Uncomplicated UTIs: Navigating Treatment Failure in the Primary Care Setting: AAPA Webinar 2024 References and Footnotes

Slide 4

uUTI = uncomplicated urinary tract infection

Slide 6

UTI = urinary tract infection, uUTI = uncomplicated urinary tract infection.

1. Schappert SM, Rechtsteiner EA. Vital Health Stat 13. 2011;(169):1-38. 2. Foxman B, Brown P. Infect Dis Clin North Am. 2003;17(2):227-241. 3. Ahmed H, et al. PLoS One. 2018;13(1):e0190521. 4. Flores-Mireles AL, et al. Nat Rev Microbiol. 2015;13:269. 5. Franklin M, et al. Poster presented at: ISPOR 2023; May 7-10, 2023. Presentation EE548.

Slide 8

UTI = urinary tract infection.

Anger J, et al. J Urol. 2019;202(2):282-289.

Slide 9

[a]Complicated UTI guidelines are currently being updated.

UTI = urinary tract infection.

1. Anger J, et al. J Urol. 2019;202(2):282-289. 2. Nicolle LE, et al. Clin Infect Dis. 2005;40(5):643-654. 3. Brubaker L, et al. Female Pelvic Med Reconstr Surg. 2018;24(5):321-335.
4. Gupta K, et al. Clin Infect Dis. 2011;52(5):e103-e120. 5. Orenstein R, Wong E. Am Fam Physician. 1999;59(5):1225-1234.

Slide 10

UTI = urinary tract infection.

1. Foxman B. Infect Dis Clin North Am. 2014;28(1):1-13. 2. Hooton TM, et al. N Engl J Med 1996;335:468-474.

Slide 12

[a]The Activity Impairment Assessment (AIA), a validated 5-item self-administered questionnaire, was used to measure the impact of uUTI on daily activities by assessing the amount of time that daily activities were impaired by uUTI symptoms. [b]Combination of non-recurrent and recurrent uUTI groups. [c]In a cross-sectional survey study of United States females ages ≥ 18 years with a self-reported UTI [d]HRQoL assessed using a modified form of short form-36, version 2 (SF-36v2) questionnaire.

HRQoL = health related quality of life; uUTI = uncomplicated urinary tract infection.

Thompson J, et al. PLoS One. 2023;18(2):e0277728.

Slide 13

[a]A total of 65 women ≥ 18 years of age with ≥ 1 uUTI and antibiotic treatment in the past year completed a qualitative, interview-based study, 40 (61.5%) from the US and 25 (38.5%) from Germany. Saturation was estimated to have been achieved after analysis of 20 US participant interviews and 17 German participant interviews. High levels of consistency were observed across the sample.

uUTI = uncomplicated urinary tract infection.

1. Grigoryan L, et al. BMC Womens Health. 2022;22(1):182. 2. Trennery CL, et al. Abstract presented at: IDWeek 2022; October 19-23, 2022; Washington, DC. Abstract 217370.

Slide 14
rUTI = recurrent urinary tract infection; UTI = urinary tract infection.
1. Scott VC, et al. J Urol. 2021;206(3):688-695. 2. Grigoryan L, et al. BMC Womens Health. 2022;22(1):182. 3. Lecky DM, et al. Br J Gen Pract. 2020;70(694):e330-e338.

Slide 16
IDSA = Infectious Diseases Society of America; UTI = urinary tract infection.
Gupta K, et al. Clin Infect Dis. 2011;52(5):e103-e120.

Slide 17
MDRO = multidrug-resistant organism.

Slide 18
UTI = uncomplicated urinary tract infection.

Slide 19
MDRO = multidrug-resistant organism; STI = sexually transmitted infection.

Slide 20
[a]This guideline is currently being updated.
AE = adverse effect; IDSA = Infectious Diseases Society of America; TMP-SMX = trimethoprim-sulfamethoxazole; UTI = urinary tract infection.
Gupta K, et al. Clin Infect Dis. 2011;52(5):e103-e120.

Slide 23
FDA = Food and Drug Administration; HRU = health resource utilization; US = United States; uUTI = uncomplicated urinary tract infection.
1. Drugs@FDA: FDA-Approved Drugs. U.S. Food and Drug Administration. Accessed April 25, 2024. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=050717. 2. Kaye KS, et al. Clin Infect Dis. 2021;73(11):1992-1999. 3. Thompson J, et al. Presented at IDWeek, September 29 – October 3, 2021, Virtual Conference. Presentation 1415. 4. Markowitz MA, et al. Int Urogynecol J. 2019;30(7):1187-1194. 5. Gupta K, et al. Clin Infect Dis. 2011;52(5):e103-e120. 6. Langner JL, et al. Am J Obstet Gynecol. 2021;225(3):272.e1–272.e11. 7. Shafrin J, et al. Antimicrob Resist Infect Control. 2022;11(1):133. 8. Gharbi M, et al. BMJ. 2019;364:1525. 9. Moon RC, et al. PLoS One. 2022;17(11):e0277713. 10. Fromer DL, et al. Poster presented at: AMCP NEXUS 2023; October 16-19, 2023. 11. Grigoryan L, et al. BMC Womens Health. 2022;22(1):182.

Slide 25
[a]Derived from natural products.
[b]Gram-negative pathogens that produce ESBLs are resistant to penicillins, cephalosporins, and monobactams.
ESBL = extended-spectrum beta-lactamase; FDA = Food and Drug Administration; uUTI = uncomplicated urinary tract infection.
1. Hutchings M, et al. Curr Opin Microbiol. 2019;51:72–80. 2. Harkins CP, et al. Genome Biol. 2017;18:130. 3. Hendlin D, et al. Science. 1969;166(3901):122–3. 4. Palmeira JD, et al. Heliyon. 2020:6(1):e03206.
5. Drugs@FDA: FDA-Approved Drugs. U.S. Food and Drug Administration. Accessed January 23, 2024. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=050717.

6. FDA. FDA Approves New Treatment for Uncomplicated Urinary Tract Infections. Published April 24, 2024. Accessed April 25, 2024. https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-uncomplicated-urinary-tract-infections#:~:text=Today%2C%20the%20U.S.%20Food%20and%20Drug%20Administration%20approved, of%20Escherichia%20coli%2C%20Proteus%20mirabilis%20and %20Staphylococcus%20saprophyticus.

Slide 27

[a]Antimicrobial resistance among E. coli was defined as non-susceptible (resistant or intermediate susceptibility results).
[b]Retrospective, multicenter, cohort study of over 1.5 million non-duplicate E. coli isolates from urine cultures collected from US female outpatients ≥ 12 years to evaluate antimicrobial resistance to FQ, NFT, or TMP-SMX and also included isolates that were ESBL-producing. The facilities included had a geographic distribution similar to that of the US as a whole.
E. coli = Escherichia coli; ESBL = extended-spectrum beta-lactamase; FQ = fluoroquinolone; NFT = nitrofurantoin; TMP-SMX = trimethoprim-sulfamethoxazole; US = United States.
Kaye KS, et al. Clin Infect Dis. 2021;73(11):1992-1999.

Slide 28

TMP-SMX = trimethoprim-sulfamethoxazole; UTI = urinary tract infection; uUTI = uncomplicated urinary tract infection.
Thompson J, et al. Presented at IDWeek, September 29 – October 3, 2021, Virtual Conference. Presentation 1415.

Slide 29

[a]Due to rounding, percentages may not add to 100% and all values ≤ 1% were assumed to be 1%. All reported data for “fosfomycin” and “others” were ≤ 1%; therefore, the data label has been omitted from the figure.
[b]Adapted from American Journal of Obstetrics & Gynecology, Vol 225, Joanna L. Langner, Kim F. Chiang, Randall S. Stafford, Current prescribing practices and guideline concordance for the treatment of uncomplicated urinary tract infections in women, Page No. 6, Copyright 2021, with permission from Elsevier and Jones JK. National disease and therapeutic index. Plymouth Meeting, PA: IQVIA; 2019.
HCP = healthcare provider; IDSA = Infectious Diseases Society of America; TMP-SMX = trimethoprim-sulfamethoxazole; US = United States; uUTI = uncomplicated urinary tract infection.
Langner JL, et al. Am J Obstet Gynecol. 2021;225(3):272.e1–272.e11.

Slide 30

UTI = urinary tract infection.
Gharbi M, et al. BMJ. 2019;364:1525.

Slide 31

[a]In a retrospective cohort study from January 2013 to December 2018, females ages ≥12 years (N = 5870) had an oral antibiotic prescription ±5 days of uncomplicated UTI diagnosis based on ICD Tenth Edition.
ED = emergency department; ICD = International Classification of Disease; IDSA = Infectious Diseases Society of America; IV = intravenous; UTI = urinary tract infection; uUTI = uncomplicated urinary tract infection.
Moon RC, et al. PLoS One. 2022;17(11):e0277713.

Slide 32

[a]Reference group: appropriate and optimal antibiotic prescriptions.

[b]After adjusting for patient characteristics and during a 12-month follow-up.

[c]Within 12 months of the index episode, and after adjustment for age group, race, ethnicity, and CCI score.

[d]In a retrospective cohort study from January 2013 to December 2018, females ages ≥12 years (N = 5870) had an oral antibiotic prescription ±5 days of uncomplicated UTI diagnosis based on ICD Tenth Edition. Appropriate antibiotic prescription was defined per the IDSA 2011 guidelines for drug class and duration. Inappropriate antibiotic prescription was defined as prescription of a second-line antibiotic as first-line therapy, prescription of two first-line therapies at the same time, or treatment duration not aligned with those detailed in IDSA 2011 guidelines. Suboptimal antibiotic prescription was defined as evidence of treatment failure: treatment failure included receipt of intravenous antibiotics, a switch to a different antibiotic, or a primary diagnosis of UTI in an acute care setting within 28 days of the index date.

CCI = Charlson Comorbidity Index; CI = confidence interval; ED = emergency department; HRU = health resource utilization; ICD = International Classification of Disease; IDSA = Infectious Diseases Society of America; RR = relative risk; UTI = urinary tract infection.

Moon RC, et al. PLoS One. 2022;17(11):e0277713.

Slide 34

UTI = urinary tract infection.

Slide 35

ACOG = American College of Obstetricians and Gynecologists; AUA = American Urological Association; AUGS = American Urogynecologic Society; CUA = Canadian Urological Association; IDSA = Infectious Diseases Society of America; UTI = urinary tract infection.

1. Nicolle LE, et al. Clin Infect Dis. 2005;40(5):643-654. **2.** Anger J, et al. J Urol. 2019;202(2):282-2893. **3.** Brubaker L, et al. Female Pelvic Med Reconstr Surg. 2018;24(5):321-335. **4.** ACOG Practice Bulletin No. 91 (2008). Obstet Gynecol 2008;111:785-94.

Slide 36

[a]Retrospective cohort study assessed the occurrence of treatment failure in 238,355 females aged ≥18 years, with an uUTI diagnosis (i.e., no evidence of complicated UTI), identified in an outpatient setting, ≥1 oral antibiotic prescription within ±5 days of diagnosis (date of initial antibiotic prescription defined the index date), and ≥1 year of continuous health plan enrollment pre- and post-index date. Treatment failure was evaluated within 28 days of index date.

[b]Assessed occurrence of treatment failure in 376,004 females aged ≥12 years with ≥1 uUTI diagnosis (i.e., no evidence of complicated UTI), with ≥1 empiric prescription of nitrofurantoin, trimethoprim-sulfamethoxazole, fluoroquinolones, fosfomycin, or beta-lactams within ±5 days of diagnosis (date of initial antibiotic prescription defined the index date), and ≥12 months of electronic health record activity before and after the index date. Incidence of treatment failure was evaluated over the first 28 days of the observation period following the index date.

IV = intravenous; UTI = urinary tract infection; uUTI = uncomplicated urinary tract infection.

1. Franklin M, et al. Poster presented at: ISPOR 2023; May 7-10, 2023. Presentation EE548 **2.** Fromer DL, et al. Poster presented at: AMCP NEXUS 2023; October 16-19, 2023.

Slide 38

[a]In a retrospective cohort study, females ages ≥ 12 years (N=376,004) had an oral antibiotic prescription ± 5 days of uncomplicated UTI diagnosis and at least 12 months of electronic health record data activity before and after index date.

Rx = prescription; UTI = urinary tract infection; uUTI = uncomplicated urinary tract infection.

Fromer DL, et al. Poster presented at: AMCP NEXUS 2023; October 16-19, 2023.

Slide 40

[a]Treatment failure defined as needing more than one line of antibiotics in an uncomplicated urinary tract infection episode.

[b]In an interview-based study of females ≥ 18 years of age in the United States and Germany females with ≥ 1 uUTI and antibiotic treatment in the past year.

Grigoryan L, et al. BMC Womens Health. 2022;22(1):182.

Slide 41

[a]Healthcare resource utilization and costs were assessed for the index uUTI episode (per ICD-10-CM codes) in females ages ≥ 18 years who had received an oral antibiotic prescription within ± 5 days of diagnosis and had ≥1 outpatient uUTI diagnosis between October 10, 2016 and September 9, 2020. An uUTI episode was defined as a period of 28 days; in patients who experienced treatment failure, the length of the uUTI episode was extended from the date of treatment failure for an additional 28 days. Data collected from de-identified claims data.

[b]Satterthwaite approximation statistical test was used to calculate the p-values to account for two different sample variances.

ED = emergency department; IV = intravenous; US = United States; UTI = urinary tract infection; uUTI = uncomplicated urinary tract infection.

Franklin M, et al. Poster presented at: ISPOR 2023; May 7-10, 2023. Presentation EE548.

Slide 42

[a]Healthcare resource utilization and costs were assessed for the index uUTI episode (per ICD-10-CM codes) in females ages ≥ 18 years who had received an oral antibiotic prescription within ± 5 days of diagnosis and had ≥1 outpatient uUTI diagnosis between October 10, 2016 and September 9, 2020. An uUTI episode was defined as a period of 28 days; in patients who experienced treatment failure, the length of the uUTI episode was extended from the date of treatment failure for an additional 28 days. Data collected from de-identified claims data.

[b]Outpatient costs were defined as: emergency room, outpatient hospital visit, office visit, laboratory and radiology test, home health, durable medical equipment, and outpatient 'other' costs.

ED = emergency department; IV = intravenous; US = United States; UTI = urinary tract infection; uUTI = uncomplicated urinary tract infection.

Franklin M, et al. Poster presented at: ISPOR 2023; May 7-10, 2023. Presentation EE548.

Slide 43

HRQoL = health related quality of life; HRU = health resource utilization; uUTI = uncomplicated urinary tract infection; UTI = urinary tract infection.

1. Schappert SM, Rechtsteiner EA. Vital Health Stat 13. 2011;(169):1-38. 2. Anger J, et al. J Urol. 2019;202(2):282-289. 3. Brubaker L, et al. Female Pelvic Med Reconstr Surg. 2018;24(5):321-335. 4. Colgan R, Williams M. Am Fam Physician. 2011;84(7):771-776. 5. Hooton TM. N Engl J Med. 2012;366:1028-37. 6. Thompson J, et al. PLoS One. 2023;18(2):e0277728. 7. Langner JL, et al. Am J Obstet Gynecol. 2021;225(3):272.e1-272.e11. 8. Kaye KS, et al. Clin Infect Dis. 2021;73(11):1992-1999. 9. Markowitz MA, et al. Int Urogynecol J. 2019;30(7):1187-1194. 10. Gupta K, et al. Clin Infect Dis. 2011;52(5):e103-e120. 11. Fromer DL, et al. Poster presented at: AMCP NEXUS 2023; October 16-19, 2023. Presentation XXXX. 12. Franklin M, et al. Poster presented at: ISPOR 2023; May 7-10, 2023. Presentation EE548. 13. Grigoryan L, et al. BMC Womens Health. 2022;22(1):182.