



Assessing the Management of Urinary Tract Infections at a Large, Urban Teaching Hospital

Advani Shreena Patel^{1*}, Rab Saira¹ and Kalokhe Ameeta²

¹Department of Pharmacy and Drug Information, Grady Health System, USA

²Department of Medicine, Emory University School of Medicine, USA

Abstract

Purpose: Despite availability of consensus guidelines for management of urinary tract infections, variability in both diagnosis and treatment of urinary tract infections has been noted in the literature.

Methods: From October 1, 2013 to March 31, 2014 we conducted a three-phase pilot study to evaluate the efficacy of a pharmacist-driven educational intervention on improving rates of guideline-based management of urinary tract infections (UTIs) at Grady Health System (GHS), a large, urban teaching hospital. The primary outcome measured was the percentage of UTIs managed in compliance with GHS guidelines before and after pharmacist intervention; guideline-based diagnosis and treatment of UTIs served as a composite indicator of guideline compliant management. Secondary outcomes included: percentage of UTIs in compliance with GHS guideline-based empiric antibiotic selection and treatment duration. Additionally, total cost savings associated with GHS guideline adherence was calculated.

Results: One hundred patients were analyzed for the retrospective phase of the study. Of these, 86% were managed in compliance with guidelines. One hundred patients were analyzed for the prospective phase of the study. Of these, 98% were managed in compliance with guidelines. Empiric antibiotic selection was in compliance with guidelines 66% of the time during the pre-intervention phase, compared to 95% during the post-intervention phase. Annual cost savings based on antibiotic use avoidance resulting from pharmacist intervention were calculated as \$5,000 for a seven-day course of antibiotics.

Conclusion: Pilot findings suggest that a simple, pharmacist-driven educational intervention can impact adherence to hospital UTI management guidelines, and thus result in improved antibiotic stewardship and cost savings.

Introduction

Urinary tract infections (UTIs) are among the most prevalent of infectious diseases [1]. According to a 1997 survey, UTIs accounted for nearly seven million office visits and nearly one million emergency department visits. Of the one million emergency department visits, approximately 100,000 resulted in hospitalizations [2]. The economic impact associated with the management of UTIs is projected to exceed one billion dollars [1]. The magnitude of the potential economic and clinical implications UTIs impart, warranted the need for consensus treatment guidelines. In 1999, the Infectious Diseases Society of America (IDSA) published guidelines to direct clinical practice in the management of acute, uncomplicated cystitis and pyelonephritis in women [3]. Emergence of antimicrobial resistance among uropathogens along with studies supporting use of newer agents prompted an update to these guidelines in 2011 [4]. Additionally, IDSA published guidelines for appropriate management of asymptomatic bacteriuria and catheter-associated UTIs (CA-UTI), conditions for which clinical practice guidelines had not previously existed [5,6].

Acute cystitis is an infection of the urinary tract characterized by symptoms of dysuria, suprapubic pain, increased frequency, and/or increased urgency with urination. Diagnosis of UTI is dependent not only on the associated signs and symptoms, but also a urinary culture growing $\geq 10^2$ colony-forming units (CFUs) per milliliter (mL) of a bacterial pathogen. Acute cystitis is further categorized as either complicated or uncomplicated. This classification distinguishes between a UTI occurring in the presence of a normal genitourinary tract, an uncomplicated UTI, and one that occurs in individuals with a functional or structural abnormality of the genitourinary tract, a complicated UTI. Pyelonephritis is inflammation of the urinary tract involving the kidneys, and is characterized

OPEN ACCESS

*Correspondence:

Patel AS, Department of Pharmacy and Drug Information, Grady Health System, 80 Jesse Hill Jr Atlanta, GA 30303, USA, Tel: 404-616-0628; Fax: 404-616-0672;

E-mail: sadvani@gmh.edu

Received Date: 28 Dec 2016

Accepted Date: 14 Mar 2017

Published Date: 16 Mar 2017

Citation:

Patel AS, Saira R, Ameeta K. Assessing the Management of Urinary Tract Infections at a Large, Urban Teaching Hospital. *Ann Infect Dis Epidemiol.* 2017; 2(2): 1015.

Copyright © 2017 Patel AS. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Table 1: IDSA Guidelines for Initial Treatment of UTIs [4,5,6].

Type of UTI	Initial Treatment Recommendation	Alternative Treatment Recommendations
Acute, uncomplicated cystitis	Nitrofurantoin monohydrate 100 mg PO BID x 5 days Trimethoprim-sulfamethoxazole 160-800 mg PO BID x 3 days Fosfomycin 3 gm PO x 1 dose	Fluoroquinolones (i.e. ciprofloxacin 250 mg PO BID x 3 days) Beta-lactams (i.e. amoxicillin-clavulonate 500 mg PO BID x 3-7 days)
Pyelonephritis	Ciprofloxacin 500 mg PO BID x 7 days	Ciprofloxacin ER 1000 mg PO q day x 7 days
Catheter-associated UTI	Discontinue catheter Treatment should be directed toward isolated organism from urine culture x 7 days for patient showing prompt resolution and 10-24 days for those with delayed response	Levofloxacin 750 mg x 7 days [*]
Asymptomatic bacteriuria	Treatment is only recommended in pregnant women, patients undergoing urologic procedures with anticipated mucosal bleeding, and patients undergoing a transurethral resection of the prostate Specific antimicrobials not outlined; however a duration of 3-7 days is recommended	

^{*}Route of therapy not specified

Table 2: GHS Guidelines for Management of UTIs [12].

Category	Definition	Empiric Treatment	Definitive Treatment
Community acquired UTI	Signs/symptoms for cystitis = frequency, urgency, dysuria, suprapubic pain Signs/symptoms for pyelonephritis = cystitis	First Line Ceftriaxone 1 g q24h Severe Beta-Lactam Allergy (Anaphylaxis, throat swelling) Aztreonam 2 g q8h ----- Consider vancomycin 15 mg/kg x 1 dose, then pharmacy to dose, if there is suspicion for Enterococcus UTIs	Convert to an oral regimen active against the organism with resolution of sepsis. Preferred therapy IF susceptible to these agents:
Hospital acquired or Healthcare-associated UTI	PLUS costovertebral angle pain and tenderness or fever Urinalysis with leukocyte esterase/nitrite PLUS pyuria (WBC > 10) PLUS Clinical signs/symptoms	First Line Piperacillin-tazobactam 4.5 g q6h Second Line Ceftazidime 2 g q8h + Vancomycin 15 mg/kg x 1 dose, then pharmacy to dose Severe Beta-Lactam Allergy (Anaphylaxis, throat swelling) Aztreonam 2 g q8h +/- Tobramycin 5 mg/kg; pharmacy to dose + Vancomycin 15 mg/kg x 1 dose then pharmacy to dose, if there is suspicion for Enterococcus UTIs	Gram-negative organisms – TMP-SMX DS 1 tab BID or Cephalexin 500 mg QID Gram-positive organisms of Streptococcus and Enterococcus species – Amoxicillin 500 mg TID
Catheter-associated UTI (CA-UTI)	Signs/symptoms: new onset fever, rigors, altered mental status, flank pain/tenderness, hematuria PLUS presence of >100,000 cfu of >1 bacterial species in a single catheter urine specimen Spinal cord injury: signs/symptoms include increased spasticity, autonomic dysreflexia, sense of unease Pyuria, cloudy or malodorous urine are not diagnostic of CA-UTI	Catheter Management Discontinuation of catheter will remove source of infection as is preferred Replacement of catheter Treatment Based on urine culture and susceptibilities; if unavailable, base treatment on previous cultures if available Treat as cystitis pending urine culture and susceptibilities Treatment without removal of catheter may increase risk of relapse and resistance Duration may be for 7 days in patients with quick resolution of symptoms	Treatment of culture negative pyelonephritis: Ciprofloxacin 500 mg PO BID or TMP/SMX 1 DS tablet PO BID Duration: 7-14 days, consider shorter duration of therapy in patients with resolution of symptoms within 72 hours. Longer duration is not associated with improved clinical cure but is associated with increased drug resistance.

by costovertebral angle pain, tenderness, and fever. Microbiological findings for diagnosis of pyelonephritis are identical to those for acute, uncomplicated cystitis [5]. Catheter associated UTIs (CA-UTIs) occur in patients with indwelling urethral or suprapubic catheters. Patients present with signs or symptoms associated with a UTI that are unexplained by other sources of infection, along with $\geq 10^3$ CFU/mL of at least one bacterial species in a single catheter urine specimen. The culture may also be obtained from a midstream voided urine specimen of patients who had a catheter removed within the previous 48 hours [6]. Asymptomatic bacteriuria is defined by the presence of $\geq 10^5$ CFU/mL in either two consecutive voided urine specimens, a single clean-catch voided urine specimen, or a single catheterized specimen with $\geq 10^2$ CFU/mL [5]. Patients will not present with signs or symptoms of UTI. Of note, these definitions do not apply to certain patient populations such as immunocompromised individuals, pregnant women, and those undergoing urologic procedures. Treatment algorithms are individualized based on the classification of the UTI (Table 1). These initial treatment recommendations are based

on the epidemiology of uropathogens in the population. According to the guidelines, *Escherichia coli* accounts for 75-95% of causative pathogens for UTIs. Other common uropathogens include members of the Enterobacteriaceae family such as *Klebsiella pneumoniae* and *Proteus mirabilis* [4].

Despite the establishment of these treatment guidelines, several studies have indicated that the management of UTIs is varied [7-9]. A retrospective chart review was conducted to determine the appropriateness of antimicrobial therapy in response to urine culture results. A study evaluating bacteriuria in 137 patients from an academic hospital with an adjoining long term care facility, found that only 25% (34/137) of patients met criteria for symptomatic bacteriuria. Sixty-four percent (42/67) of the patients who had asymptomatic bacteriuria were not managed according to IDSA guidelines. Thirty-six of the patients with bacteriuria were found to have a primary source of infection at a non-urinary site. These patients received antimicrobial therapy despite lacking signs or symptoms of a UTI [7]. Furthermore, a study investigating the appropriate management of CA-UTIs at

a tertiary care hospital reviewed a total of 280 urine cultures from hospitalized patients with indwelling or condom catheters. Of the 280 cultures reviewed, 58.5% (164/280) were classified as catheter associated asymptomatic bacteriuria (CAABU). Thirty-two percent (90/280) of CAABU cases were treated for UTI despite the absence of appropriate signs or symptoms. Factors associated with inappropriate treatment included older patient age, higher white blood cell count, and patients with urine cultures positive for gram negative bacteria ($p < 0.05$). Finally, a retrospective study conducted at two Rhode Island nursing homes found that 26% (45/172) of patients received inappropriately dosed antibiotics based on the patient's creatinine clearance. Additionally, 40% (69/172) of these patients received treatment that differed from IDSA guideline recommendations. For instance, fifteen patients were initiated on a fluoroquinolone instead of sulfamethoxazole-trimethoprim for empiric therapy [8].

Appropriate management of UTIs improves clinical outcomes for patients, reduces emergence of resistant bacteria, and prevents adverse events associated with unnecessary antimicrobial therapy. For instance, one study found that those who were inappropriately treated for a UTI were 8.5 (95% CI 1.7-42.2) times more likely to develop *Clostridium difficile* associated diarrhea within three months of treatment [9]. Additionally, the IDSA guidelines note an increase in resistance among uropathogens associated with UTIs over the last decade [4]. A retrospective analysis of The Surveillance Network Database-USA in the year 2000 found 7.1% (2,768 of 38,835) of *Escherichia coli* isolated from urine cultures were resistance to three or more antimicrobial agents. A majority of these multidrug-resistance strains were resistant to sulfamethoxazole-trimethoprim, fluoroquinolones and ampicillin [10].

Given such implications for inappropriate management of UTIs, efforts must be made to align diagnosis and treatment of UTIs with evidence. A recent study, conducted by Hecker and colleagues evaluated the effect of antimicrobial stewardship interventions on adherence to uncomplicated cystitis and pyelonephritis guidelines in the emergency department [11]. Interventions included implementation of an electronic order set including institution specific recommendations for management of UTIs and a pharmacist-led audit and feedback component. Adherence to guidelines with regards to antibiotic choice and duration of therapy increased from 44% to 68% after implementation of order sets and rose further to 82% after implementation of audit and feedback.

Grady Health System (GHS), a large, urban, teaching hospital in Atlanta, Georgia, established guidelines in 2008 for managing UTIs in the inpatient setting. These guidelines were updated in 2013 (Table 2). The IDSA guidelines emphasize consulting community resistance patterns to determine appropriate empiric treatment options. The 2012 GHS antibiogram was utilized to tailor the updated 2013 UTI guidelines for the institution. For instance, a total of 2,803 *Escherichia coli* isolates were obtained from urinary cultures in 2012; only 75% of these isolates were susceptible to ciprofloxacin; therefore, quinolones are not recommended as a first line option for UTIs. Despite these recommendations, variability in the diagnosis and treatment of UTIs at GHS has been noted [12]. Such deviation of clinical practice can have a tremendous impact on patient outcomes. As such, formal evaluation of the management of UTIs at GHS is necessary in order to reduce the risk of antimicrobial resistance among uropathogens, improve stewardship of antimicrobials, decrease medication-related costs, and most importantly improve quality of care.

Materials and Methods

Patients, 18 years or older, admitted to GHS from August 1, 2013 – October 31, 2013 and January 1, 2014 – March 31, 2014 who had a UA ordered for evaluation of a potential UTI were included in the study. Patients in the intensive care or step down units during time of UA order, patients with an initial UA ordered during a weekend day, and those with a UA ordered for evaluation of non-infectious disease state, as determined through chart review, were excluded from the study.

The primary outcome measured was the percentage of UTIs managed in compliance with GHS guidelines before and after pharmacist intervention; guideline-based diagnosis and treatment of UTIs served as a composite indicator of guideline compliant management. Secondary outcomes included: percentage of UTIs in compliance with GHS guideline-based empiric antibiotic selection, percentage of UTIs in compliance with GHS guideline-based duration of therapy, and total cost savings associated with GHS-guideline based antibiotic use. Cost savings were calculated based on the drug acquisition cost for antibiotics whose use was avoided as a result of pharmacist intervention.

This study was approved by the institution's Investigational Review Board and was conducted in three phases: 1) a retrospective, pre-intervention phase serving as a control for analysis of appropriately managed UTIs, 2) an intervention phase consisting of a pharmacist-driven educational program, and 3) a post-intervention phase used to evaluate the efficacy of the educational intervention on improving adherence to GHS UTI guidelines.

The first phase consisted of retrospectively identifying patients for whom a urinalysis (UA) was ordered during August through October of 2013. This was accomplished through review of laboratory records available via 'TheraDoc', a clinical surveillance program that is linked to the hospital's electronic record system. Data was collected until 100 patients meeting inclusion criteria were identified. A standardized data collection sheet was utilized to record information from electronic medical records (EMRs). Patient parameters collected included general demographic information, UA results, indication for UA, documented signs and symptoms of UTI, antibiotics initiated, and urine culture results.

A pharmacist categorized patients' UTIs as guideline adherent or non-adherent based on whether diagnosis and treatment followed GHS established guidelines for management of UTI (Table 2). A repeat UA in a patient was treated as a new encounter if it was obtained three weeks after the initial UA.

The intervention phase took place during the months of November and December of 2013 and involved conducting five educational sessions and the provision of informational pocket cards for hospital physician staff including interns and residents on general medicine, surgery, and ambulatory care services. The pharmacist-led educational sessions consisted of a review of GHS UTI management guidelines, definitions of various categories of UTIs per IDSA guidelines, and common misconceptions associated with diagnosis and treatment of UTIs. These sessions were also held for all pharmacy staff with hopes to reinforce importance of guideline adherence at the medication verification level. Pocket cards outlining GHS UTI management guidelines in a flow chart form were distributed to physician staff throughout the intervention phase (Figure 1).

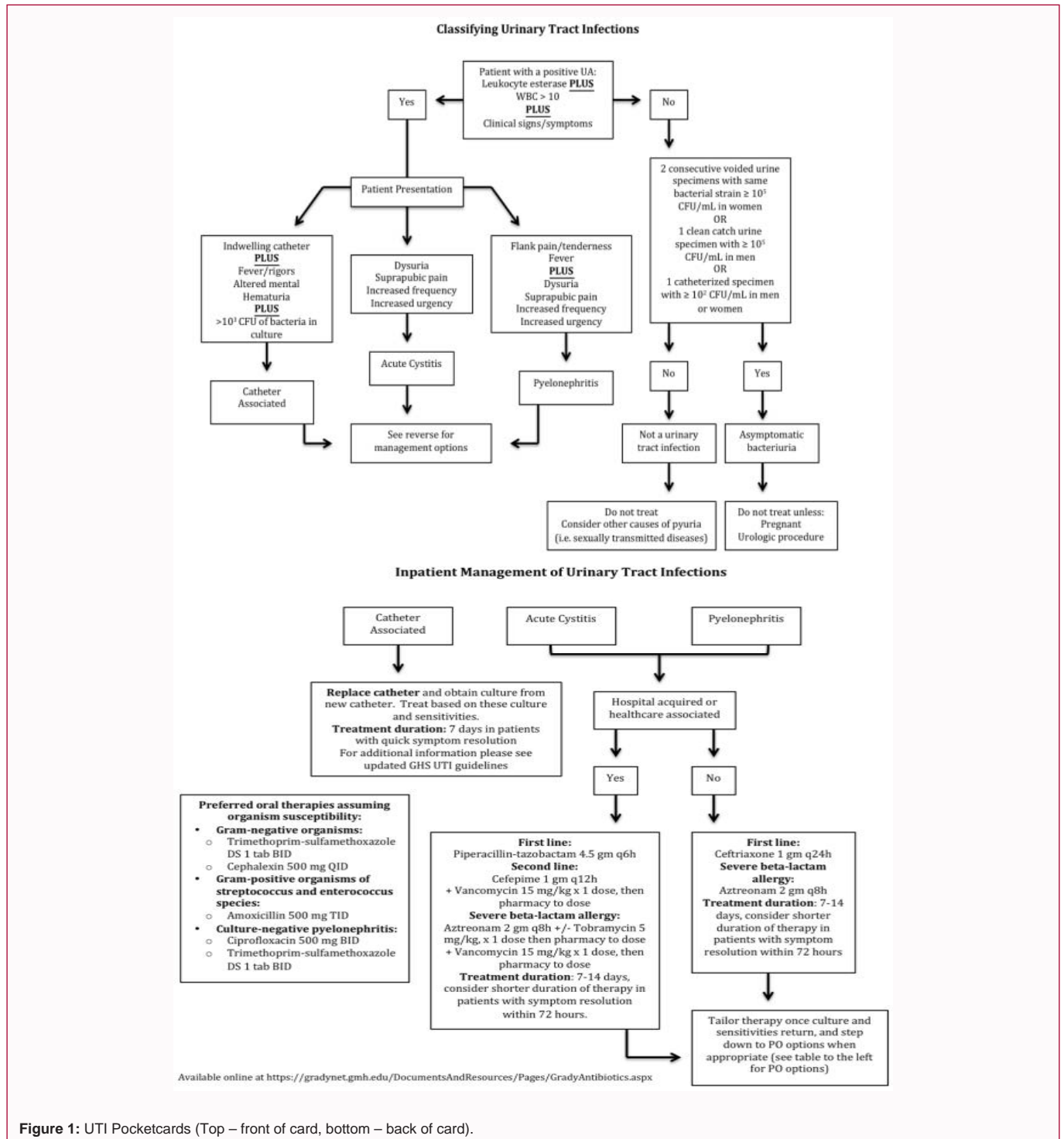


Figure 1: UTI Pocketcards (Top – front of card, bottom – back of card).

The final phase of the study consisted of a concurrent chart review of all patients, who met inclusion criteria, for whom a UA was ordered between January and March 2014. A pharmacist provided real-time feedback, mimicking the institution's current antimicrobial stewardship program, to a physician member of the treatment team if non-guideline-based UTI management was identified. Data was collected until a 100 patients meeting inclusion criteria were reached.

A sample size of 100 patients for the pre-intervention group and 100 patients in the post-intervention group was pre-determined based on feasibility To compare percentage of UTIs managed per GHS

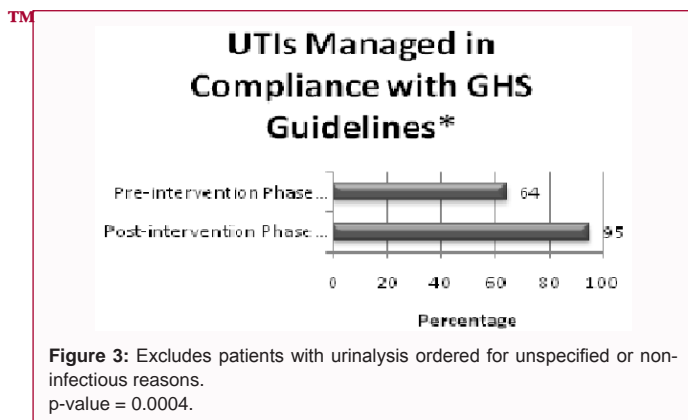
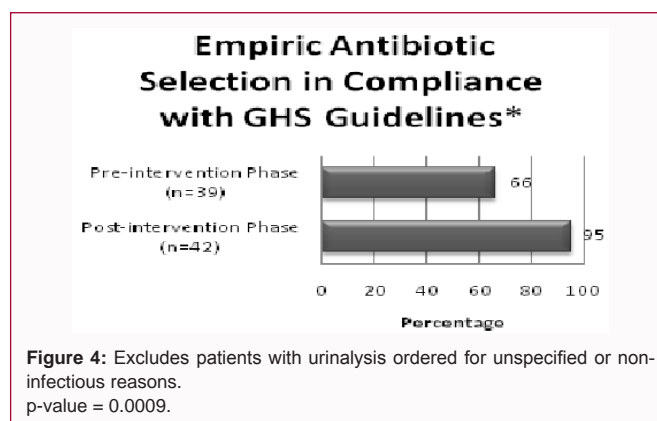
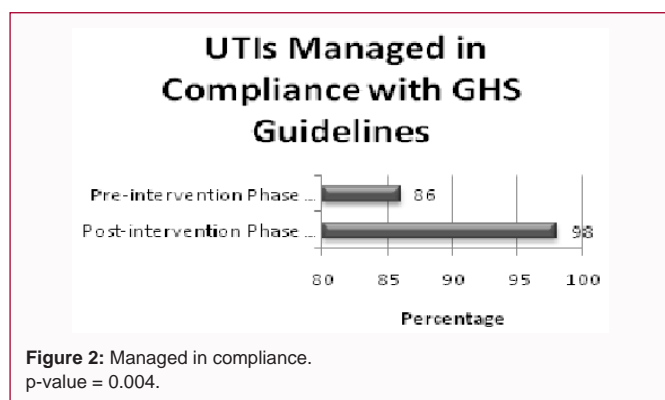
guidelines before and after pharmacist intervention, Chi-squared test or Fischer's exact test were performed with a p-value ≤ 0.05 defined as significant. Descriptive statistics were utilized to calculate incidences and cost avoidance. All statistical tests were performed using VassarStats®.

Results and Discussion

A total of 243 patients were screened during the study period, 118 during the retrospective phase and 125 in the concurrent phase. Eighteen patients were excluded in the retrospective phase and 25 were excluded during the concurrent phase. Baseline characteristics

Table 3: Patient Demographics.

	Pre-intervention Phase (n=100)	Post-intervention Phase (n=100)	p-value
Female (%)	56	54	0.887
Average Age (years, SD)	51±16	50±14	
Comorbidities (%)			
Hypertension	42	45	0.775
Diabetes	37	30	0.368
End Stage Renal Disease	24	26	0.870
Human Immunodeficiency Virus	20	24	0.608
Cancer	8	4	0.372
Ordering Service (%)			
Medicine	87	91	0.498
Surgery	11	9	0.814
Orthopedics	2	0	0.497



were similar between both groups of patients (Table 3). Cystitis was the most common type of UTI managed during both the retrospective and concurrent phases (85% vs. 80% respectively). The percentage of UTIs managed in accordance to GHS guidelines was 86% in the pre-intervention phase and 98% in the post-intervention phase (p=0.004, Figure 2). A majority of UAs were ordered for non-specified indications during both phases of the study (61% and 58%). These UAs ordered for non-specified reasons were included in the study, as evaluation of a potential UTI could not be definitively ruled out from chart review. The inclusion of these UAs may have confounded the primary outcome measure, as many of these UAs were likely ordered for evaluation of non-infectious disease states. When excluding UAs ordered for non-specified reasons, 64% of UTIs were managed in accordance to GHS guidelines in the pre-

intervention phase compared to 95% in the post-intervention phase (p = 0.0004, Figure 3).

Duration of therapy for UTIs was in accordance to GHS guidelines during both the pre and post-intervention phases. The average duration of therapy was 11.3 days during the pre-intervention phase and 10.5 days in the post intervention phase. Empiric antibiotic selection was in line with GHS-guideline recommendations 66% of the time in the pre-intervention phase and 95% during the post-intervention phase (p=0.0009, Figure 4).

During the post-intervention phase, 10% of UTIs were deemed non-compliant with GHS-guidelines; a pharmacist attempted to provide real-time feedback with recommendations for guideline-based management in all of these cases. Of the ten attempts that were made to provide feedback, the physician was unreachable on two occasions. All recommendations that were relayed were accepted. Potential cost savings were calculated based on these interventions. A total of \$483.42 was saved from the eight accepted recommendations. This savings is based solely on the cost of a seven-day course of antibiotics. Annualized cost savings was also calculated based on the savings from 8 interventions made during the three month, post-intervention phase; annual savings were projected as \$5,041.38.

The results of this study suggest that pharmacist-driven educational intervention can impact guideline adherence for UTI management. Our intervention was intended to improve both diagnosis and treatment of UTIs at GHS. As the results show, GHS guideline-adherent empiric antibiotic selection increased in the

post-intervention phase. This upward trend was largely due to the reduction of empiric use of fluoroquinolones.

Duration of therapy was in compliance with guidelines during both pre and post-intervention phases; while an average duration of 11.3 or 10.5 days was in-line with GHS guidelines, given that a majority of UTIs diagnosed were categorized as acute, uncomplicated cystitis, this may be inappropriate based on IDSA recommendations. The current GHS UTI management guidelines provide a broad range of seven to fourteen days for recommended therapy duration regardless of UTI classification. The IDSA guidelines correlate duration of therapy with type of UTI; for instance, three to seven day duration is recommended for treatment of acute, uncomplicated cystitis. Given this information and the results of this study, a change in current GHS guideline duration of therapy recommendation may be warranted.

The real-time feedback component of the study suggests that physicians at GHS are receptive to pharmacist recommendations regarding UTI management as 100% of recommendations relayed were accepted. These recommendations were largely addressing non-guideline compliant empiric antibiotic selection. Accepted recommendations resulted in cost savings calculated based on antibiotic use avoidance. The savings calculated did not include costs associated with a potential prolonged length of stay.

There were several limitations that may have impacted study outcomes. For instance, the lack of a parallel control arm limits the ability to draw a direct cause and effect relationship between intervention and outcomes. Additionally, data was collected through chart review limiting objectivity. As previously mentioned, a large number of UAs included in the study during both the pre and post-intervention phases were collected for reasons not specified in the EMRs; this ultimately led to the inclusion of UAs that may have been ordered for reasons other than evaluation of a potential UTI, thereby confounding the primary outcome. Lastly, two schools of medicine practice at GHS; only one of these schools was reached for the pharmacist-led educational sessions during the intervention phase. For the school of medicine that was reached, only a fraction of the physicians attended the educational sessions; therefore, the intervention phase was limited by inability to reach all physicians practicing at GHS. These limitations warrant a larger, randomized control trial to further validate findings from this pilot study.

Study findings suggest that a simple, pharmacist-driven educational intervention may impact adherence to hospital UTI management guidelines, and thus result in improved antibiotic stewardship and substantial cost savings. These findings need to be further validated through a larger, randomized trial containing a parallel control arm.

References

1. Colgan R, Nicolle LE, McGlone A, Hooton TM. Asymptomatic Bacteriuria in Adults. *Am Fam Physician*. 2006; 74: 985-990.
2. Schappert SM. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments. United States, 1997. *Vital Health Stat*. 1999; 143: 1-39.
3. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women, Infectious Diseases Society of America (IDSA). *Clin Infect Dis*. 1999; 29: 745-758.
4. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011; 52: e103-e120.
5. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM. Infectious Diseases Society of America Guidelines for the diagnosis and Treatment of Asymptomatic Bacteriuria in Adults. *Clin Infect Dis*. 2005; 40: 643-654.
6. Hooton TM, Bradley SF, Cardenad DD, Colgan R, Geerlings SE, Saint S, et al. Diagnosis, Prevention, and Treatment of Catheter Associated Urinary Tract Infection in Adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis*. 2010; 50: 625-663.
7. Silver SA, Baillie L, Simor AE. Positive Urine Cultures: A Major Cause of Inappropriate Antimicrobial use in Hospitals? *Can J Infect Dis Med Microbiol*. 2009; 20: 107-111.
8. Cope M, Cevallos ME, Cadle RM, Darouiche RO, Musher DM, Trautner BW. Inappropriate Treatment of Catheter-Associated Asymptomatic Bacteriuria in a Tertiary Care Hospital. *Clin Infect Dis*. 2009; 48: 1182-1188.
9. Rotjanapan P, Dosa D, Thomas KS. Potentially Inappropriate Treatment of Urinary Tract Infections in Two Rhode Island Nursing Homes. *Arch Intern Med*. 2011; 171: 438-443.
10. Sahm DF, Thornsberrry C, Mayfield DC, Jones ME, Karlowsky JA. Multidrug-Resistant Urinary Tract Isolates of *Escherichia coli*: Prevalence and Patient Demographics in the United States in 2000. *Antimicrob Agents Chemother*. 2001; 45: 1402-1406.
11. Hecker MT, Fox CJ, Son AH, Cydulka RK, Siff JE, Emerman CL, et al. Effect of a Stewardship Intervention on Adherence to Uncomplicated Cystitis and Pyelonephritis Guidelines in an Emergency Department Setting. *PLOS One*. 2014; 9: e87899.
12. Grady Health System Empiric Inpatient Treatment Guideline for Urinary Tract Infections/Pyelonephritis. 2013.