# The prevalence of empiric antibiotic use in an emergency department on children with suspected urinary tract infections: A retrospective study in Saudi Arabia

**Ahmed Mohammed Awad Alharbi [1], Saud Abdulaziz Almutairi [2], Turki Maeid Alanazi [2], Abdulkarim Farhan Alanazi [3]**

(1) Consultant - Pediatric emergency
(2) Pediatric resident
(3) Respiratory therapist

**Corresponding author:**
Saud Abdulaziz Almutairi
Pediatric resident R4
Phone: 0551531537
**Email:** S-a-gh@hotmail.com

Received: November 2022 Accepted: December 2022; Published: December 30, 2022.
Citation: Ahmed Mohammed Awad Alharbi et al. B The prevalence of empiric antibiotic use in an emergency department on children with suspected urinary tract infections: A retrospective study in Saudi Arabia. World Family Medicine. December 2022 - January 2023 Part 2; 21(1):70-76 DOI: 10.5742/MEWFM.2023.95251562

# Abstract

Objectives: The prescription of antibiotics for suspected urinary tract infection (UTI) is common practice and may result in unnecessary antibiotic exposure. Our goal was to review the diagnosis and management of UTI in an emergency department and to determine the goals of antimicrobial stewardship.

Methods: This is a single-centre, retrospective study that was conducted among children aged between 12 months and 18 years old who had been discharged from the emergency department with a diagnosis of UTI in the period between January and August 2022. Clinical information, laboratory findings, urine collection methods and urine culture results as well as details of prescribed antibiotics were gathered. The relation between urinalysis characteristics and confirmed UTI was assessed as a secondary outcome of the study.

Results: In this study, we were able to collect data for 183 children with a mean age of 4.2 (1.1-7.5) years and 82.5% of them were girls. Almost all children with UTI were discharged to home with prescribed antibiotics (98%) for a median duration of seven days ranging between 7-10 days. Among those who used antibiotics, 46.4% of the patients had negative urine cultures, resulting in 525 unnecessary antibiotic prescriptions. Presence of nitrite in the urine was the strongest and highly specific predictor of UTI (odds ratio of 20.22, P< 0.001).

Conclusions: Current practice in the management of suspected pediatric urinary tract infections in the selected emergency department resulted in significant and unnecessary exposure to antibiotics. We set goals to reduce unnecessary antibiotic exposure, including improving the accuracy of UTI diagnosis, establishing a process to discontinue antibiotic consumption for negative cultures, and standardizing the duration of antimicrobials.

Keywords: urinary tract infections, pediatrics, children, antimicrobial monitoring, urinalysis, antibiotics, empiric use, E. coli, nitrite, urine culture.

## Introduction

Urinary tract infection (UTI) is one of the main causes of intensive care consultations and is estimated to affect between 2.6% and 7.5% of children with fever annually in the US [1]. UTI is determined by the presence of growth bacteria that exceeds 105 colony-forming units per millilitre (CFU/ml) [2]. Predisposing factors leading to UTIs include female gender, Caucasian race, history of previous UTIs, dehydration, irritable bladder, diabetes, urogenital devices (e.g., urinary catheters and double-J stents), congenital urogenital malformation (e.g., vesicoureteral reflux, posterior urethral valves), phimosis, incomplete/rare voiding, and chronic constipation [3–5].

UTI in the pediatric population has symptoms of fever and occasionally symptoms of sepsis which may present as crying whilst voiding and a change in urine colour or poor stream [6]. In children older than two, symptoms include urinary urgency, frequency, enuresis, malodorous urine, dysuria, cloudy urine, and suprapubic pain or tenderness [7]. Moreover, children with pyelonephritis would experience more urinary symptoms as well as some systemic signs including fever, chills, and rigor in addition to flank pain and costovertebral angle tenderness [8].

Urinary tract infection is usually diagnosed on the basis of typical symptoms and confirmed by showing significant bacterial growth from an adequate urine sample [9]. Identification and susceptibility testing of causative bacteria usually require a turnaround time of 48 hours [10]. The clinical diagnosis of a UTI is often difficult and requires a high degree of suspicion, especially in younger children who do not always show typical symptoms. Because UTIs can develop into a potentially serious infection, clinicians often prescribe empiric antibiotics for suspected UTIs pending confirmation by culture, especially when follow-up is uncertain (i.e., emergency department [ED]). However, dipstick urinalysis has the disadvantage of lacking specificity, and this practice can lead to the prescription of unnecessary antibiotics [11]. Moreover, because of lack of continuity of care and healthcare resource constraints in acute care settings as well as the high volume of outstanding test results, many emergency departments are only able to follow-up on positive test results. As part of the Antimicrobial Stewardship Initiative, we aimed to review the practice of diagnosing and treating suspected UTIs in an emergency department to determine the frequency of empirically prescribed antibiotics for suspected UTIs that were not confirmed by urine culture and identify intervention targets to reduce unnecessary antibiotic exposure.

## Methods

This was a single-centre retrospective study that was conducted at the pediatric department at a governmental hospital in Saudi Arabia in the period between January to August 2022. In this study, we included all pediatric patients aged between 12 weeks and 18 years old who were discharged from the emergency department with a diagnosis of UTI. Exclusion criteria included patients younger than 12 weeks and those older than 18 years old, those having underlying genitourinary tract abnormalities, patients who admitted or transferred to another centre, those who received antibiotics on presentation, those who received a conditional prescription to be filled if the urine culture was positive, patients who had urine tests which had been conducted in another laboratory outside the hospital, and those who had a duplicate occurrence (more than one visit to the emergency department within the same illness period).

For all patients, charts were reviewed in order to collect data on patients' demographic factors including age and gender, clinical presentation, significant underlying co-morbidities, medical management as well as urinalysis and urine culture results. Determining the upper UTI signs and symptoms were defined as the presence of vomiting, fever or costovertebral angle tenderness while lower UTI symptoms included urgency, dysuria, frequency, or incontinence. Moreover, confirmed UTI was defined as the presence of pyuria and the presence of more than 50,000 CFU/ml or one or more uro-pathogens [12]. Furthermore, significant growth was defined with the presence of more than 50,000 CFU/ml of a uro-pathogen in addition to less than 50,000 CFU/ml of nonuro-pathogen. The semiquantitative results of leukocyte esterase (LE) were trace corresponded to 15 WBC/high power field, small (+1), moderate (+2) and large (+3) corresponding to 75, 125 and 500 WBC/high power field respectively. Presence of greater than 10*106 WBC/L which was assessed by the hemocytometer analysis of uncentrifuged urine determined the clinically significant pyuria.

urinalysis and confirmed UTIs. All estimates are presented with 95 % confidence intervals where p value of lower or equal to 0.05 was considered statistically significant.

## Results

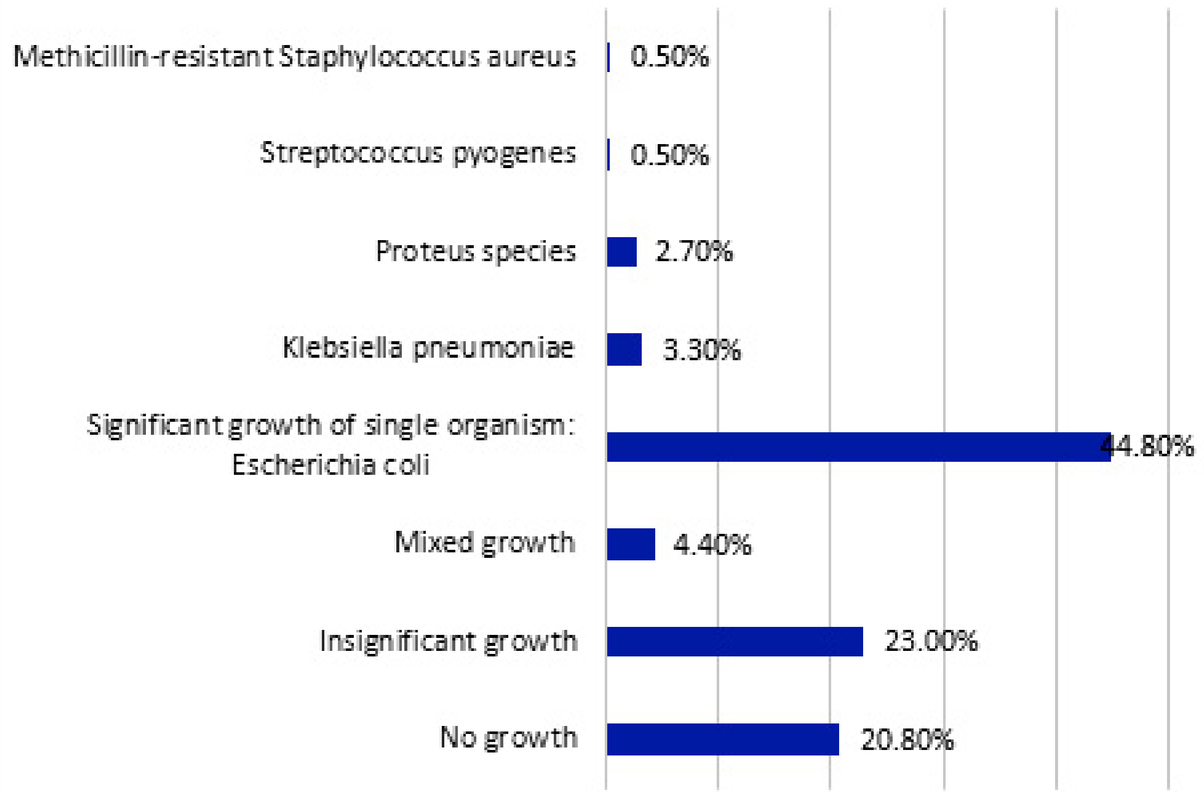
In this study, we were able to collect data for 293 patients who were discharged from the emergency department with the diagnosis of UTI which represented 2.5 % of the total ED visits during the period of the study. Among this population, 110 patients were excluded from the analysis because of being admitted (26), urine culture results (25) which were not ordered for ten patients or had been done elsewhere for 15 patients, having underlying genitourinary tract abnormalities (23), being on UTI prophylaxis (2), transferred to another institution (6), duplicate (3), being younger than 12 weeks (6), having conditional antibiotic prescriptions (7) and having a urine culture test which was conducted during therapeutic antibiotic (12). The study was conducted among 183 patients and their data were included in the analysis. Most of the patients were females (82.5 %) with a mean age of 4.2 years old and ranging between 1.1 and 7.5 years old. Most of the specimens were collected by midstream urine (65.8 %), and catheterization was used to collect specimens in 33.3% of the patients. Signs and symptoms of upper UTI were reported in 54.1% of the pediatric patients while lower UTI symptoms and signs were reported in 41.5% (Table 1).

**Table 1. Demographic Characteristics of Study Population (n = 183)**

| Variable | | Count | Percent |
|---|---|---|---|
| Age, y | Median (IQR) | 4.2 (1.1–7.5) | |
| **Gender** | Male | 32 | 17.4 % |
| | Female | 151 | 82.6 % |
| **Urinary symptoms (n = 175)** | Upper | 99 | 56.6 % |
| | Lower | 76 | 43.4 % |
| **Urine collection method** | Catheter | 61 | 33.3 % |
| | Midstream urine | 119 | 65.0 % |
| | Bag | 2 | 1.1 % |
| | Not specified | 1 | 0.6 % |
| **Urinalysis (n = 180)** | LE negative | 10 | 5.5 % |
| | LE trace | 33 | 18.3 % |
| | LE positive | 137 | 76.1 % |
| | Nitrite positive | 42 | 23.3 % |

Moreover, we found that 44.8 % of the patients had significant growth of a single organism of Escherichia coli while 4.4% had mixed growth while klebsiella pneumoniae presented in 3.3% of the patients. On the other hand, 23% of the patients had insignificant growth and 20.8% had no growth (Figure 1).

**Figure 1: Urine culture results**




This study reported that almost all patients with suspected UTIs were discharged home on antibiotics (98.4%). The most commonly prescribed antibiotic was cephalexin which was prescribed for 57.2% of the patients followed by amoxicillin-clavulanic acid (prescribed for 26.7%). The mean duration of using the antibiotics was 7 days which ranged between 7 and 10 days. In general, most of the antibiotic choices and duration were compatible with local UTI guidelines based on the susceptibility pattern. Among 88 patients with negative urine cultures (38 no growth, 42 insignificant growth and 8 mixed growth), 85 patients received antibiotics despite negative urine cultures and none of these patients received a call to stop the antibiotics which indicated that 46.4 % of those with prescribed antibiotics were for negative cultures.

**Table 2: Prevalence of prescribing of antibiotics in children with suspected UTI and type of antibiotic used**

| | | | |
|---|---|---|---|
| Antibiotic prescription for negative culture | | 85 | 46.4 % |
| Antibiotic prescription for positive culture | | 95 | 51.9 % |
| Total antibiotic prescriptions* | Total | 180 | 98.4 % |
| | Amoxicillin | 3 | 1.7 % |
| | Amoxicillin/clavulanic acid | 48 | 26.7 % |
| | Cefixime | 8 | 4.4 % |
| | Cephalexin | 103 | 57.2 % |
| | Ciprofloxacin | 3 | 1.7 % |
| | Nitrofurantoin | 3 | 1.7 % |
| | TMP/SMX | 9 | 5.0 % |
| Duration of antibiotics (day) | Median (IQR) | 7 (7–10) | |

*1 patient received 2 antibiotics.

TMP/SMX indicates trimethoprim/sulfamethoxazole.

The results of this study showed that urine LE on point-of-care testing was associated with the presence of pyuria on microscopy where the odds of microscopic pyuria were found to increase as the LE results increased from traces to +3 (P< 0.001). The sensitivity and specificity of LE and nitrite positivity are presented in Table 3. Furthermore, the presence of nitrites in the urine analysis was found to be the strongest predictor of UTO (OR=20.22, 95 % confidence interval of 5.95: 68.71, P < 0.001). Depending on subgroup analysis of urine samples collected by catheter, it was found that the presence of nitrites was 100 % predictive of UTI and had (OR=11.51, 95 confidence interval of 3.15: 42.06, P < 0.001) for other samples. Moreover, LE results of +2 and +3 were predictors of UTI in all specimens however this did not reach the statistical significance (OR= 28.96, and 4.07, 95 % CI= 7.78: 107.84 and 0.88: 18.87, P < 0.001 and 0.096 respectively). However, on subgroup analysis, LE results of +2 was only significant predictor of UTI in catheter specimens (Table 4).

**Table 3. Test Performance for LE and Nitrite Detection**

| | | Sensitivity, % | Specificity, % | PPV, % | NPV, % |
|---|---|---|---|---|---|
| **All specimens** | LE* | 83.0 | 32.6 | 57.4 | 63.6 |
| | Nitrite | 43.6 | 97.7 | 95.3 | 61.3 |
| Catheter specimens | LE* | 86.0 | 41.2 | 78.7 | 53.8 |
| | Nitrite | 51.2 | 100 | 100 | 44.7 |
| **Non catheter specimens** | LE* | 82.0 | 31.4 | 46.1 | 71.0 |
| | Nitrite | 36.0 | 95.7 | 85.7 | 67.7 |

*Positive result considered to be ≥ +1.
NPV indicates negative predictive value; PPV, positive predictive value.

**Table 4: Predictors of UTI (Univariable Analysis)**

| Variable | OR (95% CI) | P | Catheter Only, OR (95% CI) | P | Other, OR (95% CI) | P |
|---|---|---|---|---|---|---|
| Nitrite positive | 20.22 (5.95–68.71) | <0.001 | NA* | | 11.51 (3.15–42.06) | <0.001 |
| LE neg | REF | | REF | | REF | |
| Trace | 0.65 (0.15–2.83) | 0.568 | 0.83 (0.04–16.99) | 0.906 | 0.49 (0.09–2.81) | 0.423 |
| 1+ | 1.18 (0.31–4.58) | 0.806 | 1.86 (0.10–34.44) | 0.678 | 0.91 (0.19–4.30) | 0.909 |
| 2+ | 4.07 (0.88–18.87) | 0.073 | NA* | | 2.15 (0.38–12.20) | 0.390 |
| 3+ | 3.35 (0.81–13.90) | 0.096 | 4.67 (0.22–97.50) | 0.321 | 2.5 (0.49–12.89) | 0.273 |
| Pyuria | 8.12 (3.73–17.67) | <0.001 | 5.46 (1.43–20.88) | 0.013 | 9.46 (3.37–26.60) | <0.001 |

*Unable to estimate—predicts success perfectly.
NA indicates non-applicable; neg, negative; REF, reference

## Discussion

Urinary tract infections are responsible for a large number of intensive care visits and antibiotic prescriptions issued to children. We found that about 50% of patients with a suspected UTI based on symptoms or a dipstick urinalysis had a negative urine culture. This highlights the limited specificity of clinical assessment and rapid urinalysis testing in an acute care setting [9] and results in significant and unnecessary exposure to antibiotics.

Outpatient visits for UTIs place a significant burden on health care use and economic cost [13]. Promotion of rapid diagnosis is critical to reduce health care costs and potential complications, including pyelonephritis, abscess formation, and subsequent kidney scarring. However, the performance of the LE and nitrite assays in urine differs. Leukocyte esterase has good sensitivity, 83% on average, and increases to 94% in clinically suspected UTI. However, it is of poor quality for detecting UTIs in children (64%-92%). Many conditions can lead to a false-positive result, including fever [9]. On the other hand, urinary nitrites have good quality (98%) but poor sensitivity (53%) [9]. The same results were found in this study where most of the patients who had a positive nitrite test had a positive urine culture especially among catheter specimens. Moreover, an absence of nitrite in addition to low- level LE is associated with the lowest predictive value for UTI. Therefore, empiric treatment according to the guided strategy should be conducted for patients with nitrite positive results or those with nitrite negative specimens but with +1 or more LE on catheter specimens and +2 or more on other specimens. This could increase the accuracy of UTI diagnosis and avoid several days of unnecessary exposure to antibiotics. According to the strategy proposed in our study, if this had been followed it could have avoided antibiotic usage for 75 patients and avoided 587 days of unnecessary antibiotic therapy. Moreover, seventeen patients (23 %) would have had a delay in initiating antibiotics for culture-confirmed UTI. However, according to the strategy, 27 patients would have received unnecessary antibiotics for negative urine culture (217 of antibiotic days). Delaying the early initiation of antibiotics is linked with increasing the risk for renal scarring [14], therefore, evaluation of a larger study population using this type of strategy is required to determine the long-term effect on patients.

Approximately half (46.4%) of the patients who received antibiotic treatment for a suspected UTI had a negative urine culture. Watson et al. noted a similar finding that 49% of patients with suspected UTI had negative urine cultures [15]. The practice of empiric therapy for all patients with antibiotics, although it can prevent serious complications of a UTI, is associated with high and unnecessary prescriptions of antibiotics, which leads to a lower value of care and higher costs for the health system. Moreover, this practice of using empirical antibiotic for all suspected patients can cause antimicrobial-associated adverse reactions and increase the rate of development and selection of antimicrobial resistance [16–18]. In a previous study conducted by Garraffo et al., the authors showed that antibiotic exposure in the pediatric population in the 12 months preceding a UTI diagnosis is associated with increasing the risk of bacterial resistance particularly with amoxicillin, cotrimoxazole and first/ third- generation cephalosporin [19].

However, the pattern of resistance depended on the type of antibiotic to which the patients were exposed [19]. Moreover, the increase in the duration of antibiotic exposure is associated with the increased risk of developing of antimicrobial resistance [20]. Although, the impact of using of brief course of antibiotics until a culture is reported negative for bacterial resistance is not clear [10]. Without a proper follow-up of urine results, prescribing antibiotics to a child with a UTI diagnosis may lead to frequent urinalysis with all future febrile illnesses.

There are several antimicrobial stewardship strategies that have been proposed in different infection syndromes including some skin infections and pneumonia [21]. In a previous study conducted by Saha et al., the authors implemented a standard antibiotic discontinuation protocol for patients with a negative urine culture [11]. This practice outlined by Saha et al., was associated with an increase in the rate of antibiotic discontinuation from 4 % to 84 % and helped avoiding 3429 antibiotic unnecessary days for 29 months [11]. In the current study, the lack of such protocol led to 525 unnecessary antibiotic days during seven months. Moreover, another potential area of antimicrobial stewardship is standardizing the antibiotic prescription duration. In the current study, 41 % of the prescriptions of antibiotics were for 10 days or longer although, recent guidelines recommend 7 – 10 days of therapy with antibiotic in patients with UTI [9].

This study had some limitations including its retrospective nature where details of patients' clinical data may not be well documented. Moreover, some patients with UTIs may have been missed as they were discharged with an alternative diagnosis without urinalysis or urine culture. In addition, some patients were instructed to follow-up with their primary physicians and it is not clear whether any subsequent clinician changed the initial antibiotic management plan.

In conclusion, this study highlights the results that the current practice in our department in management of pediatric UTI often results in significant and unnecessary use of antibiotics. This knowledge would help to develop antimicrobial stewardship interventions that aimed to improve the antibiotic prescriptions practice in the emergency departments in order to reduce the unnecessary antibiotic associated adverse events and decrease the costs to the healthcare systems. This study identified potential strategies in order to reduce the unnecessary exposure of antibiotic by improving the diagnostic accuracy of UTIs, discontinuing antibiotics for negative cultures, and standardizing antimicrobial duration.

## References

1. Sood A, Penna FJ, Eleswarapu S, et al. Incidence, admission rates, and economic burden of pediatric emergency department visits for urinary tract infection: Data from the nationwide emergency department sample, 2006 to 2011. J Pediatr Urol. 2015;11(5):246.e1-246.e8. doi:10.1016/j.jpurol.2014.10.005
2. Larcombe J. Clinical evidence: Urinary tract infection in children. BMJ. 1999;319(7218):1173-1175. doi:10.1136/bmj.319.7218.1173
3. Shaaban OA, Mahmoud NA, Zeidan AA, Kumar N, Finan AC. Prevalence and Resistance Patterns of Pediatric Urinary Tract Infections in Bahrain. Cureus. Published online December 31, 2021. doi:10.7759/cureus.20859
4. Gondim R, Azevedo R, Braga AANM, Veiga ML, Barroso Jr. U. Risk factors for urinary tract infection in children with urinary urgency. Int braz j urol. 2018;44(2):378-383. doi:10.1590/s1677-5538.ibju.2017.0434
5. Simon C, Everitt H, Dorp F van, Hussain N, Nash E, Peet D. Oxford Handbook of General Practice. (Edition F, ed.). Oxford Medical Handbooks; 2020.
6. Vasudev AS, Shah NK. Algorithms in Pediatrics. Jaypee Brothers Medical Publishers; 2017. https://www.jaypeebrothers.com/pgDetails.aspx?book_id=9789351521600
7. Leung AKC, Wong AHC, Leung AAM, Hon KL. Urinary Tract Infection in Children. Recent Pat Inflamm Allergy Drug Discov. 2019;13(1):2-18. doi:10.2174/1872213X13666181228154940
8. Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: an overview of diagnosis and management. BMJ Paediatr Open. 2019;3(1):e000487. doi:10.1136/bmjpo-2019-000487
9. KB R. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128:595-610.
10. Alghounaim M, Ostrow O, Timberlake K, Richardson SE, Koyle M, Science M. Antibiotic Prescription Practice for Pediatric Urinary Tract Infection in a Tertiary Center. Pediatr Emerg Care. 2019;Publish Ah. doi:10.1097/PEC.0000000000001780
11. Saha D, Patel J, Buckingham D, Thornton D, Barber T, Watson JR. Urine Culture Follow-up and Antimicrobial Stewardship in a Pediatric Urgent Care Network. Pediatrics. 2017;139(4). doi:10.1542/peds.2016-2103
12. Leber AL E. Urine culture. In: Clinical Microbiology Procedures HandbooK. ASM Press; 2016:3.12.1–3.12.33.
13. FREEDMAN AL. UROLOGIC DISEASES IN NORTH AMERICA PROJECT: TRENDS IN RESOURCE UTILIZATION FOR URINARY TRACT INFECTIONS IN CHILDREN. J Urol. 2005;173(3):949-954. doi:10.1097/01.ju.0000152092.03931.9a
14. Shaikh N, Mattoo TK, Keren R, et al. Early Antibiotic Treatment for Pediatric Febrile Urinary Tract Infection and Renal Scarring. JAMA Pediatr. 2016;170(9):848. doi:10.1001/jamapediatrics.2016.1181
15. Watson JR, Sánchez PJ, Spencer JD, Cohen DM, Hains DS. Urinary Tract Infection and Antimicrobial Stewardship in the Emergency Department. Pediatr Emerg Care. 2018;34(2):93-95. doi:10.1097/PEC.0000000000000688
16. Abbo L, Hooton T. Antimicrobial Stewardship and Urinary Tract Infections. Antibiotics. 2014;3(2):174-192. doi:10.3390/antibiotics3020174
17. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ. 2010;340(may18 2):c2096-c2096. doi:10.1136/bmj.c2096
18. Paschke AA, Zaoutis T, Conway PH, Xie D, Keren R. Previous Antimicrobial Exposure Is Associated With Drug-Resistant Urinary Tract Infections in Children. Pediatrics. 2010;125(4):664-672. doi:10.1542/peds.2009-1527
19. Garraffo A, Marguet C, Checoury A, et al. Urinary tract infections in hospital pediatrics: Many previous antibiotherapy and antibiotics resistance, including fluoroquinolones. Médecine Mal Infect. 2014;44(2):63-68. doi:10.1016/j.medmal.2013.12.002
20. Hillier S, Roberts Z, Dunstan F, Butler C, Howard A, Palmer S. Prior antibiotics and risk of antibiotic-resistant community-acquired urinary tract infection: a case–control study. J Antimicrob Chemother. 2007;60(1):92-99. doi:10.1093/jac/dkm141
21. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016;62(10):e51-e77. doi:10.1093/cid/ciw118