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# Evaluation of a disease state management guideline for urinary tract infection

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ABSTRACT

A urinary tract infection (UTI) disease state management guideline, including risk-based antimicrobial recommendations, Foley catheter management and transitions of care, was implemented. This study evaluated the outcomes associated with implementation of the guideline. A retrospective study was conducted between 1 July 2013 and 30 September 2013 (pre-implementation) and between 1 July 2014 and 30 September 2014 (post-implementation). Symptomatic patients treated for UTI within 24 h with an identified pathogen were included. Risk-based patient groups were community-acquired UTI, healthcare-associated UTI, or extended-spectrum β-lactamase (ESBL) history in prior 12 months. Recommended antimicrobials were ceftriaxone, cefepime ± vancomycin, or doripenem ± vancomycin, respectively. Given the low post-implementation guideline adherence, pre- and post-groups were combined to evaluate potential guideline value. Length of stay (LOS) decreased when guidelines were followed [5 (IQR 4–7) days vs. 6 (IQR 4–8) days; $P = 0.03$] or appropriate therapy (according to in vitro susceptibilities) was given [5 (IQR 4–7) days vs. 6 (IQR 4–9) days; $P = 0.03$]. Those receiving guideline-recommended antimicrobials were more likely to have appropriate therapy within 24 h (84.4% vs. 64.2%; $P < 0.001$). On multivariate analysis, intensive care unit (ICU) admission and admission from home were associated with longer and shorter LOS, respectively. Despite less than anticipated adherence, these data suggest that the established disease state management guideline can improve outcomes in patients admitted with UTI.


## 1. Introduction

Urinary tract infection (UTI) and pyelonephritis are commonly encountered infections. In 2005, the US Centers for Disease Control and Prevention (CDC) estimated that UTIs accounted for ca. 4 million visits to outpatient providers in the USA [1]. *Escherichia coli* is a common causative pathogen of UTIs, but other Enterobacteriaceae also play a causative role.

Research has identified the presence of risk factors differentiating community-acquired (CA) and healthcare-associated (HA) UTIs and has demonstrated that these differences result in infections with very different epidemiology. One study demonstrated that compared with community-onset pyelonephritis, patients with HA pyelonephritis were less likely to have *E. coli* as the causative pathogen and were more likely to have resistant pathogens, such as extended-spectrum β-lactamase (ESBL)-producers [2]. Two other reports have also document differences in bacterial aetiology, with differences in the percentage of patients with *Pseudomonas aeruginosa* and ESBL-producing organisms being notably different [3,4]. Patients with HA pyelonephritis also have more organ dysfunction, longer hospital length of stay (LOS) and a less robust response to antimicrobial therapy [3]. These data highlight important differences and strongly suggest these two entities require different empirical considerations for their treatment and management.

Given these findings, an investigation was undertaken at our institution to determine the differences seen in the patient population presenting with UTI. *P. aeruginosa* was most commonly seen in HA infections, and ESBL-producers were most commonly seen in those who had previous documentation of an ESBL within the past year [5]. Upon construction of a disease state antibiogram looking at susceptibilities of urinary pathogens only, susceptibilities of Gram-negative causative pathogens varied widely depending on pre-existing risk factors, with no one pathogen dominating the

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antibiogram results. Because of these differences in susceptibilities, empirical therapy was less likely to be appropriate for patients with HA infection or in those with an ESBL history. Inappropriate empirical therapy was also associated with a longer hospital LOS. Delays in appropriate antimicrobial therapy were associated with increased costs, which were not reimbursed, resulting in a financial loss for the institution [6].

Based on these findings, a disease state management guideline was implemented. This guideline grouped patients based on risk factors and outlined appropriate empirical antimicrobial therapy, Foley catheter management, considerations for obtaining cultures, de-escalation strategies and duration of therapy. The purpose of the present study was to evaluate the impact of the guideline on patient clinical outcomes and the financial impact to the institution as measured by LOS.

## 2. Methods

### 2.1. Patient selection

This was a single-site, observational study examining patients with UTI admitted to Hartford Hospital (Hartford, CT), which is an 867-bed mixed academic and teaching tertiary care centre, during two time periods: 1 July 2013 through 30 September 2013 (pre-implementation); and 1 July 2014 through 30 September 2014 (post-implementation). Patients admitted during this time period were identified for study inclusion via diagnostic codes from the International Classification of Diseases, 9th revision (ICD-9). Patients with a diagnosis code of 599, 590 or 595 listed as the primary or secondary reason for admission, who were ≥18 years of age, who were treated for a UTI within 24 h of admission and who had a pathogen isolated on culture were included in the study. In addition, patients included in the study must have had at least one of the following symptoms of UTI documented: fever (temperature ≥38 °C sustained for ≥1 h, or a one-time reading of ≥38.3 °C); chills or rigors; nausea/vomiting; altered mental status; costovertebral angle tenderness; suprapubic or flank pain; dysuria; urinary frequency; urinary urgency; or haematuria. Patients with missing cost records were excluded from the economic analysis. The study was approved by the Hartford Hospital Institutional Review Board with a waiver of informed consent.

### 2.2. Guideline description

The disease state management guideline stratified patients into the following categories: those with documented isolation of an ESBL-producing organism within the past 12 months (EH group); those admitted from a long-term care or skilled nursing facility, those who received antimicrobials within 3 months prior to admission, or those who were hospitalised within the past 3 months (HA group); and all others (CA group). Empirical antibiotic selection in the guideline was based on risk factors associated with each group, and not based on severity of illness; thus, providers were encouraged to choose an antibiotic regimen that would be active against the most likely causative pathogen. The guideline stressed obtaining urinalysis and cultures prior to initiation of antimicrobial therapy, as well as Foley catheter management, which included removing urinary catheters whenever possible and changing urinary catheters when removal was not possible.

Empirical antimicrobial treatment was outlined in the guideline as follows: doripenem with or without vancomycin was recommended for the EH group; cefepime with or without vancomycin was recommended for the HA group; and ceftriaxone was recommended for the CA group. De-escalation strategies were also outlined based on pathogens isolated on culture and listed preferred antimicrobials in addition to alternative options. If providers chose to maintain the patient on a β-lactam, intravenous (i.v.) therapy was permitted until the time of discharge, provided that the i.v. agent chosen was the narrowest spectrum possible. Antimicrobial recommendations included in the guideline were based on a previously constructed disease state antibiogram [5]. The recommended duration of therapy for those who responded favourably within 72 h of antimicrobial initiation was 7 days. For those who responded to therapy more slowly or had nephrolithiasis, a 14-day course of antimicrobials was recommended. The guideline also suggested consideration of alternative durations of therapy for immunocompromised patients. Prescribers and pharmacists were educated on the origin and contents of the guideline prior to implementation, and adjustments were made to the institution's medication electronic ordering system.

### 2.3. Cultures

Urine and blood cultures were analysed using MicroScan (Dade Behring, Inc., West Sacramento, CA). Enterobacteriaceae isolated on blood culture were considered UTI pathogens if the urine was considered the likely source by the medical provider. Species producing an inducible AmpC β-lactamase (*Serratia*, *Providencia*, *Morganella morganii*, *Citrobacter* and *Enterobacter* spp.) were considered to be resistant to first- to third-generation cephalosporins regardless of MicroScan results [7,8]. Resistant pathogens were defined as *P. aeruginosa*, ESBL-producing organisms or AmpC-producing species.

### 2.4. Outcomes

Difference in LOS was the primary outcome of interest. Adherence to the guideline was also assessed as an outcome of interest. Adherence to guideline recommendations in terms of empirical antimicrobial therapy selection, obtaining cultures, de-escalation and Foley catheter management were assessed. A de-escalation opportunity was defined as an instance in which a patient was initiated on a β-lactam antimicrobial with activity against *P. aeruginosa* or a carbapenem, but the pathogen identified on culture did not require activity against *Pseudomonas* and/or a carbapenem. De-escalation occurred when therapy was switched from a β-lactam with activity against *Pseudomonas* or a carbapenem to a non-antipseudomonal β-lactam, non-carbapenem or any other agent as allowed per the guideline for de-escalation (i.e. ciprofloxacin, trimethoprim/sulfamethoxazole, etc.). Additional outcomes of interest included LOS, re-admission rates within 30 days of discharge, and UTI-related re-admissions within 30 days (defined as re-admission with an ICD-9 code of 599, 590 or 595 listed as primary or secondary reason for admission). Cost data were collected ≥6 months post-discharge. Total drug costs were calculated by multiplying the institution average price per day by the number of days the patient received the drug.

### 2.5. Statistical analysis

Statistical analysis was performed using SigmaPlot v.12.0 (Systat Software, Inc., San Jose, CA). Continuous variables were assessed via *t*-test or Mann–Whitney rank-sum test, as appropriate. Dichotomous variables were assessed via $\chi^2$ test or Fisher's exact test, as appropriate. A *P*-value of $<0.05$ was considered statistically significant. A backward stepwise regression was performed to examine the impact of multiple factors on LOS and cost. Factors with a *P*-value of $\leq 0.2$ on univariate analysis were included in the backward stepwise regression model.