Figure 2: **Mean costs for the 12-month post-index* period by time interval§**

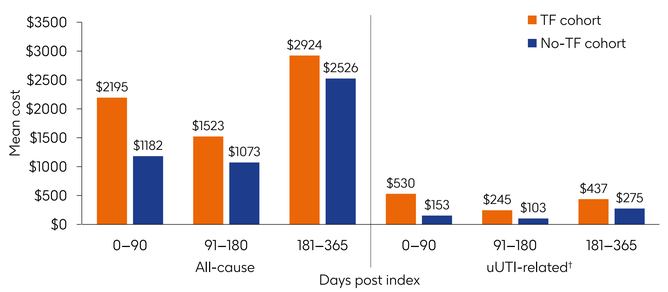

Table 2: **Baseline patient characteristics for the matched TF and no-TF cohorts**

	TF cohort (n=3957)	No-TF cohort (n=3957)	p-value‡
Age at index, years, mean (SD)	53.0 (21.0)	53.4 (20.7)	0.353
Elixhauser index, mean (SD)	1.23 (4.92)	1.38 (4.97)	0.202
Baseline healthcare costs $, mean (SD)	3089 (6783)	2796 (6328)	**0.047**
Race, n (%)			0.505
White/Caucasian	3772 (95.3)	3781 (95.6)	
Asian	54 (1.4)	59 (1.5)	
Black/African American	53 (1.3)	49 (1.2)	
Other/unknown	34 (0.9)	37 (0.9)	
Native American/Pacific Islander	22 (0.6)	20 (0.5)	
Not disclosed	22 (0.6)	11 (0.3)	
Index year, n (%)			1.000
2017	1488 (37.6)	1488 (37.6)	
2018	891 (22.5)	891 (22.5)	
2019	595 (15.0)	595 (15.0)	
2020	547 (13.8)	547 (13.8)	
2021/2022	436 (11.0)	436 (11.0)	
Baseline uUTI count, n (%)			0.675
0	3154 (79.7)	3177 (80.3)	
1	700 (17.7)	687 (17.4)	
2	77 (1.9)	78 (2.0)	
≥3	26 (0.7)	15 (0.4)	
Baseline hospitalizations, n (%)			0.981
0	3734 (94.4)	3750 (94.8)	
1	170 (4.3)	155 (3.9)	
2	45 (1.1)	44 (1.1)	
≥3	<10 (<0.3)	<10 (<0.3)	
Baseline ED visits, n (%)			**0.025**
0	3037 (76.8)	3155 (79.7)	
1	596 (15.1)	524 (13.2)	
2	176 (4.4)	153 (3.9)	
3	85 (2.1)	60 (1.5)	
4	31 (0.8)	33 (0.8)	
≥5	32 (0.8)	32 (0.5)	
Baseline urological or nephrological procedure, n (%)	84 (2.1)	85 (2.1)	1.000
Baseline diabetes, n (%)	628 (15.9)	628 (15.9)	1.000

Table 3: **HCRU during the index uUTI episode and 12-month post-index period in matched TF and no-TF cohorts**

	All-cause HCRU			uUTI-related† HCRU		
	TF cohort (n=3957)	No-TF cohort (n=3957)	p-value‡	TF cohort (n=3957)	No-TF cohort (n=3957)	p-value‡
During the index uUTI episode						
≥1 inpatient visit, n (%)	124 (3.1)	19 (0.5)	**<0.001**	68 (1.7)	<10 (<0.3)	S¶
≥1 ED visit, n (%)	754 (19.1)	299 (7.6)	**<0.001**	500 (12.6)	186 (4.7)	**<0.001**
≥1 outpatient hospital visit, n (%)	2572 (65.0)	1944 (49.1)	**<0.001**	1400 (35.4)	914 (23.1)	**<0.001**
≥1 physician's office visit, n (%)	3397 (85.8)	2809 (71.0)	**<0.001**	2473 (62.5)	1959 (49.5)	**<0.001**
≥1 lab/imaging test, n (%)	3634 (91.8)	2871 (72.6)	**<0.001**	2771 (70.0)	2069 (52.3)	**<0.001**
Mean number of physician's office visits [median] (SD)	2.1 [2] (1.3)	1.4 [1] (0.8)	**<0.001**	1.4 [1] (0.7)	1.1 [1] (0.3)	**<0.001**
Mean number of lab/imaging tests [median] (SD)	2.5 [2] (2.2)	1.5 [1] (1.0)	**<0.001**	1.6 [1] (1.1)	1.1 [1] (0.3)	**<0.001**
0–90 days post index						
≥1 inpatient visit, n (%)	184 (4.7)	79 (2.0)	**<0.001**	93 (2.4)	21 (0.5)	**<0.001**
≥1 ED visit, n (%)	922 (23.3)	513 (13.0)	**<0.001**	534 (13.5)	229 (5.8)	**<0.001**
≥1 outpatient hospital visit, n (%)	3059 (77.3)	2681 (67.8)	**<0.001**	1527 (38.6)	1015 (25.7)	**<0.001**
≥1 physician's office visit, n (%)	3603 (91.1)	3216 (81.3)	**<0.001**	2567 (64.9)	2055 (51.9)	**<0.001**
≥1 lab/imaging test, n (%)	3736 (94.4)	3243 (82.0)	**<0.001**	2839 (71.8)	2164 (54.7)	**<0.001**
Mean number of physician's office visits [median] (SD)	2.8 [2.0] (2.0)	2.2 [2.0] (1.6)	**<0.001**	1.5 [1.0] (0.8)	1.2 [1.0] (0.5)	**<0.001**
Mean number of lab/imaging tests [median] (SD)	3.5 [3.0] (3.4)	2.3 [2.0] (2.1)	**<0.001**	1.8 [1.0] (1.3)	1.2 [1.0] (0.7)	**<0.001**
91–180 days post index						
≥1 inpatient visit, n (%)	123 (3.1)	84 (2.1)	0.183	51 (1.3)	24 (0.6)	**0.081**
≥1 ED visit, n (%)	465 (11.8)	359 (9.1)	**0.009**	120 (3.0)	55 (1.4)	**<0.001**
≥1 outpatient hospital visit, n (%)	2461 (62.2)	2225 (56.2)	**<0.001**	393 (9.9)	225 (5.7)	**<0.001**
≥1 physician's office visit, n (%)	2313 (58.5)	2049 (51.8)	**<0.001**	487 (12.3)	303 (7.7)	**<0.001**
≥1 lab/imaging test, n (%)	2218 (56.1)	1917 (48.5)	**<0.001**	552 (14.0)	328 (8.3)	**<0.001**
Mean number of physician's office visits [median] (SD)	2.2 [2.0] (1.7)	2.1 [2.0] (1.5)	**0.002**	1.4 [1.0] (0.9)	1.2 [1.0] (0.6)	0.064
Mean number of lab/imaging tests [median] (SD)	2.8 [2.0] (3.2)	2.4 [2.0] (2.5)	**<0.001**	1.8 [1.0] (1.8)	1.5 [1.0] (1.4)	**0.029**
181–365 days post index						
≥1 inpatient visit, n (%)	226 (5.7)	186 (4.7)	0.536	82 (2.1)	56 (1.4)	0.418
≥1 ED visit, n (%)	716 (18.1)	666 (16.8)	0.822	165 (4.2)	140 (3.5)	0.831
≥1 outpatient hospital visit, n (%)	3060 (77.3)	2933 (74.1)	**0.050**	558 (14.1)	386 (9.8)	**<0.001**
≥1 physician's office visit, n (%)	2986 (75.5)	2745 (69.4)	**<0.001**	658 (16.6)	472 (11.9)	**<0.001**
≥1 lab/imaging test, n (%)	2879 (72.8)	2714 (68.6)	**0.005**	730 (18.5)	529 (13.4)	**<0.001**
Mean number of physician's office visits [median] (SD)	3.4 [3.0] (2.8)	3.1 [2.0] (2.6)	**<0.001**	1.6 [1.0] (1.2)	1.4 [1.0] (0.8)	0.052
Mean number of lab/imaging tests [median] (SD)	4.0 [2.0] (4.9)	3.6 [2.0] (4.2)	**0.011**	2.3 [1.0] (2.8)	2.1 [1.0] (3.1)	**0.030**

*Footnotes for all RESULTS Tables and Figures: *Index date is defined as the first ABX within ± 5 days of the uUTI diagnosis. †uUTI-related was defined as diagnosis code for uUTI on the same calendar day as the HCRU or prescription being considered. ‡Statistical differences were determined via chi-square test for categorical variables and Wilcoxon rank sum (2-group comparison) or Kruskal–Wallis test (≥3-group comparison) for continuous variables. §All costs were statistically significantly higher for the TF cohort versus the no-TF cohort across all time intervals (p<0.001). ¶Statistically significant, but not reportable as it is based in part on a cohort grouping with cell size <10. Bold font in p-values represents statistical significance (p<0.05). S, statistically significant.*

Conclusions

- Various forms of HCRU, notably inpatient and ED visits, were significantly greater for patients with TF compared to patients without TF
- Commensurate with greater HCRU, costs were significantly higher for patients with TF versus those without TF for the index uUTI episode and across all time intervals assessed

- Greater proportions of the TF cohort experienced all-cause inpatient stays (3.1% vs 0.5%; p<0.001) and ED visits (19.1% vs 7.6%; p<0.001) versus the no-TF cohort during the index uUTI episode, and at each timepoint during the 12-month post-index period (**Table 3**)

Abbreviations

ABX, antibiotic; ED, emergency department; EHR, electronic health record; HCRU, healthcare resource utilization; IDN, Integrated Delivery Network; IV, intravenous; MS-DRG, Medicare Severity-Diagnosis Related Group; PSM, propensity score matching; RVU, relative value unit; S, statistically significant; SD, standard deviation; TF, treatment failure; US, United States; UTI, urinary tract infection; uUTI, uncomplicated urinary tract infection.

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