Teasing out Asymptomatic Bacteriuria From UTI: *When to Treat (and With What)*

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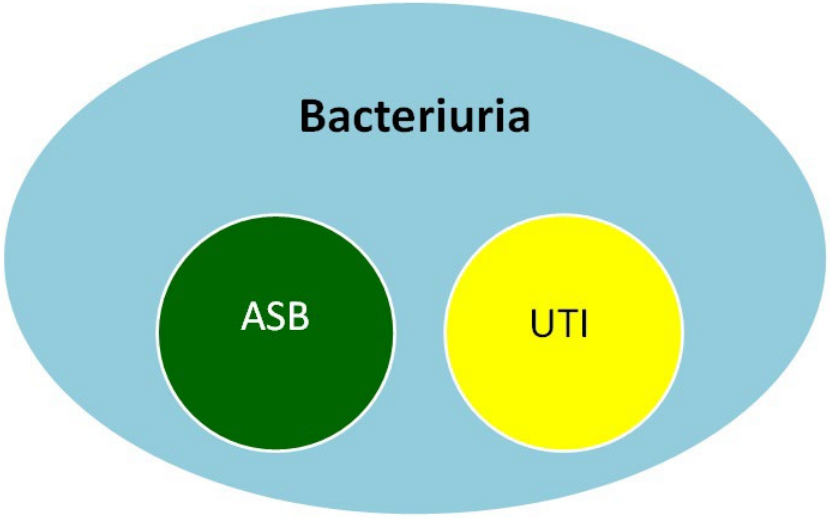


Disclosures

None

Questions to be Answered

- What distinguishes UTI from asymptomatic bacteriuria?
- When is treatment for asymptomatic bacteriuria indicated?
- What are my antibiotic choices in treating UTI?
- How long should I treat?
- Are there prevention strategies for UTI?

What are the TRUE signs and symptoms of UTI?

Classic symptoms directly attributable to the GU tract

- Urinary frequency
- Urgency (new)
- Dysuria
- Flank pain or CVA tenderness

GU symptoms to consider in certain situations (in the absence of other etiologies)

- Acute hematuria
- Pelvic/suprapubic discomfort

Systemic symptoms that may indicate UTI (esp. in patients who cannot communicate symptoms) in the absence of other etiologies

- Fever
- Change in mental status/delirium
- "Sense of unease" or increased spasticity in spinal cord injury

Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America (idsociety.org)

What are NOT true signs and symptoms of UTI?

- Change in urinary sediment
- Foul odor or change in odor of urine
- Pyuria (typically only helpful in ruling out UTI when not present)
- Positive leukocyte esterase (another way of measuring pyuria)
- Positive nitrite (indicates presence of bacteria that produce nitrite)

Causes of Malodorous Urine

- Bacterial colonization/infection (due to production of ammonia from bacterial ureases)
  - Not all infecting bacteria have urease
  - Not all bacteria that make urease cause symptomatic infection
- Dehydration (urinary concentration)
- Fecal contamination
- Ketosis
- Asparagus intake

Reasons for Overtreatment of ASB

- Historical misunderstanding:
  - ASB discovered in pregnant women
  - Bladder thought to be sterile
- Lack of knowledge about guidelines
  - Misunderstanding of pyuria
  - Unawareness of ASB as distinct from UTI
- Inherent biases—treat a positive test
- Fear of withholding antibiotics
- Social norms

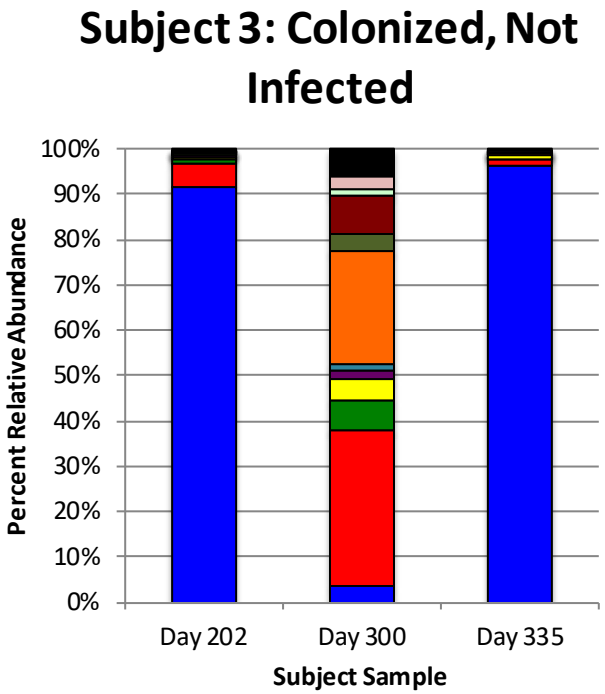
- Drekonja et al, AJIC 2014; Trautner et al, AJIC 2014; Lee et al, BMC Infect Dis 2015

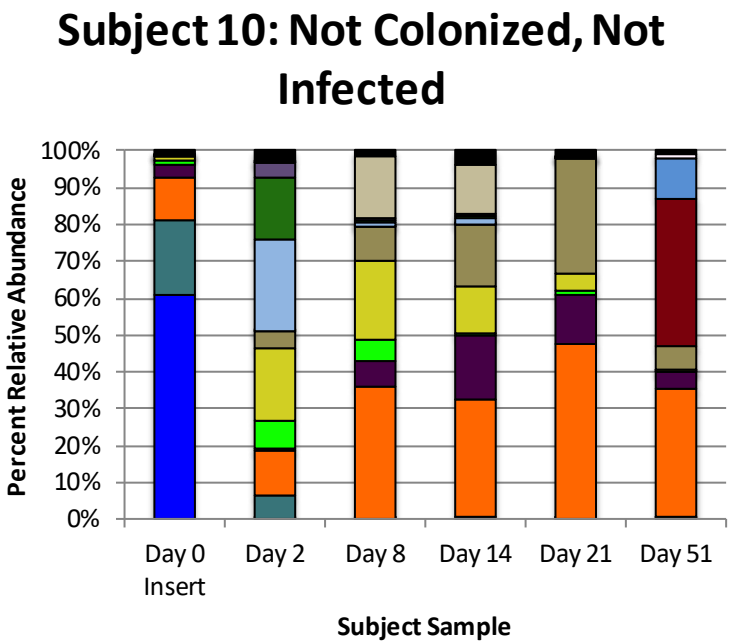
The bladder isn't sterile!
Definitely not in catheterized patients.
Microbiome studies using 16s rRNA sequencing are defining the urinary microbiota.

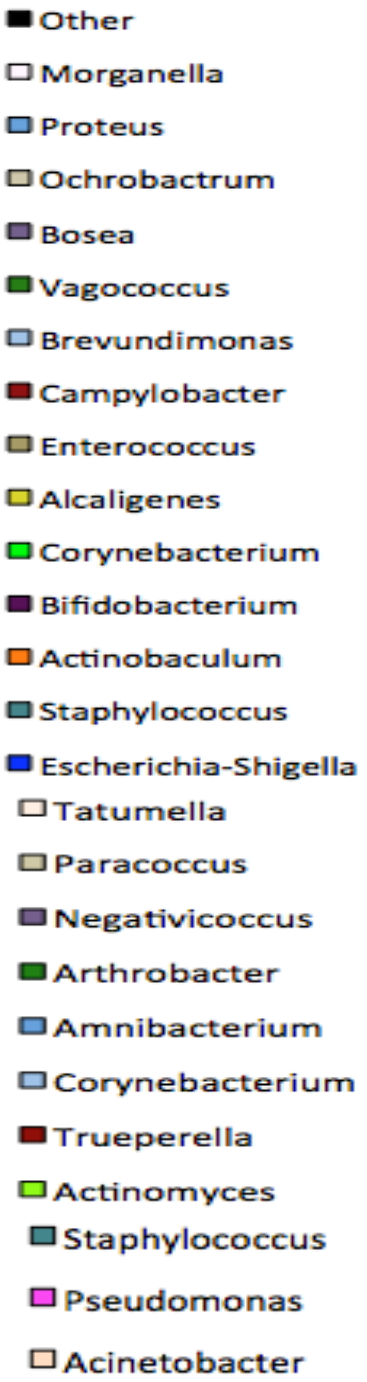
Warren et al, JID 1982

Wolfe and Brubaker, European Urol 2015
Lewis, Front Cell Infect Microbiobe 2012
Hilt, J Clin Microbiol 2014
Fouts, J Translat Med 2012

Microbiota of Catheterized Bladders







Asymptomatic patients

Horwitz et al, J Infection, 2015

Prevalence of Asymptomatic Bacteriuria

Population	Prevalence
Healthy women	1-5% (premenopausal) 2-10% (pregnant) 3-9% (postmenopausal)
Persons with diabetes	11-16% (women) 0.7-11% (men)
Elderly persons in the community	11-16% (women) 4-19% (men)
Elderly persons in long-term care facilities	25-50% (women) 15-50% (men)
Persons with indwelling catheter use	3-5% per day (short term) 100% (long term, e.g., 30d or more)

Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America (idsociety.org)

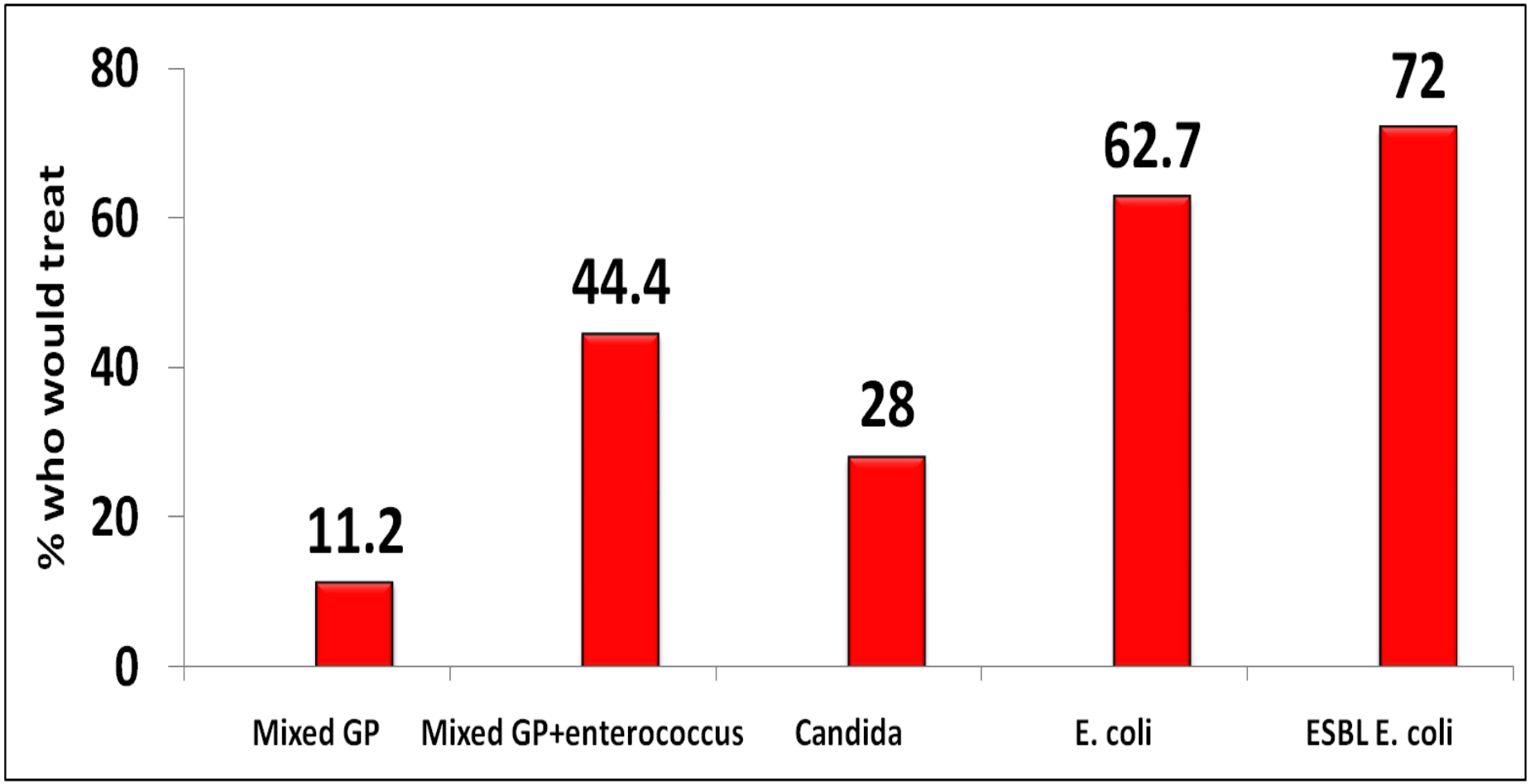
Survey of Nursing Home Personnel

- Licensed personnel (N=822)
  - 60% recognized that screening cultures on admission are not indicated
  - 36% understood that pyuria does not distinguish ASB from UTI
- Unlicensed personnel (N=804)
  - 27% recognized fever but not urine color, odor, or cloudiness as a CAUTI symptom)

AHRQ Safety Program for Long-Term Care: Preventing CAUTI and Other HAIs
http://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/cauti-ltc/index.html

Trautner et al, ICHE 2016

Organism type drives inappropriate antibiotic use for ASB



Trautner et al, Am J Infect Control 2014

Bacteria in the urine after being blamed for everything

Recommendations Against Treating ASB

- "Choosing Wisely" Campaign addresses harmful or wasteful medical practices
  - Creates top 5 lists of practices to avoid
- Treatment of ASB makes the top 5 list for:
  - Australia (Royal College of Pathologists)
  - Canadian Urologic Society
  - American Academic of Pediatrics
  - American Geriatrics Society
  - Society for Post-Acute and Long-Term Care
  - IDSA

- Jung et al, Infection 2016

IDSA Asymptomatic Bacteriuria Guidelines: Highlights from Recent Update

- Screening for/treat ASB in pregnancy (at one of initial visits): rx 4-7d
- Guidance for older, functionally/cognitively impaired patient with nonlocalizing symptoms
  - Assess for other causes
  - Treat if fever and other systemic signs c/w sepsis
- No recommendation for/against screening for/treating ASB at time of catheter removal

Clin Infect Dis 2019 Mar 21. doi: 10.1093/cid/ciy1121

IDSA Asymptomatic Bacteriuria Guidelines: Highlights from Recent Update

- ASB in transplant/immunocomp patients
  - Do not screen for/treat ASB in renal transplant >1mo (data insufficient for/against <1mo)
  - Do not screen for/treat ASB in other SOT
  - No recommendation for/against screening/treating in high-risk neutropenia (ANC<100 x ≥ 7d)

Clin Infect Dis 2019 Mar 21. doi: 10.1093/cid/ciy1121

IDSA Asymptomatic Bacteriuria Guidelines: Highlights from Recent Update

- ASB in surgical patients
  - Do not screen for/treat ASB for pts undergoing nonurologic surgery
  - Screen for/treat ASB in endoscopic urologic procedures associated with mucosal trauma (1-2 doses periprocedure)

Clin Infect Dis 2019 Mar 21. doi: 10.1093/cid/ciy1121

Urologic Procedures and "Mucosal Trauma"

Yes: Screen for/Treat ASB

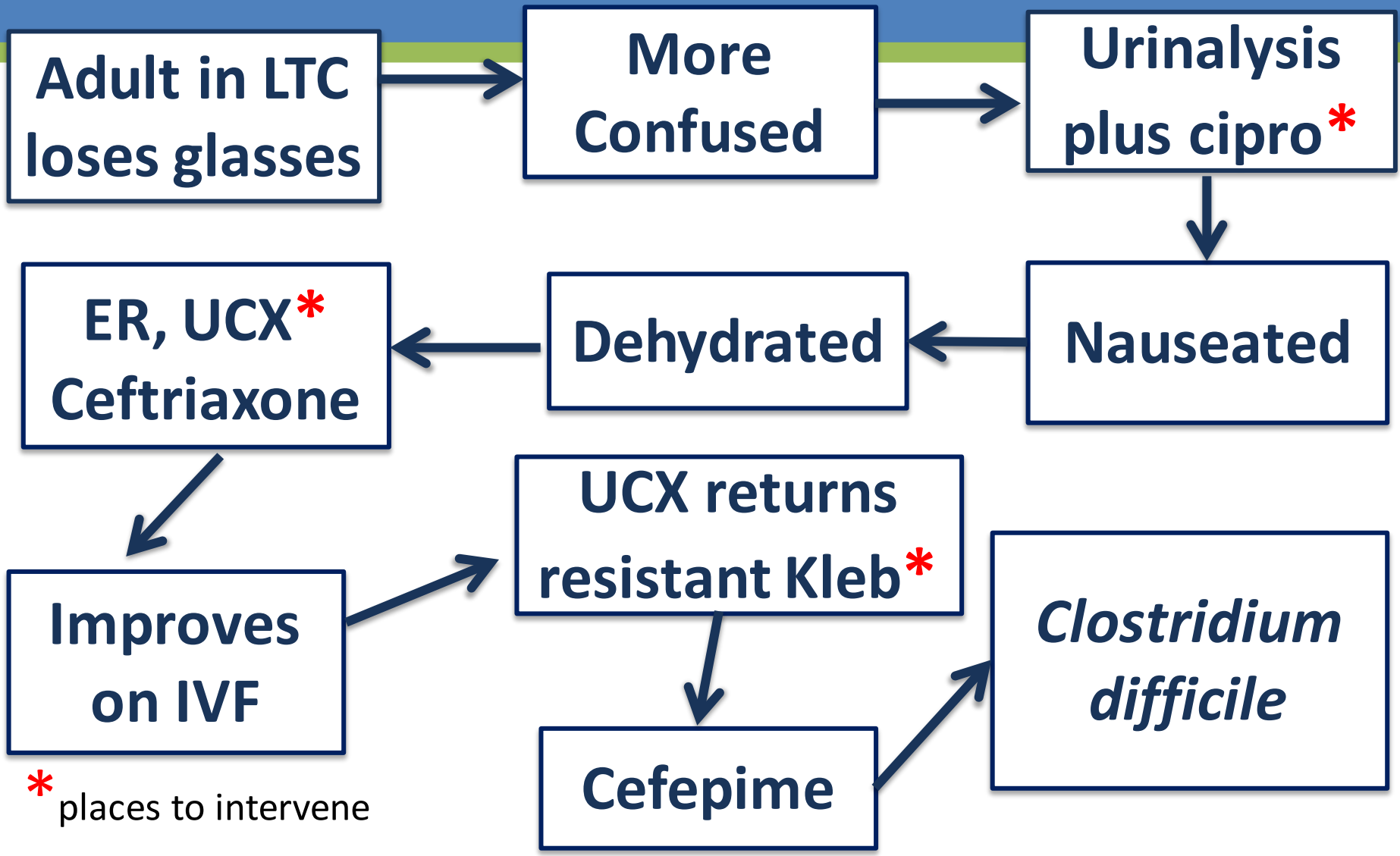
- TURP
- Ureteroscopy including lithotripsy, percutaneous stone surgery
- Cystoscopy involving mucosal biopsy

No: Don't Screen/Treat

- Uncomplicated catheter removal/exchange
- Diagnostic cystoscopy
- Cystoscopy including removing of internal ureteric stents
- Artificial urine sphincter
- Penile prosthesis implantation

Clin Infect Dis 2019 Mar 21. doi: 10.1093/cid/ciy1121

What happens in real life?



*places to intervene

Criteria For Diagnosing and/or Treating UTI in Long-Term Care: *Non-Catheterized Patients*

- Updated McGeer criteria (designed for surveillance and benchmarking, NOT for when to treat):
  - At least one of the following
    - Dysuria or acute pain, swelling, tenderness of testes, epididymitis, or prostate
    - Fever or leukocytosis AND at least one of the following (need two if no fever or leukocytosis):
      - CVAT
      - Suprapubic pain
      - Gross hematuria
      - New or increased incontinence, urgency, or frequency
  - PLUS positive urine culture (no more than 2 pathogens)

- Nace DA, *et al.* JAMDA 2014;15:133-139.

Criteria For Treating UTI in Long-Term Care: *Non-Catheterized Patients*

- 2005 Loeb Criteria: Minimal criteria for initiating antimicrobials
  - Positive urine culture and dysuria, OR
  - Positive urine culture and 2 or more of the following:
    - Fever
    - Urgency
    - Flank pain
    - Urinary incontinence
    - Shaking chills
    - Frequency
    - Gross hematuria
    - Suprapubic pain
- Nace DA, *et al.* JAMDA 2014;15:133-139.

From the Loeb Criteria Authors

- The original SHEA (Loeb) criteria were developed for the general NH population and did not take into consideration the unique characteristics of residents with profound cognitive impairment who are nonverbal…fever alone may be adequate evidence to justify antimicrobial initiation for a suspected UTI so long as there are no additional symptoms (e.g., new cough) to suggest an alternative source of infection."

- Nace DA, *et al.* JAMDA 2014;15:133-139.

Is There A Less Complicated Way Forward for NH Patients?

- Cooper Urinary Surveillance tool: developed by nurse practitioner in Ann Arbor for nurses to initiate evaluation for UTI
- Patients with indwelling catheters must exhibit two of the following new or acutely worse symptoms:
  - Fever >2°F above baseline or >100°F, chills, or new-onset hypotension
  - Flank/suprapubic/testicular pain or tenderness
  - Urine character change or purulent discharge around insertion site
  - Worsening of mental or functional status

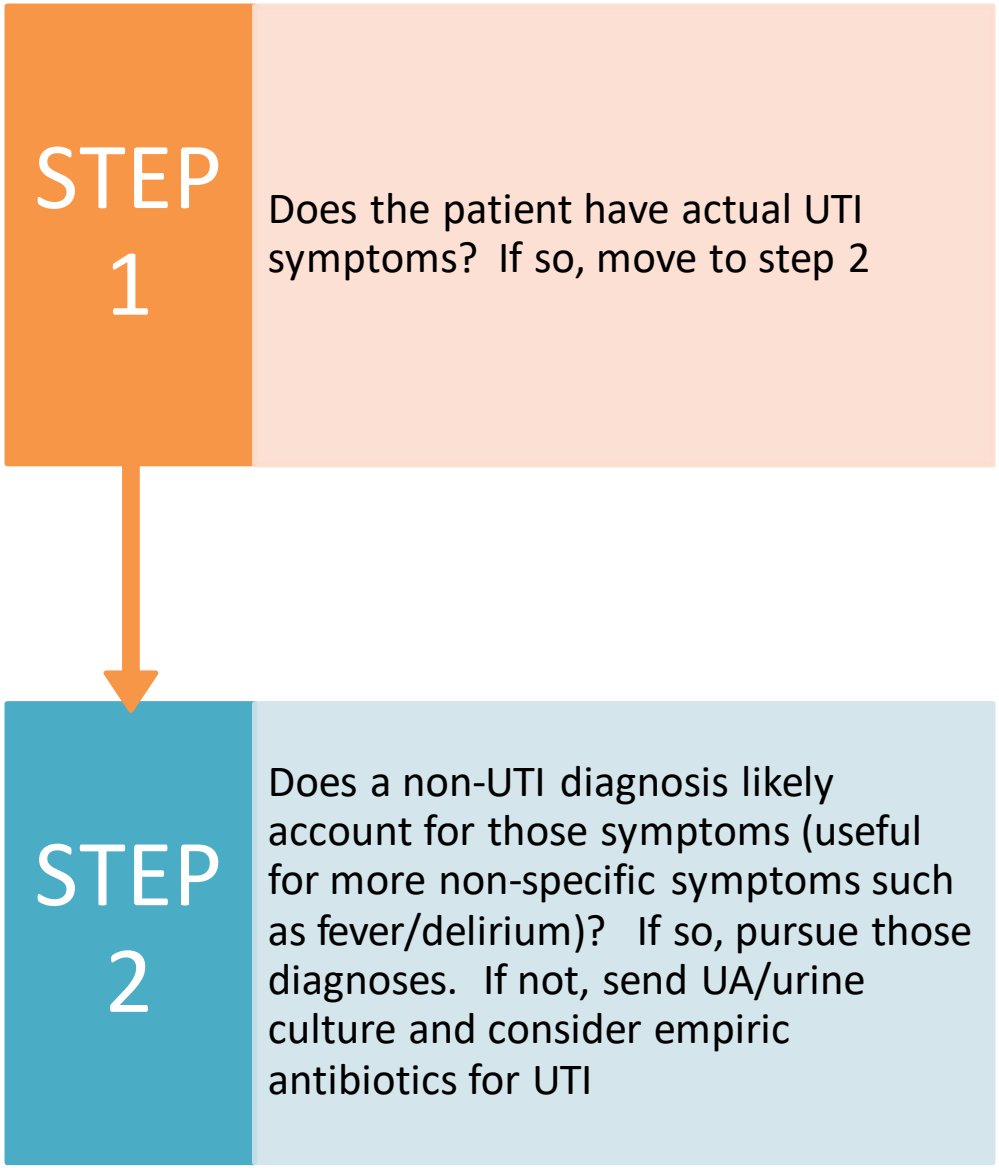
- Cooper DL, *et al.* Annals of Long-Term Care 2017;25(2):36-43

Cooper Urinary Surveillance Tool *Non-catheterized patients*

- Three of the following new or acutely worse symptoms required for initiation of evaluation for UTI:
  - Fever >2°F above baseline or >100°F
  - Dysuria, frequency, or urgency
  - Flank/suprapubic/testicular pain or tenderness
  - Change in urine character
  - Worsening mental or functional status

- Cooper DL, *et al.* Annals of Long-Term Care 2017;25(2):36-43

Algorithmic-based approach to UTI workup



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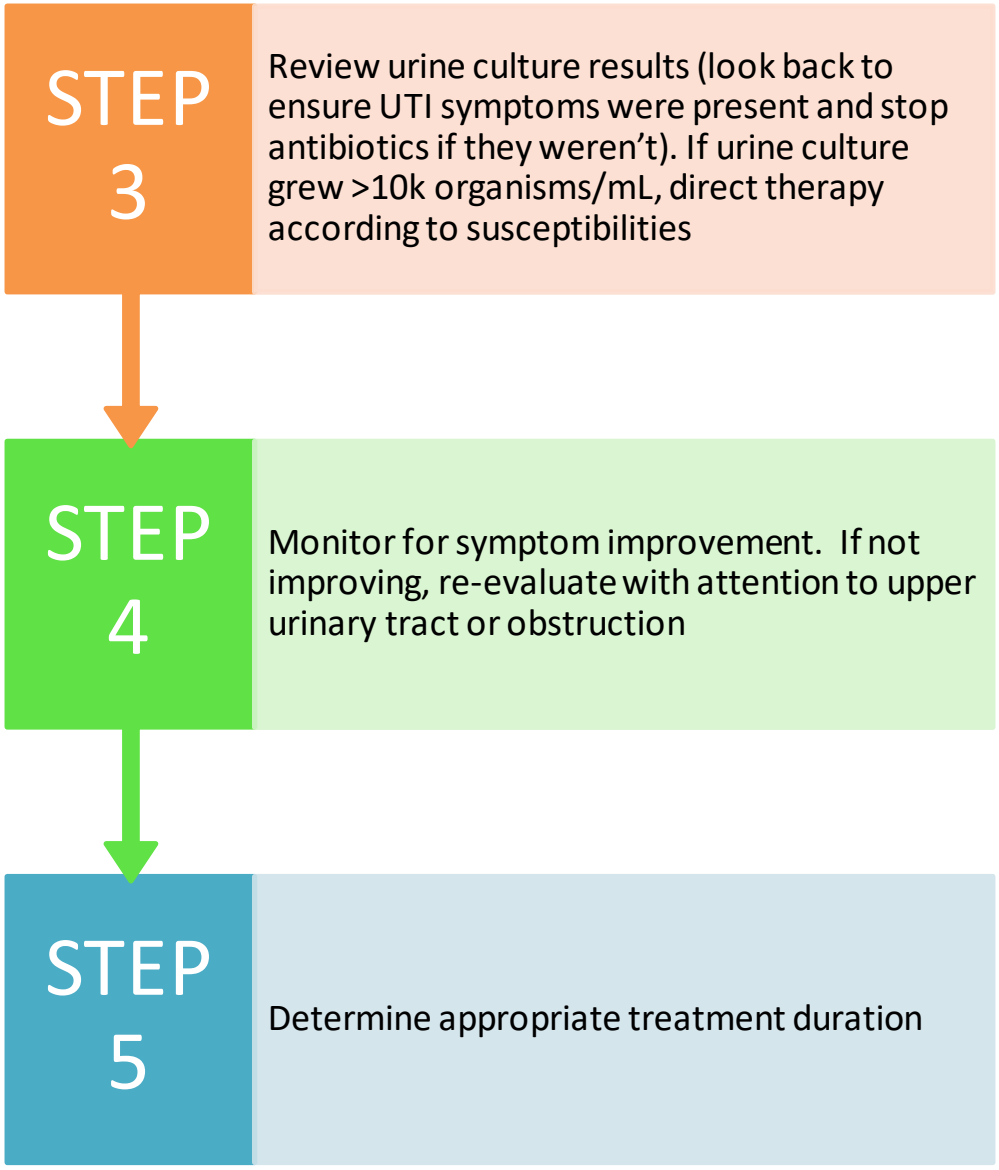


Antibiotic Treatment for UTI: General Guidelines

- Breadth of coverage will depend on setting and degree of illness
  - Patient presenting from non-healthcare setting who does not appear systemically ill likely does not require broad-spectrum Gram-negative coverage pending culture results
- Consider IV therapy for more severe disease and when patient cannot tolerate oral therapy
- *Follow up culture results to ensure your therapy is appropriate and to narrow it when able*

Organisms Associated with Non-Catheter-Associated UTI

- *Escherichia coli* by far most common (75-95%)
- Occasional other Enterobacterales, esp. *Proteus mirabilis, Klebsiella pneumoniae*
- *Staphylococcus saprophyticus*

Organisms Associated with Catheter-Associated UTI

- *Escherichia coli* most common (overall < 1/3 of all isolates)
- Other GNRs: *Klebsiella, Serratia, Citrobacter, Enterobacter, Pseudomonas, Proteus, Morganella*
- Gram-positive cocci: Enterococcus, coagulase-negative staphylococci
- (*Candida* species: typically represent colonization, rarely true infection)

- Short term catheterization typically associated with isolation of one organism, while long-term catheterization associated with polymicrobial cultures

Antibiotic Treatment for UTI: Oral Options

- β-Lactams/cephalosporins
  - Cephalexin 500mg po bid-qid
    - Better Gram-negative coverage than you think
  - Amoxicillin-clavulanate, cefdinir, cefaclor, cefpodoxime
  - Avoid in acute pyelonephritis unless IV agent given first; dose on higher side for bacteremia/upper tract disease
- Trimethoprim-sulfamethoxazole (TMP-SMX), typically 1 DS tab bid (normal renal function)
  - Monitor potassium and creatinine if renal insufficiency is present, especially if on ACE-inhibitor or ARB
  - Avoid if resistance prevalence is known to exceed 20% or if used for UTI in the previous 3 months
- Ciprofloxacin 250-500mg po bid
  - Avoid co-administration with tri- and divalent cations (aluminum, magnesium, calcium, iron, zinc) that lower absorption (e.g. tube feeds)
  - Know your local resistance patterns

Antibiotic Treatment for UTI: Other Oral Options

- Nitrofurantoin 100mg bid
  - Avoid if early pyelonephritis or complicated disease is suspected
  - Rare but serious side effect: interstitial pneumonitis
- Fosfomycin 3gm (single dose for uncomplicated cystitis; q3d for ~3 doses otherwise)
  - Avoid if early pyelonephritis or complicated disease is suspected
  - Should only be used for *E. coli*
  - May be of use in prostatitis (more extended course)

Antibiotic Treatment for Complicated UTI or Pyelonephritis:

IV Options (non-MDR organisms suspected)

- Ertapenem 1g IV q24h
  - Very broad coverage (though misses *Pseudomonas*)
- Ceftriaxone 1-2g IV q24h
  - Somewhat less-broad GNR coverage than ertapenem
  - Also misses *Pseudomonas*
- Ciprofloxacin 400mg IV q12h
  - Decent activity against most outpatient Gram-negative isolates at VA GLA but much more spotty against nosocomial isolates (~50% resistance in *E. coli, Klebsiella, Proteus, Pseudomonas*)

Antibiotic Treatment for Complicated UTI or Pyelonephritis:
IV Options (MDR organisms suspected)

- Aminoglycoside
- Piperacillin-tazobactam
- Cefepime
- Meropenem

- Gram-positive coverage (vancomycin, linezolid) is often considered empirically, though enterococci and coag neg staph tend to be of lower virulence
- MRSA is an uncommon cause of UTI (and when found in the urine should prompt investigation of occult bacteremia)

Duration of Treatment: Uncomplicated UTI

Cystitis in women

- Single-dose: fosfomycin
- 3 days: TMP-SMX, fluoroquinolones
- 5 days: nitrofurantoin
- 3-7 days: β-lactams/cephalosporins

Pyelonephritis

- Typically 7 days
  - 5 days: levofloxacin 750mg qd
  - 14 days: oral TMP-SMX

“Complicated” has been Complicated

- Can refer to:
  - Any UTI in males
  - Recent urologic surgery
  - Presence of urologic instrumentation
  - Pyelonephritis
  - Bacteremia associated with UTI

New Definition of "Complicated"

(from upcoming IDSA guidelines for complicated UTI)

- Infection beyond the bladder
  - Pyelonephritis
  - CAUTI
  - Febrile or bacteremic UTI

Duration of Treatment: Complicated and Catheter-Associated UTI

- 7 days in most cases (even with bacteremia)
- Consider extending treatment to 10-14 days if response is delayed
- Can consider 3 day course for women age ≤ 65 who develop UTI without upper tract symptoms after a catheter has been removed

Management of Recurrent UTI

- Make sure it's actually recurrent
  - Is it just ASB?
  - Are there other etiologies that can explain symptoms?
    - Interstitial cystitis/bladder pain syndrome
    - Vulvovaginitis
    - Gonorrhea/chlamydia/mycoplasma urethritis

Strategies for recurrent simple cystitis in women

- Evaluate for anatomic abnormalities (e.g., cystocele, nephrolithiasis)
- Avoidance of spermicide
- Increase fluid intake
- Topical estrogen in postmenopausal women
- Antimicrobial prophylaxis can be *considered* in select cases
  - ?methenamine with vitamin C
  - Nitrofurantoin, trimethoprim +/- sulfamethoxazole, beta-lactams are options, but expect resistance to emerge over time
  - Post-coital prophylaxis in select cases (doxyPEP?)

Antibiotic Prophylaxis for Recurrent Catheter-Associated UTI?

- A few studies do show some reduction in symptomatic UTI with a short course (≤ 72h) of antibiotics starting immediately prior to catheter placement for surgical procedures
- For long-term catheterization, antibiotic prophylaxis likely reduces bacteriuria in the first ~4 days of catheterization, an effect that wanes over time

BUT…

Antibiotic Prophylaxis for Recurrent Catheter-Associated UTI?

- Potential for benefit for prophylaxis in the vast majority of both short- and long-term catheterization is outweighed by:
  - Increased risk for subsequent infection with resistant organisms
  - Adverse effects of antibiotic therapy
    - Antibiotic-associated diarrhea, including *C. difficile*-associated colitis
    - Allergic reaction
    - Idiosyncratic effects (tendon rupture with fluoroquinolones, interstitial pneumonitis with nitrofurantoin)
- Rarely indicated

Recommendations To Reduce Catheter-Associated UTI

- Hand hygiene (particularly in catheter placement and handling)
- Aseptic technique and sterile equipment
- Securing catheter properly: keep catheter below bladder and drainage bag below catheter
- Maintaining closed, sterile drainage
- Catheterize only when necessary
- Remove unneeded catheters
- Don’t check a urine culture in a patient without symptoms!

When Is Urinary Catheterization Needed?

- Urinary obstruction
- Urinary retention
- Urologic or contiguous surgery
- Measuring urine output in critically ill patients

- Convenience should not be the only reason!

Avoid the one-point restraint…

When Is Urinary Incontinence an Indication for Catheterization?

- At patient request when other measures to treat incontinence have failed
- Comfort care in terminal illness
- To avoid contamination of wounds (i.e. sacral decubiti)—theoretical; no data to actually support this indication

Alternatives to Indwelling Catheterization

- Condom catheterization
  - Generally preferred for management of incontinence with low postvoid residual in patients who are not cognitively impaired
  - More comfortable/less painful than indwelling catheterization
  - Likely lower risk for bacteriuria
  - Less urethral trauma, but watch for external trauma/ulceration
- Intermittent catheterization
  - Neurogenic bladder retention

SPECIAL ARTICLE

Are Physicians Aware Of Which of Their Patients Have Indwelling Urinary Catheters?

Sanjay Saint, MD, MPH, Jeff Wiese, MD, John K. Amory, MD, Michael L. Bernstein, MD, Uptal D. Patel, MD, Judith K. Zemencuk, MA, Steven J. Bernstein, MD, MPH, Benjamin A. Lipsky, MD, Timothy P. Hofer, MD, MS

- 288 providers on 56 medical teams in 4 teaching hospitals given a list of their current patients and asked which ones had an indwelling urinary catheter
- Of all the patients with an indwelling urinary catheter:

•21% of students unaware
•22% of interns unaware
•27% of residents unaware
•38% of attendings unaware

Am J Med 2000; 109:476-80

Physician Awareness and Urinary Catheter Use

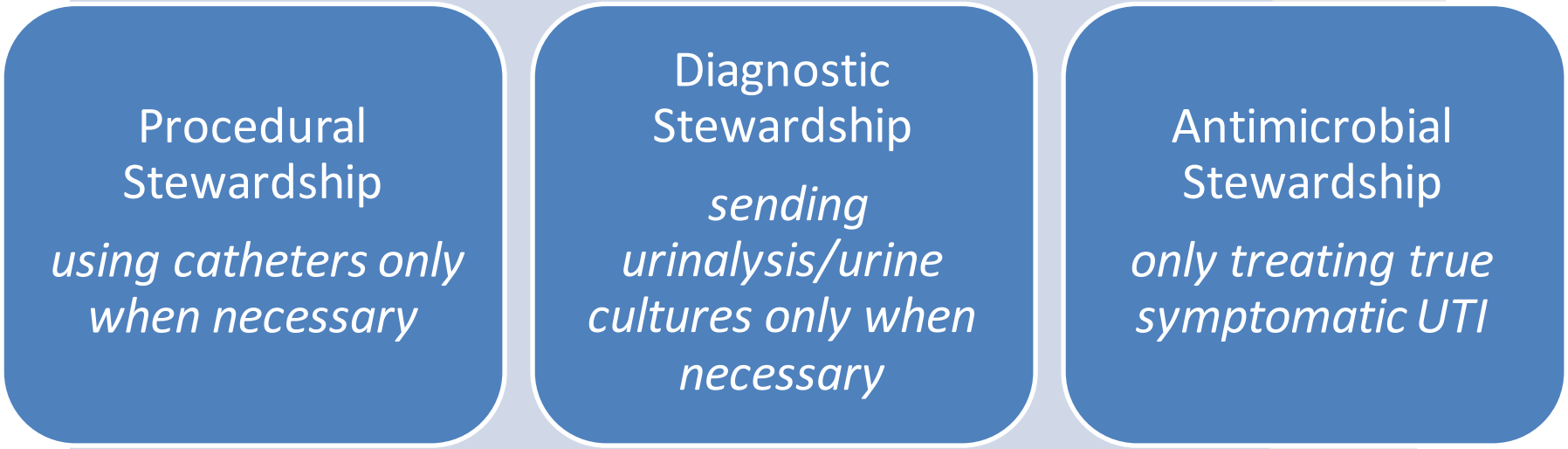
- Catheter use considered inappropriate in 31% of catheterized patients
- Among patients with inappropriate catheterization, physicians unaware of catheter use in 41% of observations
- Catheterization more likely to be appropriate if responders were aware of the catheter ($p<0.001$)

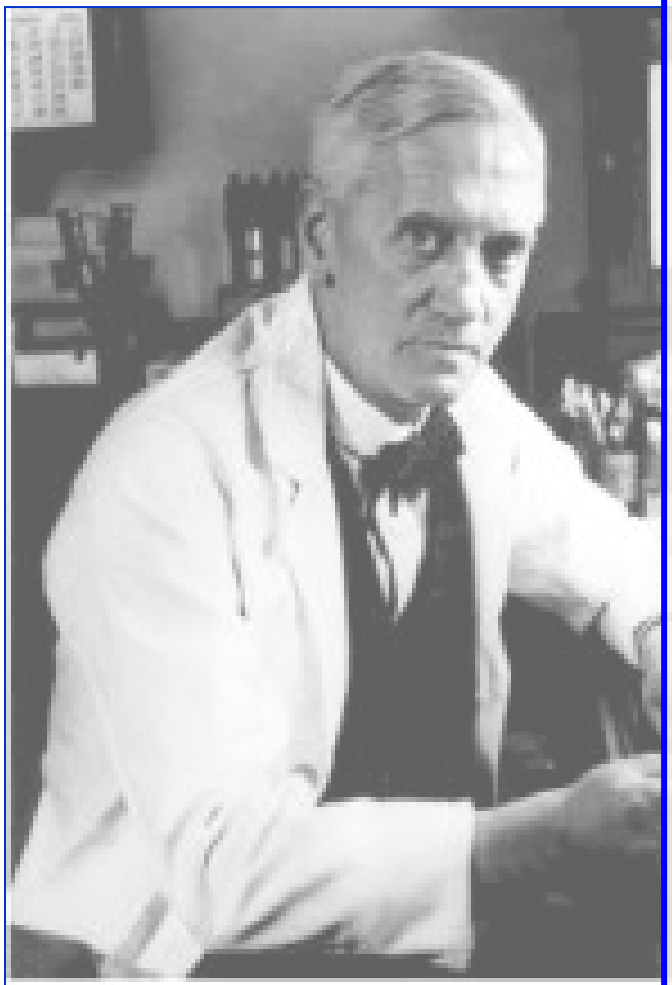
Saint S, *et al. Am J Med* 2000; 109:476-80

Consequences of Urinary Catheterization in Long-Term Care Facilities (LTCFs)

- Approximately half of all bacteremias in LTCFs are of urinary tract origin
- Urinary catheterization estimated to increase risk of bacteremia 39-fold
- Increased mortality among LTCF patients with long-term indwelling catheters
  - Unclear if this is due to bacteriuria or other confounding factors

Stewardship in UTI management





The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed on to other individuals and perhaps from there to others until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save. In such cases the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."

~ Sir Alexander Fleming, New York Times, June 26, 1945

write about antimicrobial stewardship in the style of Shakespeare

Oh, antimicrobial stewardship, a noble cause indeed,
To safeguard the potency of drugs that fight the deadliest breed
Of microbes that would do us harm, and ravage flesh and bone.
For if we use these drugs with care, their power can be known.

But if we treat these drugs with scorn, and use them without thought,
The microbes will grow stronger still, and can no longer be fought.
Thus, we must be vigilant, and use these drugs with care,
To preserve their strength, and keep them potent, beyond compare.

For if we fail in this endeavor, and let these drugs grow weak,
The consequences could be dire, and the cost of victory bleak.
Let us be mindful, then, in how we use these drugs of power,
And in doing so, safeguard our health, in this, our darkest hour.

Thanks to my UTI/ASB partners in crime!

- Barbara Trautner, MD PhD
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- Ashni Patel, PharmD
- Matthew Goetz, MD

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