Financial Burden of Recurrent Urinary Tract Infections in Women: A Time-driven Activity-based Cost Analysis

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OBJECTIVE To utilize Time-Driven Activity-Based Costing to quantify costs of managing recurrent urinary tract infections (RUTI) in women.

METHODS RUTI was defined as ≥2 UTIs in 6 months or ≥3 UTIs in 12 months. A care-delivery value chain outlined RUTI management (visits, urine studies, and imaging) for acute UTI followed by a form of long-term prevention. Prevention strategies included conservative therapy (Cranberry tablets, D-mannose, or *lactobacillus*); Estrogen therapy if postmenopausal; Antibiotic use (self-start, postcoital, or continuous regimens); or intravenous antibiotics in case of drug-resistance or intolerance. Costs of each resource were largely obtained from the Medicare Physician Fee Schedule, GoodRx and local pharmacy pricing, and institutional expenses. The capacity cost rate was defined as cost of resources per minute of care. Individual costs were summed to estimate overall expense of initial RUTI workup and annual cost for each long-term prevention strategy.

RESULTS Cost of acute RUTI workup ranged from $390 to $730. Acute antibiotics cost ranged from $10 for oral trimethoprim-sulfamethoxazole to $3970 for intravenous Ertapenem. Annually, mean cost of conservative therapy ranged from $50 for D-mannose to $1290 for vaginal estradiol ring, and antibiotic use for self-start $40, postcoital $60, and continuous $190. Capacity cost rate ranged from $0.003/min for urine culture to $80/min for estrogen ring.

CONCLUSION Using Time-Driven Activity-Based Costing, costs of RUTI management were efficiently determined. This offers new perspectives for patient counseling and long-term decision making. UROLOGY 128: 47–54, 2019. © 2019 Elsevier Inc.

Urinary tract infections (UTIs) are the most common outpatient bacterial infection, accounting for 0.9% of clinic visits and over $2 billion dollars annually.[1] Over 80% of reported UTIs occur in women[2]; over 50% of all women develop at least 1 UTI in their lifetime.[1] As many as 25% of these women may develop a second infection, while 5% may eventually develop chronic recurrent UTIs (RUTI), defined as ≥2 UTIs in 6 months or ≥3 in 12 months. While past RUTI literature focused largely on premenopausal women, there is increasing interest in studying the growing population of postmenopausal patients who tend to have higher recurrence rates.[3]

Existing RUTI therapies include conservative management, topical estrogens, and various antibiotic regimens.[4-7] Cranberry supplements and D-mannose may decrease enteric uropathogen type 1 and P fimbriae adherence to uroepithelial cells, though clinical significance is debated.[6,8] *Lactobacillus* promote natural vaginal flora, potentially protecting against uropathogens; by a similar mechanism, use of vaginal estradiol may decrease recurrence of UTIs in postmenopausal women.[4,6,7] As an alternative to daily antibiotic prophylaxis, patients with appropriate recognition of UTI symptoms and established medication compliance may choose self-start (SS) antibiotics. For UTIs associated with intercourse, postcoital (PC) antibiotics may be considered; a Cochrane review found similarly low recurrence rates in patients taking ciprofloxacin daily for 6-12 months.[9]

Though some studies have attempted to evaluate cost of specific RUTI therapies over time,[10-12] none have comprehensively quantified costs of chronic RUTI management. Costs based on individual patient data, institutional revenue or insurance reimbursement alone can vary by provider and patient, and may not reflect financial burden of RUTI to society.[13] Proposed by the Harvard Business School,[14] Time-Driven Activity-Based Costing (TDABC) is a novel strategy to define true cost of complex processes. In healthcare, TDABC derives actual expenses of patient care from costs of each stage of care delivery and each resource utilized, reducing error.[15] TDABC determines cost-efficiency by comparing each

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healthcare activity to time actively delivering care. This cost analysis project on RUTIs was specifically inspired by prior work by Laviana et al utilizing TDABC for determining costs of prostate cancer management.[13]

In this TDABC analysis, we sought to delineate costs associated with evaluation and treatment of RUTI, and compared costs of various long-term treatment options. We expected to better define costs of chronic RUTI management and to identify areas to improve cost-efficiency and value of care.

METHODS

The TDABC approach was adapted from the Harvard Business School[14] and studies that similarly utilized TDABC in healthcare settings.[13,15]

Select the Medical Condition

UTI was defined as infection of the urinary system, diagnosed by midstream clean-catch urine bacterial count of $\geq 1 \times 10^5$ colony forming units (cfu), or $\geq 1 \times 10^3$ cfu in the presence of dysuria, frequency, suprapubic pain or hematuria, and the absence of vaginal discharge or sexual symptoms.[16] RUTIs were defined as ≥2 UTIs in 6 months or ≥3 in 12 months.[17] This study included only uncomplicated RUTI, excluding patients with asymptomatic bacteriuria, structural or functional abnormalities of the urinary tract, or predisposing medical or neurologic conditions.

Define the Care-Delivery Value Chain

The care-delivery value chain (CDVC) defined a theoretical process map, detailing each step in RUTI management based on observation, expert knowledge, and institutional practice. Following initial subspecialist appointment for acute UTI, serum creatinine was obtained and urinalysis with urine culture was checked before and after antibiotic treatment.[6] After resolution of infection and in case of recurrence from bacterial persistence, current literature supports further RUTI evaluation with optional testing, including Cystoscopy, Renal Ultrasound and/or computed tomography (CT) scan.[18,19] Assuming this workup was negative and patients indeed had a confirmed uncomplicated RUTI, they were offered therapy to decrease UTI recurrence.

Preventative measures included in this study were based on current literature.[4-7,19] Conservative therapies were cranberry tablets, D-mannose or topical *lactobacillus*. Local estrogens for postmenopausal patients included topical cream or vaginal ring. Antibiotic options included: SS, or 3-5-day treatment dose course; PC, or low-dose antibiotic within 2 hours of coitus; or continuous regimens (daily low-dose for 6-12 months). Based on literature review, limited guidelines exist for acute RUTI management.[2,19,20] We selected the most commonly used antibiotics based on prior review of the literature.[21] Although Fosfomycin is a first-line recommendation per EAU guidelines, it is generally a last-resort, much costlier option in the United States with limited evidence for use in RUTI patients; therefore, it was excluded from this study.[20] Antiseptics, such as methenamine salts, were also excluded, as there is limited published data regarding dosages, cost per dose, or efficacy for RUTI.[22]

Develop Process Map

A process map incorporating all components of the CDVC is depicted in Figure 1. To better understand resources involved in long-term RUTI management, index pathways for RUTI patients were extrapolated (Fig. 2). Proposed pathways were based on menopausal status and followed a predetermined hierarchy: conservative therapy (with local estrogens if postmenopausal) was first-line, followed by either PC or SS antibiotic regimens, continuous daily antibiotics, and finally, progression to intravenous (IV) antibiotics in the event of resistance or intolerance to oral therapy.

Estimate Time

As time spent may vary between individuals, time estimates for each process in the CDVC were averaged from multiple sources. Provider estimates, CPT billing codes, published literature, and institutional data were used to estimate office-based processes. Observation and informal patient reports were used to approximate time spent for patient-directed processes, such as time spent taking an oral medication or applying vaginal cream.

Define Direct and Indirect Costs of Each Stage of the CDVC

Direct costs included resources directly affecting the patient, such as cost of personnel, equipment, space, laboratory tests, imaging, medications and billable services, while indirect costs included overhead fees and/or supporting resources. To provide a standardized cost measure, excluding institutional variation and profit margins, the 2017 Medicare Physician Fee Schedule database was queried for cost components corresponding to Current Procedural Terminology (CPT) codes, such as imaging studies and procedures. Medication and supplement costs were averaged from GoodRx, Walmart, CVS Pharmacy, Walgreens, Kroger, and Amazon pricing.[23] Institutional data were used for all other costs. Total costs were tabulated from direct and indirect costs. Average costs of each stage of care, annual follow-up expenses, and intermittent UTI treatment based on published recurrence rates, were totaled to determine overall costs.[6,24-26]

Calculating Practical Capacity and Capacity Cost Rate

Practical capacity was defined as time actively delivering care. Capacity cost rate (CCR) was calculated by dividing cost of resources by practical capacity. CCR was limited to individual processes, as a surrogate measure of cost-efficiency of each resource.

Assumptions for Calculating Total Costs

To delineate baseline costs of RUTI workup, each resource utilized, and its associated cost, was identified. RUTI workup involved initial urologic visit, urinalysis and urine culture for symptomatic patients, acute UTI antibiotic course, and possible repeat urinalysis and culture if patient continued to have symptoms. Accounting for patients with concerning features, such as malignancy or bacterial persistence, cost of further imaging with cystoscopy and upper tract imaging (Renal US, CT Urogram] was averaged and summed.

Costs of long-term management were also estimated. Annual follow-up included cost of urologic visit, and urinalysis with culture if patient continued to have symptomatic RUTI. Cost per year of use for each conservative, estrogen and antibiotic option were estimated by multiplying average cost per dose by estimated dosing frequency of each therapy. For example, published recurrence rates for each long-term prevention strategy were used to calculate additional cost of treating intermittent UTIs.[6,24-26] Frequency of PC antibiotic dosing was derived using reported rates

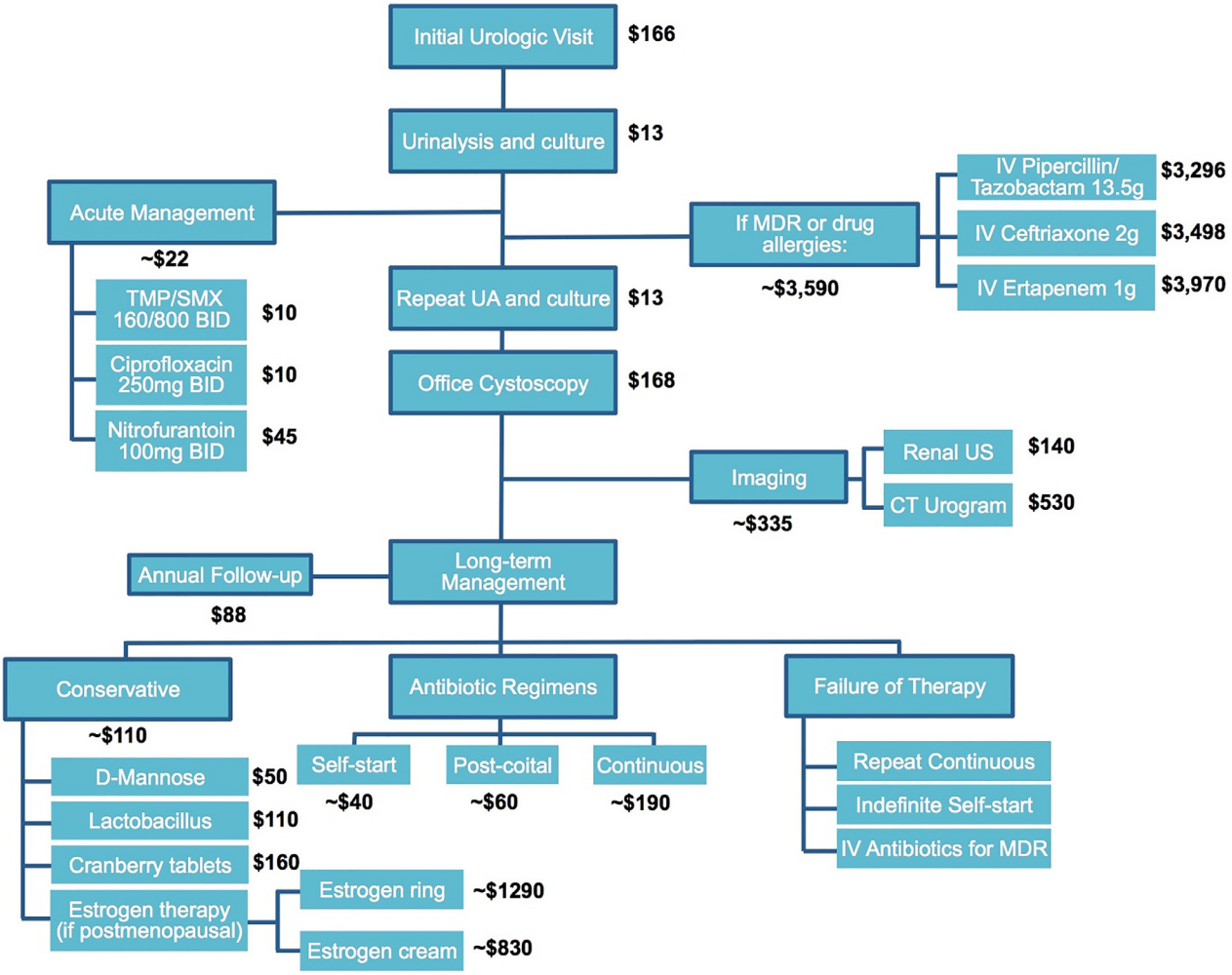

Figure 1. Care-delivery value chain. This process map, called the care-delivery value chain, represents each stage in evaluation and management of patients with RUTI, with associated cost of care. Color version available online. RUTI, recurrent urinary tract infections. (Color version available online.)

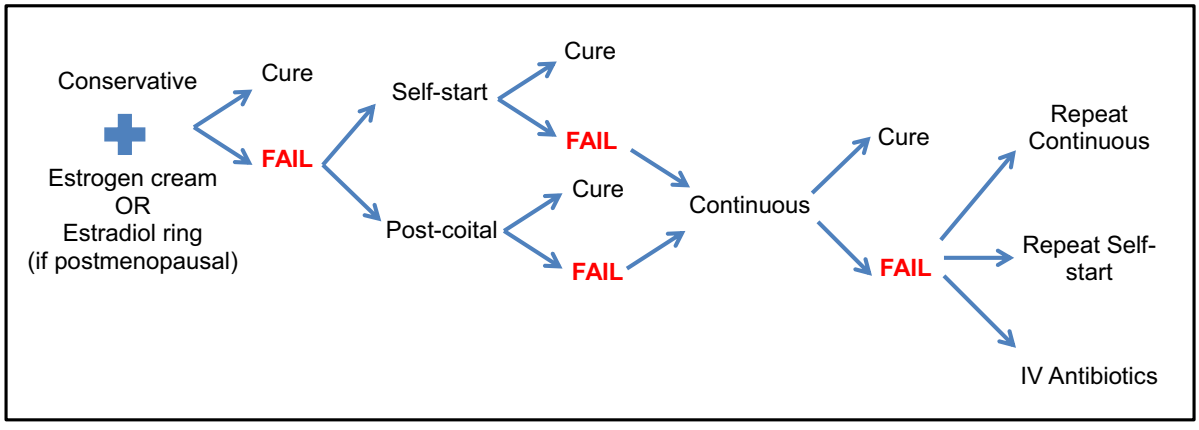

Figure 2. Proposed index pathways for long-term management of recurrent UTIs. Based on menopausal status, RUTI index patients initially trial conservative therapy, with or without local estrogen. Those who fail (≥3 infections per year), progress to self-start or postcoital antibiotics. Patients who fail then advance to daily continuous antibiotics. Finally, patients with persistent recurrence may repeat continuous or self-start regimens or may require IV antibiotics. (Color version available online.)

and expert opinion. Given cost variability between specific antibiotics and formulations, annual costs of therapy were derived from calculated averages.

RESULTS

Costs and CCR of each stage in RUTI work-up, including office appointment, urinalysis, urine culture, serum creatinine, imaging and treatment were summarized in Table 1. Although uncomplicated patients with a first UTI should be treated with a short 3-5 day course, RUTI patients may necessitate a longer antibiotic course (7 days or more) to ensure complete resolution of their infection (*mean* [$\bar{x}$] = $22): trimethoprim-sulfamethoxazole (TMP-SMX) 160/800 mg twice daily [BID] ($9), nitrofurantoin 100 mg BID ($45), or ciprofloxacin 250 mg BID ($11). After antibiotics, urinalysis and culture could be optionally repeated to ensure UTI resolution ($13 per urinalysis and culture), followed by office cystoscopy ($168). Upper tract imaging ($\bar{x}$ = $336), when indicated for persistent bacterial strains, included renal ultrasound ($142) or CT Urogram ($529).[2,17] Overall, cost of initial RUTI evaluation was estimated at $730 with optional imaging, vs $390 without. Patients who continued to have symptoms may require further follow-up visits with urine testing ($88) and intermittent UTI treatment ($\bar{x}$ = $22/infection).

Table 1. Cost and capacity cost rate of care-delivery value chain

Stages of Care-Delivery Value Chain	Estimated Cost ($)	Mean Cost Capacity Rate ($/min)
Initial urologic appointment*	166	5.54
Imaging*,†	$\bar{x}$ = 335	
Renal US	142	4.74
CT Urogram	529	26.47
Cystoscopy in office*	168	5.60
Urinalysis*	4	4.43
Urine culture*	9	0.003
Serum creatinine*	7	7.03
Acute antibiotic treatment‡ (7 d)	$\bar{x}$ = 22	
TMP-SMX 160/800 mg BID	9	1.32
Nitrofurantoin 100 mg BID	45	6.38
Ciprofloxacin 250 mg BID	11	1.52
IV antibiotics for MDR culture† (10-14 d)	$\bar{x}$ = 3390	
IV Piperacillin-Tazobactam 13.5 g	2983-3296	1.88
IV Ceftriaxone 2 g	3127-3498	7.07
IV Ertapenem 1 g	3464-3970	8.02
Total cost of RUTI workup	390-725	
Conservative therapy‡ (per year)	$\bar{x}$ = 106	
D-Mannose	49 (35-63)	0.27
Lactobacillus	110 (55-164)	0.30
Cranberry tablets	160 (110-175)	0.22
Estrogen therapy‡ (per year)		
Topical estrogen cream	830 (800-850)	10.64
Vaginal estradiol ring	1288 (1000-1600)	80.49
Long-term antibiotic use‡ (per year)		
Self-start§	40 (18-80)	4.50
Postcoital‖	58 (17-166)	2.39
Continuous¶	186 (59-574)	2.07

* Medicare Physician Fee Schedule.
† Institutional data.
‡ GoodRx and local pharmacy pricing.
§ 3-d course at treatment dose, with ~2.2 episodes/year.
‖ 1 dose within 2 hours of coitus, with ~1 dose/week.
¶ 6-mo daily course.

Patients with multidrug-resistant cultures or multiple drug allergies may require prolonged (10-14 day) IV antibiotic course, administered outpatient via peripheral intravenous central catheter (PICC). From institutional data, including total cost of PICC placement and daily infusions, outpatient IV antibiotics costs varied by medication and course length ($\bar{x}$ = $3390): Piperacillin/Tazobactam 13.5 g ($2983-$3296), Ceftriaxone 2 g ($3127-$3498), or Ertapenem 1 g ($3464-$3970).

Using local pharmacy pricing,[23] conservative therapy averaged $106/year: $35-$63 for D-mannose tablets ($\bar{x}$ = $49), $55-$165 for vaginal lactobacillus ($\bar{x}$ = $110), and $110-$175 for cranberry tablets ($\bar{x}$ = $160). For postmenopausal patients, topical estrogens were concurrently offered with conservative measures. For creams, recommended dosing was 0.5 g, administered intravaginally twice weekly. Recommended ring usage was 1 ring placed vaginally and replaced every 12 weeks. Vaginal estrogen cream, while estimated at $200 if compounded, ranged from $800 to $900 per year for traditional formulation ($\bar{x}$ = $830). Conversely, estradiol rings ranged between $1000 and $1600 per year ($\bar{x}$ = $1290).

Index patients who failed conservative therapy proceeded to SS or PC antibiotics. For SS regimens, patients self-diagnosed by UTI symptoms and positive urine dipstick (from $3 in office to $10 over-the-counter), and began a short antibiotic course, including TMP-SMX 160/800 mg BID ($3.96), ciprofloxacin 500 mg BID ($4.56), or nitrofurantoin 100 mg BID ($31.90). Given estimated recurrence of 2.2 UTIs/year on SS,[6] average cost was $40/year (CCR = $4.50/min).

For patients whom UTIs were temporally associated with intercourse, PC regimen was initiated. Following coitus, patients took 1 antibiotic dose: TMP-SMX 80/400 mg ($0.33 per dose), ciprofloxacin 125 mg ($0.38 per dose), cephalexin 250 mg ($0.55 per dose), or nitrofurantoin 100 mg ($3.19 per dose). Women with UTIs have variable reported rates of coital frequency, from less than once a month to more than 3 times per week.[24] A conservative estimate of 1 PC dose per week was used, averaging $58/year (CCR = $2.39/min).

Patients who failed SS or PC advanced to a 6-month course of continuous daily antibiotics ($\bar{x}$ = $186, CCR = $2.07/min). Costs varied by drug, from TMP-SMX 40/200 mg every other day ($24) or daily ($59), ciprofloxacin 125 mg ($68), cephalexin 250 mg ($99), TMP 100 mg ($130), or nitrofurantoin 100 mg ($574). Patients who continued to have RUTIs repeated continuous antibiotics or, if continuous antibiotics were not tolerated, switched to SS therapy. Patients with resistant cultures who failed oral antibiotics may ultimately require IV treatment.

DISCUSSION

Utilizing TDABC, financial burden of RUTI was examined from 2 perspectives: defining initial cost of RUTI workup, and then extrapolating the annual cost of each

long-term prevention modality. Initial workup for RUTI was estimated at $730, of which imaging was the most costly component ($\bar{x}$ = $336). Acute UTI treatment cost ranged from $9 for 7 days of TMP-SMX, to $3970 for 14 days of IV Ertapenem via PICC. Additional long-term management costs varied considerably among conservative therapies, from $49/year for D-mannose to $1288/year for vaginal estradiol ring. Cost of antibiotics ranged from $40/year for SS, $58/year for PC, and $186 for 6 months continuous antibiotics course. CCR ranged from $0.003/min for urine culture to $80/min for estrogen ring.

Specific treatment variables may increase long-term expenses. First, use of imaging nearly doubled the cost of workup for RUTI patients, from $390 to $730. Though only indicated in cases of bacterial persistence, upper tract imaging may be low-yield and not justify cost.[17,18] Cost of local estrogen therapy in postmenopausal patients can be significant, although it may secondarily benefit patients with concurrent genitourinary symptoms of menopause or atrophic vaginitis. Though compounded estrogens were roughly $600 per year cheaper than manufactured forms, they may be impure or less potent. Long-term use of estradiol ring specifically was $455/year costlier than any other treatment. Even in premenopausal patients, exclusive use of conservative therapies was ~$125 more costly than use of SS or PC regimens.

While conservative therapy may be perceived as "natural" with less potential for harm, we found the cost of over-the-counter supplements may accrue over time. Notably, costs of some supplements, which are not covered by insurance, were directly borne by the patient. As the Food and Drug Administration does not regulate over-the-counter supplements, different brands vary in form, dosage, concentration, and cost. One 2014 payer-perspective study found that cranberry products and other conservative therapies were less cost-effective than daily nitrofurantoin prophylaxis.[10] Other studies agreed that cranberry products were costlier than TMP-SMX prophylaxis, and the expense of treating UTI recurrence was greater over time.[11] Furthermore, one meta-analysis found that 1-year use of cranberry supplements, in comparison to placebo or antibiotic prophylaxis, was more expensive with lower efficacy.[11,12] In contrast, due to the heterogeneity of available formulations and inconclusive evidence supporting the use of mannosides and lactobacillus, the cost-benefit ratio of these therapies is unclear.

Nevertheless, conservative measures do not contribute to increase uropathogen resistance, a major disadvantage of antibiotics.[6,8] The need for IV antibiotics due to failure of therapy contributed a major additional expense. Additionally, many among these patients required intermittent oral antibiotic courses for symptomatic UTIs occurring between exacerbation episodes necessitating IV antibiotics. As a result, treatment costs were over $3300 more than comparable patients who responded to oral antibiotics. While these patients make up less than 10% of overall RUTI patients,[27] the incidence of highly resistant *Escherichia coli* and other enteric bacteria has been increasing in recent decades, accounting for an estimated 25%-54% of all uropathogens.[28] Multidrug-resistant microorganisms are associated with patient history of RUTI, inadequately treated infections, and long-term antibiotic prophylaxis.[27,29]

Patient factors, like medication tolerance and infection triggers, can also influence cost. While SS options may reduce cost of physician visits and allow more timely resolution of symptoms, infection recurrence rates were still fairly high, as the antibiotics were more therapeutic than preventative.[6,30] Alternatively, fewer doses of antibiotics were taken in PC regimens than in SS regimens, and patients had lower infection recurrence rates, ~0.3 UTI/year.[25] As medication choice ultimately depends on culture sensitivities, patients may require antibiotics with a less desirable side-effect profile, such as fluoroquinolones. Furthermore, the costs of specific antibiotics greatly differ as well; for example, for a 7-day treatment dose course, TMP-SMX may cost less than $10, while nitrofurantoin, a more commonly used medication, costs about $35 more. Considering geographic variability of medication and supplement costs, we calculated mean costs of each based on pharmacy pricing from multiple sources, including some without geographic variance (ie, Amazon, Walmart); in calculating overall average cost for each antibiotic regimen, means accounted for the most commonly prescribed drugs.

Several randomized controlled trials and reviews indicate superior efficacy of daily antibiotics over cranberry, estrogens, and SS therapy.[6] However, daily antibiotics are more costly than PC or SS regimens, roughly $128 and $146 more per year respectively. In reality, index patients who advance to continuous antibiotic regimens have likely tried and failed less "aggressive" options. Daily prophylaxis may be the only option to prevent infection and courses up to 6 months or longer can be efficacious for these patients.[30] The trade-off is greater costs, increased antibiotic dosage, and higher probability of drug resistance over time.[24,25] Additionally, a Cochrane review found that long-term daily antibiotic use was associated with oral candidiasis, gastrointestinal intolerance and rare complications such as liver injury, Steven-Johnsons' Syndrome or pancytopenia.[9] Although rates of these adverse events in RUTI patients specifically are not well described in the literature and associated costs are unpredictable, they are nevertheless significant and underscore the importance of practicing responsible antibiotic stewardship.

While the TDABC approach is advantageous, there are limitations. Our study primarily used cost and time averages of each stage in RUTI management to calculate total costs and cost efficiency. However, variables such as antibiotic choice depend on patient factors, so averages may not reflect the exact cost for every individual. Likewise, time estimates for each stage of care are subject to variability and a standardized method of data collection for time estimates was not utilized; therefore the calculated cost-efficiency may differ depending on the true time spent. Similarly, index pathways included in this cost-analysis did not include comorbidities, such as renal insufficiency or diabetes, which may affect management of real-life

RUTI patients. This study focuses purely on defining costs, and we acknowledge that the cost-benefit ratio for each treatment option depends upon many variables, including changing reimbursement patterns and institutional differences.

Still, TDABC allowed us to capture costs and time spent in acute and RUTI management at the resource level. Thus, this study is not limited by real life patient data, self-reporting bias or skewed profit margins. Using theoretical index patients better allowed us to outline the process of care delivery and treatment of RUTI. In our study, TDABC highlighted the potentially avoidable cost of imaging in RUTI workup and identified less cost-effective treatments options, such as long-term conservative therapy and topical estrogens. However, we also confirmed the greater financial burden for patients with bacterial resistant conditions, highlighting the dangers of inappropriate antibiotic use. By better defining finite costs for commonly utilized RUTI management options, this information serves as another tool for informed decision-making, and underscores the need for safe and cost-effective therapies.

CONCLUSION

Using TDABC, we found that initial RUTI workup costs between $390 and $725; judicious use of imaging may reduce this cost. Conservative therapies, particularly estrogen ring more than cream, while associated with fewer adverse events and less likelihood of resistance, were found costlier than antibiotics. Of all preventative antibiotic strategies, continuous daily antibiotics were most costly; SS courses were least costly but may be associated with high recurrence rates. Ultimately, patients with resistant infections requiring IV antibiotics faced the greatest cost of therapy.

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EDITORIAL COMMENT

This paper focuses on the significant costs of treating recurrent urinary tract infection (UTI) in females. Factors related to anatomy, hormones, menopause, and sexual activity create conditions more favorable for UTI occurrence in women. Studies have suggested that UTI is up to 30 times more common in women.

In recurrent UTI, it is estimated that less than 1.5% of women will have findings of urinary tract abnormality or other serious pelvic disease. Clearly the authors point out that indiscriminate use of expensive imaging studies or endoscopic evaluations are to be discouraged except in cases with high clinical suspicion. A large study conducted in France clearly showed that proper first diagnosis led to less costs and reduced need for imaging or other costly studies. In the majority of cases when imaging is felt to be needed, a KUB and renal ultrasound are usually sufficient.[1]

Use of holistic and dietary regimens can be effective as is pointed out however these forms of treatment are of limited success, do have associated out of pocket costs to patients, but also do not contribute to the occurrence of antibiotic resistant bacteria.

In premenopausal women with recurrent UTIs, cranberry prophylaxis has not been shown to be cost-effective compared to trimethoprim-sulfamethoxazole prophylaxis. Yet, the additional costs attributed to development of antibiotic resistance were likely higher though not defined in this reference.[2-4]

Indiscriminate use of antibiotics without proper culture and sensitivity studies to allow for treatment adjustment increases the incidence of antibiotic resistance. This is a problem of great global health concern as the rapid evolution of highly multidrug resistant strains of bacteria is occurring at an alarming rate.

Historically, studies in humans and primates to evaluate the effects of recurrent UTI on the urinary tract have led to the finding of p-fimbriated lines, *Escherichia coli (E coli)* in particular. This has given us a better understanding of the process of ascending infection as well as persistent colonization.[5]

One hope to reduce the cost of recurrent UTI and help prevent continued emergence of highly resistant bacterial strains is found in the development of vaccines. For many decades, researchers have worked on a variety of approaches in seeking to create a vaccine to prevent recurrent UTI or UTI altogether.

A recent vaccine that has raised interest favors immunoactive prophylaxis using a suspension of inactivated complete cells of different strains of *E coli*, Klebsiella pneumonia, Proteus mirabilis, and Enterococcus faecalis. The formulation allows for sublingual administration making its use easy and comfortable. The polyvalent bacterial vaccine is effective in the reduction of UTI vs continuous low-dose antibiotic prophylaxis in frail institutionalized older adults and provides an improvement in the quality of life.[6-8]

The World Health Organization estimates that 700,000+ persons die annually from bacterial infections. Some 23,000+ die in the United States according to Centers for Disease Control and Prevention (CDC) data with over 2 million illnesses annually caused by drug resistant bacteria. Estimated costs in the US are $20-25 billion in excess health expenditures and $35 billion additional for lost productivity. As a species, we are in dire need of new antibiotics, vaccines and diagnostics to end the rise of drug resistant bacteria.[9]

The clear benefit of the use of antibiotic prophylaxis to individual patients may well be outweighed by the potential harm to both patient and society due to increased frequency of every more antibiotic resistant bacteria. This is often a difficult clinical bargain for every physician to make.

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AUTHOR REPLY

There is no debating that the rising incidence of recurrent urinary tract infections (RUTI) has created a large burden on patients and our health care system. There is much needed research in this area to provide effective, expeditious, and inexpensive preventative and therapeutic options that do not contribute to increasing rates of antibiotic resistance.

RUTI is largely a bladder limited disease. Therefore, a treatment localized to the organ of interest is urgently needed. There has been some success in bladder antibiotic irrigation with gentamicin which is an option for those who already use catheterization for incomplete bladder emptying[1] as well as bladder fulguration of trigonitis to eliminate quiescent intracellular reservoirs of bacteria in the bladder mucosa.[2]

Conservative measures including adequate fluid intake, discouraging detrimental toileting behaviors as a result of chronic holding behaviors or concomitant pelvic floor dysfunction, avoidance of

bladder irritants and vaginal estrogen therapy may have some beneficial impact in this patient population for symptomatic relief and possible prevention of further RUTI.

Appropriate antibiotic stewardship while awaiting the maturation of clinical research is exceedingly important. The concern of ascending bacterial infection resulting in pyelonephritis in acute cystitis is exceedingly minimal,[3] therefore a paradigm shift in providing supportive care and symptom relief may be appropriate in patients with acute cystitis while awaiting urine culture results. Additional education on disposing of unused antibiotics as well as completing full courses of prescribed antibiotics may also be beneficial. Furthermore, over prescription of antibiotics has contributed to increasing the rates of allergy and sensitivity to antibiotics resulting in difficulties prescribing effective oral medications.[4] Considering referral to allergists to assess the ability of patients to tolerate medications listed as "allergies" can be increasingly valuable.

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