

UTIs: New Updates and Practical Approaches to Challenging Cases

4/17/25

Leslie Stewart, MD
Indian Health Service



No Disclosures



Outline



- Definitions, diagnosis and treatment of UTIs
 - New guidelines for complicated UTI coming soon
 - New approved treatments for cystitis
- Clinical challenges
 - Recurrent cystitis
 - Delirium and UTI diagnosis
 - CAUTI

Case 1



- 24yo F presents with 2 days of dysuria and urinary frequency. She denies any fevers, chills, abdominal pain, back pain or vaginal discharge.
- She is otherwise healthy, and takes no medications
- She has not been sexually active in the past year.
- On exam, she is afebrile. She has mild suprapubic tenderness, but no CVA tenderness.

- What is the diagnosis?
- What tests would you do?

UTI Definitions



Current Classification

Uncomplicated UTI: acute cystitis in afebrile, nonpregnant, premenopausal woman with no diabetes and no urologic abnormalities

Acute pyelonephritis

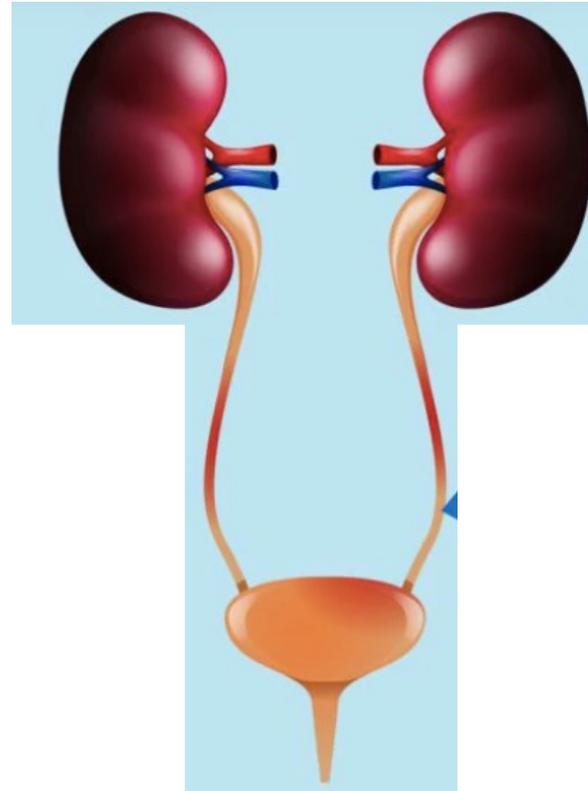
Complicated UTI: all other UTIs

UTI Definitions



Current Classification	New (Draft IDSA) Classification
<p>Uncomplicated UTI: acute cystitis in afebrile, nonpregnant, premenopausal woman with no diabetes and no urologic abnormalities</p>	<p>Uncomplicated UTI: infection confined to the bladder (in afebrile women or men)</p>
<p>Acute pyelonephritis</p>	<p>Complicated UTI: infection beyond the bladder</p>
<p>Complicated UTI: all other UTIs</p>	<ul style="list-style-type: none">- Pyelonephritis- Catheter-associated UTI (CAUTI)- Febrile or bacteremic UTI

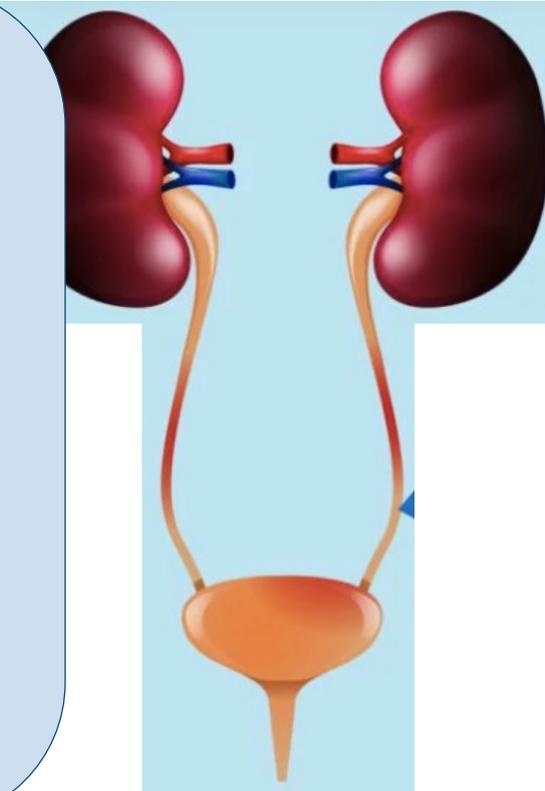
UTI Definitions



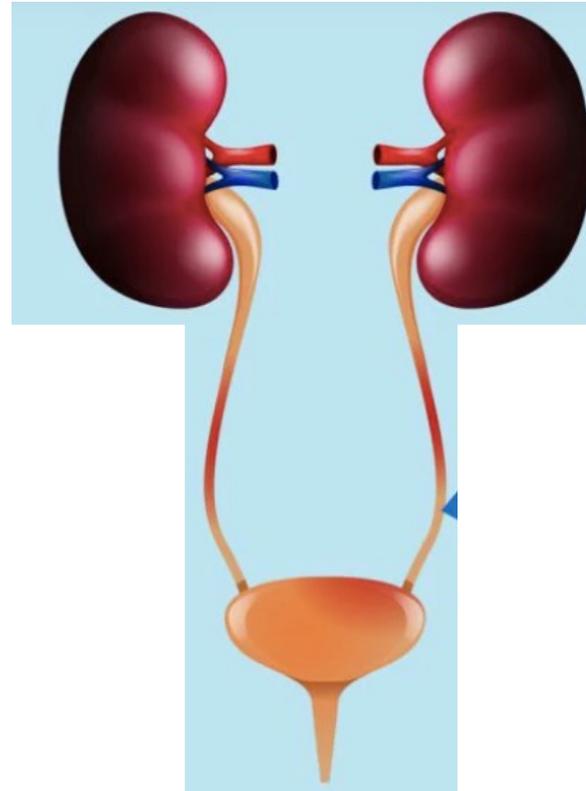
UTI Definitions

Cystitis/Uncomplicated UTI

- Symptoms: dysuria, urinary frequency/urgency, hematuria, suprapubic pain
- Treatment: nitrofurantoin, tmp-sulfa, Fosfomycin, beta-lactams
- Duration: 3-5 days



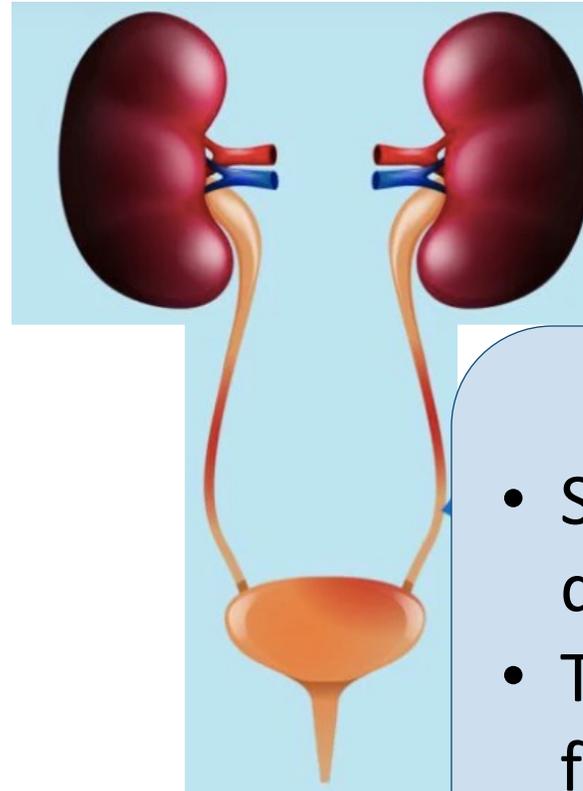
UTI Definitions



Pyelonephritis

- Symptoms: fever, back pain
- Treatment: tmp-sulfa, fluoroquinolone
- Duration: generally 7 days

UTI Definitions



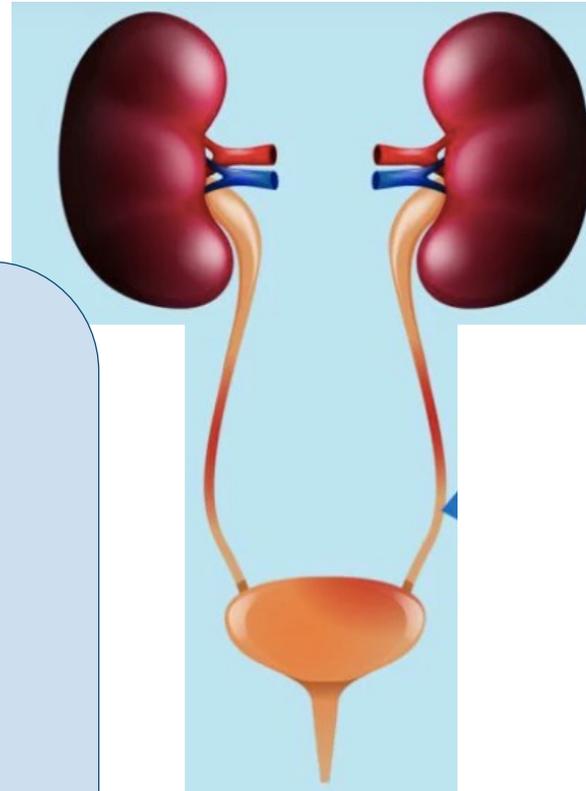
Prostatitis

- Symptoms: perineal pain, dysuria, urinary frequency
- Treatment: tmp-sulfa, fluoroquinolone
- Duration: 2-6 weeks

UTI Definitions

Urethritis

- Symptoms: dysuria, discharge
- Treatment: often STI
- Duration: 1-7 days



Case 1



- 24yo F presents with 2 days of **dysuria and urinary frequency**. She **denies any fevers**, chills, abdominal pain, back pain or vaginal discharge.
- She is otherwise healthy, and takes no medications
- She has **not been sexually active** in the past year.
- On exam, she is **afebrile**. She has mild suprapubic tenderness, but **no CVA tenderness**.

- What is the diagnosis?
- What tests would you do?

UTIs are clinical diagnoses!

There is no lab test or combination of tests that can definitively diagnose a UTI without clinical information

UTI Diagnosis: Symptoms

- Cystitis in women
 - 1 symptom of UTI: 50% positive predictive value
 - Dysuria and urinary frequency without vaginal discharge/irritation: 90% positive predictive value
- Testing with a urinalysis (with reflex to culture) helpful if
 - Diagnostic uncertainty
 - Recurrent UTI (to confirm diagnosis)
 - Concern for antibiotic resistance
 - Possible failed treatment recently
 - History of resistance
 - A lot of recent antibiotic exposure
 - Signs that infection is beyond the bladder

UTI Diagnosis: Urine culture



- Bladder is not sterile (has it's own microbiome!)
- Bacteria in a urine culture does not equal UTI

UTI Diagnosis: Urine culture

Population	Prevalence of Asymptomatic Bacteriuria
Healthy premenopausal women	1–5%
Women 70–90 years old	11–16%
Female long-term care residents	25–50%
Male long-term care residents	15–50%
Women with diabetes	9–27%
Men with diabetes	1–11%
People receiving hemodialysis	25%
Presence of indwelling urinary catheter	> 90%

UTI Diagnosis: Urinalysis

- WBC in UA (pyuria is ≥ 10 WBC/hpf)
- Helpful if negative to rule out infection
 - False negatives: pyelonephritis with obstruction, neutropenia
- Not as helpful to rule in infection
 - Premenopausal women: pyuria occurred 25% of all days on which no symptomatic urinary tract infection was diagnosed
 - Other causes of false positives: appendicitis, diverticulitis, STIs, noninfectious causes (stone, malignancy)
- Squamous epithelial cells: >100 contamination, 20-100 may be contamination (interpret results of UA and culture with caution)

UTI Diagnosis: Urinalysis



Population	Prevalence of Asymptomatic Bacteriuria	Prevalence of Pyuria in Persons with Asymptomatic Bacteriuria
Healthy premenopausal women	1–5%	32%
Women 70–90 years old	11–16%	
Female long-term care residents	25–50%	90%
Male long-term care residents	15–50%	90%
Women with diabetes	9–27%	70%
Men with diabetes	1–11%	
People receiving hemodialysis	25%	90%
Presence of indwelling urinary catheter	> 90%	50–100%

UTI Diagnosis: Urine dip stick

- Leukocyte esterase
 - Released by WBCs
 - Relatively good estimation of WBC in urinalysis

- Nitrite
 - Some bacteria reduce urinary nitrates to nitrites
 - False positives with phenazopyridine (bladder analgesic), consumption of beets



Why does this matter?

Case 2

- 62yo F with HTN, DM
- Urinalysis had been done to follow-up on microscopic hematuria
- Urinalysis → 10-20 WBC; Urine culture: >100K *E. coli*
- She feels well, has no fevers, and no urinary symptoms
- **Asymptomatic bacteriuria:** presence of bacteria in the urine, with or without pyuria, in the absence of clinical symptoms of a UTI

- *Would you treat?*
- *Which populations should be treated?*

ASB: People who are treated

- Pregnant people
- Patients who are undergoing urologic procedure with potential mucosal bleeding
- *Post-renal transplant patients in immediate transplant period?*
 - American Society of Transplantation ID COP (2019): Consider treatment if two consecutive samples $>10^5$ of the same uropathogen in the first two months post-transplant
 - IDSA (2019): Insufficient evidence to form a recommendation regarding treatment in the first month after transplant
- **NO:** everyone else! (diabetic patients, spinal cord injury, indwelling catheters, immunocompromised, people with resistant organisms)

ASB: Why not treat asymptomatic bacteriuria

- No benefit
 - RCT of antibiotics for asymptomatic bacteriuria in diabetic women
 - Screening every 3 months, maximum 3 years of follow up
 - Antibiotic therapy did not delay or decrease symptomatic UTI (40% vs 42%), hospitalization
 - More antibiotic-associated adverse effects (received nearly 5 times more days of antimicrobial therapy than the control group)
 - Other studies have not shown differences in mortality, kidney function
- Increased *C difficile* infection
 - Nursing home patients who did not meet minimum criteria for UTI: 8.5 times more likely to develop *C difficile* within 3 months of treatment
- Change in microbiome

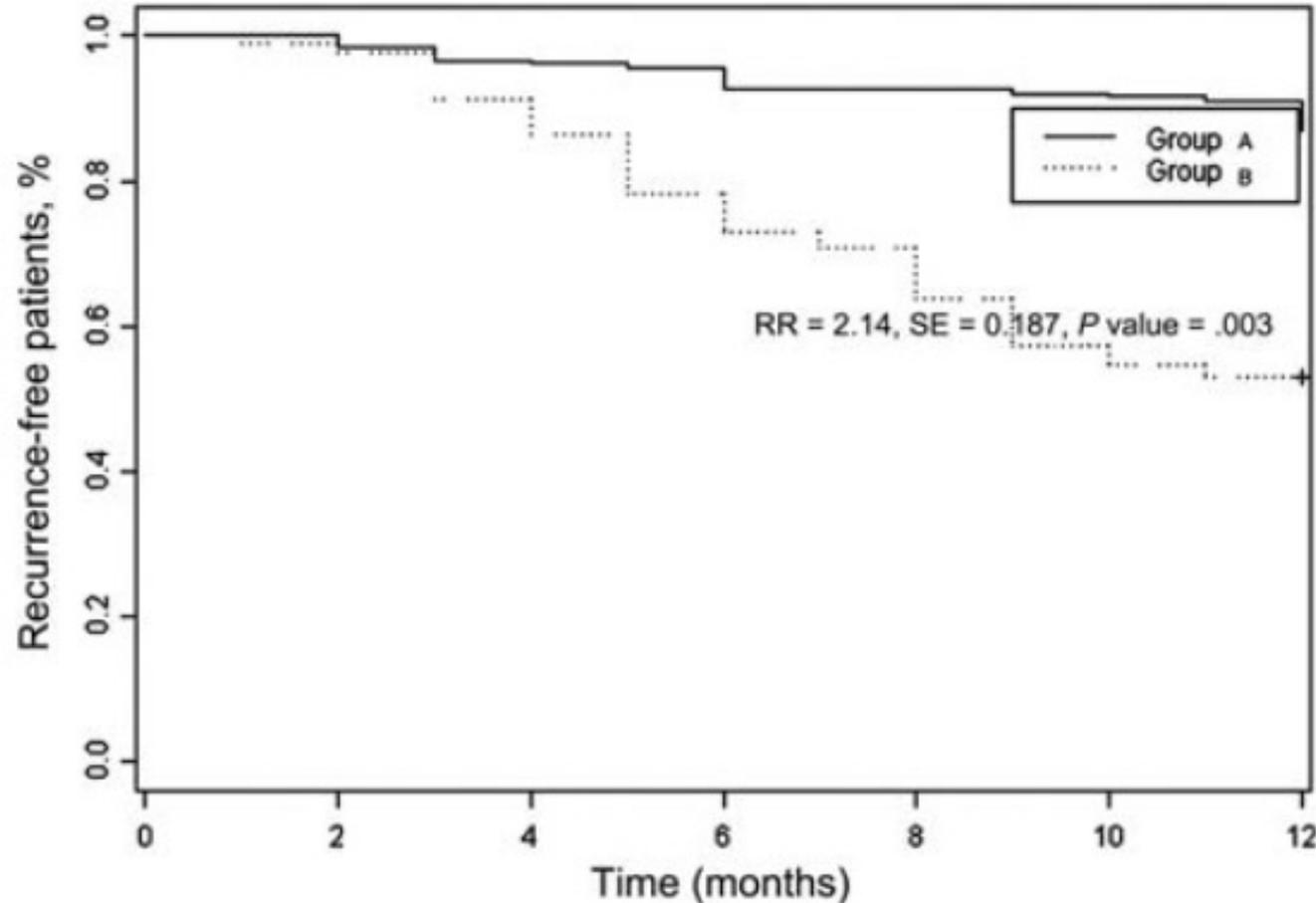
Rotjanapan Arch Intern Med 2011

Harding GK, et al. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. N Engl J Med 2002; 347:1576–83

Semetkowska-Jurkiewicz E et al. Mater Med Pol 1995; 27:91–5.

Sott A et al. Journal of clin microbio. 2001

Risks of treating ASB in patients with recurrent UTI



Group A not treated for ASB

Group B treated for ASB

Does antibiotic exposure lead to colonization by more pathogenic bacteria?



Treatment

Case 1 continued



- What antibiotic regimen would you prescribe for the patient with acute uncomplicated cystitis?
 - a) Levofloxacin 250 mg po daily X 3 days
 - b) Bactrim DS 1 tab po bid X 7 days
 - c) Cefpodoxime 100 mg po bid X 5 days
 - d) Nitrofurantoin 100 mg po bid X 5 days

IDSA- Antibiotic Regimens for Uncomplicated Cystitis

Drug (dosage)	Estimated clinical efficacy ^{ab}	Estimated microbiological efficacy ^b
 Nitrofurantoin monohydrate/ macrocrystals (100 mg twice daily for 5–7 days)	93 (84–95)	88 (86–92)
 Trimethoprim-sulfamethoxazole (160/800 mg twice daily for 3 days)	93 (90–100)	94 (91–100)
Fosfomycin trometamol (3 g single-dose sachet)	91	80 (78–83)
Pivmecillinam (400 mg twice daily for 3–7 days)	73 (55–82)	79 (74–84)
Fluoroquinolones (dose varies by agent; 3–day regimen) ^c	90 (85–98)	91 (81–98)
β-lactams (dose varies by agent; 3–5 day regimen) ^d	89 (79–98)	82 (74–98)

New treatment option: Pivmecillinam (Pivya)

- Old beta-lactam antibiotic in European guidelines for a long time (and in IDSA 2010)
- FDA approved April 2024 for treatment of women with uncomplicated UTI
- Data in women, and increasing data in men
- 185mg 3 times a day for 3 to 7 days (200mg pivmecillinam hydrochloride)
- Highly effective against *E coli*, including ESBL strains, *Klebsiella*
 - Does not cover *Enterococcus*, *Pseudomonas aeruginosa*

New: Gepotidacin (Blujepa)

- First-in-class: triazaacenaphthylene. Inhibits type II topoisomerase
- FDA approved March 2025 for treatment of females 12 and older with uncomplicated UTI caused by: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii* complex, *Staphylococcus saprophyticus* and *Enterococcus faecalis*
- Data for use came from EAGLE-2 and EAGLE-3, compared to nitrofurantoin
- 1500 mg BID for 5 days

Case 1 continued

What antibiotic regimen would you prescribe for this patient if she also had presented with fever and flank pain?

a) Clindamycin 300 mg po qid X 14 days

b) Bactrim DS 1 tab po bid X 3 days

c) Ciprofloxacin 500mg po BD X 7 days

d) Nitrofurantoin ER 100 mg po q12 X 14 days

e) Fosfomycin single dose

Draft new guidelines on complicated UTI



- Complicated UTI = infection beyond the bladder
- Four-step approach to choosing empiric antibiotic therapy for complicated UTI
 - Severity of illness
 - Septic shock, sepsis or no sepsis
 - Evaluate for risk factors for resistant organisms
 - Review culture data for the past year
 - Assess patient-specific factors
 - Allergies, drug-drug interactions, contraindications
 - Consider antibiogram
 - If septic shock ($\geq 90\%$ susceptible) or sepsis ($\geq 80\%$ susceptible)

Draft new guidelines on complicated UTI



Table 1: Potential Empiric Antibiotics for cUTI[^]--use the four steps to choose among these

Four Steps 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—use the four steps to choose among these	Alternative
Sepsis with or without shock ^{**}	Third or fourth generation cephalosporins, [*] carbapenems, [#] piperacillin-tazobactam, fluoroquinolones [^]	Novel beta lactam-beta lactamase inhibitors, [*] ceftiderocol, 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, [*] ceftiderocol, plazomicin), or older aminoglycosides [^]
Without sepsis, oral route of therapy	Fluoroquinolones [^] or oral cephalosporins (see Table 3)	Trimethoprim-sulfamethoxazole, amoxicillin-clavulanate

- Recommended treatment duration is 5-7 days in most cases

Case 3

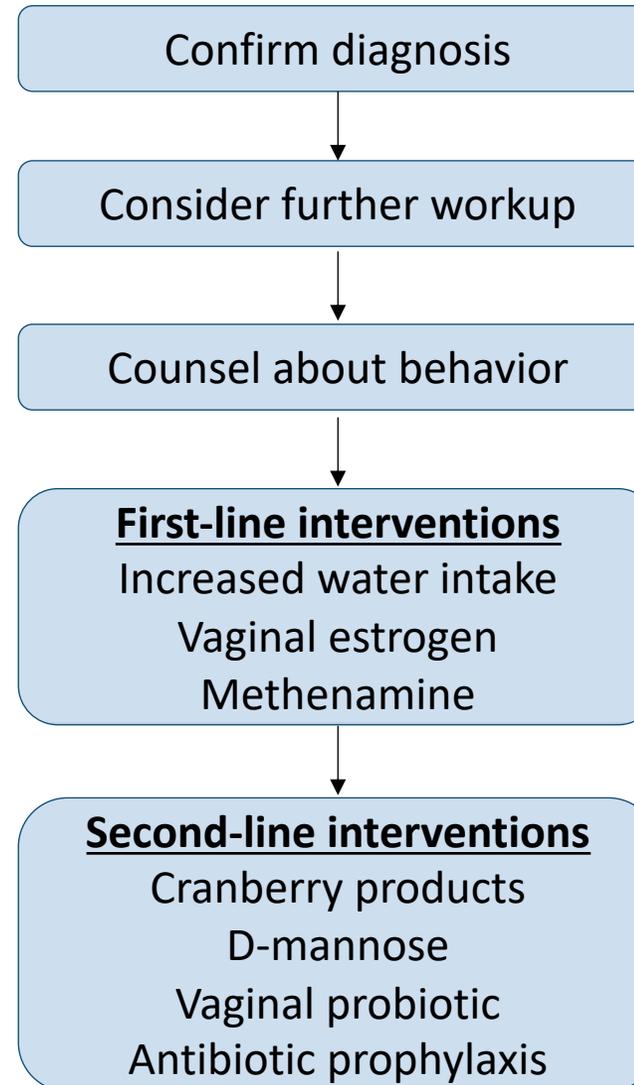
- 64yo F
- Has has had 4 episodes of cystitis in the past year, for which she usually receives treatment at a walk-in urgent care center.
- Now she wants to know how to prevent further recurrent episodes.

- *How would you counsel her?*

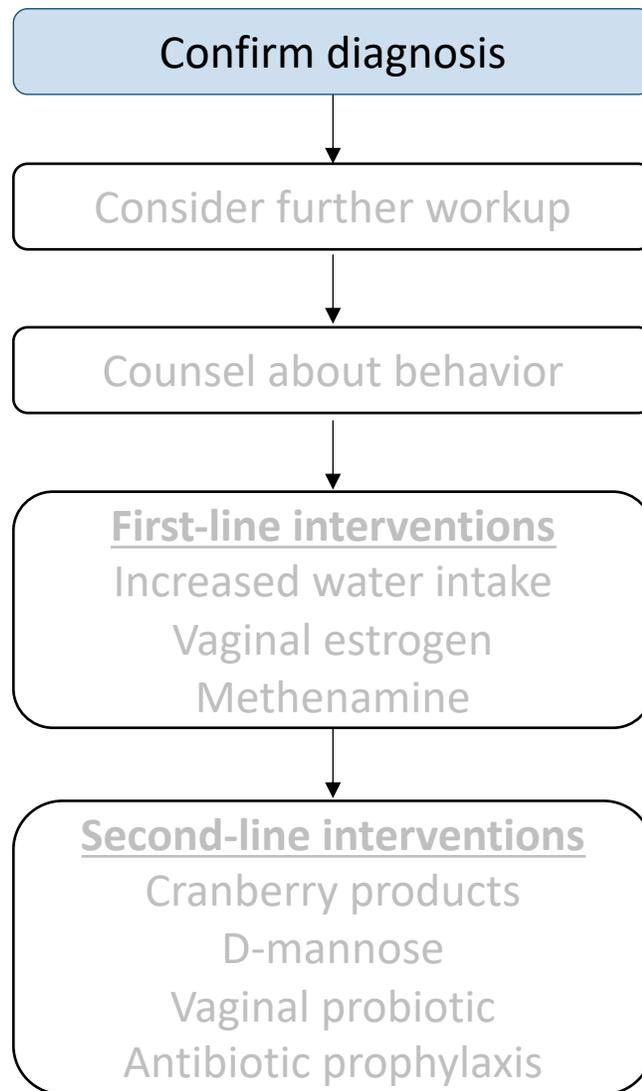
Recurrent cystitis

- Definition: ≥ 2 episodes in 6 months or ≥ 3 in a year
- Vast majority occur in women
 - Up to 25-35% of young, healthy women with no structural or functional GU tract abnormalities have recurrent cystitis
- Relapse versus reinfection:
 - Relapse: recurrent infection with the same species within 2 weeks of original treatment
→ may require thorough GU workup
 - Reinfection: clinical cure between episodes

Recurrent cystitis in women



Recurrent cystitis in women



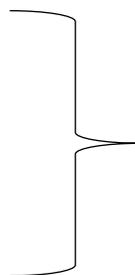
- Check urinalysis
 - If WBC<10, need to consider other etiologies
- Do physical exam

Differential diagnosis of cystitis

- Other infections
 - Vaginitis (yeast infection, trichomoniasis, bacterial vaginosis)
 - Urethritis (chlamydia, gonorrhea, HSV, etc)

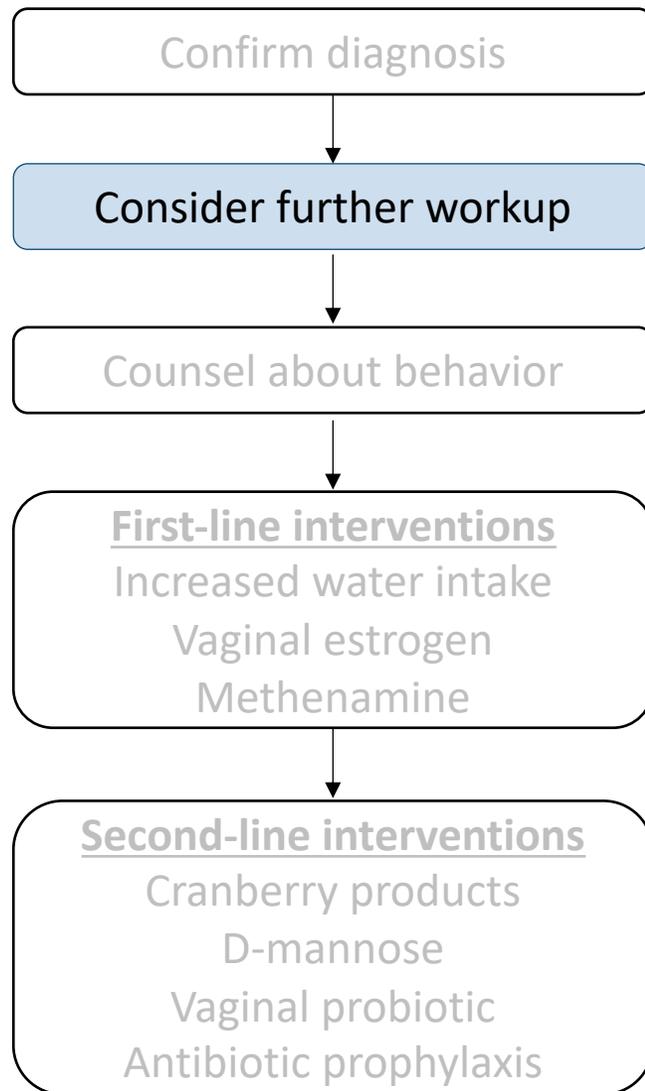
- Noninfectious causes

- Pelvic organ prolapse
- Overactive bladder
- Genitourinary syndrome of menopause
- Painful bladder syndrome (interstitial cystitis)



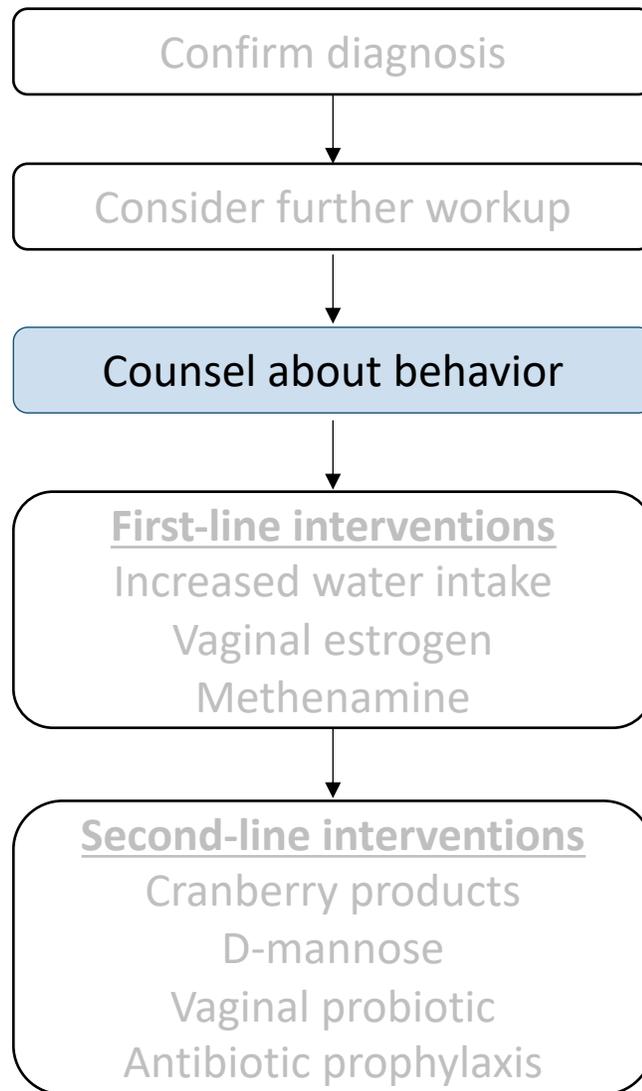
Very common in the population who presents with recurrent cystitis. Treatments overlap (vaginal estrogen, pelvic floor PT)

Recurrent cystitis in women



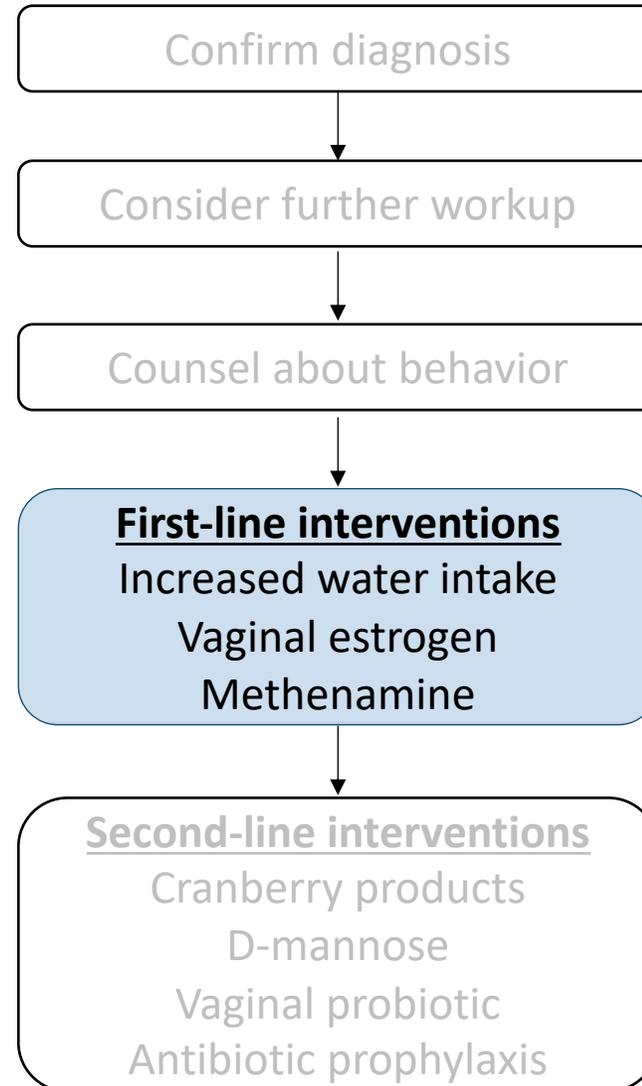
- Indications
 - Relapse
 - History of stones
 - Proteus in urine
 - Voiding issues
- Workup
 - CT or ultrasound
 - Urogynecologic evaluation

Recurrent cystitis in women



- Discuss what cystitis is
 - NOT change in odor
 - NOT cloudy urine
- Spermicides, especially with diaphragms, can increase cystitis
- Discuss constipation
- Not shown in studies: hygiene, postcoital voiding

Recurrent cystitis in women



Recurrent cystitis in women

Increased water intake

- Mechanism: dilution, increased clearance
- Evidence
 - Premenopausal women randomized to drink 1.5L more a day
 - 1.7 episodes of cystitis vs 3.2 at 12 months
 - Meta-analysis of increased fluid intake (≥ 200 ml daily)
 - Reduced the rate of UTIs (OR 0.25, 95% CI = 0.11 to 0.59, $P = 0.001$)

Recurrent cystitis in women

Increased water intake

- Cannot recommend for those on fluid restriction for heart failure, etc.
- May be difficult in those with voiding problems, incontinence
- Assess baseline intake and provide a specific goal: an increase in 1.5L or achieving >2L
- Offer practical advice
 - Scheduled phone alarms to achieve interim goals
 - Stop drinking before dinner to avoid nocturia

Recurrent cystitis in women

Vaginal estrogen

- For postmenopausal women
- Mechanism
 - Estrogen + lactobacillus → lactic acid → Low pH inhibits uropathogens
- Evidence
 - 1993 RCT of 93 postmenopausal women with recurrent UTI
 - Topical estrogen for 8 months resulted in significant reduction in UTI incidence vs. placebo (0.5 versus 5.9 episodes per patient year)
 - Meta-analysis including 1936 patients evaluated the use of vaginal estrogen
 - Significant reduction in UTIs (relative risk, 0.42; 95% CI, 0.30-0.59)

Recurrent cystitis in women

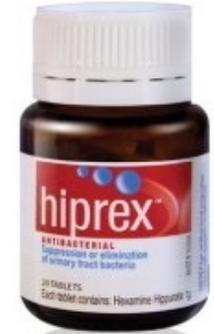
Vaginal estrogen

- Comes in many forms (cream, tab, ring)
- For cream: 1-2g daily for 2 weeks then 1g twice a week
 - Explain how to apply
- Can take up to 12 weeks to have an effect
- If patient has a history of breast cancer, can discuss with their oncologist
 - Studies have not shown an increase in breast cancer recurrence



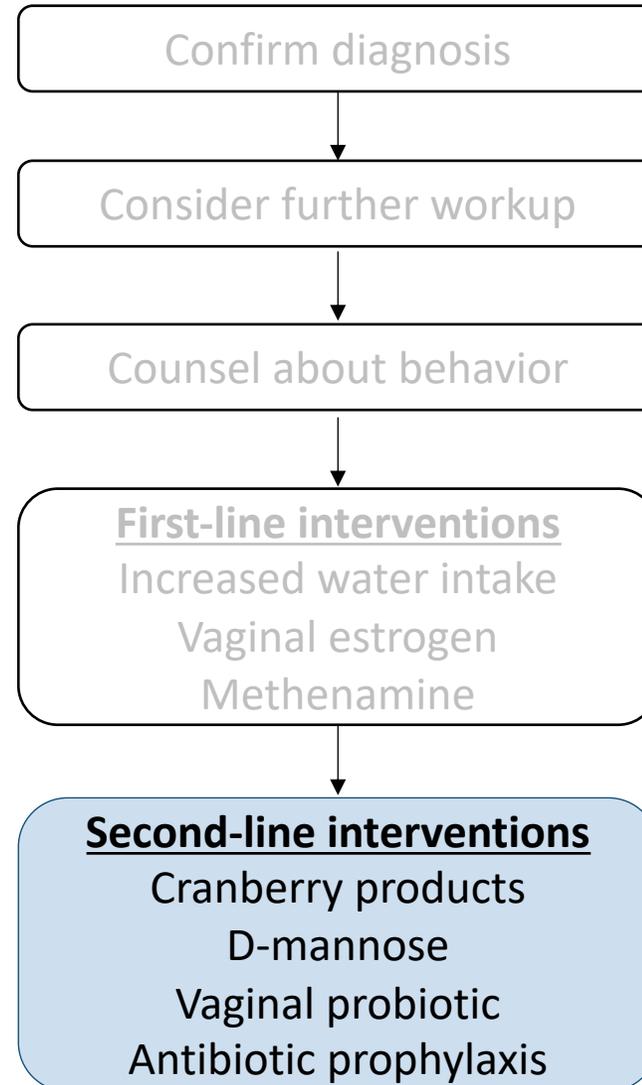
Recurrent cystitis in women

Methenamine



- Mechanism: converted to formaldehyde which inhibits bacterial growth
- Evidence
 - RCT of 92 women TMP vs methenamine: 1.5 UTIs per year in the TMP group vs 1.6 in the methenamine group
 - RCT of 240 women, methenamine not inferior to antibiotic prophylaxis
- Use
 - Dose: 1g BID
 - Avoid with GFR < 30 (poorly studied and potential for increased acid load)
 - Sometimes prescribed with vitamin C for urine acidification but methenamine hippurate itself acidifies urine, vitamin C can be associated with stones

Recurrent cystitis in women



Recurrent cystitis in women

Cranberry products



- Mechanism: inhibits adherence of uropathogens to uroepithelial cells
- Evidence
 - Data has been mixed, maybe due to different formulations
 - 2023 Cochrane meta-analysis with 6211 participants: for symptomatic, culture-verified cystitis compared to placebo or no specific treatment
 - Cranberry products RR 0.70 (95% CI 0.58 to 0.84; $I^2 = 69\%$)
 - No data to support use in older people, those with bladder emptying problems, pregnancy
- Use
 - Cranberry products containing proanthocyanidin (PCA) levels of 36mg

Recurrent cystitis in women

D-mannose

- Mechanism: prevents E coli from binding to urothelial receptors
- Evidence
 - 2023 meta-analysis of 7 trials did not show benefit
 - 2024 RCT of 598 women did not show benefit compared to placebo
- Use
 - 2g daily of D-mannose powder

Recurrent cystitis in women

Vaginal probiotic

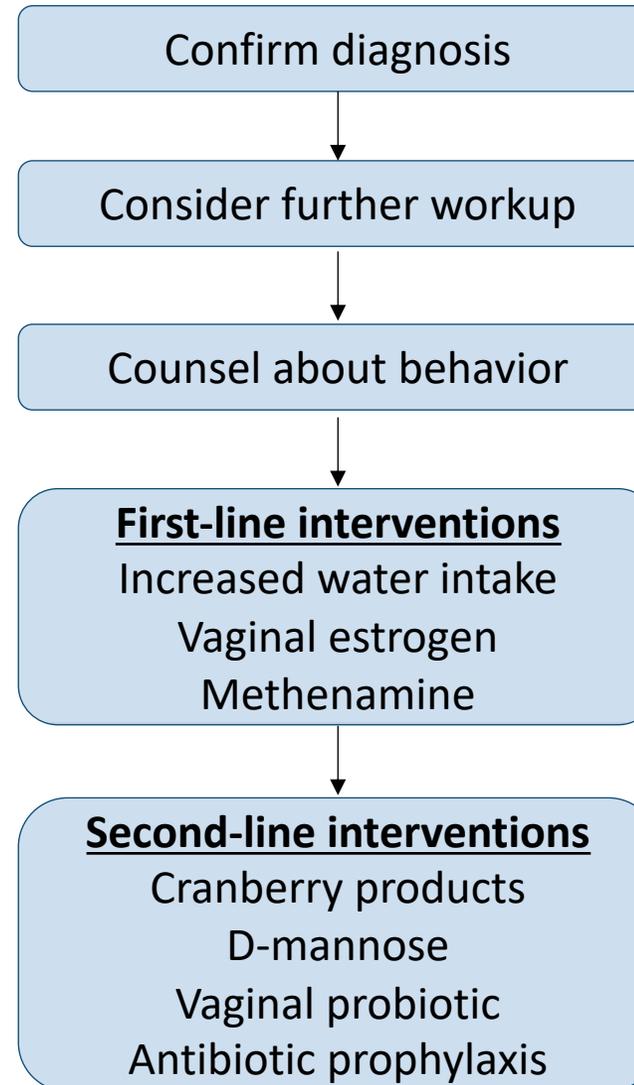
- Mechanism: restore the vaginal flora and reduce colonization of uropathogens
- Evidence
 - 2015 meta-analysis did not show benefit
 - 2024 placebo-controlled RCT of 174 premenopausal women with recurrent UTI
 - Vaginal probiotic groups (one also had oral probiotic) had lower UTI recurrence at 4 months

Recurrent cystitis in women

Antibiotic prophylaxis

- Continuous antibiotics
 - 2004 Cochrane review of women with cystitis: clinical recurrence of UTI per patient-year was significantly reduced (RR 0.15, 95% CI 0.08-0.28)
 - 2017 meta-analysis restricted to post-menopausal women RR 0.7
 - Return to prior rate when antibiotics stopped
- Postcoital antibiotics
 - For people whose infections are temporally related to intercourse
- Intermittent self-treatment (pill in pocket)
 - Relationship with PCP important: need to take as directed and call if not better

Recurrent cystitis in women



What about men?

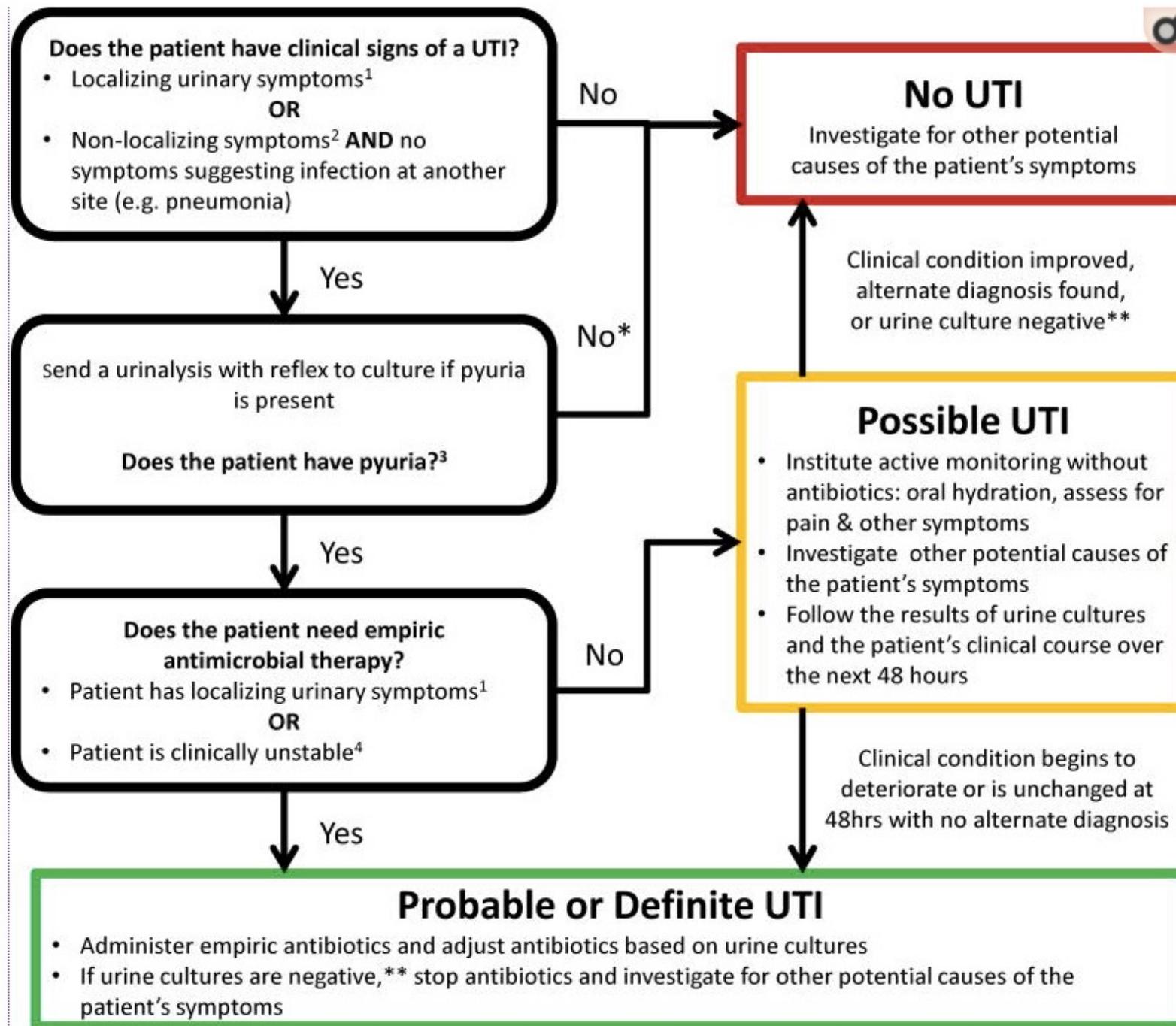
- Low threshold for further evaluation, but urologic evaluation is not always necessary
- Always think about prostatitis
 - Fever, pelvic or perineal pain, or obstructive symptoms
 - Nitrofurantoin, beta-lactams and fosfomycin do not achieve reliable tissue concentrations in the prostate
 - Usually treat with TMP-sulfa or fluoroquinolone
- No studies have evaluated the optimal duration of antibiotics in men with cystitis

Case 4

- 90yo F with HTN, DM, dementia who is brought in by family for being more confused
- Has had several similar presentations in the past year usually treated with IVF and antibiotics for possible “UTI” and gets better.
- Patient does not have any symptoms
- Vital signs are normal, no abdominal tenderness or CVA tenderness
- *How would you manage this patient?*

Delirium and Possible UTI

- Urinalysis/urine dip not often helpful in elderly populations
 - Bacteriuria in up to 50%
 - Pyuria in up to 90%
 - Often co-exist with delirium: volume depletion, incontinence
- Cystitis does not cause systemic illness- shouldn't have an altered level of consciousness in most patients without fever, leukocytosis, sepsis
- Bacteriuric episodes in nursing home residents
 - Significantly associated with subsequent isolation of multi-drug resistant bacteria
 - Not associated with changes in mental status or admission to hospital for UTI
- Anchoring to UTI because of a “positive” UA can miss the true diagnosis





In older patients with functional and/or cognitive impairment with bacteriuria and delirium (acute mental status change, confusion) and without local genitourinary symptoms or other systemic signs of infection (eg, fever or hemodynamic instability), **we recommend assessment for other causes and careful observation rather than antimicrobial treatment** (strong recommendation, very low-quality evidence).

Chronic indwelling catheter

- 97% will have pyuria
- 100% colonized
- Cloudy appearance or foul smell of the urine \neq bacteriuria or UTI
- Urine samples for culture should be obtained by removing the indwelling catheter and taking sample from new catheter
- CAUTI treatment: 5 to 7 days



Take Home Points

- UTI is a clinical diagnosis, but not always easy
 - Urinalysis (no pyuria) can be helpful to rule out infection
- Think about where infection is and the type of patient when choosing an antibiotic and duration
- Asymptomatic bacteriuria: treat in pregnant women and patients undergoing urologic procedure with mucosal bleeding
- Some patients may benefit from interventions to prevent UTIs, but have to consider carefully
- Delirium + bacteriuria does not equal UTI
- Urine tests are even less helpful for patients with catheters



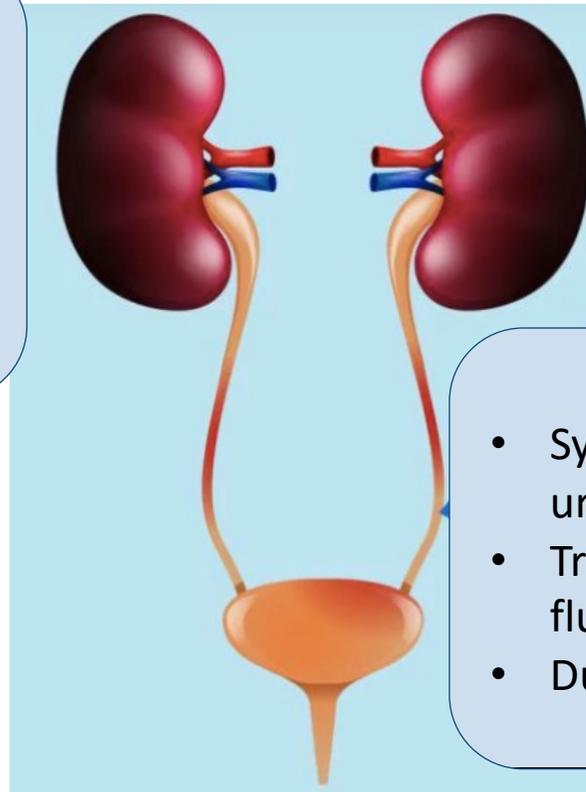
UTI Definitions

Cystitis/Uncomplicated UTI

- Symptoms: dysuria, urinary frequency/urgency, hematuria, suprapubic pain
- Treatment: nitrofurantoin, tmp-sulfa, Fosfomycin, beta-lactams
- Duration: 3-5 days

Urethritis

- Symptoms: dysuria, discharge
- Treatment: often STI
- Duration: 1-7 days



Pyelonephritis

- Symptoms: fever, back pain
- Treatment: tmp-sulfa, fluoroquinolone
- Duration: generally 7 days

Prostatitis

- Symptoms: perineal pain, dysuria, urinary frequency
- Treatment: tmp-sulfa, fluoroquinolone
- Duration: 2-6 weeks