Clinical Pearls 2018

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Directions to De-prescribing in Older Adults

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I have no actual or potential conflicts of interest to disclose.
I am not here as a representative of the VA and any opinions expressed are my own and do not necessarily represent the views of the Department of Veterans Affairs or the United States of America

Learning Objectives for Pharmacists

Discuss risks of polypharmacy in older adults and approaches to de-prescribe in this population

Review updated tools to assist with safe prescribing in older adults

Polypharmacy

- 44% of men and 57% of women aged 65+ take ≥ 5 medications per day!
- Over 50% of older adults use at least 1 OTC medication daily
- Nearly 2/3 of older adults use at least one dietary supplement daily
- 15% of older adults use a combination of drugs at risk for a major drug interaction

Qato, DM et al., *JAMA Intern Med* . 2016 April ; 176(4): 473–482.

Why are Older Adults at risk for Medication-Related Problems?

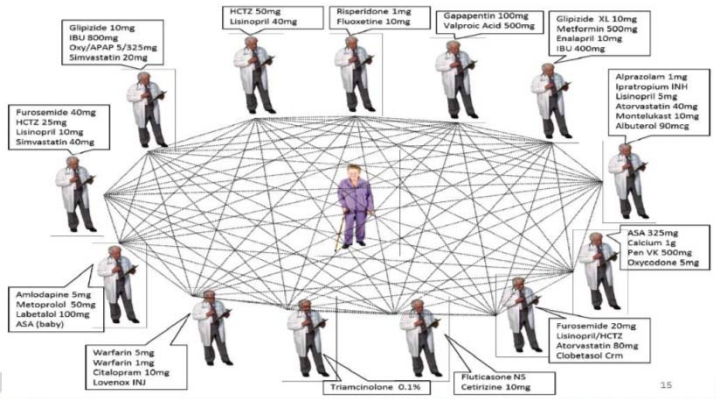
Medication Multipliers

- High # of chronic diseases
- Numerous prescribers
- Frequent use of OTC meds
- Multiple pharmacies
- Increased use of high risk medications

Additional Risk Factors

- Lack of trained professionals in geriatrics
- Underrepresented in trials
- Pharmacokinetic changes
- Pharmacodynamic changes
- Memory impairment

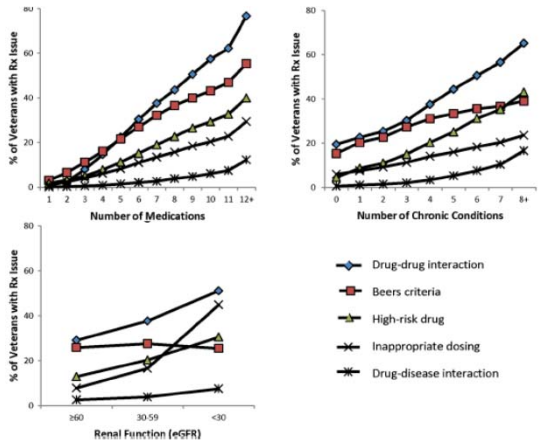
Will the real prescriber please stand up…



Risks of Polypharmacy

- Adverse Drug Events
- Falls
- Hospitalizations
- Mortality
- Decline in Cognition
- Decline in Function

Fried, TR et al., J Am Geriatr Soc. 2014 December ; 62(12): 2261–2272



Steinman MA et al., J Gen Intern Med. 2014 March; 29(10):1379–86

De-prescribing Defined

The planned and supervised process of

DOSE REDUCTION or STOPPING

of medication that may be

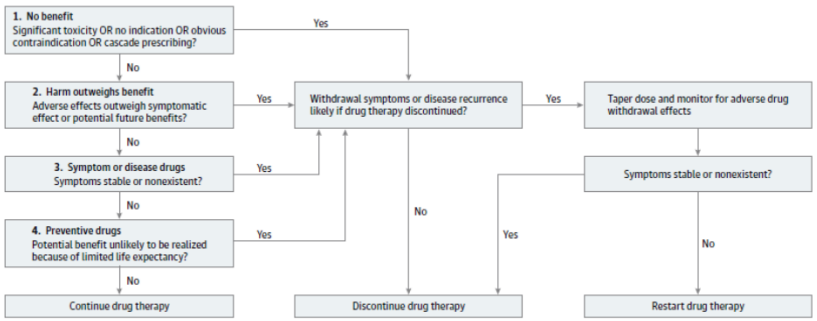
CAUSING HARM
and/or
NO LONGER PROVIDING BENEFIT

3 steps to De-prescribing

1. Perform a comprehensive medication review
   (Appropriateness/Adherence/Adverse Drug Reactions)
2. Match medications to medical conditions/diagnoses
3. Identify and discontinue unnecessary & inappropriate medications

The Process of De-prescribing

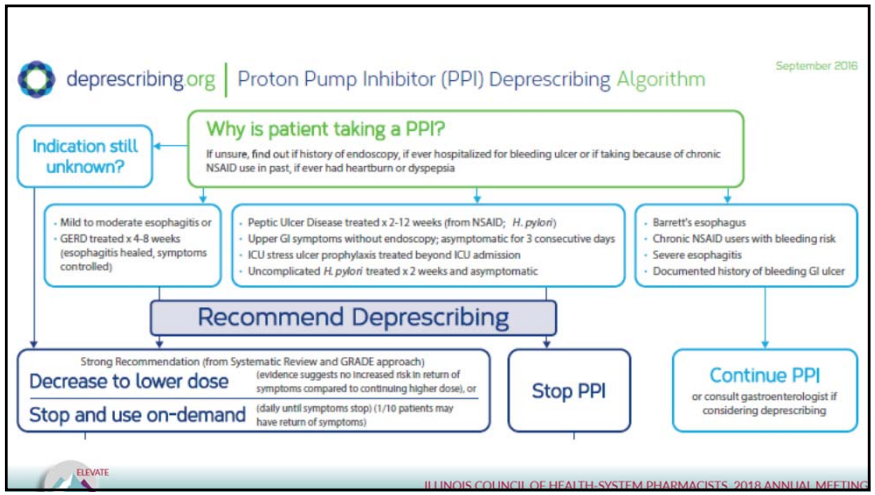
Figure. Algorithm for Deciding Order and Mode in Which Drug Use Could Be Discontinued



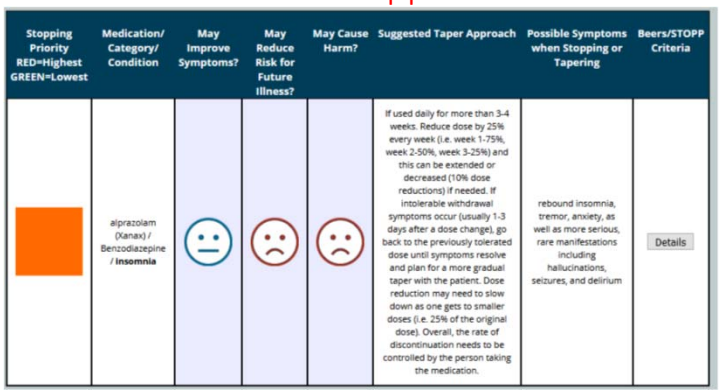
Scott I et al., *JAMA Internal medicine,* 2015; 175(5), 827-834.

De-prescribing

IF the medication is not effective or not indicated
STOP the medication
IF the medication is overprescribed
STOP the medication or DECREASE the dose
IF the medication causes current symptoms
DECREASE the dose or SWITCH to a safer alternative
IMPLEMENT Non-pharmacologic approaches
IF the medication is potentially inappropriate
SWITCH to a safer alternative



MedStopper



Available at: http://medstopper.com/. Accessed August 11, 2018

Case

- BO is an 86 y/o male who presents to the geriatrics clinic for the first time with his wife
- He is interested in reducing medication costs and burden
- He has had 3 falls in the past 2 months during the mid-day hours
- Wife is concerned with more unsteady gait and worsening cognition in the past month
- No dizziness or lightheadedness. (+) BLE peripheral neuropathy that impairs ability to get a good nights sleep. He had a cough 3 weeks ago and went to a Minute Clinic and this is now improved. No other complaints

Case

PMH: CAD s/p CABG 2010, hyperlipidemia, HTN, BPH, GERD, peripheral neuropathy, DJD s/p L hip replacement 10 yrs. ago and R knee replacement ~20 yrs. ago, insomnia

Pertinent Labs: Scr 1.1, LDL 82, HDL 61, Trigs 76

-all other relevant labs are wnl

Vitals: 125/80, HR 66 bpm, RR 18, pain score is 3

Reconciled Med List

- Aspirin 81mg EC daily
- Clopidogrel 75mg daily
- Finasteride 5mg daily
- Fish oil 500mg daily
- Gabapentin 400mg bid
- Pantoprazole 40mg qam
- Simvastatin 40mg qbedtime
- Tamsulosin 0.4mg qbedtime
- Tramadol 50mg q8h PRN for pain
- Metoprolol SA 50mg daily
- Clorazepate 7.5mg qbedtime
- Codeine/Guaifenesin 10mg/100mg q6h PRN cough
- Dicyclomine 10mg tid with meals

Which of BO's medications would you put the highest priority on de-prescribing?

A. Clorazepate 7.5mg qbedtime
B. Clopidogrel 75mg daily
C. Dicyclomine 10mg tid with meals
D. Fish Oil 500mg daily
E. Codeine/Guaifenesin 10/100mg q6h PRN for cough

Beers Criteria 2018

Original Beers Criteria – 1991

- Explicit criteria for determining inappropriate medication use in nursing home residents

1997

- Expanded to all adults older than 65 years

2003

2012

- American Geriatrics Society took ownership

2015

- Added renal dose adjustments table, drug interaction table, companion papers (how to use; alternatives)

2018

What is the Purpose of the Beers Criteria?

- Identify potentially inappropriate medications that should be avoided in many older adults
- Reduce adverse drug events and drug related problems
- Improve medication selection in older adults
- Designed for use in any clinical setting; also used as an educational, quality, and research tool
  - Not applicable to hospice and palliative care

Beers Criteria – Key Tables

- **Table 2** – Potentially inappropriate drugs to avoid
  - Organized by organ system and therapeutic category
- **Table 3** – Drug-Disease or Drug-Syndrome
  - May exacerbate disease or condition
- **Table 4** – Medications to use with caution
- **Table 5** – Drug-Drug Interactions
  - Non anti-infectives
- **Table 6** – Renal dosing table – No major changes in 2018
  - Non anti-infectives

Table 2 Changes – Potentially Inappropriate

Added / Changed

- Metoclopramide – duration update to up to 12 weeks
- Sliding Scale insulin (SSI) language modified

Removed

- Ticlopidine
- Guanabenz, Guanfacine, Methyldopa, Reserpine (>0.1mg/day)
- Meprobamate
- Ergoloid Mesylates
- Pentazocine

Table 3 Changes – Drug Disease / Syndrome

Added / Changed

- SNRI's with h/o falls or fracture
- Reduced opioid level of evidence with falls to MOD
- Add pimavanserin as exception for PD

Removed

- Chronic seizures or epilepsy as a condition
- Insomnia as a condition
- H2 antagonists with dementia; reduced quality of evidence to LOW for delirium

Table 4 Changes – Meds to use with Caution

Added / Changed

- DPP-4 inhibitors with HFrEF
- Dextromethorphan/Quinidine
- Trimethoprim/Sulfamethoxazole in patients on ACEI or ARB with reduced CrCl
- Aspirin for primary CV proph. changed to ≥ 70 y/o
- Rivaroxaban ≥ 75 y/o

Removed

- Vasodilators

Table 5 Changes – Drug Interactions

Added / Changed

- Opioids/Benzos – overdose risk
- Opioids/Gabanoids – overdose
- Antiepileptics + ≥2 CNS drugs
- Warfarin/Ciprofloxacin
- Warfarin/Macrolides
- Warfarin/ Trimethoprim/Sulfamethoxazole

Removed

- ACEI + amiloride or triamterene and changed to:
- Avoid ≥1 Potassium raising med
  - ACEI
  - ARB
  - Aliskerin
  - K+ sparing diuretics

Pop Quiz Hot Shot!

Which of the following is a medication related update in the 2018 Beers criteria?

A. Aspirin should be used with caution for primary CV prophylaxis in those ≥80 y/o
B. Venlafaxine use is potentially inappropriate for those with a h/o falls or fracture
C. Metoclopramide is potentially inappropriate if used ≥ 6 weeks
D. Warfarin and amoxicillin is a drug interaction to be avoided in older adults

Questions?

References

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Pharmacogenomics: An Inpatient Perspective

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ILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2018 ANNUAL MEETING

Conflict of Interest Declaration

James Lee, PharmD, has no actual or potential conflicts of interest to report.

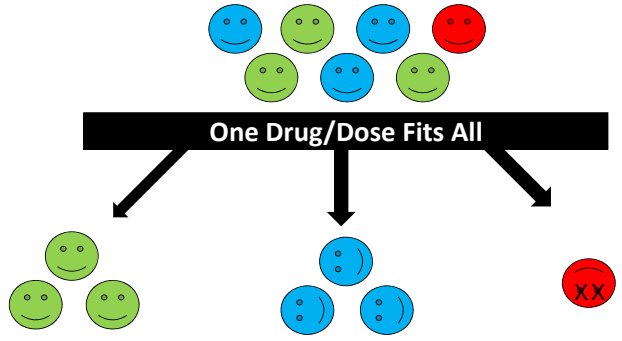
ILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2018 ANNUAL MEETING

Learning Objective - Pharmacist

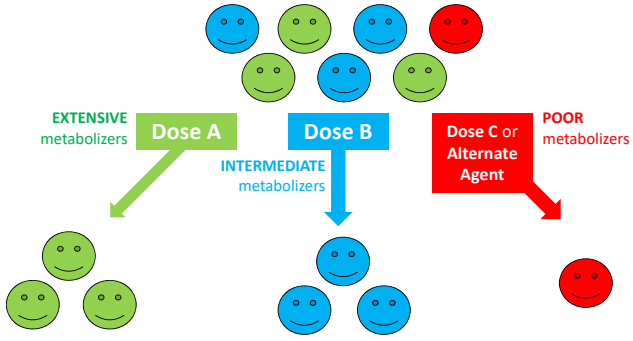
Describe considerations for implementing and applying pharmacogenomics (PGx) testing in the inpatient setting.

ILLINOIS COUNCIL OF HEALTH-SYSTEM PHARMACISTS 2018 ANNUAL MEETING

Today's Standard Approach



A Tailored Approach



Using PGx to choose between therapeutic equals

Avoid medication-related adverse events and safely achieve optimal treatment outcomes
- Improve treatment safety
- Reduce hospitalizations

Advance patient understanding of individual health and health risk
- Improve medication adherence

Reduce medication spending waste
- Reduce care costs associated w/ empiric drug selection and dosing

Common Gene-Drug Pairs

Drug Metabolism & Transporter Function
- **CYP2D6**: **TCA/SSRI** (dosing/selection), **codeine** (toxicity: conversion to morphine)
- **CYP2C9**: **warfarin** (w/ VKORC1: dosing), **phenytoin** (w/ HLA-B*15-02)
- **CYP2C19**: **TCA/SSRI** (dosing/selection), **clopidogrel** (bioactivation), **voriconazole** (dosing)
- **DPYD**: **fluoropyrimidines** (toxicity)
- **TPMT**: **thiopurines** (toxicity)
- **SLCO1B1**: **simvastatin** (myopathy)

Human Leukocyte Antigen Carrier Status → hypersensitivity
- **HLA-B*57:01**: abacavir
- **HLA-B*58:01**: allopurinol
- **HLA-B*15:02 / HLA-A*31:01**: carbamazepine, oxcarbazepine
- **HLA-B*15:02**: phenytoin

Interpretation, Translation, Intervention

Clinical Pharmacogenetics Implementation Consortium (CPIC)

- Develops peer-reviewed, expert consensus guidelines
- Evidence from preclinical functional and clinical data, and disease-specific consensus guidelines
- Assist clinicians with **HOW** to **translate** and **apply** test results
- Address implementation process and barriers

Considerations: It Takes a Team & Commitment

Support For PGx Within Your Institution

- **Institutional value:** Priority of PGx; Investment/opportunity or a cost?
- **Clinician interest & expertise:** pharmacist, physician, other advanced practitioners
- **Physician champion**
- **Interdepartmental support:** IT build/support, clinical department utilization
- **Support personnel:** administrative, research, student support

Be prepared for consistent education drives

Considerations: Who, What, & How to Test

Selecting Patients (WHO)

- **Higher risk** patients
- Patient level **suboptimal treatment outcomes**
- **Institutional level outcomes** with room for improvement

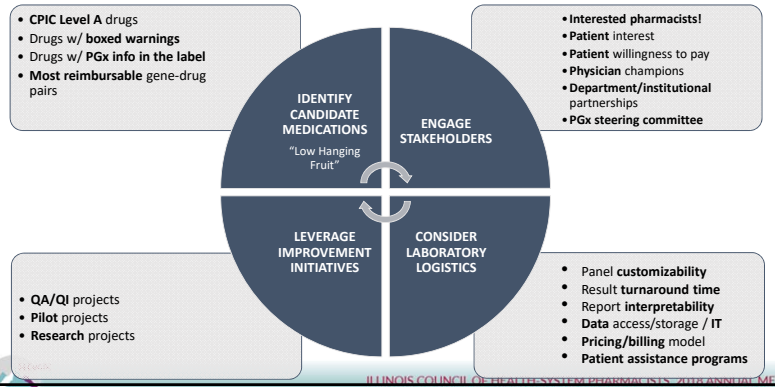
Testing Approach (WHEN & HOW)

- **Reactive** vs pre-emptive testing
- **Single** gene vs multigene (consider commonly prescribed medications)
- **In-house** vs third party laboratory

Reimbursement: Billing Model / Cost Perspective

- Will provider bill?
- How is patient billed?
- Focus on **global cost savings** vs revenue generation

Multi-prong Planning & Implementation



Which of the following should be considered when implementing pharmacogenomics in the inpatient setting?

A. A multi-pronged approach incorporating internal and outside stakeholders in the planning and implementation process is essential.
B. Consider implementing pharmacogenomics testing for commonly prescribed medications rated as CPIC Level C.
C. Pharmacists should lead the effort and solicit feedback from outside the pharmacy department as needed.
D. CPIC guidelines provide guidance on determining which settings pharmacogenomic testing should be implemented in.

Updates on *Clostridium difficile*

Nick Van Hise, PharmD, BCPS
Infectious Disease Pharmacy Specialist/Research Coordinator
Metro Infectious Disease Consultants

Learning Objectives - Pharmacists

- State *Clostridium difficile* infection (CDI) treatment recommendations consistent with the 2018 IDSA guidelines based on patient-specific factors
- Recall treatment considerations for reducing the risk of *Clostridium difficile* recurrence

Potential Conflicts

- Related to Cdiff
  - Principal Investigator for a Phase II Clinical Trial study for FMT funded by Finch Therapeutics
- Unrelated to Cdiff
  - Speaker bureau for antibacterial agents for Melinta, Astellas, and Merck

All conflicts were resolved through peer review

Background

- *C. difficile* is a gram-positive, anaerobic, spore-forming rod
- Leading cause of hospital-acquired diarrhea
- >250,000 cases per year
- $1.1 billion per year in the United States
- Mortality 1-2.5%
- Complications: toxic megacolon, *C. difficile*-associated arthritis, septicemia

Aslam S, et al. *Lancet Infect Dis.* 2005.
Brito GA, et al. *J Infect Dis.* 2002.

Economic Impact

- Attributable costs per episode: $3,791 - $4,846
- Annual US healthcare costs: $433 - $797 M
- Overall costs per hospitalization case-control
  - 85% higher costs for CDI ($55K vs. $28K)
  - 99% longer length of stay (21.1 vs 10 days)
- Special populations per episode
  - Recurrent: $13,655 - $18,067
  - IBD, surgical inpatient, ICU: $90K

Kyne L, et al. *Clin Infect Dis.* 2002.
Dubberke ER, et al. *Clin Infect Dis.* 2008.
Ghantoji SS, et al. *J Hosp Infect.* 2010.
Pakyz A, et al. *Pharmacother.* 2011.

Pathogenesis

- 3 events must occur for the development of *C. difficile* infection (CDI)
  1. Disruption of normal intestinal flora
  2. Exposure to *C. difficile*
  3. Inadequate host immune response

Owens RC, et al. *Clin Infect Dis.* 2008.
Howell MD, et al. *Arch Intern Med.* 2010.
Kelly CP, et al. *NEJM.* 2008.

Diagnosis

- Onset usually 1-2 days after antibiotic initiation
- Can be as long as 10 weeks after discontinuation of antibiotic
- Diagnosis:
  - Diarrhea (≥3 unformed stools/24 hrs for ≥ 2 days)
  - PLUS Positive *C. difficile* toxin in stool sample
  - OR pseudomembranes seen in the colon
- Colonization versus infection
  - NAAT
  - Toxin
  - GDH
- The key is symptoms: ≥3 bouts of diarrhea in a 24 hour period

Peterson LR, et al. *Ann Intern Med.* 2009.
McDonald LC, et al. *Clin. Inf. Diseases.* 2018.
Bobo LD, et al. *Chest.* 2011.

Acquisition of *Clostridium difficile*

- Acquisition usually in hospital
- Commonly cultured from inanimate objects
- Can persist for 40 days
- Acquisition rate 13% with a stay of 2 weeks and 50% when stay > 4 weeks
- Share a room→3.2 days

Schroeder, MS. *Am Fam Physician*, 2005;71:921-28.

Initial Mild to Moderate CDI Treatment

- Previous guidelines recommended metronidazole as first line therapy
- Update removed metronidazole from the guidelines
- First therapy:
  - Oral Vancomycin for 10 days
  - Fidaxomicin for 10 days
- Caveats:
  - Accessibility of vancomycin or fidaxomicin is not an option, metronidazole can be considered for mild to moderate CDI
  - Fidaxomicin should be considered over vancomycin in pts at high risk for recurrence

McDonald LC, et al. *Clin. Inf. Diseases*. 2018.

66yo WF prevents with intra-abdominal infection secondary to diverticulitis. Patient rapidly improved with fluids and IV antibiotics. Pt discharged on augmentin to finish a 7 day course. Upon discharge, the patient begins to have diarrhea with 6-7 bouts of diarrhea a day and is PCR positive for Cdiff.

What is the most appropriate therapy?

A. Metronidazole PO 500mg every 8 hours for 10 days
B. Vancomycin 125mg PO QID (four times daily) for 10 days
C. Vancomycin 250mg PO QID (four times daily) for 10 days
D. Fecal Microbiota Transplant

Initial Severe to Fulminant Treatment

- Severe:
  - Vanco 125mg every 6 hours OR
  - Fidaxomicin 200mg BID
- Fulminant:
  - Vanco 500mg every 6 hours PO or NG PLUS metronidazole IV 500mg every 8 hours
  - Rectal instillation of vanco every 6 hours should be considered in situations of ileus (500mg in 1L NS)

McDonald LC, et al. *Clin. Inf. Diseases*. 2018.

Severe CDI

- Vancomycin 500mg PO every 6 hours
- Fidaxomicin 200mg every 12 hours

- Fulminant CDI: standard of care for severe plus
  - If ileus, consider rectal instillation of vancomycin
  - Metronidazole 500mg IV every 8 hours

McDonald LC, et al. *Clin. Inf. Diseases*. 2018.

Demotion of Metronidazole

- Higher cure rates with vancomycin compared to metronidazole
- Increased resistance with metronidazole to clostridium difficile isolates
- MIC_{90} 0.25-1 mcg/mL
- Resistance: 6%
- Rapid oral absorption (6-15% in stool)
- Stool concentrations
  - 9.3 ± 7.5 ug/g (wet)
  - 1.2 ug/g (formed)
- Failures
  - Decreased mucosal inflammation?
  - Increased absorption?
  - MIC drift?
  - Poor concentration/MIC ratios

Chow AW, et al. *Antimicrob Agents Chemother.* 1985.
Pelaez T, et al. *Antimicrob Agents Chemother.* 2002.
Bolton RP, et al. *Gut.* 1986.

Which of the following are reasons for why metronidazole was removed from the first line treatment of mild to moderate CDI (Cdiff infection)?

A. Metronidazole resistance
B. Poor concentration/MIC ratios due to MIC drift
C. High cost of metronidazole
D. Lack of availability of metronidazole
E. A&B
F. All of the above

Other Dosage Schemes for Recurrence

- Vancomycin tapered pulse:
  - 125mg PO q6 for 10 to 14 days
  - 125mg PO q12 for 7 days
  - 125mg PO once daily for 7 days
  - 125mg PO every 2 or 3 days for 2 to 8 weeks
- Fidaxomicin 200mg PO BID
- Fidaxomicin 200mg BID on days 1-5, then once daily on alternate dates on days 7-25*

*Not yet in IDSA guidelines

McDonald LC, et al. *Clin. Inf. Diseases*. 2018.
Guery, et al. *The Lancet Infectious Diseases*. 2018.

Recurrent CDI Treatment

- Tapered pulse vancomycin
- Pulse fidaxomicin
- Fecal Microbiota Transplant (FMT)
- Bezlotoxumab (Zinplava®)

McDonald LC, et al. *Clin. Inf. Diseases*. 2018.

Fecal Microbiota Transplant (FMT)

- Single healthy donor with necessary screening performed
- Healthy, monogamous donor→ criteria not specified in IDSA guidelines
  - Refer to FDA Guidance of 2016 to criteria to meet for FMT
- Various pharmaceutical company FMT products
  - Seres Pharma. ®
  - Rebiotix®
  - Finch Therapeutics® (working with OpenBiome®)

Gough E, et al. *Clin Infect Dis.* 2011.
Kelly CR, et al. *J ClinGastroenterol.* 2012.
Kao, D, et al. *JAMA.* 2017.

Prevention of Recurrence

- Antimicrobial Stewardship
  - Minimize frequency, duration of high risk antibiotics
  - Implement a coordinated stewardship program following IDSA/SHEA Stewardship Update of 2016
  - Restrictions of specific classes that are associated with highest rates of CDI
  - PPI restriction

McDonald LC, et al. *Clin. Inf. Diseases*. 2018.

Prevention of Recurrence

- Oral vancomycin prophylaxis
  - Should be considered in high risk patients on broad spectrum antibiotics who have a history of CDI
  - If previous CDI even was greater than 1 year ago, evidence is weaker
  - Dosage varies between 125 to 250mg daily to BID→ likely should be based upon pts baseline bowel movement status
- High risk criteria to consider:
  - Time since last recurrence
  - Severity of previous recurrences
  - Hx. of FMT or bezlotoxumab
  - Frailty of patient

McDonald LC, et al. *Clin. Inf. Diseases*. 2018.

THANK YOU FOR LISTENING! QUESTIONS OR COMMENTS?