Urinary Tract Infections in Adults:
Frequent Questions, Urgent Dilemmas, Burning Answers

Andrew Urban MD
Infectious Disease and HIV Care
Madison, WI

CONTINUING EDUCATION COMPANY

1

Disclosure

I have no financial interests or relationships to disclose.

CONTINUING EDUCATION COMPANY

2

84-year-old Woman

- Lives in Arizona
- Travels to Florida to visit her son, 3-4 times per year
- Every time she visits she gets a UTI
- She is in a Florida Urgent Care and wants an antibiotic
- How would you help her?
  - Florida Urgent Care
  - Arizona Primary Care

3

Urinary Tract Infections in Adults

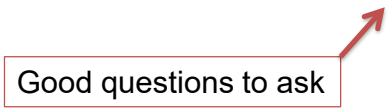
- Diagnostic areas of confusion
- A deeper look at UTI antibiotics
- Recurrent Infections

4

Risks for Drug Resistant Uropathogens

- Indwelling catheter
- Recurrent UTIs
- Male UTI

- Past 3-6 months
  - Urine cx showing resistance
  - Antibiotic use
  - Inpatient, LTACH, LTCF stay
  - International Travel



Microbiol Spectrum 4(6);UTI-0021-2015 Curr Opin Infect Dis. 2021 Oct; 34(5): 423–431

5

Infection of the Urinary Tract

- Asymptomatic
  - High levels of bacteriuria but no attributable symptoms
  - Clinical significance = huge area of antibiotic misuse
- Symptomatic
  - Clinical diagnosis supported or refuted by labs
  - Laboratory tests are inherently non-specific
  - The diagnosis is usually straightforward, but can be quite difficult in those unable to sense - SCI, catheters, cognitive

6

Symptomatic UTI Categorization

- Acute Cystitis – limited to bladder, lower tract
- Acute Pyelonephritis – upper tract, kidney
  - IDSA 2010 Guidelines: non-pregnant, pre-menopausal women with no known urologic abnormalities or comorbidities
- Recurrent Cystitis
  - AUA, EUA Guidelines: non-pregnant women, no structural or functional abnormality or comorbidity

Infectious Disease Society of America, Clin Infect Dis 2011;52(5):e103
https://www.auanet.org/guidelines-and-quality/guidelines/recurrent-uti

7

Symptomatic UTI Categorization

- Uncomplicated UTI
  - Implies acute cystitis in healthy non-pregnant women
  - Tract is structurally and neurologically intact
- Complicated UTI
  - All adults with everything else

Note
UptoDate likes the word “simple" instead of uncomplicated

8

Complicated UTI – Everything Else

Diverse Groups Each with Unique Management Considerations

- Male UTI
- Catheter Associated (CAUTI)
- Recurrent UTI in other populations
- Immunocompromised
- Metabolic problems
- Structural abnormalities
- Neurologic abnormalities
- Pregnancy
- Renal Transplant
- Elderly
  - Community dwelling
  - LTC dwelling
- Drug resistant pathogens

9

IDSA PRACTICE GUIDELINES CURRENT

Complicated Urinary Tract Infections (cUTI): Clinical Guidelines for Treatment and Management

Published July 17, 2025 **Last Updated** July 17, 2025

New classifications of uUTI and cUTI

Old Classifications	New Classifications
Uncomplicated UTI: Acute cystitis in afebrile nonpregnant premenopausal women with no diabetes and no urologic abnormalities	**Uncomplicated UTI: Infection confined to the bladder** in afebrile women or men
Acute Pyelonephritis: Acute kidney infection in women otherwise meeting the definition of uncomplicated UTI above	**Complicated UTI: infection beyond the bladder** in women or men • Pyelonephritis • Febrile or bacteremic UTI • Catheter-associated (CAUTI) • Prostatitis* (*not covered by these guidelines)
Complicated UTI: All other UTIs	

10

Urine Culture Colony Counts
Clinical Interpretation in Adults

≥ CFU/ml	Population	Comments
10^{2*}	Women uncomplicated cystitis	Coliforms, voided urine
	Straight Cath obtained	Less contamination, lower cutoff
10^3	Men	Voided urine
10^4	Pyelonephritis	Voided urine up to 95% of cases
10^5	Asymptomatic bacteriuria	Higher cutoff for increased specificity

*Labs may not quantify below 10^3 CFU/mL so 10^3 can be used

ASM Spectrum 2016 NEJM 2013;369:1883 NEJM 1982;307:4634

11

Antibiotics for UTI
A Deeper Look

12

24-year-old Woman

- Abrupt onset of dysuria, frequency
- UA 50 WBC/HPF
- Urine culture grows 10^3 CFU/mL *Proteus mirabilis*
  - Susceptibility pending

Choice?

A. Cefpodoxime 100 mg BID x 7 days
B. Doxycycline 100 mg BID x 7 days
C. Nitrofurantoin 100 mg BID x 5 days
D. TMP/SMX DS 1 tab BID x 3 days

Acute Uncomplicated Cystitis

IDSA Guidelines 2010 Empiric Therapy

Recommended Agent	Comments
Nitrofurantoin 100 mg BID x 5 days	Avoid if early pyelonephritis suspected
TMP/SMX DS 1 BID x 3 days	Avoid if local resistance > 20% Avoid if used for UTI in previous 3 mos
Fosfomycin 3gm po once	Avoid if early pyelonephritis suspected
Alternate Agents	**Why Alternate**
Fluoroquinolone	Side effects, resistance, collateral issues
Beta-lactams	Less efficacy, closer follow-up, longer duration of treatment needed

Infectious Disease Society of America, Clin Infect Dis 2011;52(5):e103

15

Nitrofurantoin

- Therapeutic concentration reached in urine only
  - Do not use for pyelonephritis
  - Minimum CrCl 40-60 cc/min (check local guidance)
- Be aware of holes in the spectrum
  - Activity < 50% : Klebsiella, Enterobacter
  - Usually resistant: Pseudomonas, Proteus, Serratia
- Adverse effects rare but serious
  - Pulmonary, Hepatic, Neurologic

16

Trimethoprim-Sulfamethoxazole

- Empiric use can be limited by resistance
  - Avoid if local *E. coli* resistance > 20% (check antibiogram)
  - Risks: TMP/SMX use or international travel past 3-6 mos
- When active
  - Highly effective, well tolerated, 3 day course for AUC
  - Watch dosing in renal impairment, drug-drug interactions

17

Fosfomycin

- 3gm oral sachet, expensive, broad spectrum
  - Indication uncomplicated UTI *E coli* and Enterococcus
  - Less reliable for Pseudomonas, Klebsiella, Serratia, Enterobacter (*fos*A hydrolase gene)
- Resistance testing very limited (call your lab)
  - Resistance can emerge with repeated use
- Do not use for pyelonephritis
  - Complicated UTI often dosed 3gm q72h x 3 doses
  - Emerging data for prostate infections

18

Beta-lactams for UTI

- Less eradication of GI and GU reservoirs
  - Need a longer duration of therapy
- Unique roles
  - Cephalexin inexpensive, good UTI agent if active
  - Isolates with resistance to first-line agents
  - Ceftriaxone single dose for outpatient pyelonephritis

AUC = acute uncomplicated cystitis

19

FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects

We have determined that fluoroquinolones should be reserved for use in patients who have no other treatment options for acute bacterial sinusitis, (ABS), acute bacterial exacerbation of chronic bronchitis (ABECB), and uncomplicated urinary tract infections (UTI) because the risk of these serious side effects generally outweighs the benefits in these patients. For some serious bacterial infections the benefits of fluoroquinolones outweigh the risks, and it is appropriate for them to remain available as a therapeutic option.

www.fda.gov

20

Fluoroquinolones for UTI

- Avoid for acute uncomplicated cystitis
  - Reserve for inability to use first-line agents
  - 3 day course levofloxacin or ciprofloxacin
- Unique roles (bioavailability, sites of action, spectrum)
  - Resistance to first-line agents
  - Oral therapy, outpatient pyelonephritis
  - Step-down oral treatment, Gram-negative urosepsis
  - Prostate infections
  - Complicated UTI

21

Urine Culture - *E. coli*

Drug	S/R
TMP/SMX	R
Nitrofurantoin	R
Levofloxacin	R
Ciprofloxacin	R
Cephalexin	R
Cefepime	R
Piperacillin/tazobactam	R
Amoxicillin/clavulanate	R
Gentamicin	R
Meropenem	S

22

Treatment of ESBL Acute Cystitis

- Preferred*
  - TMP/SMX or nitrofurantoin
- Alternates*
  - Fluoroquinolones, carbapenems, aminoglycosides (SD), fosfomycin (less reliable if non-*E.coli* pathogen)

SD – single dose IV

*IDSA 2023 Guidance on the Treatment of Antimicrobial Resistant Gram-negative Infections

23

Clinical Guidelines | June 2021

Appropriate Use of Short-Course Antibiotics in Common Infections: Best Practice Advice From the American College of Physicians

Best Practice Advice 3:

In women with uncomplicated bacterial cystitis, clinicians should prescribe short-course antibiotics with either nitrofurantoin for 5 days, trimethoprim–sulfamethoxazole (TMP–SMZ) for 3 days, or fosfomycin as a single dose. In men and women with uncomplicated pyelonephritis, clinicians should prescribe short-course therapy either with fluoroquinolones (5 to 7 days) or TMP–SMZ (14 days) based on antibiotic susceptibility.

Ann Int Med 2021;174(6):822

24

Newly Approved Agents

- Pivmecillinam (4/24)
  - Uncomplicated UTI in women
  - Beta-lactam prodrug of mecillinam, TID dosing, Europe
  - Active vs some MDR-GNR, no pseudomonas or Gram pos
- Sulopenem + probenecid (10/24)
  - Uncomplicated UTI in women w/ limited or no oral options
  - Penem, new beta-lactam class
  - Broad spectrum, no pseudomonas or enterococci
- Gepotidacin (3/25)
  - Uncomplicated UTI in women
  - Triazaacenaphthylene, new class topoisomerase inhibitor
  - Broad spectrum including quinolone resistant

25

Complicated UTI

- Host underlying conditions, pathogens, drug-resistance much more diverse
- General principles
  - Empiric therapy often broader spectrum (quinolones, beta-lactams with broader Gram-negative coverage)
  - Reliance on past and present microbiology data
  - Targeted therapy based on culture data
  - Longer treatment durations often needed

26

Table 1.1: Potential Empiric Antibiotics for cUTI^ prior to using the four-step approach to choose among these options

Four-Step Approach to choose among these antibiotics: Assess (1) severity of illness, (2) risk factors for resistance, (3) patient-specific considerations, and (4) if septic, consider the antibiogram. See discussion below for details of the four steps.

Condition of the Patient	Preferred	Alternative
Sepsis with or without shock**	Third or fourth generation cephalosporins,* carbapenems,# piperacillin-tazobactam, fluoroquinolones&	Novel beta lactam-beta lactamase inhibitors,+ cefiderocol, plazomicin, or older aminoglycosides%
Without sepsis, IV route of therapy	Third or fourth generation cephalosporins,* piperacillin-tazobactam, or fluoroquinolones&	Carbapenems,# newer agents (novel beta lactams-beta lactamase inhibitors,+ cefiderocol, plazomicin), or older aminoglycosides%
Without sepsis, oral route of therapy	Fluoroquinolones& or trimethoprim-sulfamethoxazole	Amoxicillin-clavulanate or oral cephalosporins (see **Table 3.1**)

IDSA 2025 Guidelines

27

In patients presenting with complicated UTI (cUTI) with a clinical response to therapy, should total duration of antibiotics be prolonged to >7 days rather than shorter (<=7 days)?

Recommendations:

I. In patients presenting with complicated UTI (including acute pyelonephritis) and who are improving clinically on effective therapy, we suggest treating with a shorter course of antimicrobials, using either 5-7 days of a fluoroquinolone (conditional recommendation, moderate certainty of evidence) or 7 days of a non-fluoroquinolone antibiotic (*conditional recommendation, very low certainty of evidence*), rather than a longer course (10-14 days).

II. In patients presenting with complicated UTI with associated Gram-negative bacteremia and who are improving clinically on effective therapy, we suggest treating with a shorter course (7 days) of antimicrobial therapy rather than a longer course (14 days) (*conditional recommendation, low certainty in the evidence*).

IDSA 2025 Guidelines

28

Recurrent UTI

29

24-year-old Woman

- Abrupt onset of dysuria, frequency
- UA 50 WBC/HPF
- Urine culture grows 10^4 CFU/mL *Proteus mirabilis*
- This is her third infection in a year with *P. mirabilis*

30

Most Important Next Step?

A. Workup for stones
B. Workup for estrogen deficiency
C. Workup for incomplete bladder emptying
D. Recommend low-dose TMP/SMX prophylaxis
E. Recommend cranberry juice

31

Recurrent Infections

- Relapse
  - Same organism over and over
  - Suggests a persistent focus
- Reinfection
  - Different organism each time
  - Suggests a reason for recurrency

32

The Properties of *Proteus mirabilis*

- Multiple virulence factors
  - Biofilm, proteases, swarming motility
  - Urease producer → struvite stones
  - Infected stones must be fully eradicated to clear UTIs
- Antibiotic considerations
  - Not active: nitrofurantoin, tetracyclines
  - High resistance: TMP/SMX
  - Less resistance: B-lactams, FQ, fosfomycin

Microbiol Spectr. 2015 October ; 3(5)

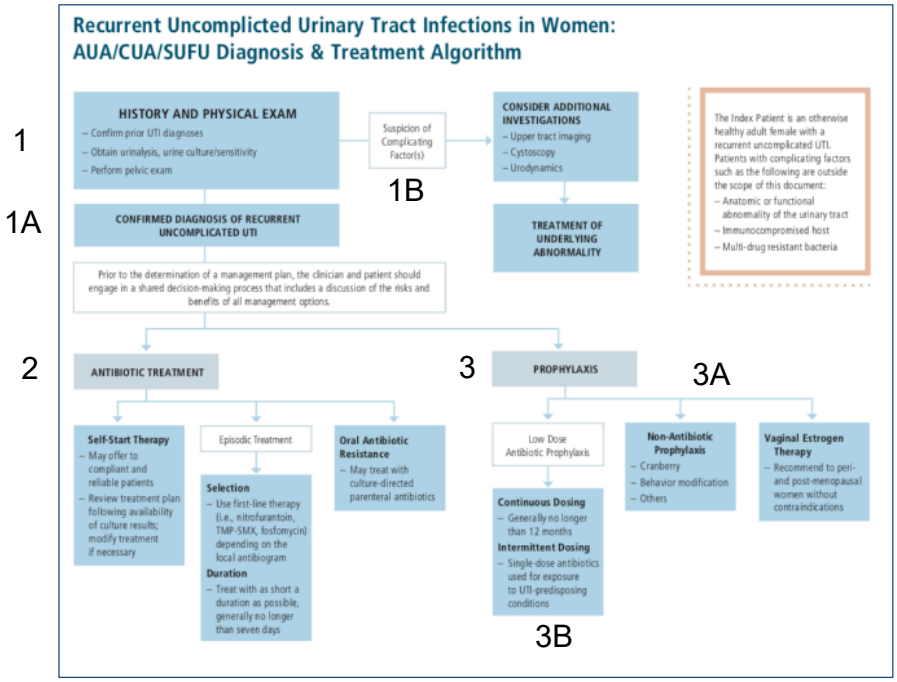
33

Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline

- Definition
  - Two separate culture-proven episodes of acute bacterial cystitis and associated symptoms within 6 months or 3 episodes within a year
- Population
  - Healthy adult female with recurrent uncomplicated UTI
  - No anatomic or functional urinary tract abnormality, immunocompromise, or multi-drug resistant bacteria

https://www.auanet.org/guidelines-and-quality/guidelines/recurrent-uti

34



35

History

- Confirming the diagnosis of recurrent UTI
  - Linking episodes with true symptoms and plausible pathogens (past micro and antibiotic review)
  - Obtaining fresh UA/Urine culture with new episodes
- Assessing risk factors for workup and interventions
  - Poor response/early relapse, persistent hematuria, cancer risks, stone risks, upper tract disease, incomplete emptying, timing of UTI w/sexual activity, others

36

78*year-old Man*

- RA*, immunosuppressives*
- Recurrent *P. aeruginosa* UTI, now resistant to levo and ciprofloxacin after 3 courses of oral quinolones over 5 mos*
- Treated with IV cefepime, symptoms partially improved*
- Another UA and culture sent as incomplete response
  - Urine culture showed no growth*
  - UA showed persistent hematuria*
  - Cystoscopy = large bladder tumor

* Red flags

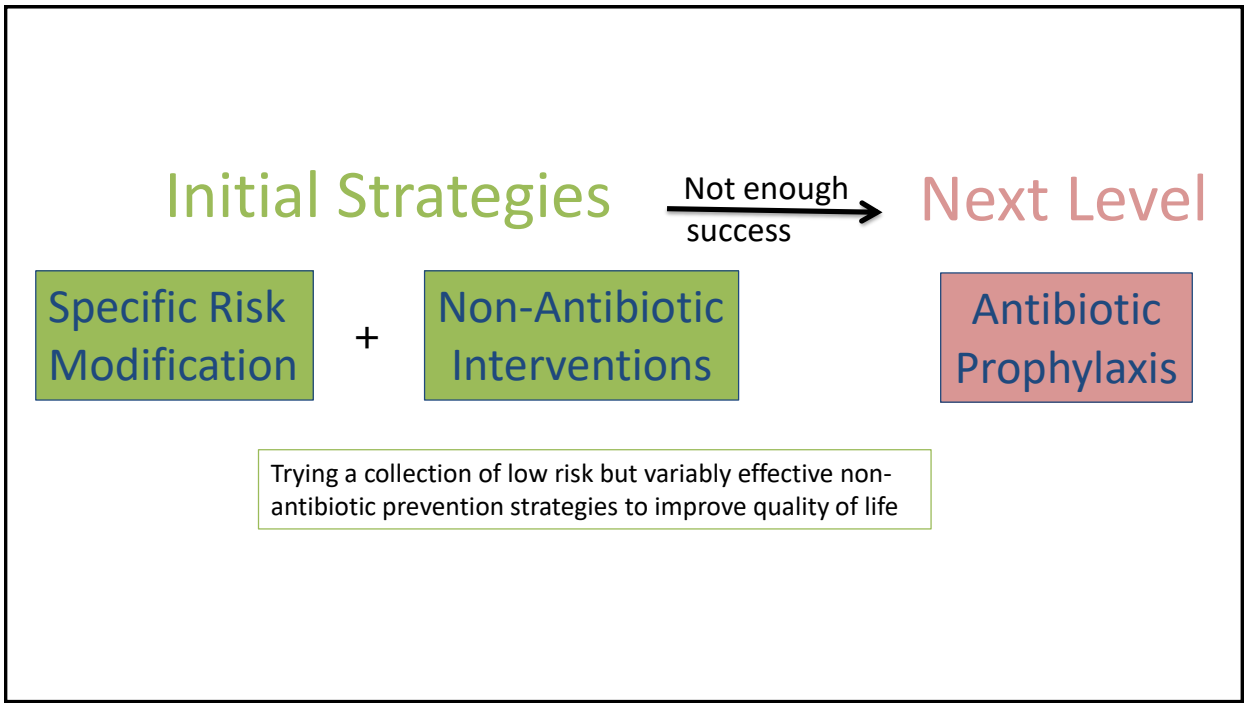
37

High Residual Urine: A Critical Issue

Bladder Outlet Obstruction or Bladder Dysfunction Often Overlooked In Progressive Cases

- Urine is a culture media where microbes grow
  - The more often one has high residual, the more likely a microbe will get lucky
- Antibiotic resistance is a numbers game
  - Resistance predicated on organism burden and persistence, is apt to emerge with high residual urine

38



39

Non-Antibiotic

- Cranberry
  - Proanthocyanidins (PAC) inhibit adherence of type 1 fimbriated *E. coli* to the uroepithelial cell receptors
  - Cochrane 2023 update (50 studies) reduces risk of recurrent UTI
  - Many products, consider PAC concentration
- D-mannose
  - Binds to type 1 pili of *E. coli* blocking adhesion to uroepithelial cells
  - Longer time to UTI recurrence vs TMP/SMX
  - Similar recurrence as NTF, both were better than placebo

J Clin Urol 2014;7:208
World J Urol 2014;32(1):79

40

Non-Antibiotic

- Vaginal estrogen
  - Peri-/post-menopausal women w/ no contraindications
  - Restores epithelium, normal flora (lactobacilli), lowers pH, antimicrobial peptides
  - Reduces UTI recurrence by 50%
- Lactobacillus probiotics
  - Idea is to normalize vaginal flora, benefit in reducing recurrent UTI risk unclear

41

Effectiveness of Prophylactic Oral and/or Vaginal Probiotic Supplementation in the Prevention of Recurrent Urinary Tract Infections: A Randomized, Double-Blind, Placebo-Controlled Trial

Varsha Gupta,[1] Paola Mastromarino,[2] and Ritu Garg[3]

Table 4. Time to the First Symptomatic Urinary Tract Infection Recurrence in the Treatment Groups

Parameter	Group[a]	Number of Patients With UTI Recurrence	Time to the First Symptomatic UTI (d)	*F*-value	*P* Value
Mean time to the first symptomatic UTI, d	G1	42	69.33	27.37	<.001
	G2	34	71.91		
	G3	27	123.88[b,c]		
	G4	24	141.87[b,c]		

Abbreviation: G, group; UTI, urinary tract infection.

[a]G1 used oral placebo + vaginal placebo; G2 used oral probiotic + vaginal placebo; G3 used oral placebo + vaginal probiotic; and G4 used oral probiotic + vaginal probiotic.

[b]$P < .05$ (vs G1 in post hoc Bonferroni test).

[c]$P < .05$ (vs G2 in post hoc Bonferroni test).

Clinical Infectious Diseases® 2024;78(5):1154–61

42

JAMA Internal Medicine | Original Investigation

Effect of Increased Daily Water Intake in Premenopausal Women With Recurrent Urinary Tract Infections

A Randomized Clinical Trial

Thomas M. Hooton, MD; Mariacristina Vecchio, PharmD; Alison Iroz, PhD; Ivan Tack, MD, PhD; Quentin Dornic, MSc; Isabelle Seksek, PhD; Yair Lotan, MD

Funding/Support: This study was funded by Danone Research, which sells bottled water, including Evian that was used in this study.

140 healthy, recurrent UTI, who drink <1.5L H_20 daily

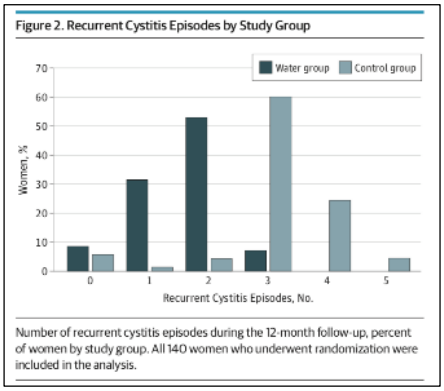
Drink 1.5L daily + baseline vs baseline amount

UTI frequency over 12 months

Water group

Fewer UTI 1.7 vs 3.2, p<0.001)

Fewer Abx 1.9 vs 3.6, p< 0.001)



43

Methenamine – The Resurgence

- Methenamine salts
  - Hippurate (dosed BID) and mandelate (dosed QID)
  - FDA approved 1967 to prevent recurrent UTI
- Hydrolyzed in acidic urine to formaldehyde and ammonia
  - Formaldehyde denatures proteins, nucleic acids
- Requires acidic urine pH and dwell time
  - pH < 6 (use urine pH strips and oral ascorbic acid)
  - Challenge with urea-splitting organisms (Proteus, Pseudomonas)

HIPREX package insert, accessdata.FDA.gov;

44

Methenamine

- Caveats
  - Contraindicated in renal insufficiency, severe liver insufficiency, severe dehydration. Do not use with sulfonamides (combination can precipitate out)
  - Generally well tolerated, check LFTs periodically
  - Watch for bladder irritation, hematuria, dysuria
- Several recent studies in renal transplant
  - Reduction in UTIs, well tolerated

HIPREX package insert, accessdata.FDA.gov;

Progress in Transplantation 2022;32(1):67
Transpl Infect Dis 2019;21(3):e13063
Transpl Infect Dis 2020;22(2):e13247

45

ALTAR Trial

Alternative to Prophylactic Antibiotics for the Treatment of Recurrent UTI in Women

- Women, recurrent UTI, n = 240
  - Median 6 UTI in 12 mos prior
  - Mean age 50, 59% peri-/post-menopausal
- Methenamine hip BID vs Daily antibiotic x 12 months
  - Randomized, open label, non-inferiority
- Incidence of treated UTI during time on preventive Rx
  - 1.38 (MHip) vs 0.89 (Abx) episodes/person/year (so not inferior)
  - Similar rates of adverse effects

BMJ 2022;376:e068229

46

Antibiotic Prophylaxis

- Post-coital UTI
  - Single dose
- Continuous
  - 3-6 months (clinical trials 6-12 months)
- Usual agents
  - TMP/SMX, nitrofurantoin, cephalexin, and others

https://www.auanet.org/guidelines-and-quality/guidelines/recurrent-uti

47

Long-Term UTI Antibiotic Prophylaxis

- Work diligently on these first
  - Structural, stone, neurologic, high residual urine
  - Non-antibiotic interventions
- Antibiotic prophylaxis works but has a price
  - Selection of resistant pathogens, reversion back to recurrent UTI when off prophylaxis
  - Be sure to document and monitor for side effects

Microbiol Spectrum 4(6);UTI-0021-2015
/www.auanet.org/guidelines-and-quality/guidelines/recurrent-uti

48

Initial Strategies → Not enough success → Next Level

Specific Risk Modification + Non-Antibiotic Interventions

- Sexual activity related
- Incomplete emptying
- Structural issues
- Abx/bacteria mismatch

- Cranberry
- Hydration
- Vaginal estrogen
- D-mannose
- Methenamine

Antibiotic Prophylaxis

- 3-6 month trial

Trying a collection of low risk but variably effective non-antibiotic prevention strategies to improve quality of life

49

Let's Recap: 84-year-old woman

- Lives in Arizona
- Travels to Florida to visit her son, 3-4 times per year
- Every time she visits, she gets a UTI
- She is in a Florida Urgent Care and wants an antibiotic
- How would you help her?
  - Florida Urgent Care
  - Arizona Primary Care

50