GO WITH THE FLOW: A CASE-BASED APPROACH TO RECURRENT UTIS

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Washington State Department of HEALTH

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WASHINGTON STATE SOCIETY FOR POST-ACUTE AND LONG-TERM CARE MEDICINE

Speaker Introduction

KEVIN CLAY, MD
&
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Disclosures

- Dr. Kevin Clay and Dr. Jessica Zering have no financial relationships with an ineligible company relevant to this presentation to disclose.

- Dr. Erica Stohs has the following financial relationships to disclose:
  - Grant/Research Support from: Merck & Co, Inc & BioMerieux for investigator-initiated studies

All relevant financial relationships have been mitigated

Disclosures

- None of the planners have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients

- Jessica Zering, PharmD, will be discussing off-label use of the following medications in this presentation:
  - Vaginal estrogen for recurrent urinary tract infection (rUTI)

Housekeeping

This presentation is intended to provide guidance, but does not replace clinical judgement

Please type any questions into the chat box. The moderator will review & select questions to answer live for 10 minutes following the presentation

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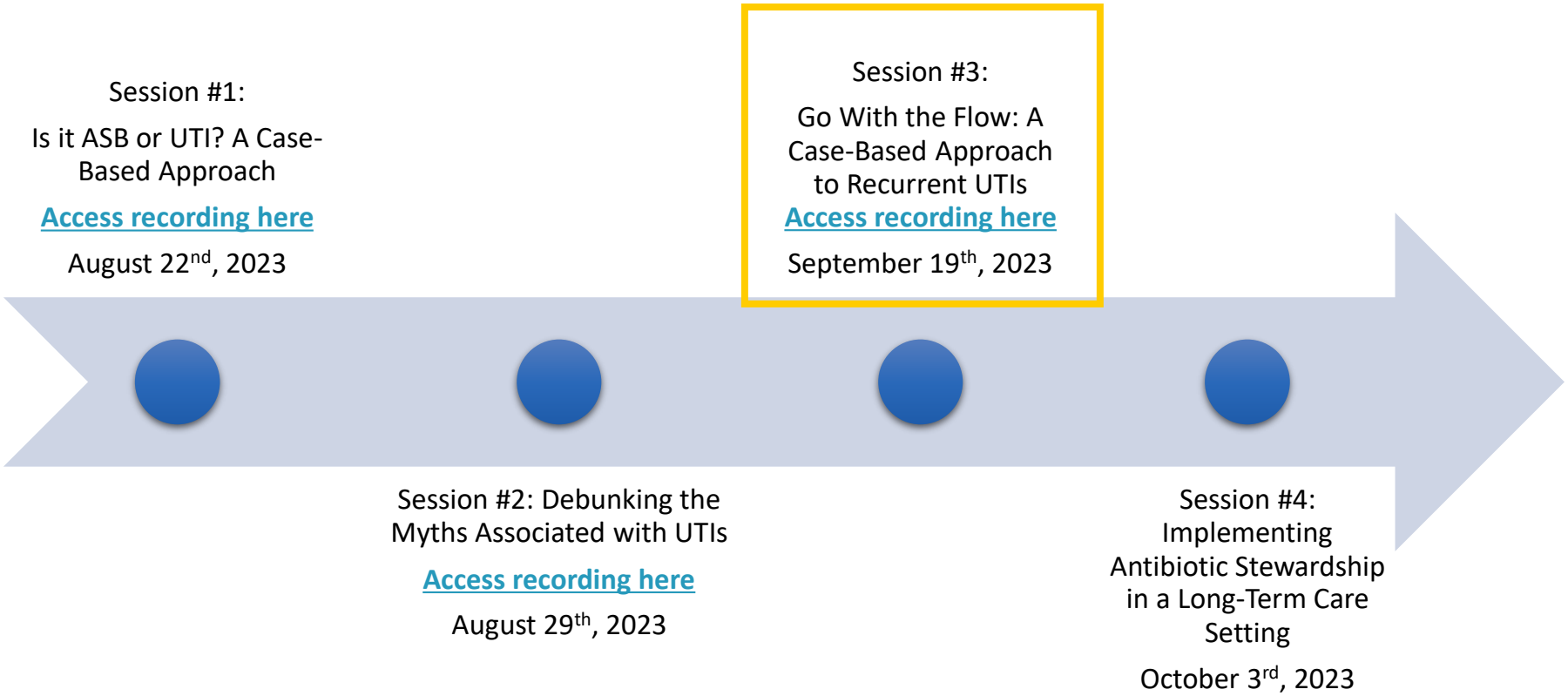
Series Timeline



Learning Objectives

1. Recognize the definition, diagnosis, & etiologies of recurrent urinary tract infection in the context of a patient case
2. Describe common myths surrounding recurrent urinary tract infection
3. Identify strategies for managing recurrent urinary tract infections
4. Describe stewardship strategies and metrics that can be used to measure successes

Poll Question #1

- True or False:
  - Recurrent UTIs are defined as 2 infections in 6 months

Poll Question #2

- True or False:
  - Antibiotic suppression is the only treatment option for recurrent UTIs

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INTRO TO RECURRENT UTIS

Kevin Clay, MD

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UTI

It is <u>essential</u> to distinguish between ASB and true UTIs!

UTI Facts

- UTIs are the most common outpatient infections in the US
- About 1 in 4 women with 1 UTI episode will go on to develop frequent recurrences

- Between 50% and 60% of adult women will have at least 1 UTI in their life
- The prevalence of UTIs in women > 65 years is approximately double the rate seen in the female population overall

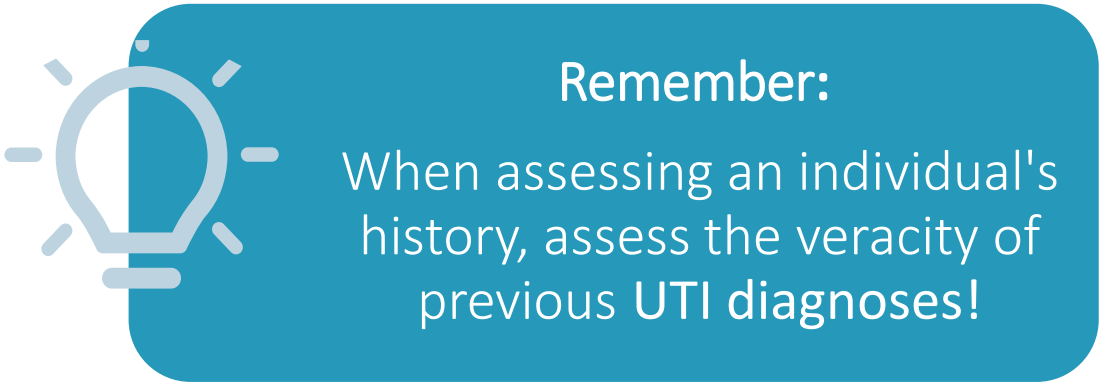
Medina, M et al. Ther Adv Urol. 2019 May;11:3-7
Chris Harding et al. BMJ 2022;376:bmj-2021-0068229

Definition of Recurrent UTI

- More than 2 infections in 6 months
- More than 3 infections in a year
  - Symptoms plus positive culture

Vs.

- **Relapsed UTI**: re-emergence of UTI due to the same bacterial species within 2 weeks of completion of treatment



Aydin A, et al. Int Urogynecol J. 2015;26(6):795-804.

Differential Diagnosis of Recurrent UTI

- Reflux at the ureteral vesicle junction (children, young adults)
- Kidney or urethral stones
- Vaginal atrophy in post-menopausal women
- Incomplete bladder emptying/Urinary stasis
  - Obstruction (prostate hypertrophy or other pathology such as cancer)
  - Neurogenic bladder
- Other: catheter dysfunction, GI-GU fistula

Indications for Investigation of Recurrent UTIs

If your patient has this…	Rule out this
Prior urinary tract surgery or trauma	Surgical / anatomic complication
Hematuria (gross or microscopic) after UTI resolution	Stones, GU cancer
Previous bladder or renal calculi	Recurrent stones
Straining, weak stream, intermittency, hesitancy	Obstruction (consider BPH, prostate pathology)
High post-void residual	Obstruction, neurogenic bladder, incomplete bladder emptying

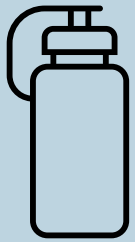
Dayson et al. Can Urol Assoc J. 2011 Oct; 5(5): 316–322.

Indications for Investigation of Recurrent UTIs

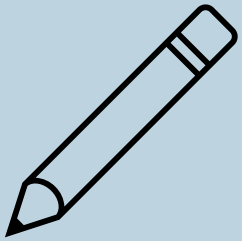
If your patient has this…	Rule out this
Urea-splitting bacteria (Proteus, Yersinia)	Stones (staghorn calculi)
Relapsed UTI (recurrent UTI with the same organism within 2 weeks of completing therapy)	Calculi, abscess, retained foreign body (i.e. ureteral stent)
Prior abdominopelvic malignancy	Tumor compression, post-surgical stricture
Concurrent diabetes mellitus	Poor blood glucose control
Pneumaturia, fecaluria, anaerobic bacteria	GI-GU fistula
Recurrent pyelonephritis	Abscess, infected renal cyst

Dayson et al. Can Urol Assoc J. 2011 Oct; 5(5): 316–322.

Non-Pharmacologic Management

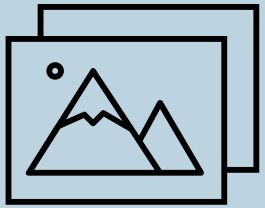


Assess fluid intake and hydration status



Assess post-void residuals & schedule voids or caths

Address underlying conditions & review medications

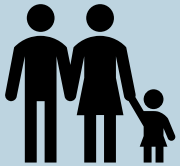


Advanced imaging and/or referrals

Non-Pharmacologic Management Cont'd

Don't underestimate the value of good peri-care!

Foley care and maintenance, especially if stool-incontinent



Education of resident, family and staff

(Stay tuned for Session #4)

Icon on the left and on the right created by Freepik – Flaticon

Case

- Mr. Johnson is an 82 y/o man who enjoys spending time with his newest grandchild
- Due to a spinal cord injury, he has performed self-catheterization 3 times daily for many years and has done well.
- He suddenly starts having recurrent UTIs presenting with fevers
- Culture shows *E. coli* sensitive to nitrofurantoin

Poll Question

- Which of the following options is NOT part of initial management?
  - A. Observe catheterization w/post-void residual
  - B. Order an ultrasound
  - C. Refer to Urology for further evaluation
  - D. Order nitrofurantoin x 6 months for UTI prophylaxis

Answer

- Which of the following options is NOT part of initial management?
  - A. Observe catheterization w/post-void residual
  - B. Order an ultrasound
  - C. Refer to Urology for further evaluation
  - **D. Order nitrofurantoin x 6 months for UTI prophylaxis**

Case Wrap-Up

- Mr. Johnson had high post-void residuals after observed catheterizations.
- Bladder ultrasound revealed moderate sediment and a bladder diverticulum.
- Gentamicin bladder irrigation was performed in the urology office and cleared the sediment.
- Recommendation: scheduled catheterizations every 4-6 hours moving forward to prevent urinary retention and bladder overdistension. Consider suprapubic catheter in the future.
- (Please note: In a patient with a chronic catheter, the bag should always be below the level of the bladder, and catheters should be exchanged every month.)

Case

- Mrs. Diaz is an 84 y/o retired elementary school teacher with 3 confirmed UTI infections in 9 months
  - She is reporting pain with urination and is having new incontinence
  - During her previous episodes, urine cultures have revealed *K. pneumoniae* and *E. coli* > 100k CFUs
  - You are starting empiric therapy with sulfamethoxazole/trimethoprim
  - What else should you consider in your plan of care?

Clinical Next Steps

- Perform a physical exam (inclusive of genitourinary exam)
- Ensure hydration, hygiene, and scheduled voids
  - Includes good catheter care, when applicable
- Obtain renal and bladder ultrasound to evaluate an underlying cause
- Arrange for Urology and ID care as needed
- If no obvious underlying cause, consider pharmacologic management for recurrent UTIs (in addition to the acute treatment plan)

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MEDICATION MANAGEMENT OF RECURRENT UTIS

Jessica Zering, PharmD, BCIDP, BCPS, CAPM

Case Cont'd

- Mrs. Diaz has completed the course of antibiotic therapy for her acute UTI episode
- You would now like to start her on rUTI prophylaxis
- Mrs. Diaz's past medical history is significant for breast cancer, which occurred 15 years ago & remains in complete remission
  - She is not currently on tamoxifen or an aromatase inhibitor

Poll Question

- True or False:
  - Mrs. Diaz's cancer history is an absolute contraindication to vaginal estrogen

Recurrent Uncomplicted Urinary Tract Infections in Women: AUA/CUA/SUFU Diagnosis & Treatment Algorithm

HISTORY AND PHYSICAL EXAM
- Confirm prior UTI diagnoses
- Obtain urinalysis, urine culture/sensitivity
- Perform pelvic exam

Suspicion of Complicating Factor(s)

CONSIDER ADDITIONAL INVESTIGATIONS
- Upper tract imaging
- Cystoscopy
- Urodynamics

TREATMENT OF UNDERLYING ABNORMALITY

The Index Patient is an otherwise healthy adult female with a recurrent uncomplicated UTI. Patients with complicating factors such as the following are outside the scope of this document:
- Anatomic or functional abnormality of the urinary tract
- Immunocompromised host
- Multi-drug resistant bacteria

CONFIRMED DIAGNOSIS OF RECURRENT UNCOMPLICATED UTI

Prior to the determination of a management plan, the clinician and patient should engage in a shared decision-making process that includes a discussion of the risks and benefits of all management options.

ANTIBIOTIC TREATMENT

Self-Start Therapy
- May offer to compliant and reliable patients
- Review treatment plan following availability of culture results; modify treatment if necessary

Episodic Treatment

Selection
- Use first-line therapy (i.e., nitrofurantoin, TMP-SMX, fosfomycin) depending on the local antibiogram

Duration
- Treat with as short a duration as possible, generally no longer than seven days

Oral Antibiotic Resistance
- May treat with culture-directed parenteral antibiotics

PROPHYLAXIS

Low Dose Antibiotic Prophylaxis

Continuous Dosing
- Generally no longer than 12 months

Intermittent Dosing
- Single-dose antibiotics used for exposure to UTI-predisposing conditions

Non-Antibiotic Prophylaxis
- Cranberry
- Behavior modification
- Others

Vaginal Estrogen Therapy
- Recommend to peri- and post-menopausal women without contraindications

Non-Antibiotic Prophylaxis of UTIs

Vaginal Estrogen Therapy

- Prevention of rUTI considered an off-label use
- Beers Criteria:
  - "Vaginal cream or vaginal tablets: acceptable to use low-dose…for the management of…recurrent lower urinary tract infections"
- American Urology Association (AUA):
  - "Clinicians should recommend vaginal estrogen therapy to all… post-menopausal women with rUTI to reduce the risk of rUTI"

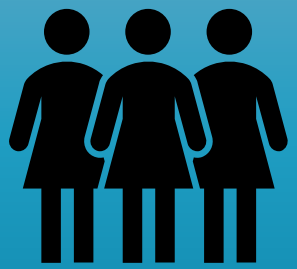
Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289
American Geriatrics Society Beers Criteria Update Expert Panel. Journal of the American Geriatrics Society. 2023;71(7): 2052 – 2081

Type of Study:

- Randomized, double-blind, placebo-controlled

Intervention + Methods:

- Estriol vaginal cream vs. placebo
- Vaginal pH + cultures measured at 1 & 8 months of treatment, urine samples obtained at monthly clinic visits, diary entries kept to assess for compliance



Population:

- 93 women split between both groups
- Average age = 65 years old

Raz, R & Stamm, W. NEJM. 1993 Sep;329(11):753-6

Result

- Annualized median incidence of UTIs in estrogen group vs placebo:
  - 0.5 vs. 5.9 per patient year, P <0.001
- Estrogen-treated patients used fewer antibiotics for UTI
- Increase in vaginal lactobacilli growth noted

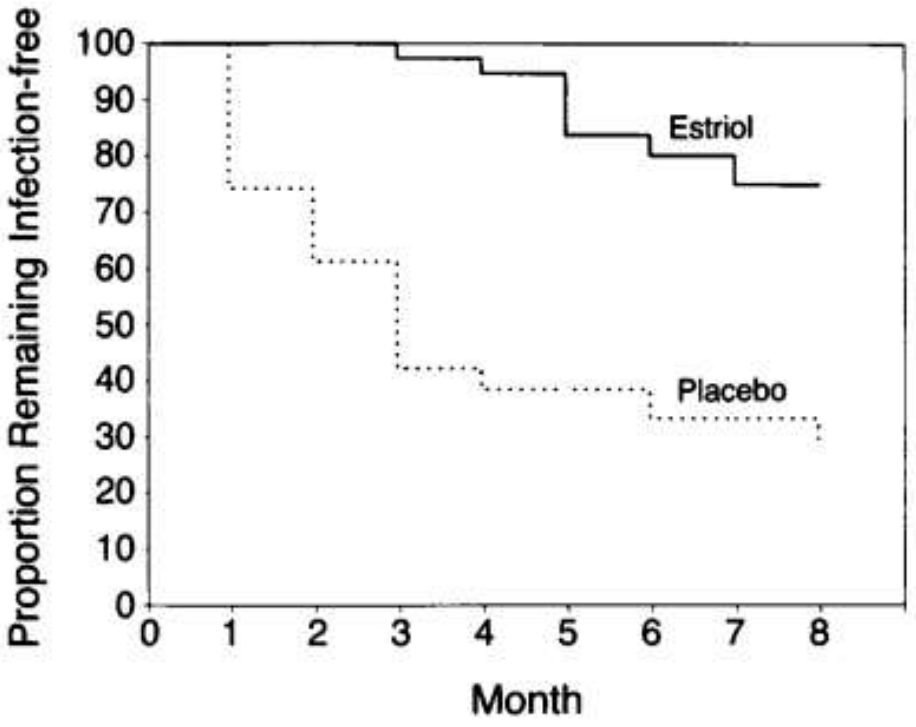


Figure 1. Kaplan–Meier Analysis Showing the Cumulative Proportions of Women Remaining Free of Urinary Tract Infections in the Estriol and Placebo Groups (P<0.001 by the Log-Rank Test).

Raz, R & Stamm, W. NEJM. 1993 Sep;329(11):753-6

Contraindications Listed in Package Insert

- Undiagnosed abnormal genital bleeding
- Known, suspected, or history of breast cancer/estrogen-dependent neoplasia
- Active DVT, PE, arterial thromboembolic disease or history of these conditions
- Known liver dysfunction/disease
- Known protein C, protein S, or antithrombin deficiency or other known thrombophilic disorders

Pfizer. Conjugated estrogens vaginal cream. Pfizer; 2018

What If the Patient Has a Cancer History?

- Vaginal estrogen is not associated with systemic effects
  - Lower serum estrogen concentrations vs. systemic therapy
- American Congress of OB/GYNs (ACOG):
  - Low-dose vaginal estrogen may be used after risk and benefits discussion in individuals with a history of breast cancer, including those on tamoxifen
  - If on aromatase inhibitors: use after shared decision making between patient, gynecologist, and oncologist

Raz, R & Stamm, W. NEJM. 1993 Sep;329(11):753-6
Gill, C et al. JAMDA. 2020 Jan;21(1):P46-54
ACOG Committee on Clinical Consensus. Obstet Gynecol. 2021 Dec 1; 138(6):950-960

Case Cont'd

- After a discussion with Mrs. Diaz about risks vs. benefits, you have decided to start her on vaginal estrogen cream
- She reports that she is symptom-free upon follow-up 6 months later!

Cranberry

- Considered a dietary supplement (not an FDA-approved drug)
- May offer cranberry prophylaxis (capsules, juice)
  - Note that juice studies have used a variety of juices and cocktails
  - Caution in diabetic patients
  - May interact with warfarin (mixed evidence)

Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289
Gill, C et al. JAMDA. 2020 Jan;21(1):P46-54

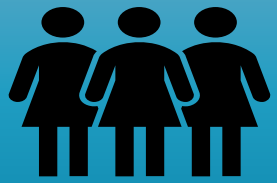
Evidence for Recommendation

Number of Studies:

- 8 RCTs

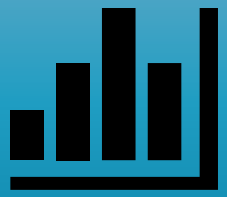
Interventions:

- Cranberry vs. placebo/no cranberry & cranberry vs. antibiotic
- 6 mos, 12 mos



Populations:

- Women 18 years of age and up



Endpoints:

- Recurrence of UTI

Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289

Results

- Decreased risk of experiencing at least 1 UTI recurrence than placebo or no cranberry
- No significant difference between cranberry vs. antibiotics
  - Based on only 2 trials
- Some studies in older adults have shown no difference in rate of rUTI
  - Only trial that showed a difference may have been confounded by ASB cases

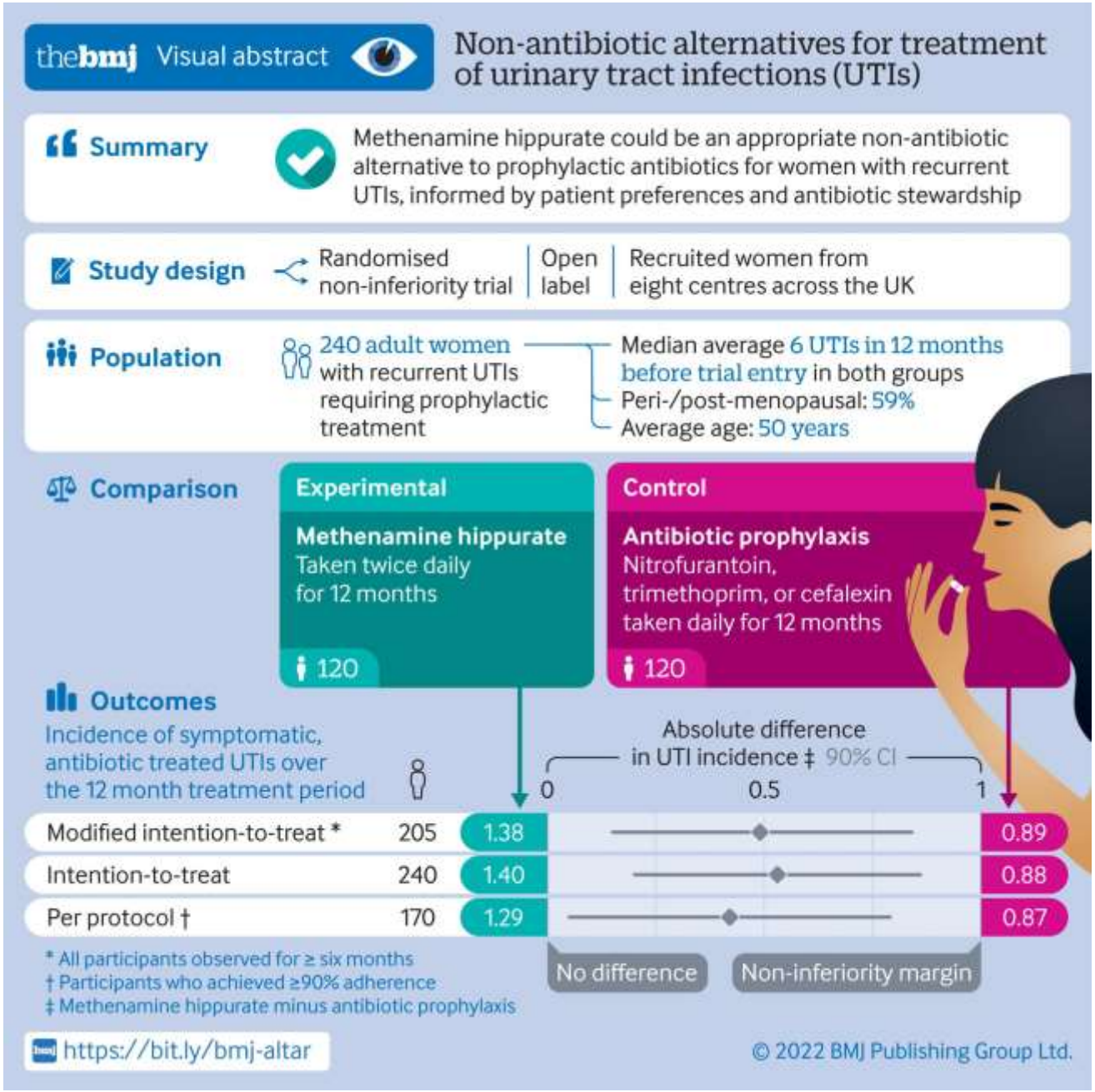
Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289
Gill, C et al. JAMDA. 2020 Jan;21(1):P46-54

Other Non-Antibiotic Prophylaxis Options

Methenamine Hippurate

- Works by acidifying the urine, which prevents bacterial invasion of the urinary tract
- Approved by the FDA for the prophylactic treatment of UTIs

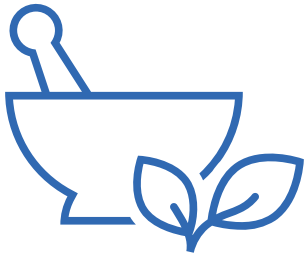
Gill, C et al. JAMDA. 2020 Jan;21(1):P46-54



Chris Harding et al. BMJ 2022;376:bmj-2021-0068229

Results

- Both treatments similarly reduced urinary tract infections
  - Low rate of adverse events also noted
  - Treatment satisfaction rates were equal between both groups
- Methenamine hippurate could be an appropriate non-antibiotic alternative to prophylactic antibiotics in women with recurrent UTIs



Chris Harding et al. BMJ 2022;376:bmj-2021-0068229

D-Mannose

- Considered a dietary supplement (not an FDA-approved drug)
- A simple sugar that prevents bacterial adhesion to the cells in the urinary tract

Gill, C et al. JAMDA. 2020 Jan;21(1):P46-54

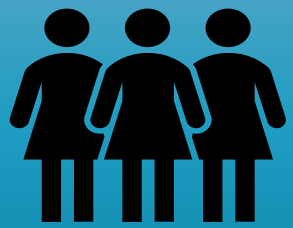
Cochrane Review

Number of Studies:

- 7 RCTs

Interventions:

- D-mannose vs. nitrofurantoin/no treatment
- D-mannose plus dietary/vitamin/herbal supplements vs. antibiotic
- Duration Range: 15 days – 24 weeks



Populations:

- 719 total adult participants (primarily women)
- Older adults in residential/long-term care facilities were included

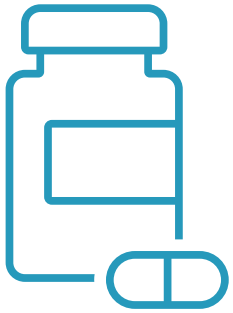
Cooper, T et all. Cochrane Database Syst Rev. 2022 Aug 20;8(8):CD013608

Result

- Review found a lack of high-quality RCTs testing the efficacy of D-mannose in any population
  - Limited sample sizes, lack of standardized dosing regiments, variable definitions of UTI, variable outcome measures
- No recommendation for or against the use of this to prevent UTIs can be made

Gill, C et al. JAMDA. 2020 Jan;21(1):P46-54
Cooper, T et all. Cochrane Database Syst Rev. 2022 Aug 20;8(8):CD013608

Antibiotic Prophylaxis of UTIs



Wait!

- Pause BEFORE starting antibiotic prophylaxis
  1. Does this person truly have recurrent UTI?
  2. Has a complete evaluation been performed to rule out treatable underlying predisposing conditions?
  3. Have non-antibiotic prophylaxis options already been tried?

AMDA Infection Advisory Subcommittee Statement

Although antibiotics may reduce the risk of recurrent, uncomplicated UTIs, the potential harms associated with long-term use, coupled with the prevalence of multidrug-resistant organisms among PALTC residents, argues against long-term antibiotic prophylaxis.

Similarly, because of concerns about selection for multidrug-resistant organisms, systemic antibiotics should not be used to prevent infection in residents with short- or long-term indwelling urinary catheters

Ashraf, M et al. JAMDA. 2020 Jan;21(1):12-24

Recurrent UTI Antibiotic Prophylaxis

- May represent up to 70% of all prophylactic antibiotics prescribed in nursing homes
- 14% of prophylactic use for this indication is in patients ≥ 65 years of age
- Evidence gap regarding this practice in patients ≥ 65 years old
  - Duration, appropriateness, necessity

Sloane, P et al. JAMDA. 2020 Sep; 21(90):1181-1185
Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289

Evidence for AUA Guideline Recommendation

Number of Studies:

- 28

Common Antibiotics:

- Nitrofurantoin, sulfamethoxazole-trimethoprim (SMZ/TMP), trimethoprim (TMP)

Average Duration of Prophylaxis:

- 6-12 months

Average Ages:

- 30-40 years & ≥ 50 years

Most of the relevant RCTs were published prior to 1995

Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289

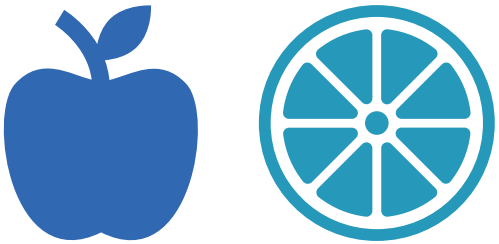
Findings

- Antibiotics were associated with a decreased likelihood of experiencing ≥ 1 UTI recurrence vs. placebo or no antibiotics
  - Daily dosing regiment
  - RR = 0.26, 95% CI 0.18 – 0.37
- Antibiotics were also associated with increased risk of adverse events
  - RR = 1.73, 95% CI 1.08 – 2.79

Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289

Comparison

- 8 trials compared nitrofurantoin to other agents
  - Fosfomycin, TMP, SMZ/TMP, cefaclor, norfloxacin
- No differences found in risk of recurrence between agents
- Nitrofurantoin was associated with an increased risk of any adverse event
  - RR ≈ 2.00 – 2.40



Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289

Antibiotic Prophylaxis Choices

Review antibiogram & history of urine cultures/antibiotic use before prescribing

Antibiotic	Clinical Considerations
Nitrofurantoin	Avoid for long-term suppression as per Beers Criteria
Fluoroquinolones	Not recommended
SMZ/TMP or TMP alone	High resistance rates, may require lab monitoring, renal dosing, potentially deadly interactions with ACE inhibitors
Cephalexin	Assess for allergy to cephalexin
Fosfomycin	Uncommon - logistical & insurance coverage issues

Anger, J et al. Journal of Urology. 2019 Aug; 202(2): 282-289
American Geriatrics Society Beers Criteria Update Expert Panel. Journal of the American Geriatrics Society. 2023;71(7): 2052 – 2081
Antoniou T et al. JAMA. 2010;170(12):1045-1049

Antimicrobial Stewardship for Recurrent UTIs

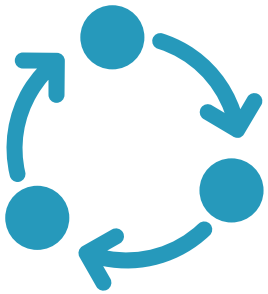
Stewarding rUTIs

- Assess if residents have true rUTI vs. ASB
  - Use Loeb Criteria for acute UTI (see 1st presentation)
- Clarify duration/indication of prophylaxis
- Consider trial of non-antibiotic options before using antibiotic prophylaxis

CDC. Limit Prolonged Antibiotic Prophylaxis for Urinary Tract Infection

Methods & Metrics

- Educate providers, build/write non-antibiotic options into order sets
- Educate residents and families
- Track antibiotic starts or days of therapy
  - Aim for decreases in both over time



Takeaways

- Assess if the resident truly has recurrent UTI prior to prescribing prophylaxis
- Try non-antibiotic prophylaxis first (see table below)

Drug Name	Effective in Older Adults?
Vaginal estrogen (off-label indication)	Yes!
Methenamine hippurate	Likely – data show efficacy in post menopausal women
Cranberry	Maybe – data show efficacy in younger adults
D-Mannose	Unknown

Poll Question #1

- True or False:
  - Recurrent UTIs are defined as 2 infections in 6 months

Poll Question #2

- True or False:
  - Antibiotic suppression is the only treatment option for recurrent UTIs

Resources

Guidance for Creating/Maintaining Stewardship Programs

- WA DOH's AMS Resources for Nursing Homes
- CDC's Core Elements of Antibiotic Stewardship for Nursing Homes
- CDC's Core Elements of Antibiotic Stewardship for Nursing Homes Checklist
- Washington State Society for Post-Acute and Long-Term Care Medicine

Antibiotic Guide

- UW's Centers for Stewardship in Medicine (UW-CSiM) Antibiotic Guide

Clinical Guidance

- Infectious Diseases Society of America (IDSA) - Uncomplicated Cystitis and Pyelonephritis Guideline
- Infectious Disease Society of America (IDSA) - Management of Asymptomatic Bacteriuria

Education (Residents and Families)

- Antibiotics for UTI in Older Adults (Eng)
- Antibiotics for UTI in Older Adults (Spanish)
- To implement: Put into resident orientation, hand these to residents and families when an antibiotic isn't a part of the care plan, print these and put them on tables near facility entrance

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QUESTIONS?

wa-paltc

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Join Us Next Time…

- October 3rd, 2023: Implementing Antibiotic Stewardship in a Long-Term Care Setting
  - Come & get your stewardship questions answered by our multidisciplinary panel of experts!
  - Register here

- Access previous webinars here:
  - UTI RESOURCES | WA-PALTC

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