A Practical Approach to Drug Interactions

Focusing on Prescribing Antibiotics

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Objectives

01 Discuss antibiotics on the Beer's list (and other considerations for antibiotic therapy in older adults)

02 UTI treatment in older adults - updates from the 2025 IDSA guidelines on complicated urinary tract infections

03 Develop patient-specific medication management plans for complex patients receiving anticoagulants, GLP-1 receptor agonists, and other commonly prescribed therapies

04 Identify major drug interactions with linezolid and review counseling points for patients

Antibiotics and the older adult - what does the Beer's list say?

Safety Concerns

Only medication listed under the "anti-infective" section is nitrofurantoin

Concern for particularly long term use for UTI suppression:

- pulmonary toxicity
- hepatotoxicity
- neuropathy

Renal Threshold:
Do not use with CrCl <30 ml/min

Conflicting renal dosing

Beers list: okay if CrCl >30 ml/min and short term
FDA original labeling: contraindicated if crcl <60 ml/min
UK MHRA: avoid if eGFR is less than 45 ml/min

Clinical Efficacy

Decreased efficacy?

- Won't work for cUTI including pyelonephritis
- Inactive against Proteus, pseudomonas and Serratia

Alternatives endorsed for UTI prophylaxis

Hormonal Strategy

Vaginal Estrogen

First line strategy in postmenopausal women

Note: Beers criteria does not endorse systemic estrogen

Conservative Care

Nonpharmacologic Methods

Interventions:

- Increased fluid intake
- Methenamine
- Cranberry
- D-mannose

Evidence quality is mixed, but these are considered low-risk interventions.

Pharmacotherapy

Alternative Antibiotics

Recommended Agents:

Trimethoprim

Fosfomycin

Chronic UTI – Reviewing Anticholinergic Medications

Anticholinergic Classes to Evaluate

Antidepressants
Amitriptyline, clomipramine, desipramine, doxepin (>6mg/day), imipramine, nortriptyline, paroxetine

Antiemetics
Prochlorperazine, promethazine

Antihistamines (First Generation)
Diphenhydramine, doxylamine, hydroxyzine, meclizine, promethazine

Antimuscarinics
Darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, trospium

Antiparkinsonian Agents & Antispasmodics
Benztropine, trihexyphenidyl, hyoscyamine, dicyclomine, scopolamine

Skeletal Muscle Relaxants
Cyclobenzaprine, orphenadrine



New classifications of uUTI and cUTI

Old Classifications

Uncomplicated UTI:
Acute cystitis in afebrile nonpregnant premenopausal women with no diabetes and no urologic abnormalities



Acute Pyelonephritis: Acute kidney infection in women otherwise meeting the definition of uncomplicated UTI above



Complicated UTI: All other UTIs

New Classifications

Uncomplicated UTI: Infection confined to the bladder in afebrile women or men

Complicated UTI: infection beyond the bladder in women or men

- Pyelonephritis
- Febrile or bacteremic UTI
- Catheter-associated (CAUTI)
- Prostatitis* (*not covered by these guidelines)



Antibiotics for Uncomplicated UTI (uUTI)

uUTI Diagnostic Criteria & Exclusions

Expanded Diagnostic Criteria

- Infection confined to the bladder in afebrile patients
- uUTI can occur in:
  - Males
  - Patients with diabetes
  - Immunocompromised

Notable Exclusions (usually complicated)

- Presence of a catheter
- Intermittent catheterization
- Urologic stents
- Percutaneous nephrostomy tubes

Treatment Options

Nitrofurantoin
5 days

Sulfamethoxazole-trimethoprim
3 days

Fosfomycin
Single dose

Shorter Antibiotic Durations for Complicated UTIs (cUTI)

Definition & Exclusions

Definition of cUTI

- Infection extending beyond the bladder (e.g. pyelonephritis, bacteremia)

Guideline Exclusions

- Pregnancy
- Prostatitis

Outpatient Treatment

Preferred Options

- Fluoroquinolone
- Sulfamethoxazole/trimethoprim

Alternative Options

- Amoxicillin-clavulanate
- Oral cephalosporins

Duration of Therapy

Fluoroquinolones
5–7 days

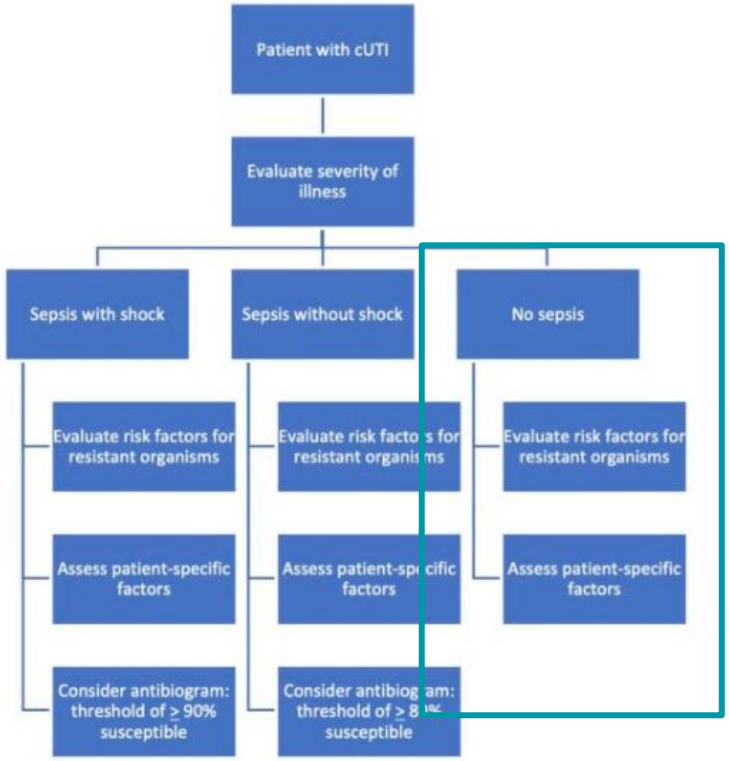
Non-fluoroquinolone
7 days

Gram-negative bacteremia
7 days

*Patients with severe sepsis, severe immunosuppression, or those with an indwelling urinary catheter may require a different approach and potentially longer durations (10-14 days), and this should be considered on a case-by-case basis.

https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/

Four-Step Approach to Choosing Empiric Antimicrobial Therapy for cUTI



Risk Factors for Resistant Organisms

Recent antibiotic use

- Suggest avoiding fluoroquinolones as treatment if patient exposed in past 12 months (conditional recommendation, low certainty of evidence)
- Recent hospitalizations
- History of MDRO
- International travel to areas with high rates of antibiotic resistance

Patient-Specific Factors

- Allergies
- Contraindications
- Drug-drug interactions
- Previous cultures/Antibiogram

https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/

Antibiotic selection

Table 1.2: Dosing of oral antibiotics for complicated UTI (in alphabetical order)

Table 1.2: Dosing of oral antibiotics for complicated UTI

Drug	Oral absorption (%)	Urinary excretion (%)	Dose for patients with normal renal function	Refs:
Amoxicillin-clavulanate	80 (amoxicillin)[61] variable (clavulanate)[62]	50-70 (amoxicillin)[61] 25-40% (clavulanate)[61]	875mg-125mg every 12 to 8 hours[52-55,63-67] Other regimens may be more effective[a]	
Cefixime	50[68]	50[68]	400mg once daily[26]	
Cefpodoxime	50[68]	~30[68]	200mg to 400mg every 12 hours[51,55,72]	
Ceftibuten	75-90[68]	56[68]	9mg/kg daily (children)[b] 400mg daily or 200mg every 12 hours (adults)[73,74]	
Cefuroxime	52[68,70]	50[68,70]	500mg every 12 hours[55,71]	
Cephalexin	90[68]	90[68]	500mg to 1000mg every 6 hours[50,52-54,63-66,69] Other regimens may be more effective[a]	
Ciprofloxacin	70[75]	40-50[75]	500mg to 750mg every 12 hours[50,55,65,76,77]	
Levofloxacin	99[78]	64-100[78]	500mg to 750mg daily[21,50,72,77]	
Other oral beta-lactams (e.g. amoxicillin, cefadroxil, cefaclor, cefdinir)	Comparative clinical outcomes data vs highly bioavailable oral alternatives are more limited and/or discouraging; consider use with infectious disease pharmacist consultation if alternatives are not available.			
Trimethoprim-sulfamethoxazole	70-90[79]	84 (sulfamethoxazole), 66 (trimethoprim)[79]	800mg-160mg every 12 hours[55,76]	

[a]Despite routine use of optimized dosing, the majority of studies comparing switch to oral beta-lactams versus fluoroquinolones or trimethoprim-sulfamethoxazole for cUTI have found inferior outcomes with oral beta-lactams when amoxicillin-clavulanate or cephalexin were the predominant oral beta-lactams being used.
[b]Ceftibuten is the sole oral beta-lactam in this table with modern randomized, controlled trial data for cUTI in both children in adults; however, while it produced comparable clinical outcomes versus trimethoprim-sulfamethoxazole in children, in adults relapses were higher with ceftibuten versus norfloxacin.

Notably missing - Cefdinir



Oral absorption: **16%–25%**

Urinary excretion: **11%–18%**

DOI: 10.1002/jhm.13415

CHOOSE WISELY®: THINGS WE DO FOR NO REASON™

Journal of Hospital Medicine shm

Things We Do for No Reason™: Prescribe cefdinir for treatment of common infections

https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/
Trautner BW et al. *Clin Infect Dis*. 2025.

CKD and antibiotics

uUTI

- **Nitrofurantoin** 5 days - avoid use if CrCl <30 ml/min
- **Bactrim:** 3 days - dose adjustment for crcl 15-29ml/min, avoid with crcl <15 ml/min
- **Fosfomycin:** single dose - no dose adjustments for oral packets!

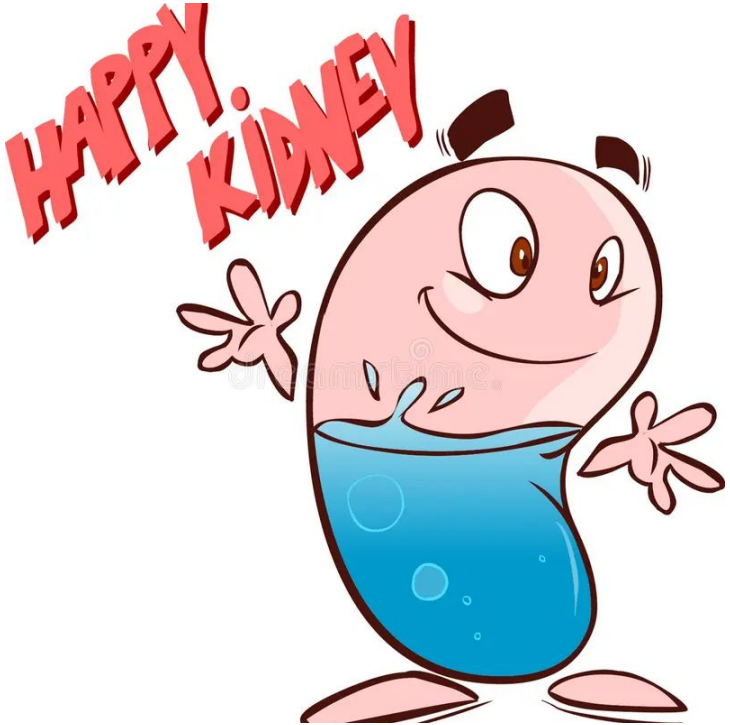
cUTI

- **Fluoroquinolones (levofloxacin, ciprofloxacin)** - dose adjust for crcl <50 ml/min
- **Amoxicillin clavulanate** - dose adjustment for crcl <30ml/min
- **Cefixime** - dose adjustment for crcl <60 ml/min
- **Cefpodoxime** - dose adjustment for crcl <30 ml/min
- **Cefuroxime** - dose adjustment for crcl <30 ml/min
- **Cephalexin** - dose adjustment for crcl <30 ml/min

Antibiotics that don’t need to be adjusted for CKD

No Dose Adjustment Required

- Doxycycline
- Dicloxacillin
- Minocycline
- Linezolid
- Azithromycin
- Erythromycin
- Clindamycin
- Moxifloxacin
- Fosfomycin



Sulfamethoxazole-trimethoprim: When to Worry

Bactrim is a great drug – remember to check a few things

Allergies

- **Allergies:** Always verify patient history
- ~5-7% of patients are labeled with sulfonamide antibiotic allergy
  - Second only to penicillin
- 95% of non-HIV patients with sulfonamide antibiotic allergy label tolerated a full-dose TMP-SMX challenge

Major Drug Interactions

Potassium Supplements: Consider holding during therapy

High-Risk Combinations:

- ACEi / ARB / ARNI / spironolactone, eplerenone

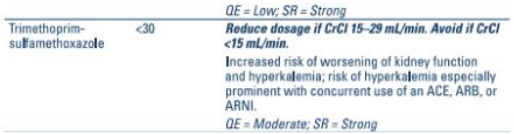
Added Risk:

- **+18 additional cases** of hyperkalemia per 1,000 patients treated
- **7x** the risk of hyperkalemia requiring hospitalization compared with those taking amoxicillin and an ACEI/ARB

Magnitude & Timing of potassium changes

- **Serum Potassium Rise:** Typically increases by **~0.6 mmol/L**.
- **Onset Timeline:** Gradual onset over **3–10 days**.
- **Dose Dependence:** Effect is directly dose-related

Dosing Guidelines in Renal Impairment



QE = Low; SR = Strong

Trimethoprim-sulfamethoxazole	<30	***Reduce dosage if CrCl 15–29 mL/min. Avoid if CrCl <15 mL/min.*** Increased risk of worsening of kidney function and hyperkalemia; risk of hyperkalemia especially prominent with concurrent use of an ACE, ARB, or ARNI.

QE = Moderate; SR = Strong

- **CrCl 15–29 mL/min:** Reduce dosage
- **CrCl <15 mL/min:** Avoid use

Hyperkalemia Risk (uUTI >66 yrs):

- • **0.46%** with Bactrim vs **0.14%** with amoxicillin

Trimethoprim Use for Urinary Tract Infection and Risk of Adverse Outcomes in Older Patients: Cohort Study. BMJ. 2018.
Drug Allergy; A 2022 Practice Parameter Update. The Journal of Clin Immunology 2022

Supportive Therapies in UTI Management

- **NSAIDS**
  - Avoid with CKD, CHF, HTN
  - Kidney injury with ACEI combination
  - Drug - Drug interaction with aspirin

- **Phenazopyridine**
  - Avoid with CrCl <50 ml/min
  - Risk of AKI, hemolytic anemia and methemoglobinemia
  - 2 day limit

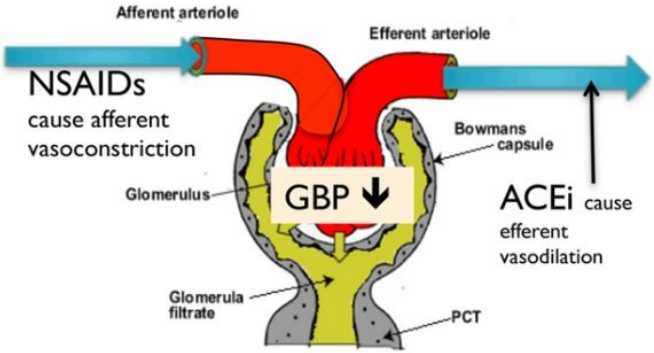


Figure 2. Effects of angiotensin-converting enzyme inhibitors and NSAIDs on glomerular blood pressure.

SGLT2 Inhibitors: Managing Infection Risks

Guidance on safety, continuation, and indications for holding therapy

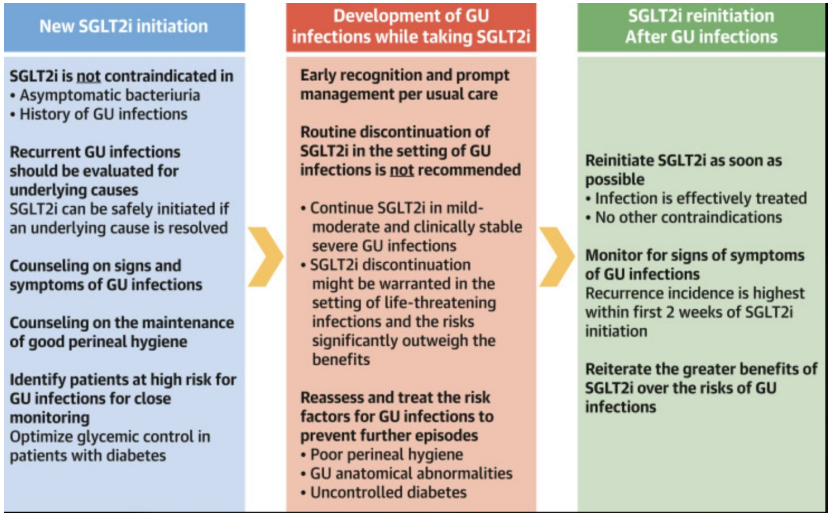
Infection Risk & Safety Profile

- **FDA Warning:** Advises on UTIs & genital yeast infections; prompt recognition/treatment required
- **Beers Criteria:** Monitor for urogenital infections and ketoacidosis. Most concern with older adult women in the first month of therapy
- **Yeast Infections:** Consistently increased across evidence
- **UTI Risk:** Small increase with mixed findings
  - 2025 Danish Cohort: ~10% 1-yr UTI risk (similar to GLP-1)

Clinical Management & Hold Criteria

- **Mild UTIs:** SGLT2i can generally be safely continued
- **When to Hold SGLT2i Therapy:**
  - Urosepsis, pyelonephritis, or Fournier's gangrene
  - Poor oral intake, vomiting, or volume depletion
- **Recurrent GU Infections:**
  - Carefully weigh risk vs. benefit before reinitiation or continuation

Management Algorithm



- **Initiation:** Safe in asymptomatic bacteriuria / history of GU infections
- **During Infection:** Continue in mild/stable; reassess risk factors
- **Reinitiation:** Restart as soon as treated and clinically appropriate

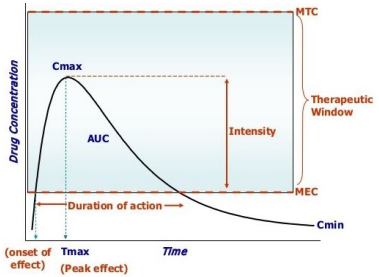
1. Kittipibul V, et al. Genitourinary tract infections in patients taking SGLT2 inhibitors. J Am Coll Cardiol. 2024.
2. Ljungberg C, et al. Risk of urogenital infections in people with T2D initiating SGLT2is vs GLP-1RAs: Danish cohort study. Diabetes Care. 2025.

Other Medications to Think About – GLP-1s

Key absorption impacts, drug interactions, and clinical management guidance

Absorption & Antibiotics

- **General Absorption Effect:** Reduced Cmax & delayed Tmax, but overall AUC unchanged
- **Antibiotic Interactions:** No specific antibiotic drug interactions known
  - Fluoroquinolones theoretically impacted, unlikely clinically relevant
- **H. Pylori Eradication:** Improved eradication rates on semaglutide



Impact on Specific Drugs

- **Levothyroxine:** Drug levels were **INCREASED** when co-administered with oral semaglutide.
- **Oral Contraceptives:** Birth control levels were **DECREASED** with tirzepatide (mostly during initiation and dose increases)
- **Summary:** Impact on medication absorption is overall mixed and drug-specific

Side Effects & Sick-Day Holds

- **GI Adverse Effects:** General GLP-1 risk of nausea and diarrhea may be confounded by concurrent antibiotic use
- **Sick-Day Hold Criteria:** Should hold GLP-1s in patients with significant systemic illness or poor oral intake
- **Clinical Action:** Evaluate hydration status and hold therapy during acute gastrointestinal or systemic illness

1. Calvarysky B, et al. Drug Saf. 2024. (Covers absorption, AUC, and overall interaction data)
2. ADA Standards of Care in Diabetes—2026, Section 6. (Sick-day holds) | 3. Mounjaro prescribing info (FDA); Ness A, et al. Helicobacter. 2025.

Sulfonylurea Drug Interactions

1.6–4x Increased Risk of Hospitalization or ED Visit for Hypoglycemia Within 14 Days

Interacting Antibiotics & Mechanisms

- **Sulfamethoxazole / trimethoprim**
  CYP2C9 inhibition; direct sulfonylurea-like effect
- **Ciprofloxacin**
  Closes beta-cell K-ATP channels (↑ insulin release)
- **Levofloxacin**
  Closes beta-cell K-ATP channels (↑ insulin release); possible P-gp inhibition
- **Metronidazole**
  CYP2C9 inhibitor → increased sulfonylurea plasma levels
- **Clarithromycin**
  P-gp inhibitor → increased sulfonylurea plasma levels

Clinical Management

Action Required

Hold or reduce sulfonylurea dose if an interacting antibiotic must be co-prescribed

Patient Counseling

- Educate on signs & symptoms of hypoglycemia (shakiness, sweating, confusion, dizziness)
- Advise frequent blood glucose monitoring during antibiotic course
- Ensure patient has fast-acting carbohydrates available for immediate treatment

1. Parekh TM, et al. Hypoglycemia after antimicrobial drug prescription for older patients using sulfonylureas. JAMA Intern Med. 2014.
2. American Diabetes Association. Standards of Care in Diabetes—2026, Section 13: Older Adults. Diabetes Care. 2026.

Other Medications to Think About – PPIs

Epidemiology, inappropriate utilization, and de-prescribing recommendations

Prevalence & Usage

- **Global Prevalence:** 1 in 4 adults worldwide uses a PPI
- **Older Adults:** 40% of adults older than 70 are prescribed PPI therapy



Inappropriate Prescribing

- **Indication Deficit:** **Up to 2/3** of PPI prescriptions lack an appropriate medical indication
- **Overuse Risk:** Chronic unindicated use increases exposure to adverse effects without clinical benefit

Gastrointestinal	
Proton-pump inhibitors ■ Dexlansoprazole ■ Esomeprazole ■ Lansoprazole ■ Omeprazole ■ Pantoprazole ■ Rabeprazole	***Avoid scheduled use for >8 weeks unless for high-risk patients (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathologic hypersecretory condition, or demonstrated need for maintenance treatment (e.g., because of failure of drug discontinuation trial or H2-receptor antagonists).*** Risk of *C. difficile* infection, pneumonia, GI malignancies, bone loss and fractures. *QE = C. difficile, bone loss, and fractures: High. Pneumonia and GI malignancies: Moderate; SR = Strong*

De-Prescribing Guidance

- **Tapering Protocol:** Tapering to discontinuation is likely more effective than abrupt stop
- **Rebound Management:** Gradual withdrawal helps manage and suppress rebound acid hypersecretion

Clinical Recommendation

Routine reassessment of indication is recommended to identify candidates for PPI dose reduction or discontinuation.

AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review. Gastroenterology. 2022. Targownik LE, Fisher DA, Saini SD.

Antibiotic Adverse Effects

Risk Stratification for Antibiotic-Associated Diarrhea

Risk Continuum for Diarrhea

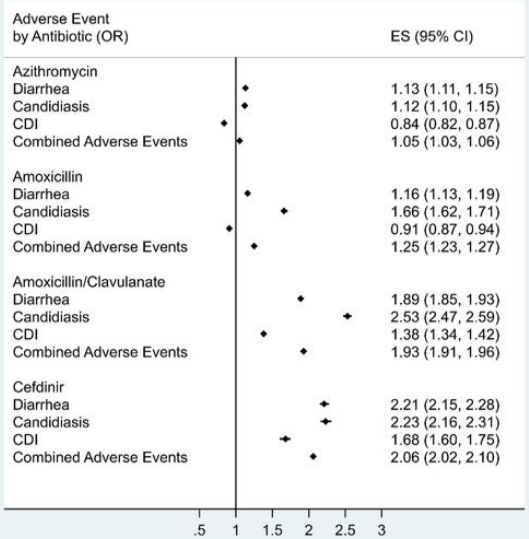
HIGHEST RISK Associated with greatest frequency of diarrhea

- **Clindamycin**
- **Amoxicillin-clavulanate** (10–25% incidence)
- **2nd & 3rd Gen Cephalosporins** (cefdinir, cefuroxime)
- **Fluoroquinolones**

LEAST LIKELY Preferred choices when minimizing GI disruption

- **Doxycycline**
- **Macrolides**
- **Amoxicillin**

Odds Ratios for Adverse Events



1. Clostridium difficile and other adverse events from overprescribed antibiotics for acute upper respiratory infection. J Intern Med. 2023.
2. Zhang J, Chen L, Gomez-Simmonds A, Yin MT, Freedberg DE. Antibiotic-Specific Risk for Community-Acquired Infection in the US From 2008 to 2020. Antimicrob Agents Chemother. 2022.

Antibiotic Adverse Effects – C. diff

High-risk agents, exposure cumulative impact, and patient pre-dispositions

Highest Risk Antibiotics (CDC)

- **Clindamycin**
- **Higher-Generation Cephalosporins** (cefdinir, cefixime, cefpodoxime)
- **Fluoroquinolones**

Additive Exposure Matters

- **Multiple Antibiotics:** Exposure to 2–4 or 5+ antibiotics increases hazard ratio to **2.5** and **9.6** respectively (vs. 1 antibiotic)
- **Extended Duration:** 10 and 14 day regimens increase risk by **12%** and **27%** compared to 7-day courses

Patient Risk Factors

- **High-Risk Meds:** Chemotherapy, PPIs
- **Prior History:** C. diff colonization or past infection
- **Procedures:** GI procedures or abdominal surgery
- **Demographics:** Advanced age

Probiotics

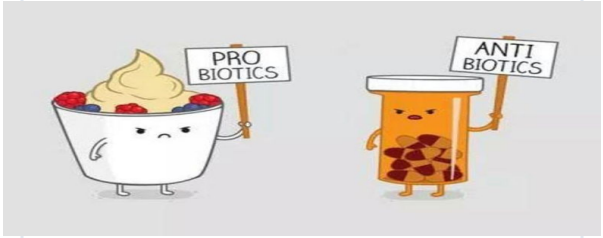
Evidence quality, administration timing, and clinical efficacy considerations

Evidence Quality

- **Inconsistent Data:** Evidence is overall inconsistent, relying on case reports and small, poorly designed non-randomized studies
- **AGA Rating:** The American Gastroenterological Association rates the evidence quality as "low"

Administration & Timing

- **Dosing Separation:** Administer at least 2 hours before or after antibiotics to maximize efficacy
- **Early Start:** Give as close to antibiotic start as possible (within 24–48 hours yields most benefit)

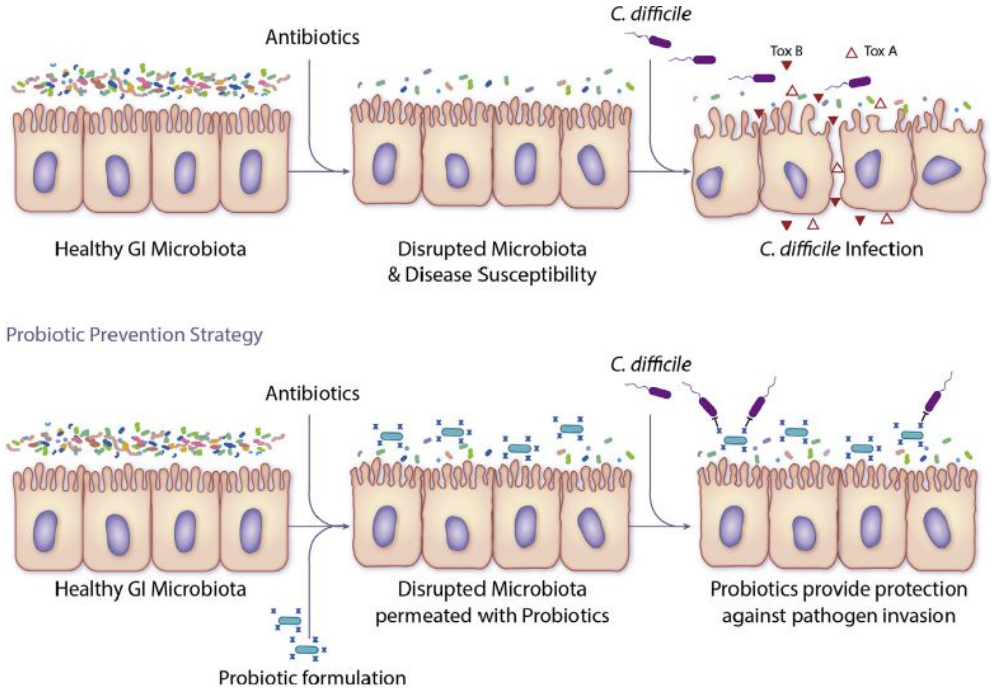


Primary Indications

- **AAD Prevention:** Shows most benefit in preventing antibiotic-associated diarrhea
- **C. difficile:** Demonstrates efficacy in reducing Clostridium difficile risk

Probiotics: Mechanism of Action

Disruption of GI microbiota and protective strategy against C. difficile



Anaerobe 41 (2016) 51–57

Probiotics: Precautions & Evidence

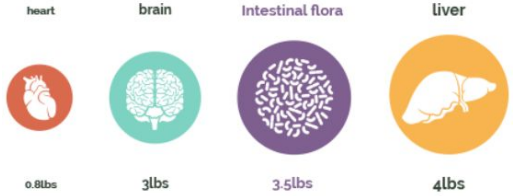
High-risk patient populations, adverse effects, and strain evidence

Avoid in Patients

- **Immunosuppressed:** cyclosporine, tacrolimus, chemotherapy
- **Compromised GI Integrity:** short gut syndrome, IBD, acute pancreatitis
- **Pregnancy:** Use with caution
- **Prosthetic Heart Valves:** Risk of bacteremia / endocarditis

Safety & Evidence Base

- **Adverse Effects:** Flatulence, bloating, diarrhea
- **Strongest Clinical Evidence:** Lactobacillus (Culturelle) & Saccharomyces boulardii (Florastor)



Probiotic Strains



How to Prevent Clostridium Difficile

Key clinical strategies to minimize C. diff infection risk

Core Interventions

- **PPI De-escalation:** De-escalate off PPIs whenever clinically appropriate
- **Antibiotic Duration:** Utilize short-course antibiotic therapy

Lower-Risk Antibiotics

Prefer narrow-spectrum options when indicated:

- Narrow-spectrum penicillins (without beta-lactamase inhibitor)
- Doxycycline
- Azithromycin
- Sulfamethoxazole-trimethoprim

Clinical Considerations

**** Antibiotic Risk Note**

All antibiotics carry an association with causing C. diff infections; however, targeted narrow-spectrum options demonstrate lower comparative risk.

Linezolid: Drug Interactions & Safety

Mechanism, serotonin toxicity incidence, and outpatient risk management

Mechanism & Toxicity Risk

- **Mechanism:** Weak, reversible MAO inhibitor.
- **Low Toxicity Incidence:** 2023 systematic review (84 studies) found very low serotonin toxicity rates:
  - **Monotherapy:** 0.0050%
  - **+ Serotonergic Drug:** 0.0134%
- **Rapid Resolution:** All cases resolved within 24–48 hours post-discontinuation
- **Dosing Strategy:** Risk is **not** dose-related; do not empirically reduce doses

Outpatient Management

- **Individualized Care:** Assess patient's capacity to detect signs and symptoms of Serotonin Syndrome (SS)
- **High-Risk Populations:** Unrecognized SS risk increases in patients who live alone or have dementia
- **Antidepressant Risks:** Discontinuation carries severe risks (withdrawal, depression/anxiety recurrence, suicidal ideation)

Serotonin Syndrome Signs

Symptoms usually occur within hours of a new/increased drug dose. Stop serotonergic meds immediately if observed.

Mental Status Changes

- Agitation or restlessness, confusion, insomnia

Autonomic Effects

- Fever / hyperthermia, tachycardia
- High BP / sweating, dilated pupils, diarrhea

Drug Interaction Risk Table

Co-prescribed agents categorized by Serotonin Syndrome risk tier

Suggestions	Drugs
Contraindicated	**MAOIs**: isocarboxazide, moclobemide, phenelzine, selegiline (high dose), tranylcypromine
High Risk	citalopram, escitalopram, methadone
Medium Risk	**Serotonergic Agents**: amitriptyline, amphetamine, buspirone, clomipramine, cocaine, codeine, cyclobenzaprine, desipramine, dextroamphetamine, dextromethorphan, doxepin, fentanyl, fluvoxamine, imipramine, levodopa, LSD, MDMA (Ecstasy), meperidine, mescaline, methamphetamine, metoclopramide, mirtazapine, naratriptan, nortriptyline, paroxetine, phentermine, rizatriptan, sibutramine, sumatriptan, tramadol, trazodone, vilazodone, vortioxetine, zolmitriptan
	Bone Marrow Suppressors: clozapine, cladribine, carbamazepine, some chemotherapeutic agents, azathioprine
Low Risk	amantadine, bromocriptine, brompheniramine, bupropion, carbamazepine, chlorpheniramine, clozapine, desvenlafaxine, dihydroergotamine, diphenhydramine, dolasetron, droperidol, duloxetine, fluoxetine, granisetron, lithium, olanzapine, ondansetron, quetiapine, reserpine, risperidone, ritonavir, sertraline, St. John's wort, tetrabenazine, valproate, venlafaxine, ziprasidone
Monitor Closely	**Adrenergic Drugs**: pseudoephedrine, epinephrine, norepinephrine, dopamine, or dobutamine

Research by Kevin Pasquali PharmD, BCPS, BCIDP

Elbarbry F and Moshirian N, "Linezolid-Associated Serotonin Toxicity: A Systematic Review," European Journal of Clinical Pharmacology, July 2023 (PMID 37129603)

DOAC Drug Interactions vs. Warfarin Interactions

Comparing monitoring requirements, contraindications, and dosing adjustments

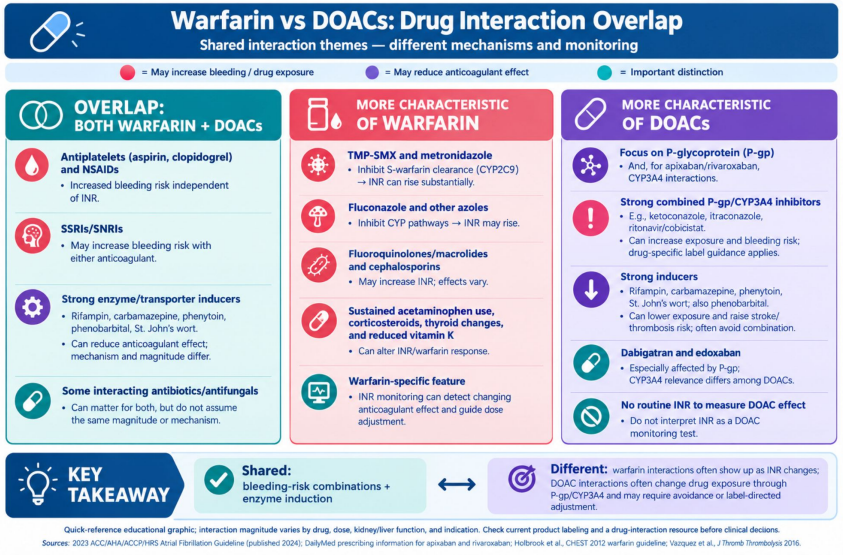
Warfarin Interactions

- **Contraindicated:** None
- **INR Impact:** MANY medications affect INR!
- **Beers Criteria Notable Interactions:** Amiodarone, ciprofloxacin, erythromycin, clarithromycin, sulfamethoxazole/trimethoprim, SSRIs

DOAC Interactions

- **General Guidance:** Refer to individual agents
- **Contraindicated:** Strong CYP 3A4 inducers (e.g., rifampin)
- **Dose Adjustments Required:** Dronedarone, ketoconazole, itraconazole, ritonavir

Drug Interaction Overlap Reference Chart



Inhibiting Enzymes vs. Inducing Enzymes

Time course, onset/offset predictability, and CYP enzyme impact

Inhibitors (e.g., Fluconazole)

- **Onset:** Usually immediately after first dose
- **Offset:** Fairly predictable (can calculate 5 half-lives)

Inducers (e.g., Rifampin)

- **Onset:** May take weeks
- **Offset:** Unpredictable and slow (2–4 weeks awaiting enzyme degradation)
- **Key Factors:** Half-life of medication AND enzyme de-induction (~7.7 days)

Cytochrome P450 (CYP) Enzymes

Key substrates, inhibitors, and inducers reference guide

Cytochrome P450 (CYP) Enzymes

Key Substrates, Inhibitors and Inducers

Inhibitors generally increase substrate drug levels | Inducers generally decrease substratse drug levels

CYP Enzyme	Key Substrates	Inhibitors ↑ Drug Levels	Inducers ↓ Drug Levels
CYP3A4/5 *Metabolizes >50% of drugs*	• Statins (simvastatin, atorvastatin) • Calcium channel blockers (CCBs) • Cyclosporine/tacrolimus • Midazolam • Sildenafil • Direct oral anticoagulants (DOACs)	Strong: • Clarithromycin, itraconazole, ketoconazole, voriconazole, posaconazole, ritonavir/cobicistat, grapefruit Moderate: • Erythromycin, diltiazem, verapamil, fluconazole, amiodarone	• Rifampin • Carbamazepine • Phenytoin • Phenobarbital • St. John's wort • Enzalutamide • Efavirenz • Dexamethasone
CYP2D6	• Codeine/tramadol (prodrugs) • Tamoxifen • Metoprolol • Tricyclic antidepressants (TCAs) • Venlafaxine • Dextromethorphan	• Fluoxetine • Paroxetine • Bupropion • Quinidine • Terbinafine • Duloxetine • Amiodarone • Diphenhydramine	*No significant inducers*
CYP2C9	• Warfarin • Phenytoin • Sulfonylureas • NSAIDs • Losartan	• Amiodarone • Fluconazole • Metronidazole • Trimethoprim-sulfamethoxazole (TMP-SMX) • Fluoxetine	• Rifampin • Carbamazepine • Phenobarbital • Phenytoin • Enzalutamide
CYP2C19	• Clopidogrel (prodrug) • Proton pump inhibitors (PPIs) • Citalopram	• Fluvoxamine • Fluoxetine • Fluconazole • Omeprazole/esomeprazole • Isoniazid	• Rifampin • Carbamazepine • Phenytoin
CYP1A2	• Theophylline • Clozapine • Olanzapine • Tizanidine • Caffeine	• Ciprofloxacin • Fluvoxamine • Oral contraceptives	• Smoking *(clinically significant)* • Phenytoin • Rifampin
CYP2C8	• Repaglinide • Pioglitazone • Paclitaxel	• Gemfibrozil • Clopidogrel	• Rifampin

1. Horn JR, Hansten PD. Disaster: failing to consider the time course of drug interactions. *Pharm Times*. 2006;72:30.
2. Reitman ML, Chu X, Cai X, et al. Rifampin's acute inhibitory and chronic inductive drug interactions. *Clin Pharmacol Ther*. 2011;89:234-242.

Summary & Key Takeaways

Essential principles for optimal antimicrobial stewardship and clinical prescribing

01

Prescribing

Being a prescriber is complex and nuanced

Correct antibiotic choice: Knowing the first choice antibiotic for the spectrum of diseases you treat

Patient Individualization: Recognize and develop a tailored clinical plan when standard regimens aren't appropriate for your specific patient

02

Healthcare Team Value

Leverage interprofessional expertise for superior patient outcomes

Collaborative Care: Engage clinical pharmacists, infectious disease specialists, and nurses to optimize therapeutic choices

Shared Decision-Making: Connecting with your patient and meeting them where they are

03

Active De-Prescribing

Prioritize medication reconciliation and polypharmacy reduction

Interaction Prevention: Systematically evaluate and discontinue unnecessary agents to prevent severe adverse drug interactions

Safety & Efficacy: Re-evaluate therapy duration regularly to minimize long-term risks

Questions?

Feel free to email me! Laura.king900@commonspirit.org

