ARLG
Antibacterial Resistance Leadership Group

Straining for the best outcomes: Top controversies in *C. difficile* management

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March 3, 2023

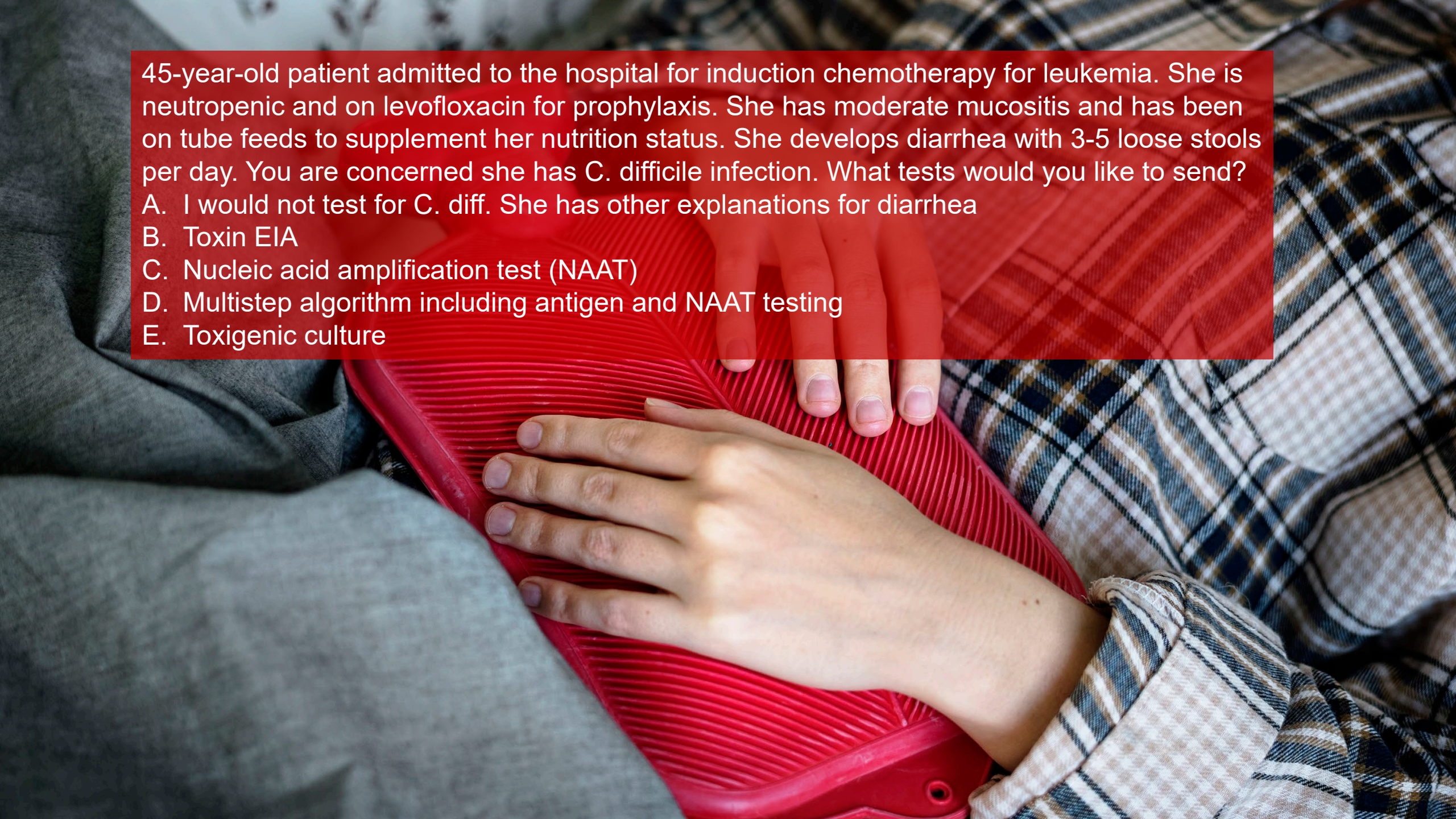
Disclosures

- Sarah:
  - Funding for clinical research studies to UCSF from Gilead, Pfizer, F2G, Regeneron, Chan Zuckerberg Initiative, and NIH
  - Personal consulting fees from Genentech and Janssen/J+J
  - Clinical Events Committee compensation from Shinogi, Basilea, DCRI
- Mike:
  - Funding for clinical research studies to Emory from NIH and CDC

Objectives

- Describe top controversies in *C. difficile* diagnosis and management
- Understand emerging and newer *C. difficile* therapies
- Summarize gaps in the literature and future areas for research
- Apply this knowledge to your treatment setting

TREAT + NAAT / - AG?



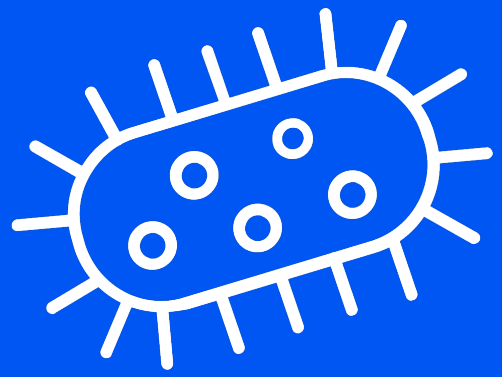
45-year-old patient admitted to the hospital for induction chemotherapy for leukemia. She is neutropenic and on levofloxacin for prophylaxis. She has moderate mucositis and has been on tube feeds to supplement her nutrition status. She develops diarrhea with 3-5 loose stools per day. You are concerned she has C. difficile infection. What tests would you like to send?

A. I would not test for C. diff. She has other explanations for diarrhea
B. Toxin EIA
C. Nucleic acid amplification test (NAAT)
D. Multistep algorithm including antigen and NAAT testing
E. Toxigenic culture

“Send stool for C. diff x 3”

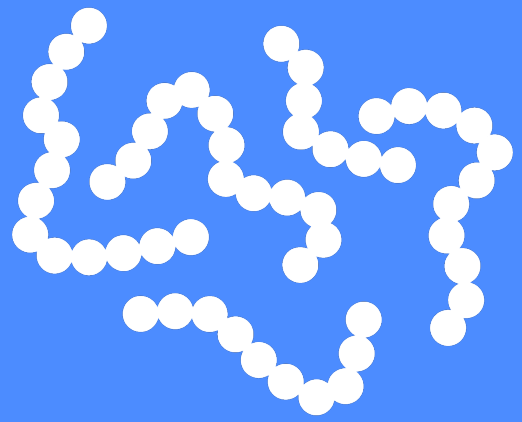
Bartlett JG and Gerding DN CID 2008; 46: S12-18; Manabe YC, et al. Ann Intern Med 1995; 123:835–40

Diagnostic testing



Glutamate dehydrogenase Ag (GDH)

- Bacterial detection
- Sn but not Sp



Enzyme immunoassay (EIA), toxins A+B

- Protein detection
- ↓Sensitivity
- ↑Specificity

Polymerase chain reaction (PCR):

- Toxin-producing gene
- ↑Sensitivity
- ↓Specificity

Additional tests (“reference standards”)—selective toxigenic culture and cell culture cytotoxicity assay—are time-consuming and impractical for routine clinical use

Crobach MJT et al. Clin Microbiol Infect 2009; 15(12): 1053-56; Eastwood K et al. J Clin Microbiol 2009; 47(10): 3211-3217; Planche T et al. Lancet Infect Dis 2008; 8(12): 777-784

Some facts

Most diarrhea in the hospital is not *C. diff*

C. diff colonization is common in certain populations

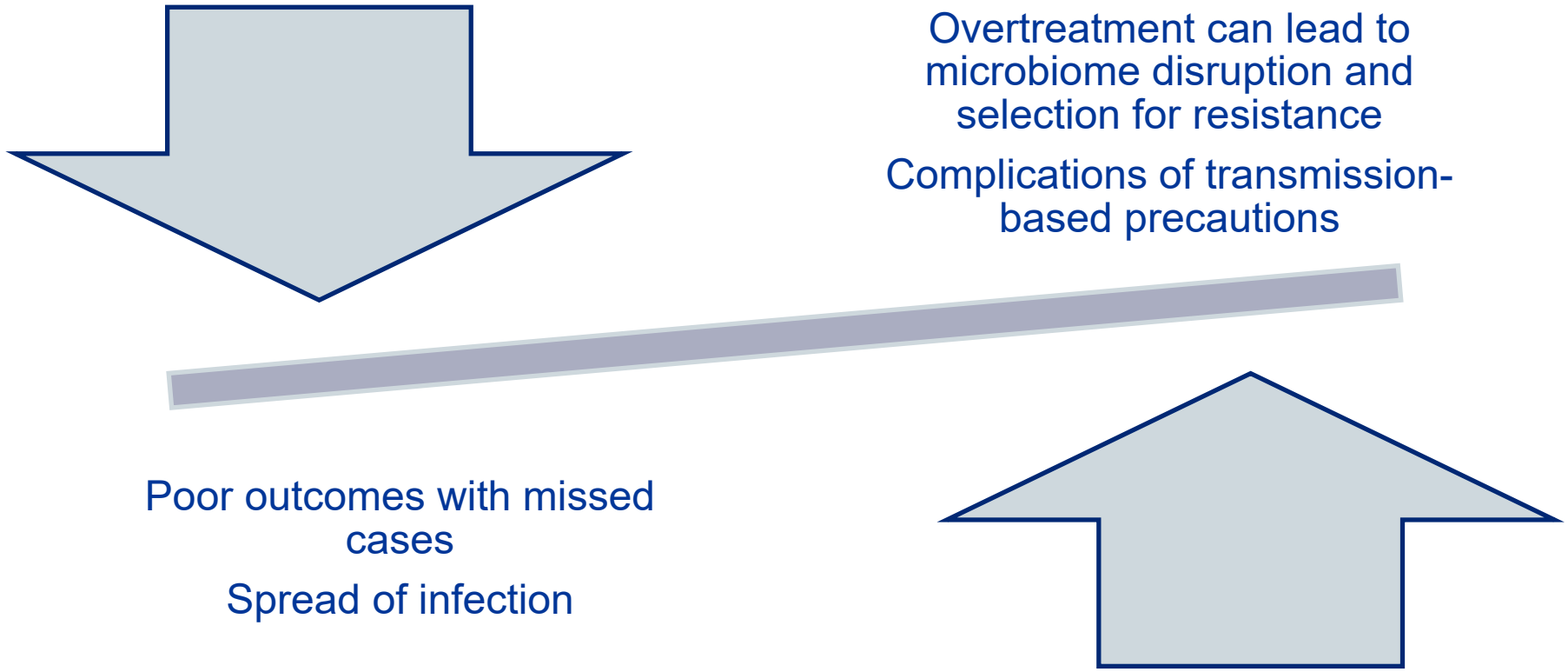
Causes of non-*C. diff* diarrhea and risk factors for C. diff have significant overlap

Test performance depends on pre-test probability

Different toxin tests vary in sensitivity

Fang FC, Polage CR, Wilcox MH. J Clin Microbiol 2017; 55(3): 670-680

Trade-offs


Overtreatment can lead to microbiome disruption and selection for resistance
Complications of transmission-based precautions
Poor outcomes with missed cases
Spread of infection

What do the guidelines say?

IDSA

- Target patients with unexplained new-onset diarrhea (≥3/24h)
- Use stool toxin test as part of a multistep algorithm rather than NAAT alone
  - Exception: Institutional limitations on stool testing population

ESCMID

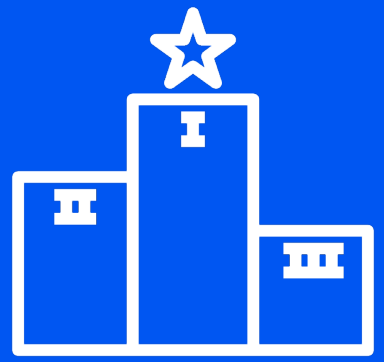
- Test only unformed stool
- Interpret tests in clinical context
- Use 2-step algorithm

Crobach MJT et al. Clin Microbiol Infect 2009; 15(12): 1053-56; McDonald LC et al. Clin Infect Dis 2018;66(7):e1–e48

Quick takes

Switch to NAAT testing ↑incidence by 43-67%

3% of PCR-only cases vs. 39% with +EIA or CCA had complication
(can find other studies w/ similar complications)



Toxin levels correlate w/ dz severity, complications, & recurrence

PCR-only patients can transmit *C. diff* to others

Gould CV et al. Clin Infect Dis 2013; 57:1304–1307; Longtin Y et al. Clin Infect Dis 2013; 56(1):67-73; Alonso CD et al. Clin Infect Dis 2022; 74(12): 2142-2149; Origuen J et al. Clim Microbiol Infect 2018; 24(4): 414-421; Mawer DPC et al. Clin Infect Dis 2017; 64(9): 1163-1170

What do most observational studies examine?

Wrong population

Pts with positive NAAT test on therapy for CDI

Detectable toxin

Undetectable toxin

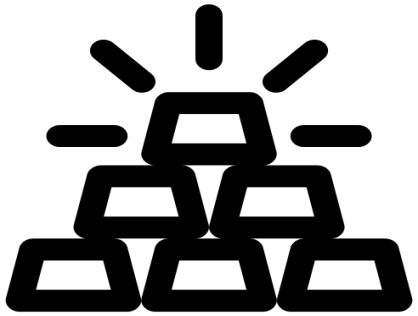
Clinical outcomes

Wrong outcomes

Pts with diarrhea

Test A

Test B

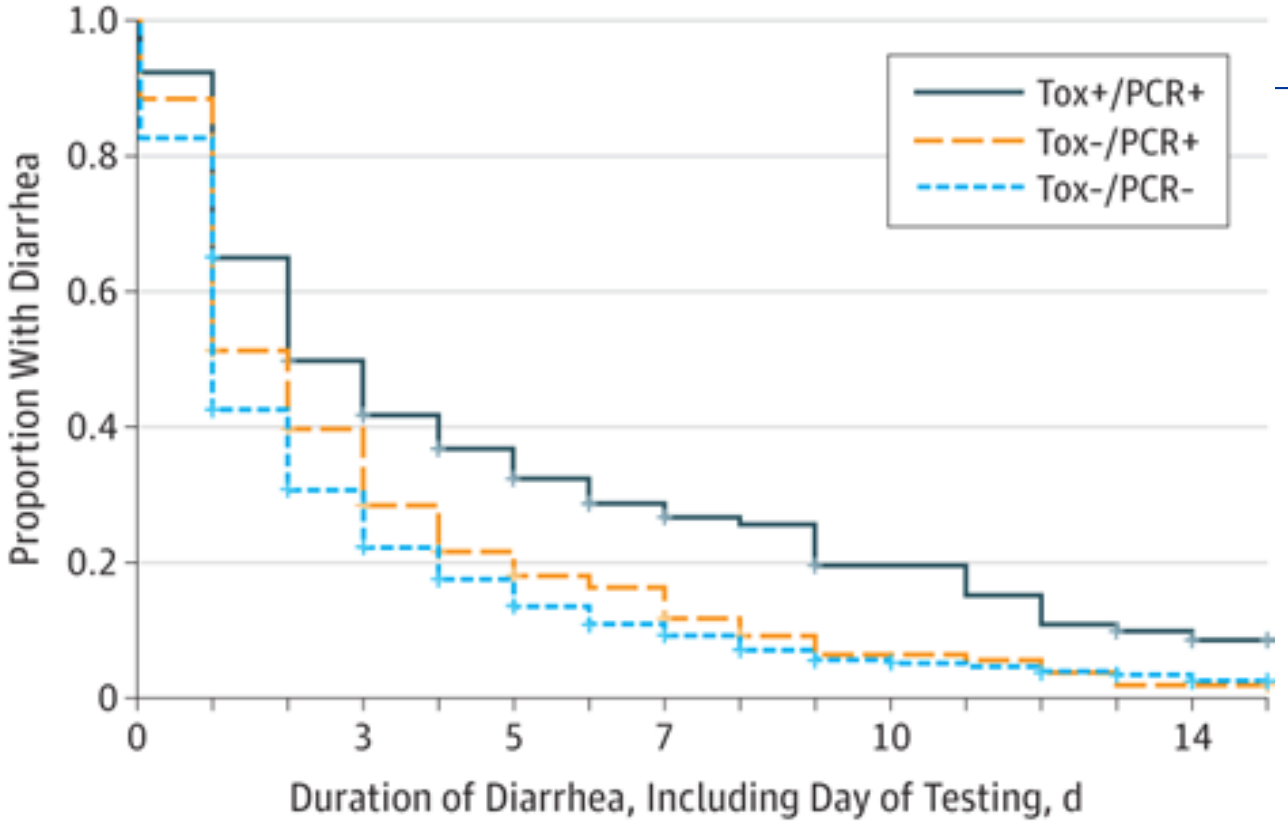


Analytical sensitivity

CDI overdiagnosis

- 21% +PCR
- Of these, 44% + toxin
- Toxin-/PCR+
  - ↓bacterial load
  - ↓abx
  - ↓diarrhea
  - No CDI-complications

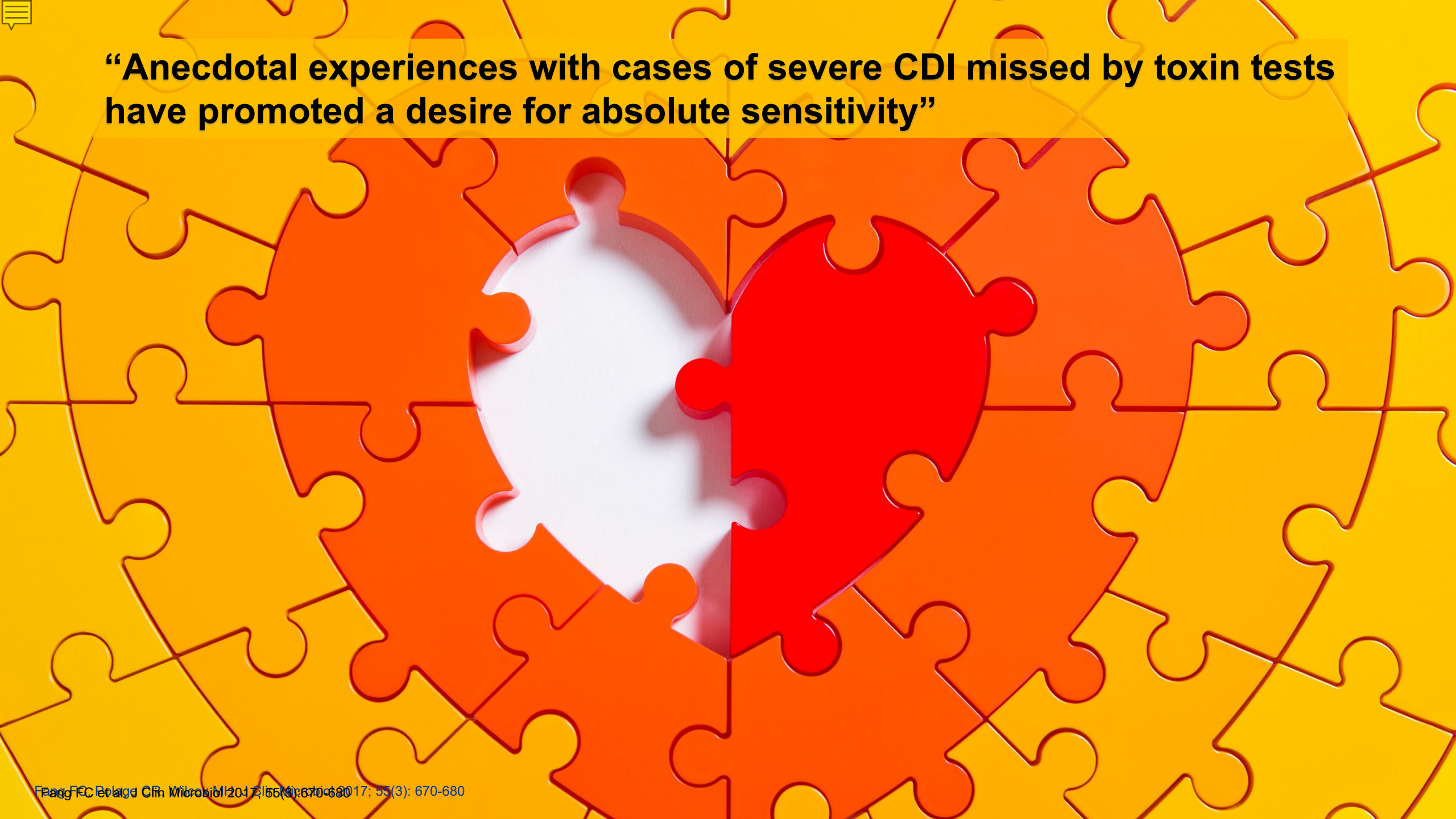
Similar results reported in the UK and at Stanford



No. at risk						
Tox+/PCR+	131	62	41	29	25	8
Tox-/PCR+	162	60	29	21	10	2
Tox-/PCR-	1123	328	172	99	42	23

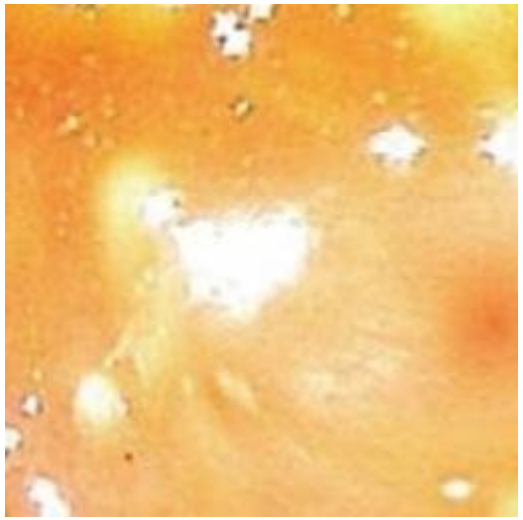
Polange CR et al., JAMA Intern Med. 2015 Nov;175(11):1792-801; Baker I et al. J Hosp Infect 2012; 84(4):311-315; Hogan CA et al. J Clin Microbiol 2022; 60(6): e02187-21

“Anecdotal experiences with cases of severe CDI missed by toxin tests have promoted a desire for absolute sensitivity”



Fang FC et al. J Clin Microbiol 2017; 55(3): 670-680

Anecdotal counterpoints



- Pt with toxic megacolon, leukemoid reaction, pseudomembranes.
- Initial toxin testing negative, later positive

Table 7. FALSE-NEGATIVE RATE OF DIAGNOSTIC STUDIES FOR FULMINANT *CLOSTRIDIUM DIFFICILE* COLITIS

	Colectomy	Autopsy	False-Negative Rate
Endoscopy	1/18	1/2	10%
Computed tomography scan	0/30	0/9	0%
Fecal leukocytes	6/10	0/0	60%
Toxin assay	3/33	3/15	12.5%

"toxin assay was negative, and he was sent home. After three weeks, he returned to the hospital with severe abdominal pain, watery diarrhea, severe sepsis, and multiple organ failure"

Dallal RM et al. Ann Surg 2002; 235(3): 363-72; Sayedy L et al. World J Gastrointest Endosc 2010; 2(8): 293-7; Stefan MS and Gupta E Am J Case Rep 2010; 11:237-240

Particular concern in immunocompromised hosts

Retrospective cohort of pts with symptoms and stool samples sent to University Hospital Basel

Toxin EIA +
(N = 274)

Toxigenic culture +
EIA negative
(N = 206)

12,481 stool specimens submitted
480 (3.8%) with toxigenic C diff + symptoms
N = 2 with TC+ and asymptomatic

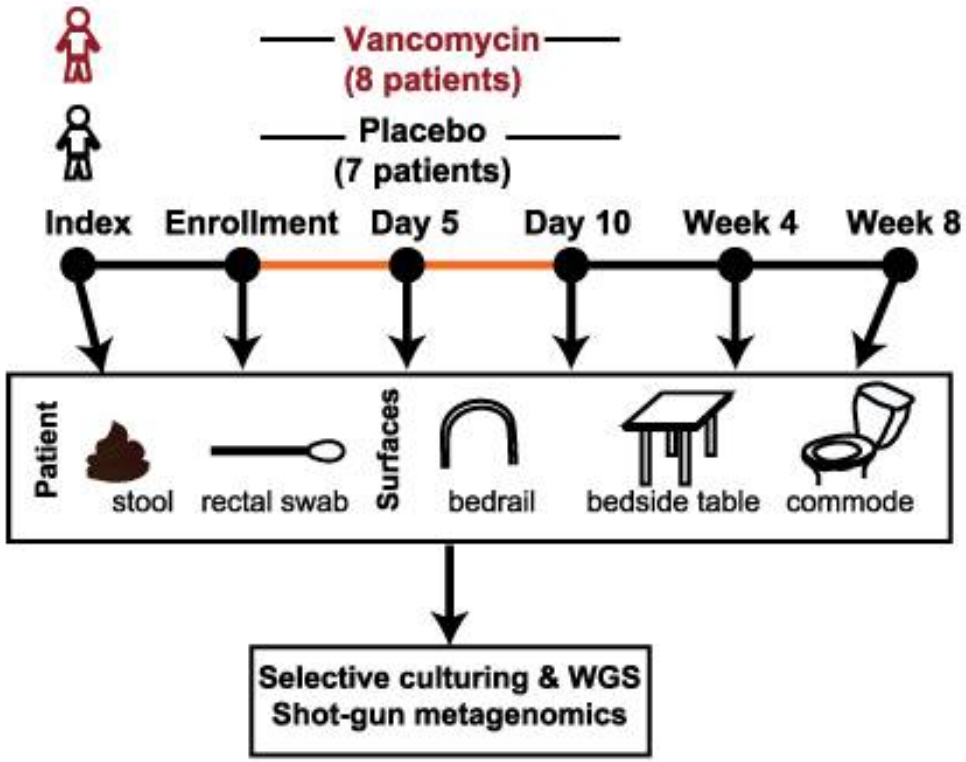
10 (3.6%) **Not treated** **42 (20.4%)**

Significant predictors for EIA-/TC+ on multivariate analysis included **high-dose steroids** (aOR 2.97, 1.5-5.9) and **leukopenia** (aOR 2.5, 1.2-5.2)

EIA-negative disease had similar crude and CDI-attributable mortality, recurrence, and need for surgery

Erb S et al. Clin Microbiol Infect 2015;21(11):998.e9-998.e15

Pilot RCT demonstrates effects of PO VAN on colonized pts



Key takeaways:

- Limited power
- 80% of PBO vs. 71% of VAN-treated patients remained colonized post-treatment
- There were differences in gut microbiota and resistomes between groups
- One PBO patient later had a positive EIA and was treated
- Numerical increase in *E. faecium* abundance

What would be the optimal study design to determine the best testing approach?

- Include: Patients with diarrhea and no alternative explanation
- Exclude: High-risk features, severe immunocompromise
- Double-blind RCT

Randomization

- Report only EIA results
- Report both EIA and NAAT results
- Report only NAAT results

Outcomes

- CDI complications
- CDI treatment
- CDI rates/spread
- Mortality
- Readmission
- Microbiome analysis

Significant uncertainty exists about the significance and management of toxin-negative/NAAT-positive C diff testing

Future directions may include:

-Better tests (host biomarkers, ultrasensitive toxin testing, Ct values) to discriminate disease from colonization

-Better preventative treatment strategies (live biotherapeutic products)

-More effective infection control strategies

WHEN IS THE BEST TIME TO TREAT WITH LBP/FMT?

Case

67 year old man with end-stage renal disease on peritoneal dialysis and recent admission for septic shock with *Enterobacter cloacae* bacteremia treated with two weeks of meropenem.

He developed diarrhea (*C. difficile* PCR +/toxin -) treated with PO vancomycin for 7 days.

He was readmitted 21 days after last dose of vancomycin with fulminant *C. difficile* colitis (PCR +/toxin +) and shock. He was initially treated with enteric vancomycin and IV metronidazole, then seen by ID and transitioned to fidaxomicin. He had persistent loose stools after two weeks of fidaxomicin.

Case

67 year old man with recurrent *C. difficile* and loose stooling refractory to antibiotics.

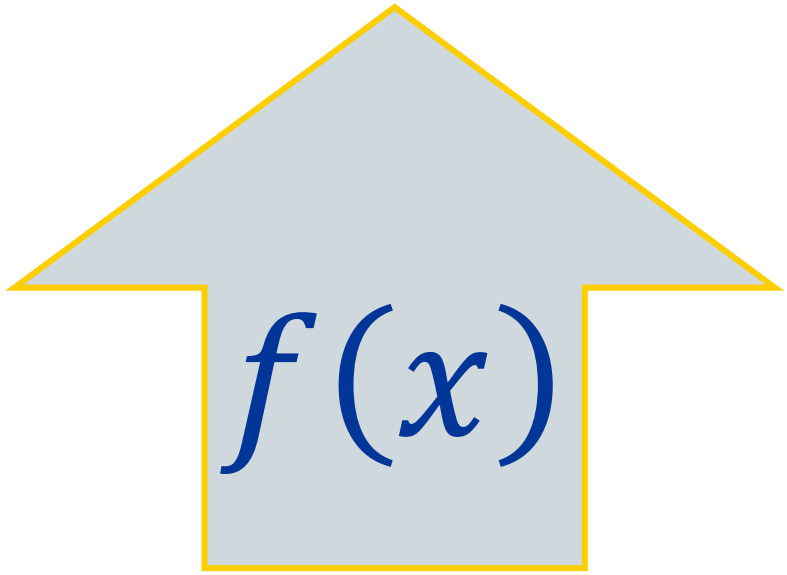
Should he be considered for FMT?

When?

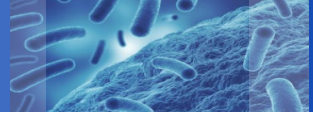
Should this patient be considered for FMT?

67 year old man with recurrent *C. difficile* and loose stooling refractory to antibiotics.

- A) No – He has only had one CDI recurrence, not two
- B) No – I'm not sure why he is having loose stool but probably not *C. difficile* anymore if it didn't respond to fidaxomicin
- C) Yes – He has antibiotic-refractory CDI, recommend FMT this admission
- D) Yes – Recommend GI referral for outpatient FMT via colonoscopy
- E) Yes – FMT seems indicated but I don't know how to get a dose



This is fundamentally different than many therapies in infectious disease.



Patients and clinicians are left with tradeoffs for timing of live biotherapeutics like FMT in the absence of validated biomarkers of gut microbiota functional potential.

Timing of LBP/FMT - Tradeoffs

PRO:
- Efficacy ~ 90% for preventing recurrence
- Limits antibiotic exposures
- Potential secondary benefits (e.g. reduced MDRO colonization and BSIs)

CON:
- Procedural risks (anesthesia, colonoscopy, discomfort from enema)
- Material risks (infection, unrecognized risks)
- Reimbursement challenges
- Limited FMT access
- Recurrence risks

Timing of FMT – IDSA & ACG Guidelines

Guideline, Date	FMT Indication(s)	Recommendation strength / Evidence quality
IDSA, 2017	• Patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments	• (Strong / Moderate)
ACG, 2021	• Second or subsequent recurrence of CDI (i.e. third or subsequent episode). • **Repeat FMT for patients with recurrence within 8 weeks of FMT** • **Severe and fulminant CDI refractory to antibiotic therapy.**	• (Strong / Moderate) • (Conditional / Very Low) • (Strong / Moderate)
IDSA, 2021	• Patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments and where appropriate screening of donor and donor fecal specimens has been performed.	• (Unchanged)

Kelly, C. Am J Gastroenterol. 2021; 116(6):1124:1147;

Timing of FMT – FDA Enforcement Policy for FMT for CDI

GUIDANCE DOCUMENT

Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation to Treat Clostridium difficile Infection Not Responsive to Standard Therapies

Guidance for Industry

NOVEMBER 2022

Download the Final Guidance Document | Read the Federal Register Notice

Final

How many FMT-eligible patients receive FMT?

After how many episodes of CDI is FMT offered to patients?

GEORGIA EIP emerging infections program

GHA Georgia Hospital Association

Among patients eligible for FMT

6%

Received FMT

94%

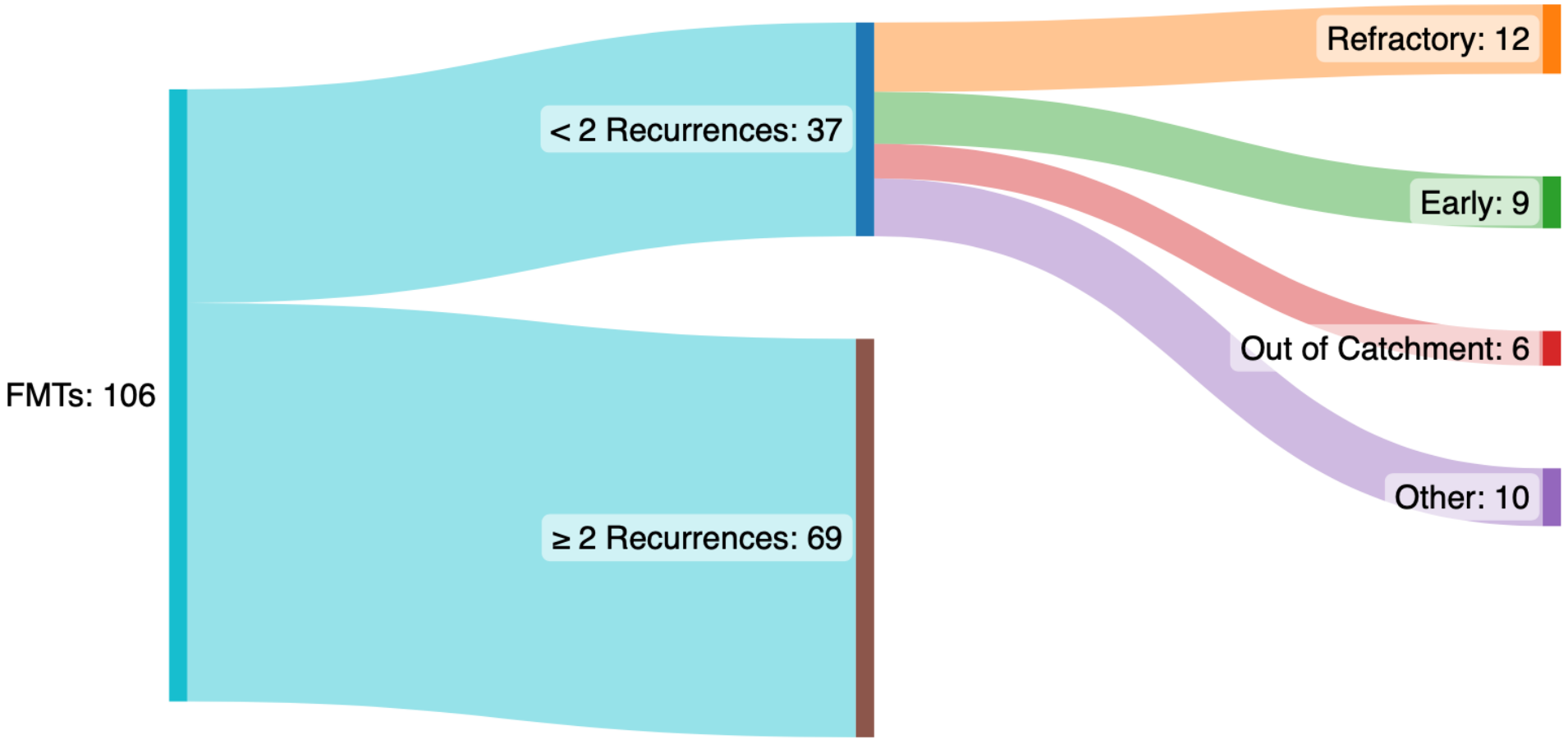
Did not receive FMT

(A guideline-recommended therapy that is 90% efficacious)

FMTs are frequently administered before Episode 3

CDI Episode	Patients (n)	Patients Treated with FMT n (%)
1	13,852	52 (0.4%)
2	3,038	75 (2.5%)
3	983	68 (7%)
4	441	35 (8%)
5	196	6 (3%)
≥6	92	10 (10%)

127 (52%) of FMTs were administered before Episode 3


FMTs: 106
< 2 Recurrences: 37
≥ 2 Recurrences: 69
Refractory: 12
Early: 9
Out of Catchment: 6
Other: 10


NON- RELEASED
CAUTION: New Drug –
Emory IRB #: 00090101
09 MAY 2019
09 MAY 2020
Lot #: 0519-02
NON- RELEASED
NON- RELEASED

Timing of FMT - Tradeoffs

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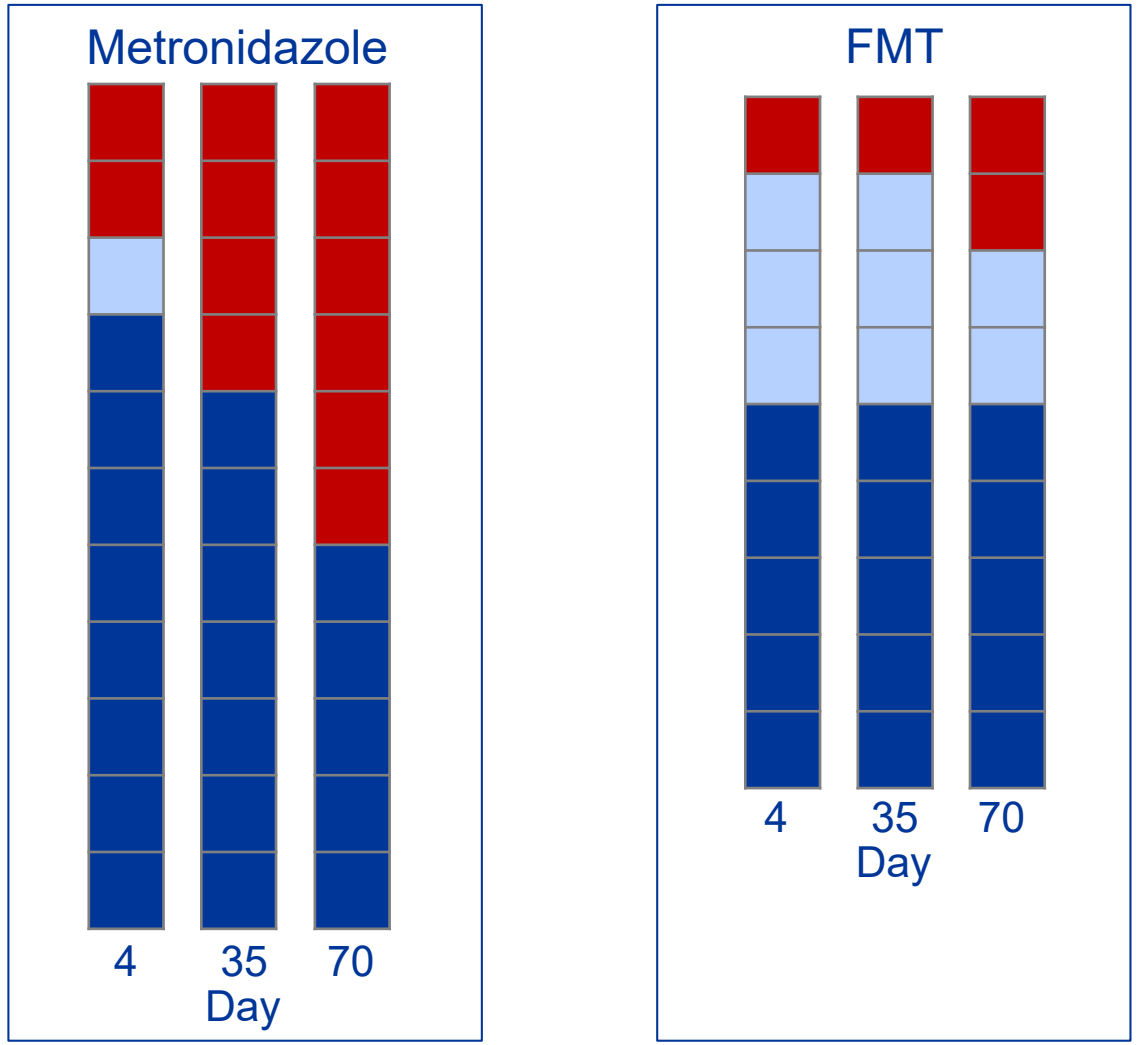
Recent data support considering FMT for primary CDI



Juul, F. NEJM. 2018; 378:2535-2536;

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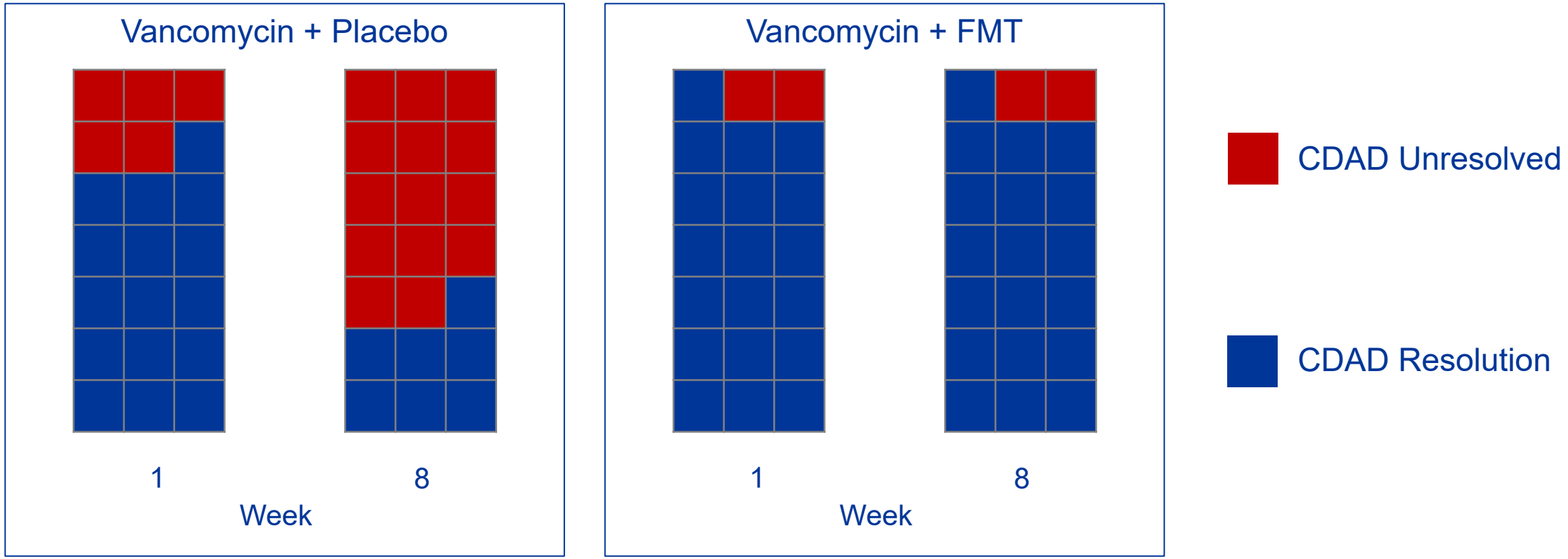


7/21, 33% Resolution at Week 8

19/21, 90% Resolution at Week 8

Braunwall, S. Lancet Gastroenterol Hepatol. 2022

What would be the most useful studies to determine the optimal time to administer FMT?

Number of CDI Episodes

Timing of repeat doses

CFUs administered

Conditioning with Antibiotics or Bowel Prep

Patient preferences

What would be the most useful study design to determine the optimal time to administer FMT?

Why participate in a clinical trial when the product is available?

Edward Jenner vaccinating a boy. Oil painting by E.-E. Hillemacher, 1884.

How can we accelerate the development of live biotherapeutic products?

Edward Jenner vaccinating a boy.
Oil painting by E.-E. Hillemacher, 1884.
CC BY 4.0, via Wikimedia Commons

Angeline Mitchell, RN…, prepares shots of the Moderna COVID-19 vaccine. 2021.
Public Domain, via Wikimedia Commons

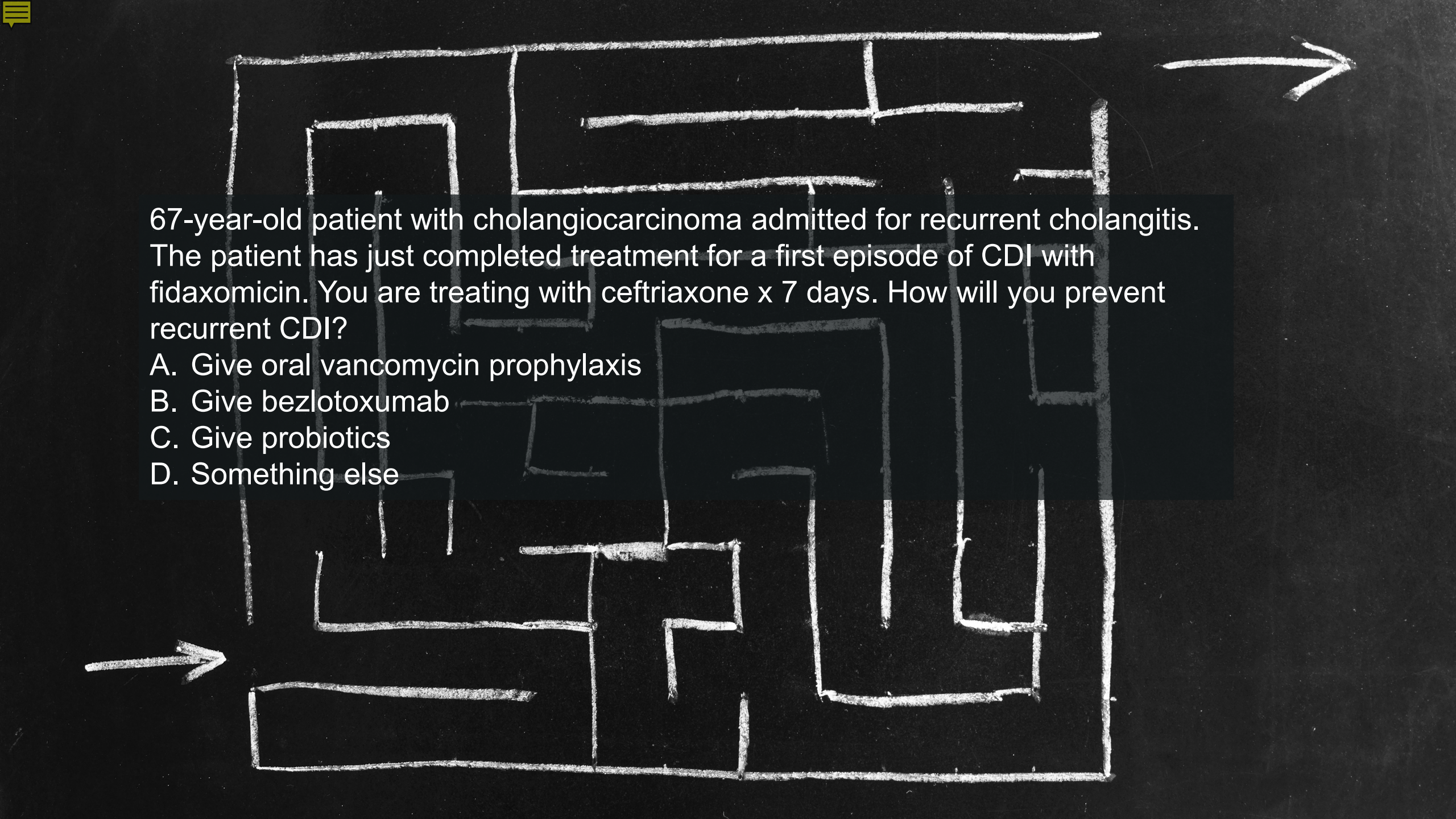
The number of dose optimization, patient preference, and operational questions may be best answered by a platform trial design.

At a minimum, we should expect data sharing and open science for microbiome trials

Case

- Two doses of Rebyota
- Good response after two doses
- Developed *Enterobacter* bacteremia treated with ciprofloxacin
- Developed recurrent diarrhea a month later
- Treated with an Emory manufactured FMT dose
- Improvement with one week of formed stools, then diarrhea
- Treated with an additional dose of Rebyota and discharged home
- Follow up: formed stools, gained 26 lb, feeling great

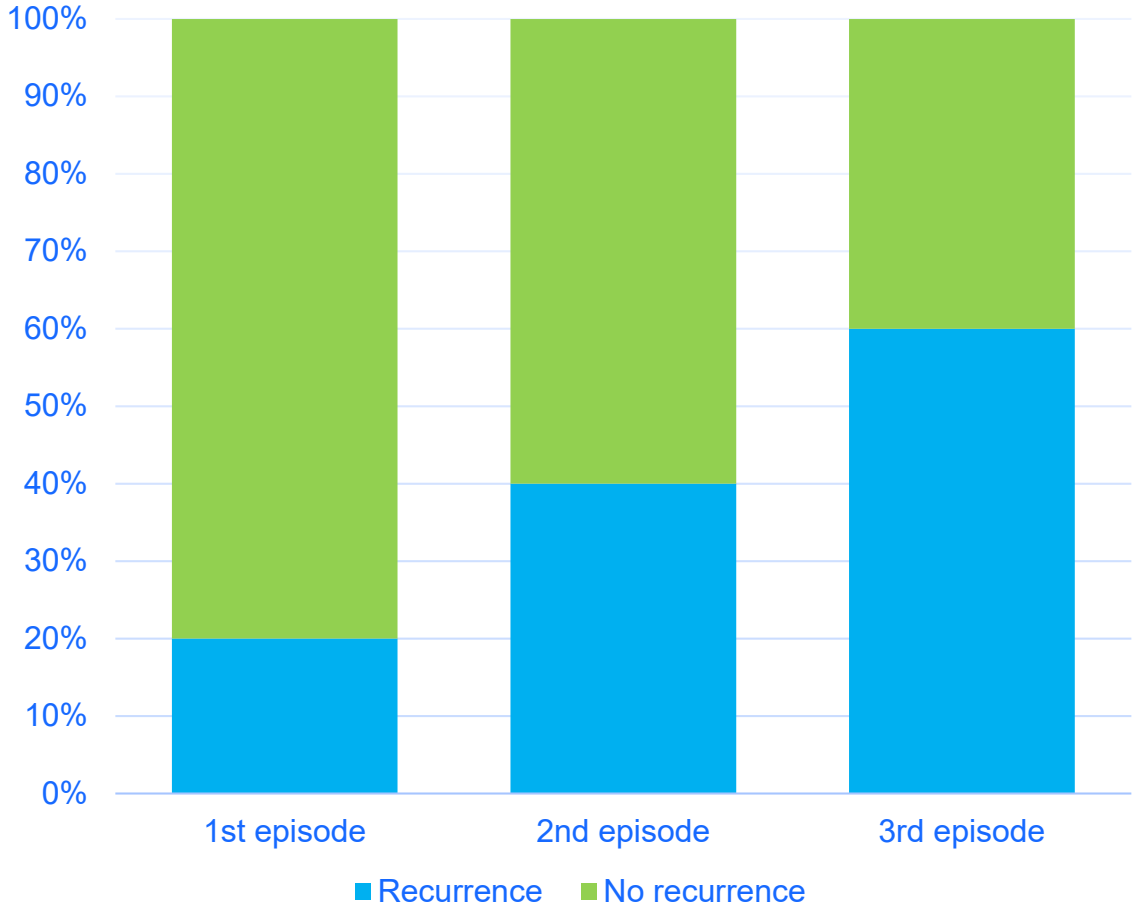
WHAT IS THE OPTIMAL STRATEGY FOR SECONDARY PREVENTION

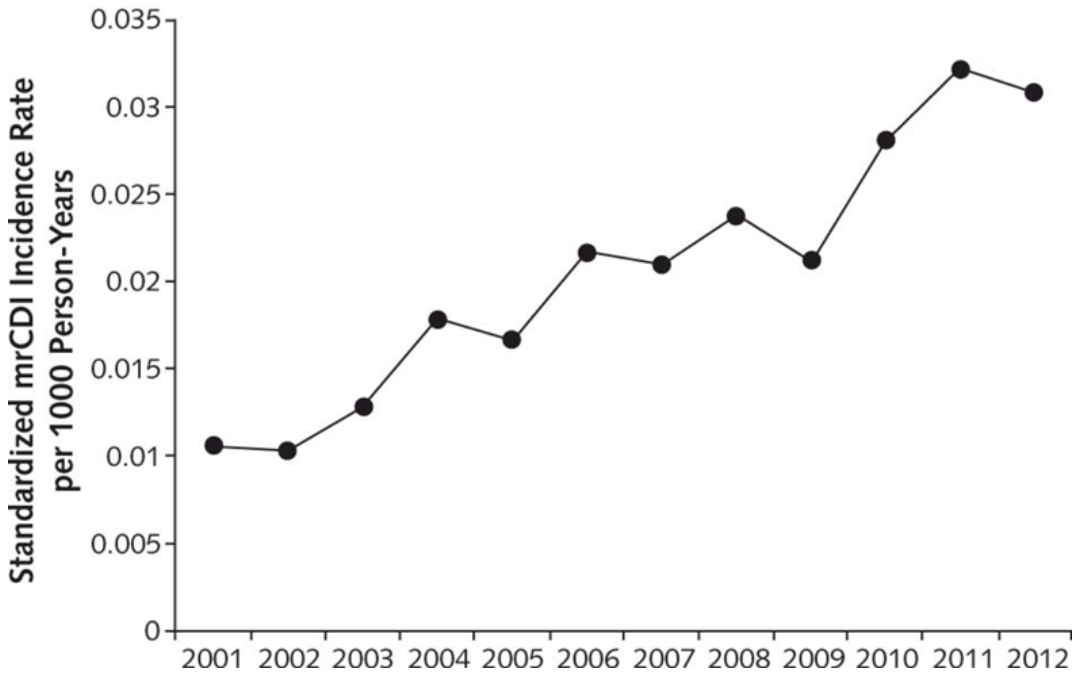


67-year-old patient with cholangiocarcinoma admitted for recurrent cholangitis. The patient has just completed treatment for a first episode of CDI with fidaxomicin. You are treating with ceftriaxone x 7 days. How will you prevent recurrent CDI?

A. Give oral vancomycin prophylaxis
B. Give bezlotoxumab
C. Give probiotics
D. Something else

Risk for recurrent CDI





Johnson S. J Infect 2009;58(6):403-10; Pepin J et al. Clin Infect Dis. 2005 Jun 1;40(11):1591-7; Ma GK et al. Ann Intern Med. 2017;167(3):152-158.

Antibiotics after CDI treatment are common

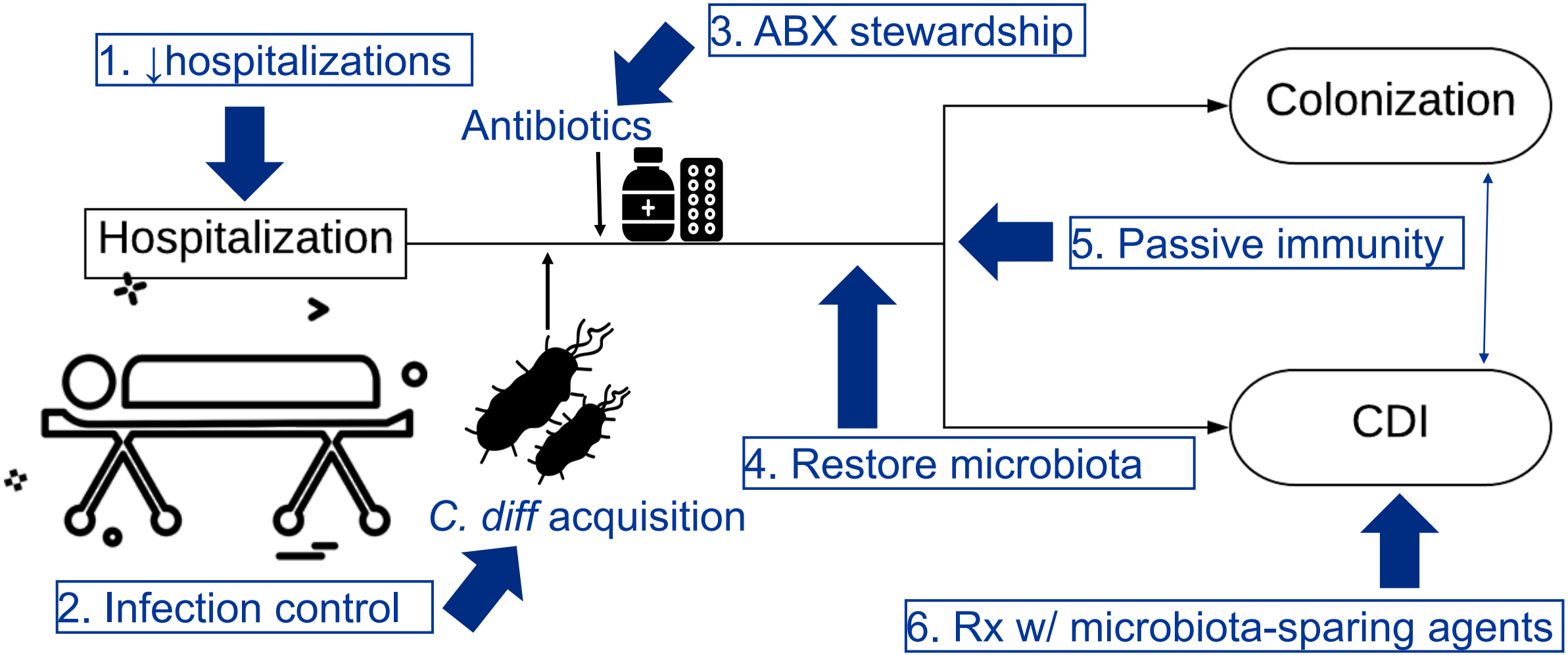
30-70% of patients with CDI receive concomitant or post-CDI treatment systemic antibiotics

Concomitant or subsequent antibiotic use ↑rCDI risk by **2-4x**

Concomitant antibiotics also decrease time to diarrhea resolution and lower cure rates

Garey KW et al. J Hosp Infect 2008; 70(4): 298-304; Deschpande A et al. ICHE 2015; 00(0): 1–9; Stevens VW et al. Infect Dis Ther 2016; 5(1):45-51; Harpe SE et al. Pharmacotherapy 2012; 32(8): 744-754; Mullane KM et al. Clin Infect Dis 2011; 53(5): 440-7

Approaches to prevent CDI



Adapted from Gerding D N , Johnson S. CID 2010;51:1306-1313

Decrease antibiotic pressure

Stop unnecessary antibiotics

Narrow therapy

Shorten courses

Stop unnecessary acid-suppressing agents

Treat with fidaxomicin

Subgroup analysis of 2 RCTs for FDX vs. VAN for primary CDI or rCDI[1]

27.5% received concomitant antibiotics during CDI treatment or 4-week follow-up

- Well-balanced between treatment assignments by spectrum and # of antibiotics

Receipt of CA resulted in:

- 8.9% ↓cure without relapse (2.5-15.4%)
- 43h longer time to resolution of diarrhea
- Differences even more pronounced for high-risk or multiple antibiotics

Outcomes by CDI treatment

	FDX	VAN	Difference
Cure	81/90 (90%)	81/102 (79%)	11% (0.2% to 20%)
Recurrence	15/89 (17%)	28/96 (29%)	-12% (-24% to -0.1%)

Should you extend or provide PO prophylaxis?

RCTs

- Open-label study of high-risk pts on systemic antibiotics randomized to PO VAN vs none: 0/50 (0%) vs. 6/50 (12%) with healthcare onset-CDI
- FDX for ppx in neutropenic pts on FQ did not meet 1º endpoint but confirmed CDI: 4.3% vs 10.7% (95% CI, 2.2% to 10.6%)
- Larger RCT expected to report results soon (http://clinicaltrials.gov/show/NCT03462459)

Observational studies

- Variable results. Most rigorous study did not demonstrate benefit except in those with only 1 prior episode. Meta-analysis showed benefit

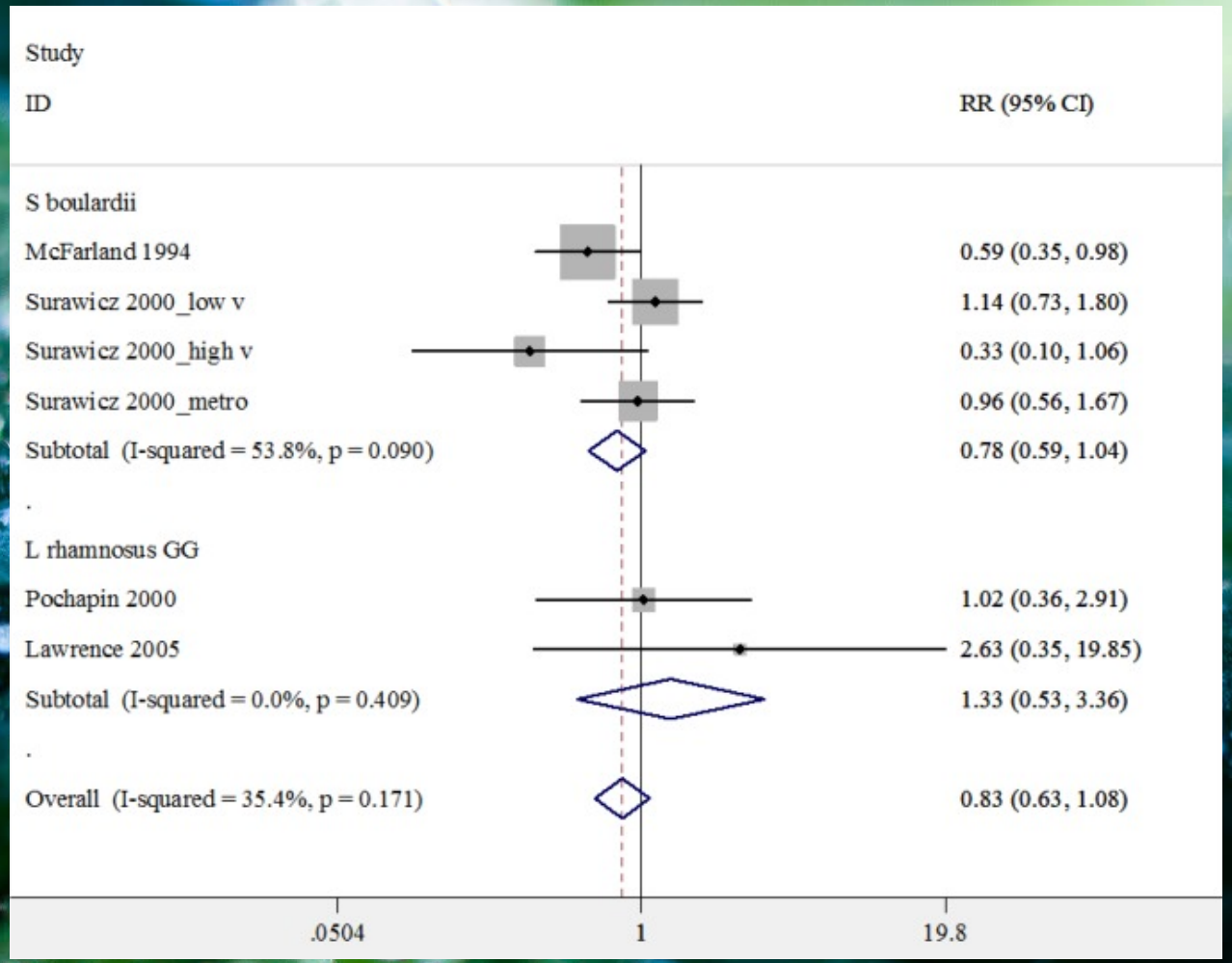
Bottom line

- Avoid for most, especially if using FDX since the benefit is to preserve the microbiome
- Consider if multiply recurrent, not candidate for FMT, or ongoing recurrences after FMT

Chang LL et al. NEJM 2023; 388: 654-656; Johnson SW et al. CID 2019:https://doi.org/10.1093/cid/ciz966; Caroff DA et al. Infect Control Hosp Epidemiol. 2019 Jun;40(6):662-667. doi: 10.1017; Mullane KM et al. Clin Infect Dis. 2019;68(2):196-203..

Probiotics for rCDI prevention

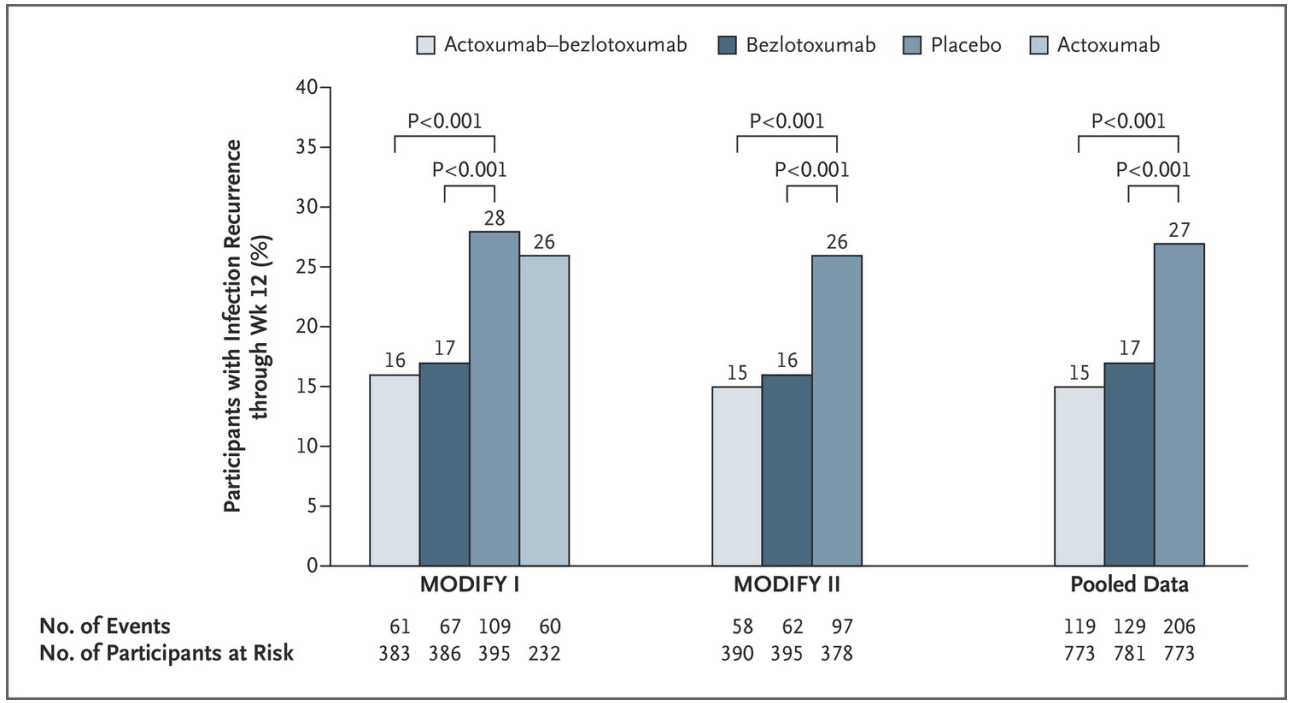
AGA: recommend against for 1° or 2° prevention; IDSA: insufficient evidence for 1° prevention, do not address 2°



McDonald LC CID 2018; Kelly C et al. The American Journal of Gastroenterology 2021; 6: 1124-27; McFarland LV Antibiotics 2015; 4(2): 160-178

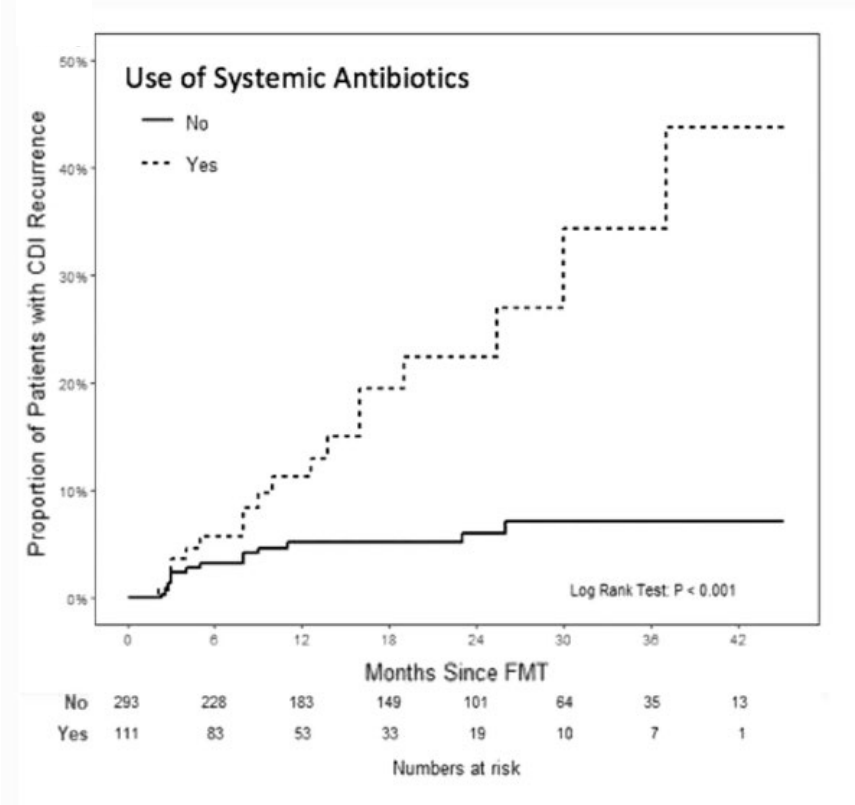
Monoclonal Abs for 2° prevention: MODIFY I and II

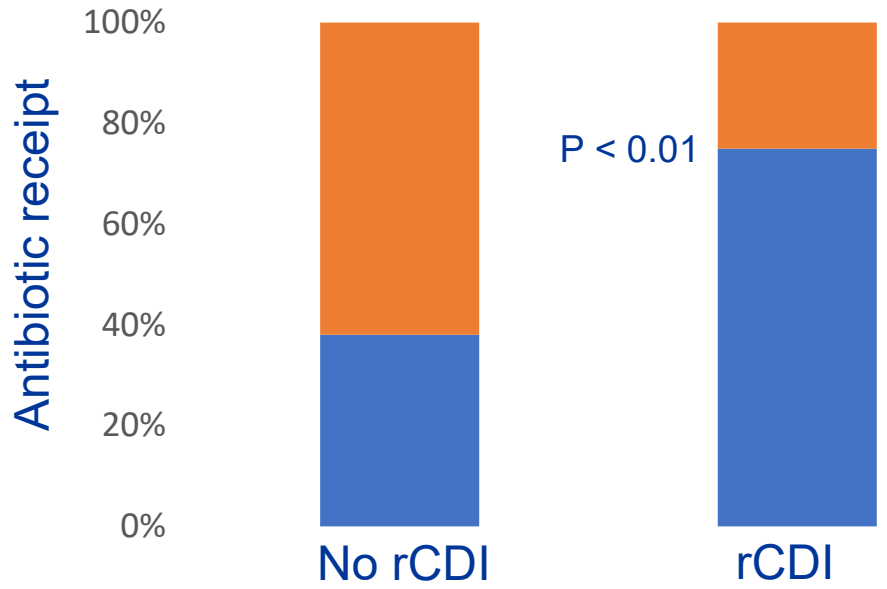
- **NNT = 10**
- Overall Δ sustained cure Bezlotux vs. SOC: 9.7% (4.8-14.5)
- 40% of patients received concomitant bx and 36% received post-rx abx
  - No formal subgroup analysis



"patients with a primary CDI episode and other risk factors for CDI recurrence… may particularly benefit from receiving bezlotoxumab" [after first episode]

Concomitant antibiotics confer risk for recurrence post FMT





Should repeat FMT or live biotherapeutic products be given at the end of antibiotic treatment?

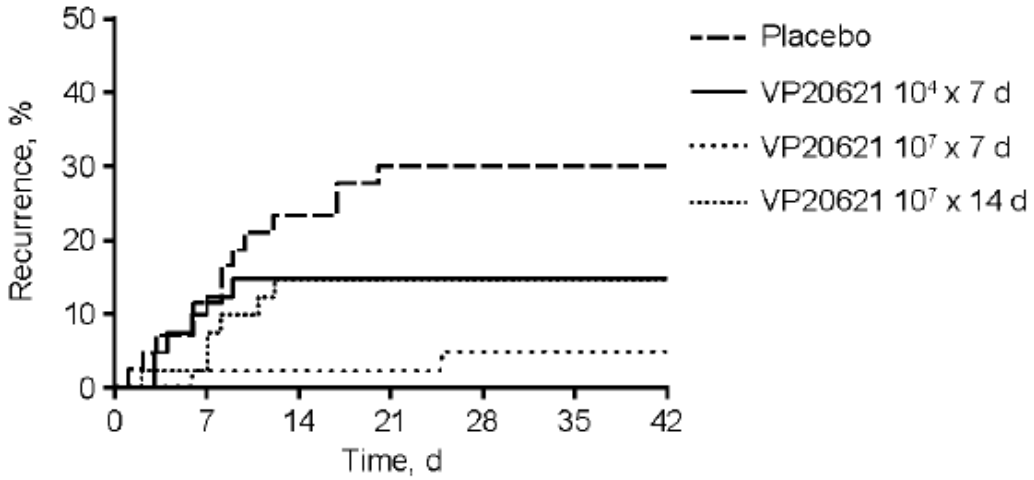
Allegretti JR et al. Dig Dis & Sci 2019; 64: 1668-1671; Saha S et al. Clin Infect Dis 2021; 73(7): e1706-e1712; Mamo Y et al. Clin Infect Dis. 2017. doi: 10.1093/cid/cix1097

Non-toxigenic C. diff for secondary prevention

- 173 patients with 1st or 2nd episode of CDI w/i 28 days (phase II)
  - 19% received additional antibiotics
  - 1-2 days after stopping CDI treatment randomized to non-toxigenic C diff (NTCD-M3) vs. placebo

Recurrence:

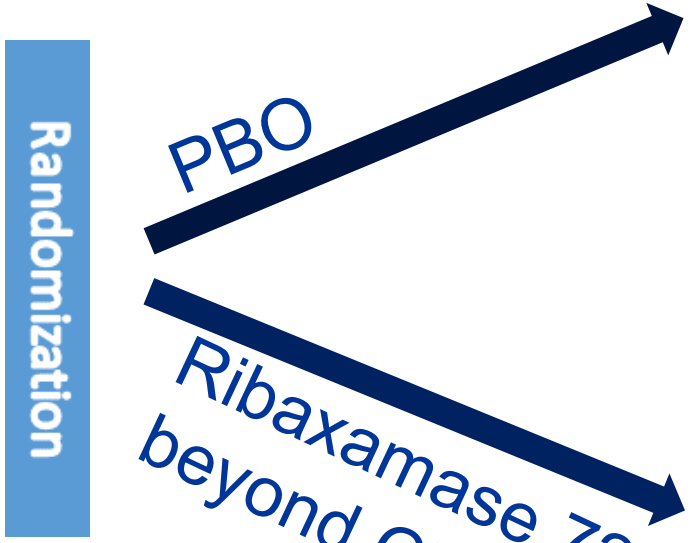
- OR 0.3; 95% CI, 0.1-0.7
- Of NTCD-M3 group, 2% for those colonized vs. 31% if not colonized
- **rCDI in the concomitant abx subgroup:**
  - **PBO: 4/8 (50%) vs.**
  - **All VP 20621: 2/25 (8%)**

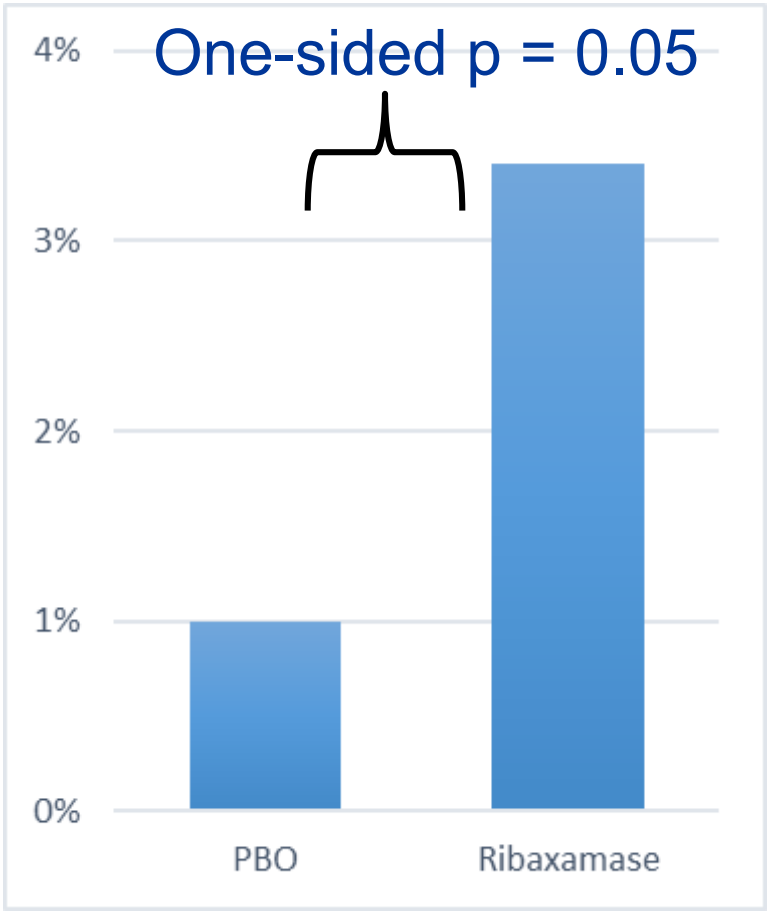


Ribaxamase

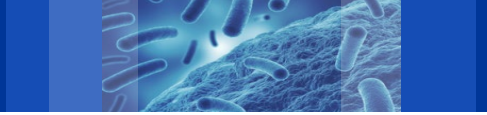
PO β-lactamase→degrade excess antibiotics in GI tract

CRO for LRTI
N = 413





Kokai-Kun JF et al. Lancet Infect Dis. 2019 May;19(5):487-496. doi: 10.1016/S1473-3099(18)30731-X



Why studies haven't answered this question

Subgroup analysis of RCT resulting in insufficient power (e.g. non-toxigenic strains, fidaxomicin)

Primary prevention (e.g. ribaximase)

Identification of risk only without intervention (e.g. FMT studies)

Observational studies with residual confounding (e.g. oral prophylaxis)

Have not examined marginal benefit of combined strategies

What would be the optimal study design to determine how to prevent rCDI in patients requiring more antibiotics?

- Include: Patients with current or recent CDI needing systemic antibiotics
- Initial treatment: fidaxomicin
- Double-blind RCT

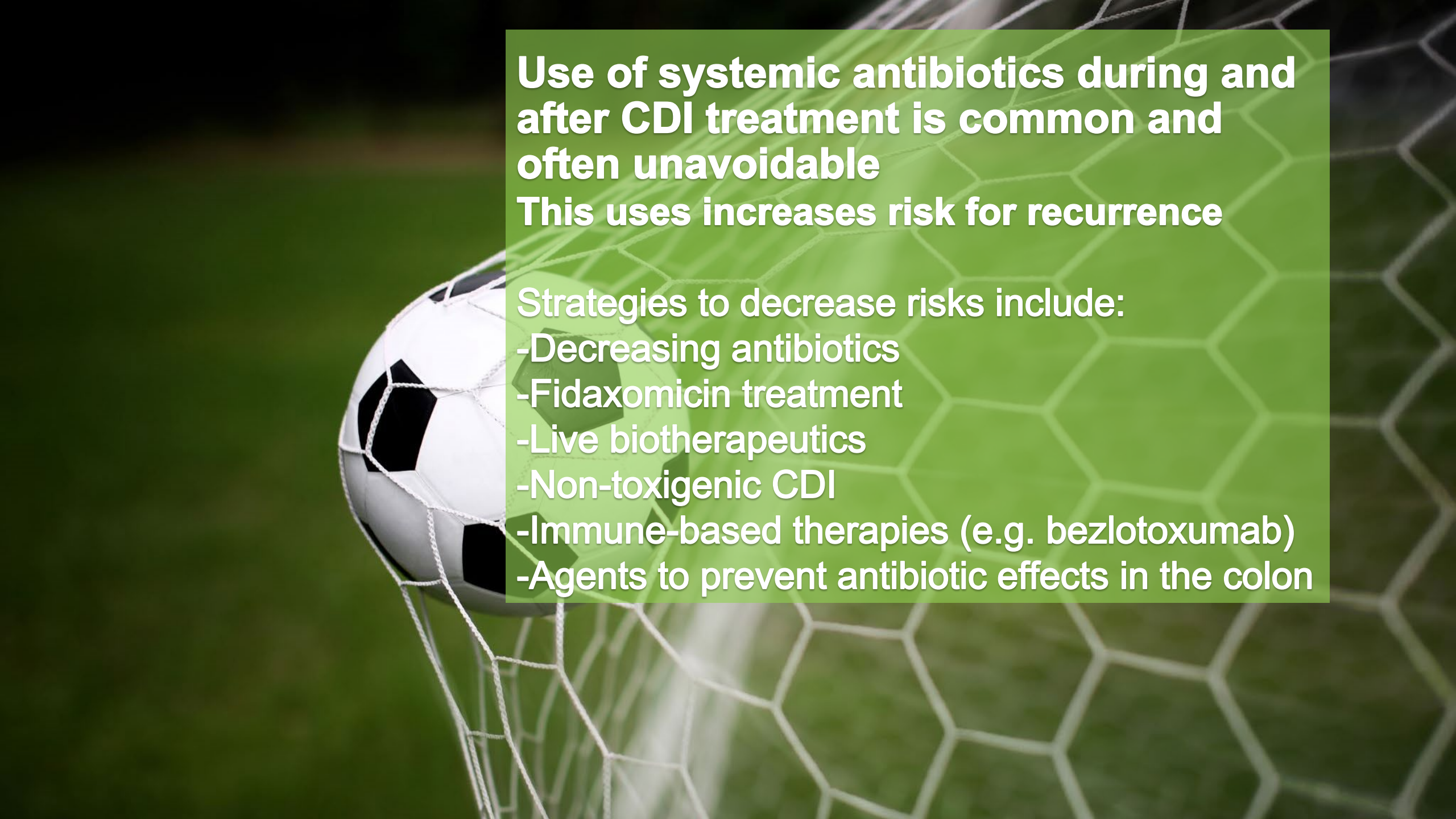
All +/- bezlotoxumab

Randomization

- FMT or live biotherapeutic post antibiotics
- Non-toxigenic *C. diff*
- Ribaxamase or colonic adsorbant
- CDI-directed oral antibiotics

Outcomes

- rCDI
- CDI complications
- Mortality
- Readmission
- Microbiome analysis



Use of systemic antibiotics during and after CDI treatment is common and often unavoidable

This uses increases risk for recurrence

Strategies to decrease risks include:

-Decreasing antibiotics

-Fidaxomicin treatment

-Live biotherapeutics

-Non-toxigenic CDI

-Immune-based therapies (e.g. bezlotoxumab)

-Agents to prevent antibiotic effects in the colon

IS IT TIME TO ADD LIVE BIOTHERAPEUTICS TO YOUR FORMULARY?

Will your institution (continue to) stock LBPs?

- A) Yes – we plan to provide the **Rebyota** rectal instillation
- B) Yes – but we are holding out for FDA review of **Seres capsules**
- C) Yes – we will continue to stock doses obtained through **OpenBiome**
- D) Yes – we will use product from an **in-house stool bank**
- E) No – the efficacy data are great but our pharmacists don't want it in the freezer.

** Please comment in the chat if you have other strategies to share for providing LBPs at your institution*

Drug Companies and Doctors Battle Over the Future of Fecal Transplants

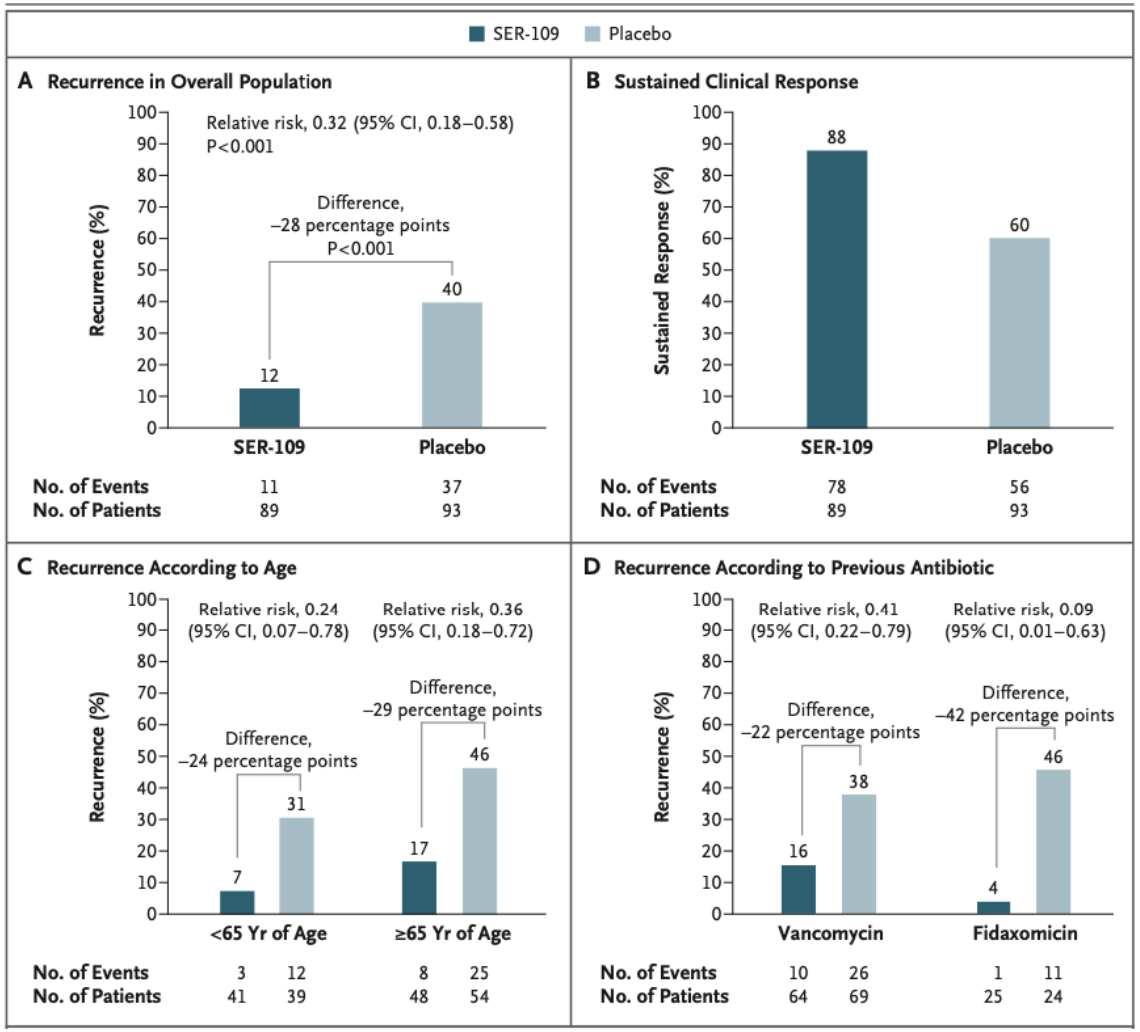
As pharmaceutical companies seek to profit from the curative wonders of human feces, doctors worry about new regulations, higher prices and patients attempting DIY cures.

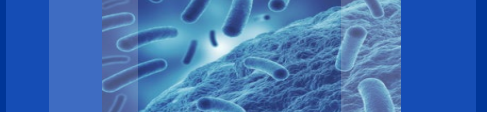
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

SER-109, an Oral Microbiome Therapy for Recurrent *Clostridioides difficile* Infection

Paul Feuerstadt, M.D., Thomas J. Louie, M.D., Bret Lashner, M.D., Elaine E.L. Wang, M.D., Liyang Diao, Ph.D., Jessica A. Bryant, Ph.D., Matthew Sims, M.D., Ph.D., Colleen S. Kraft, M.D., Stuart H. Cohen, M.D., Charles S. Berenson, M.D., Louis Y. Korman, M.D., Christopher B. Ford, Ph.D., Kevin D. Litcofsky, Ph.D., Mary-Jane Lombardo, Ph.D., Jennifer R. Wortman, M.Sc., Henry Wu, Ph.D., John G. Auniņš, Ph.D., Christopher W.J. McChalicher, B.Ch.E., Jonathan A. Winkler, Ph.D., Barbara H. McGovern, M.D., Michele Trucksis, M.D., Ph.D., Matthew R. Henn, Ph.D., and Lisa von Moltke, M.D.

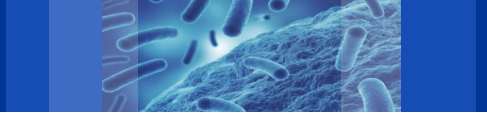

SER-109
Placebo
A Recurrence in Overall Population
Relative risk, 0.32 (95% CI, 0.18–0.58)
P<0.001
Difference,
–28 percentage points
P<0.001
Recurrence (%)
12
40
SER-109
Placebo
No. of Events 11 37
No. of Patients 89 93
B Sustained Clinical Response
Sustained Response (%)
88
60
SER-109
Placebo
No. of Events 78 56
No. of Patients 89 93
C Recurrence According to Age
Relative risk, 0.24
(95% CI, 0.07–0.78)
Relative risk, 0.36
(95% CI, 0.18–0.72)
Difference,
–24 percentage points
Difference,
–29 percentage points
Recurrence (%)
7
31
17
46
<65 Yr of Age
≥65 Yr of Age
No. of Events 3 12 8 25
No. of Patients 41 39 48 54
D Recurrence According to Previous Antibiotic
Relative risk, 0.41
(95% CI, 0.22–0.79)
Relative risk, 0.09
(95% CI, 0.01–0.63)
Difference,
–22 percentage points
Difference,
–42 percentage points
Recurrence (%)
16
38
4
46
Vancomycin
Fidaxomicin
No. of Events 10 26 1 11
No. of Patients 64 69 25 24



FDA NEWS RELEASE

FDA Approves First Fecal Microbiota Product

Rebyota Approved for the Prevention of Recurrence of Clostridioides difficile Infection in Adults



GUIDANCE DOCUMENT

Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation to Treat Clostridium difficile Infection Not Responsive to Standard Therapies

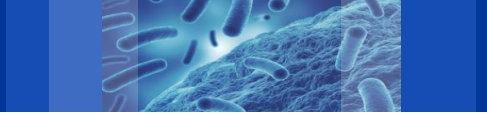
Guidance for Industry

NOVEMBER 2022

Download the Final Guidance Document | Read the Federal Register Notice

Final

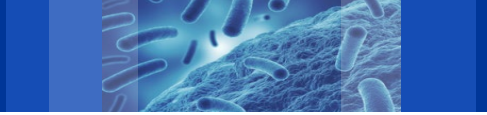
https://www.imdb.com/title/tt0101962/mediaviewer/rm1071815425



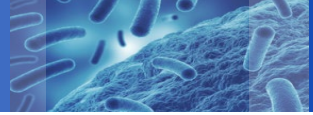
Finch to lay off 95% of staff, scrap microbiome drug study

The company blamed a range of factors in its decision, including limited funding, slower-than-anticipated trial enrollment and "broader sector trends."

Published Jan. 24, 2023



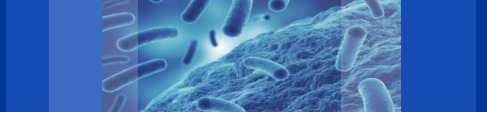
	Regulatory Status	Formulation	Cost
Rebiotix Microbiota Restoration Therapy A FERRING COMPANY	**FDA Approved**	Rectal instillation (enema)	$9,000 / dose
SERES THERAPEUTICS	FDA Review Scheduled 4/2023	Capsule	?
OPENBIOME	Pivoted to Descriptive Research, Distributing UMN Product	Instillation / Capsule (previously)	$1695 / dose + $150 shipping
FINCH	Focusing on IP	Capsule	N/A
	Focusing on non-profit provision of microbiota	Instillation / Capsule	No patient cost



LBPs on Formulary? - Unresolved Gaps

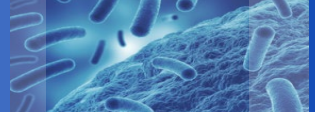
- Best practices to anticipate retreatment frequency and costs?
- Reimbursement challenges for outpatient treatment
- Need for diagnostics that accurately classify risk of recurrence and colonization resistance to support LBP stewardship

RUNNER-UP CONTROVERSIES



Several *C. difficile* controversies remain unresolved

Controversy
What is the optimal strategy for primary prevention of CDI?
Does strain of CDI matter anymore?
Can you give anti-peristaltic agents for patients with CDI?
What is the optimal treatment strategy for patients with fulminant CDI? Should we use FDX or FMT?
Does stopping acid suppressive medications improve outcomes for patients with CDI?
Should fidaxomicin be dosed with a taper?
Is diverting loop ileostomy preferred to subtotal colectomy for fulminant CDI?
Can live biotherapeutic products be used for other recurrent infections?
What management strategy leads to the best QoL in patients with CDI?
How can we get insurance to reimburse for evidence-backed strategies?



QUESTIONS?