Controversies in *Clostridioides difficile*

Diagnosis & Management & Prevention

ASC-SC Statewide Meeting

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4 May 2026

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Disclosures

No financial relationships to disclose.

Clinical recommendations in this presentation are evidence-based and free of commercial bias.

Views expressed are my own and do not reflect the infection prevention or antimicrobial stewardship policies of the Medical University of South Carolina.

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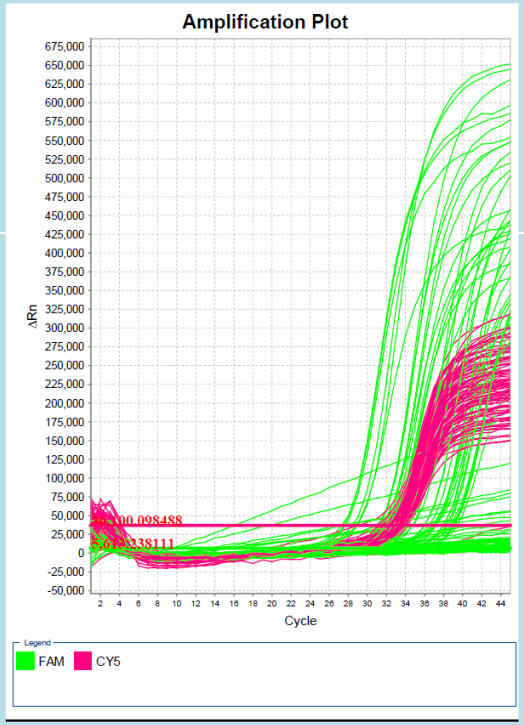
Objectives

1. Describe C. difficile metrics utilized by antimicrobial stewardship and infection control programs
2. Assess the pros and cons of various C. difficile laboratory diagnostic stewardship maneuvers
3. Identify strengths and weaknesses of current algorithms for the treatment of C. difficile, including fecal microbiota therapy
4. Evaluate infection prevention strategies for C. difficile, including the role of the asymptomatic reservoir and considerations for screening in hospital settings

"Discordant?"

How should you benchmark *C. difficile?* How do you diagnose *C. difficile?*



Photos and Figure provided by faculty

NHSN LabID Surveillance

Healthcare-facility-onset (HO) CDI defined as

- Specimen positive for *C. difficile* toxin
- Specimen collected on or after 4th hospital calendar day
- No prior positives within 14-56 days

Minimizes work for surveillance (no chart review)

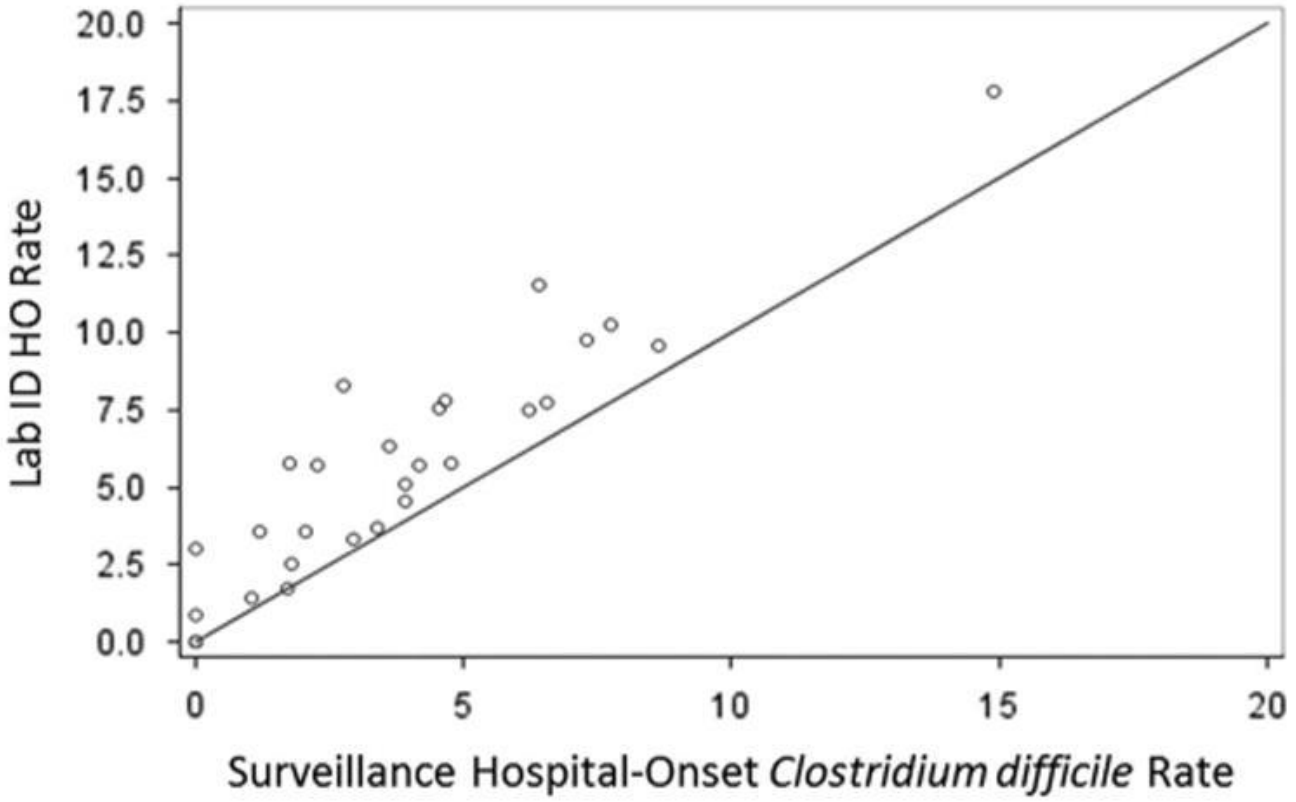
HO-HCFA CDI rate now used in public reporting

Hospital Day	HAI GI-CDI Surveillance	CDI LabID Event Reporting
-2	POA	Does not apply
-1	POA	Does not apply
Day 1 (Admission)	POA	CO
Day 2	POA	CO
Day 3	**HAI**	CO
Day 4	**HAI**	**HO**

https://www.cdc.gov/nhsn/faqs/faq-mdro-cdi.html#q10

Laboratory Surveillance for CDI

PROS	CONS
Minimizes work of surveillance	May encourage empiric treatment without testing
60-80% agreement with clinical review of symptom onset	20% of cases mis-classified as hospital-onset CDI (delayed testing)
Facilitates comparison between facilities	Inflates rates of facilities with poor test stewardship (laxatives)
Objective	Inaccurate



Gase KA et al. *Infect Control Hosp Epidemiol.* 2013 Mar;34(3):284-90
Albert K et al. *Am J Infect Control*. 2018 Sep;46(9):998-1002
Durkin MJ et al. *Infect Control Hosp Epidemiol*. 2015 Feb;36(2):125-31

Gaming the System: NHSN 2018=last test done

- NHSN adopted last test done rule in 2018
  - PCR+/EIA- is not a labID event
- Multiple centers adopted “flipped 2-step” algorithms nationwide in centers that adopted standalone NAATs
- SIRs drop dramatically (ratio of observed cases over cases predicted by NHSN model)
- Treatment of PCR+/EIA- patients (IDWeek 2019)
  - Cleveland Clinic 89%
  - Reknown Health (Reno, NV) 72%
  - University of KY 28%
  - University of Maryland 47%

Multi-step Testing Same Specimen	Testing Step	Testing Method	Documented Findings	Eligible LabID Event?
Example A	Test 1 @ 1p	NAAT	Negative	**Yes**
	Test 2 @ 1p	GDH	Positive	
Last test →	Test 3 @ 2p	EIA	**Positive**	
Example B	Test 1 @ 1p	NAAT	Positive	No
	Test 2 @ 1p	GDH	Positive	
Last test →	Test 3 @ 2p	EIA	Negative	
Example C	Test 1 @1p	GDH	Positive	**Yes**
	Test 2 @1p	EIA	Negative	
Last test →	Test 3 @2p	NAAT	**Positive**	
Example D	Test 1 @ 1p	GDH	Positive	No
	Test 2 @1p	EIA	Positive	
Last test →	Test 3 @ 3p	NAAT	Negative	

https://www.cdc.gov/nhsn/pdfs/pscmanual/12pscmdro_cdadcurrent.pdf

Impact of switching from NAAT to NAAT→EIA on CDI Incidence at 129 VA facilities

Mean infection rate for facilities using NAAT+EIA (1.91 per 10,000 patient days) was 64% lower than the average rate for facilities using NAAT alone (5.24 per 10,000 patient days)

McCauley BP, Evans ME, et al. *ICHE* 42(4):461–463, 2021.

Clinical impact of switching CDI test methodology to EIA alone: Is it safe?

Research

Original Investigation

Overdiagnosis of *Clostridium difficile* Infection in the Molecular Test Era

Christopher R. Polage, MD, MAS; Clare E. Gyorke, BS; Michael A. Kennedy, BS; Jhansi L. Leslie, BS; David L. Chin, PhD; Susan Wang, BS; Hien H. Nguyen, MD, MAS; Bin Huang, MD, PhD; Yi-Wei Tang, MD, PhD; Lenora W. Lee, MD; Kyoungmi Kim, PhD; Sandra Taylor, PhD; Patrick S. Romano, MD, MPH; Edward A. Panacek, MD, MPH; Parker B. Goodell, BS, MPH; Jay V. Solnick, MD, PhD; Stuart H. Cohen, MD

Invited Commentary

- "**OBJECTIVE** To determine the natural history and need for treatment of patients who are toxin immunoassay negative and polymerase chain reaction (PCR) positive (Tox−/PCR+) for CDI"

PCR+/EIA- patients do OK (sort of)

Table 3. Nondiarrheal Outcomes and Treatment by *Clostridium difficile* Test Group

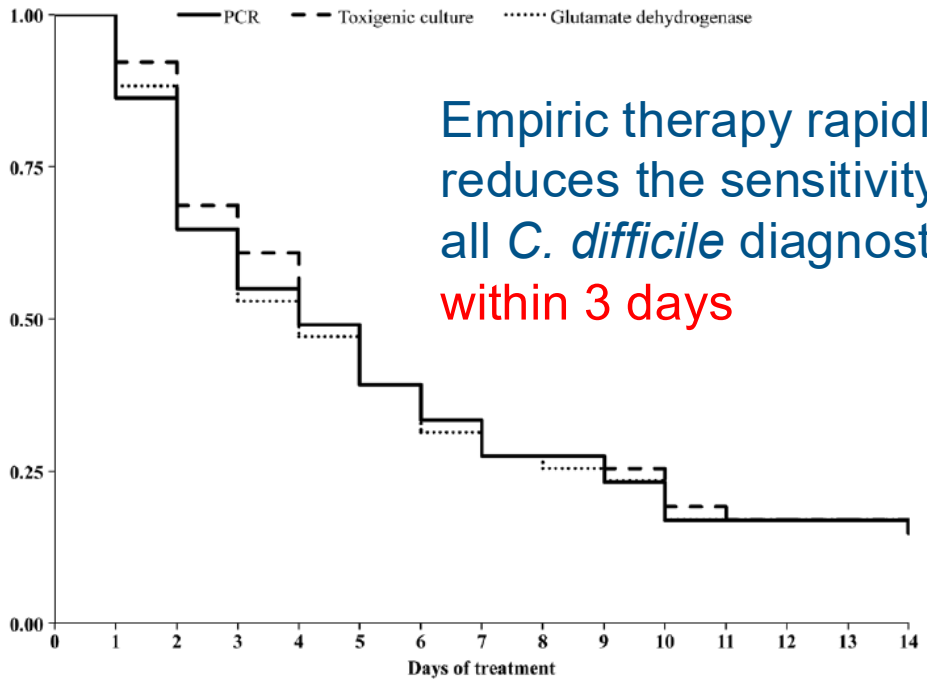
Outcome	*C difficile* Positive		*C difficile* Negative	
	Tox+/PCR+ (n = 131)	Tox−/PCR+ (n = 162)	Tox−/PCR− (n = 1123)	*P* Value[a]
***C difficile*-Related Complication or Death Within 30 d, No. (%)**				
Complication[b]	10 (7.6)	0	3 (0.3)	<.001
Death[c]	11 (8.4)	1 (0.6)	0	<.001
Complication or death	18 (13.7)	1 (0.6)	3 (0.3)	<.001
Repeat *C difficile* Testing Within 14 d, No. (%)				
Retested	14 (10.7)	61 (37.7)	374 (33.3)	<.001
Positive toxin test result	3 (2.3)	13 (8.0)	17 (1.5)	<.001
Repeat *C difficile* Testing at 15-30 d, No. (%)				
Tested	26 (19.8)	18 (11.1)	106 (9.4)	.001
Positive toxin test result	14 (10.7)	5 (3.1)	10 (0.9)	<.001
Treatment Within 14 d				
Metronidazole or oral vancomycin, No. (%)[d]	131 (100)	66 (40.7)	361 (32.1)	<.001
Duration of metronidazole or oral vancomycin, if treated, median (IQR), d	14 (11-14)	6 (3-11)	5 (2-9)	<.001
Non-*C difficile* antibiotic, No. (%)	98 (74.8)	141 (87.0)	912 (81.2)	.03
Duration of non-*C difficile* antibiotic, if treated, median (IQR), d	11 (3-14)	10 (4-14)	10 (4-14)	.13
Treatment at 15-30 d				
Metronidazole or oral vancomycin, No. (%)	75 (57.3)	35 (21.6)	137 (12.2)	<.001
Duration of metronidazole or oral vancomycin, if treated, median (IQR), d	9 (3-14)	4 (3-15)	6 (3-9)	<.001

Polage CR, et al. *JAMA Intern Med*. 2015;175(11):1792-801

Confounding effect of empiric treatment? Is there misclassification bias?

Table 1. Baseline Characteristics of the Study Population by *Clostridium difficile* Test Group

Characteristic	*C difficile* Positive		*C difficile* Negative	*P* Value[a]
	Tox+/PCR+[b] (n = 131)	Tox−/PCR+[b,c] (n = 162)	Tox−/PCR−[b,d] (n = 1123)	
Age, median (IQR), y	64 (52-71)	58 (48-68)	59 (47-71)	.12
Female sex, No. (%)	64 (48.9)	83 (51.2)	530 (47.2)	.61
Comorbidities, median (IQR)	4 (2-6)	4 (2-5)	3 (2-5)	.01
APR-DRG risk of mortality subclass 3 or 4, No. (%)	104 (79.4)	128 (79.0)	787 (70.1)	.008
Intensive care unit care on day 1 ±1 d, No. (%)[e]	30 (22.9)	57 (35.2)	435 (38.7)	.002
Hospital days before day 1, median (IQR)[e]	10 (6-24)	8 (5-12)	8 (5-12)	<.001
Admitted from health care facility, No. (%)	40 (30.5)	34 (21.0)	160 (14.2)	<.001
C difficile positive within 90 d before day 1[e]	5 (3.8)	10 (6.2)	13 (1.2)	<.001
Antibiotic days within 90 d before day 1, median (IQR)[e]	16 (7-32)	10 (4-27)	8 (4-18)	<.001
Other diarrheal or gastrointestinal inflammatory process, No. (%)[f]	8 (6.1)	27 (16.7)	161 (14.3)	.02
Metronidazole or oral vancomycin within 48 h before day 1, No. (%)[e]	3 (2.3)	32 (19.8)	184 (16.4)	<.001



Empiric therapy rapidly reduces the sensitivity of all *C. difficile* diagnostics within 3 days

Polage CR, et al. *JAMA Intern Med*. 2015;175(11):1792-801
Sunkesula VC et al. *Clin Infect Dis*. 2013;57:494-500

What happens if you choose to focus on diagnostic testing stewardship instead of infection prevention?

HYPOTHESIS: Too much testing inflates CDI incidence (CO and HO) because of asymptomatic carriers.

COROLLARY: CDI doesn't exist if you don't test for it.

The Just Say No Hypothesis

The following patient groups should not be tested for *C. difficile* (??):

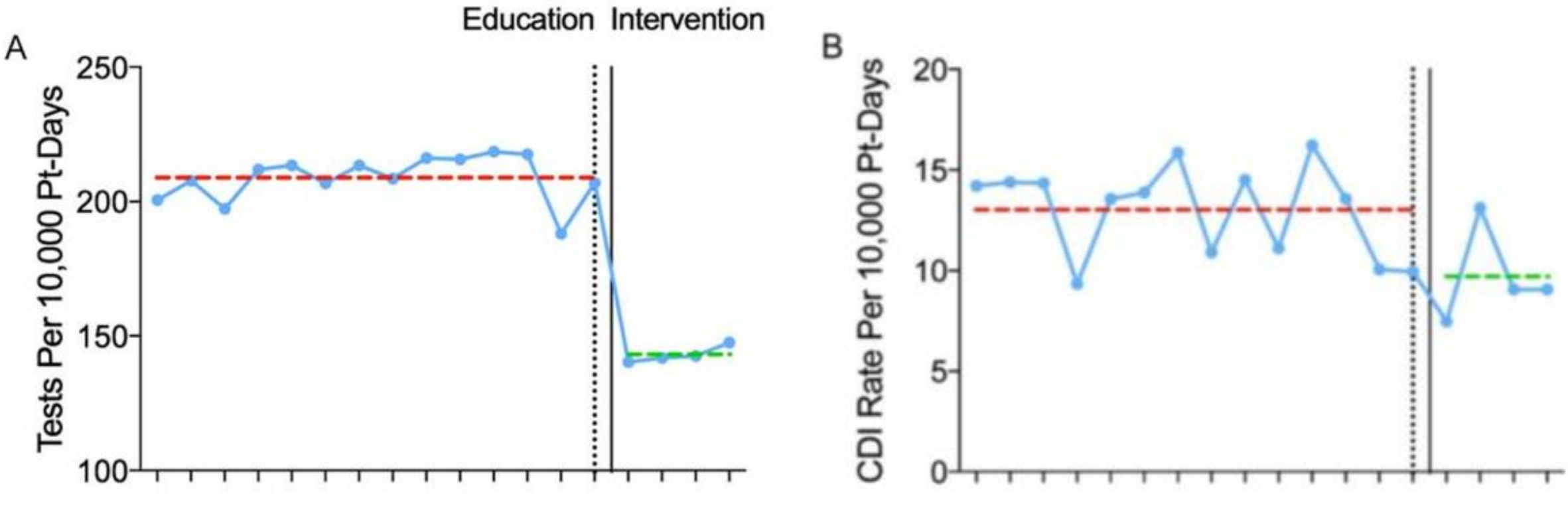
- Patients with inflammatory bowel disease
- Patients who have received laxatives within 48 hours
- Patients getting other drugs known to cause diarrhea (cancer chemotherapy)
- Patients without diarrhea

Populations at exceptional CDI Risk

Population	setting	Incidence (%)	Ref
ulcerative colitis	US (NIS)	3.73	1
Crohn's disease	US (NIS)	1.09	1
solid organ transplant	US (NIS)	2.7	2
solid organ transplant	Quebec, CA	12.4	3
lung transplant	Pittsburgh, PA	17.1	4
liver transplant	Pittsburgh, PA	11.9	4
allogeneic BMT	US (NIS)	8.4	5

1. Nguyen *Am J Gastroenterol.* 2008 Jun;103(6):1443-50
2. Pant et al. *Transpl Infect Dis*. 2012 Oct;14(5):540-7
3. Boutros et al. *Transplantation*. 2012 May 27;93(10):1051-7
4. Hong Nguyen, UPMC, personal communication
5. Guddati AK et al. Int J Hematol 2014 Jun; 99(6):758-65.

Effect of a laxative hard-stop to CDI orders



Truong CY et al. *J Clin Microbiol*. 2017 May;55(5):1276-1284.

Laxative use does not preclude diagnosis or reduce disease severity in *Clostridioides difficile* infection

Outcome	Laxatives within 48 hours (n=65)	No laxatives within 48 hours (n=144)	P-value
Severe CDI by IDSA-SHEA	43 (66%)	81 (56%)	0.224
Composite attributable outcomes (ICU admission, colectomy, death within 40 days)	7 (11%)	13 (9.0%)	0.800
CDI attributable mortality	1 (1.5%)	4 (2.8%)	0.659
Colectomy	1 (1.5%)	1 (0.7%)	0.526
CDI recurrence within 30 days	2 (3.1%)	8 (5.6%)	0.728

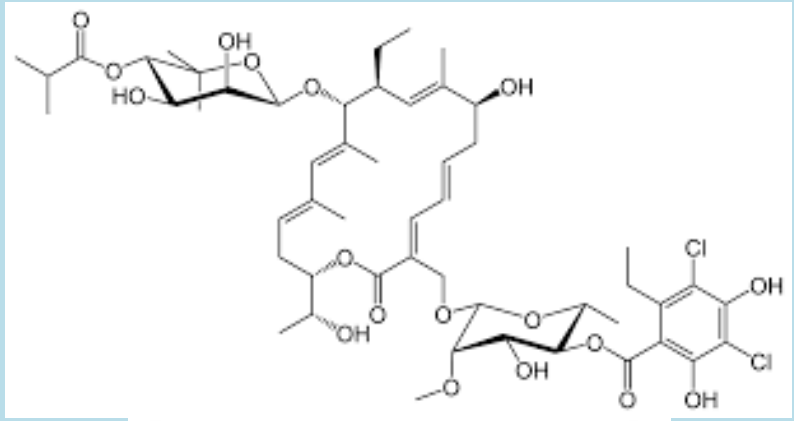
White NC. *Clin Infect Dis*. 2020 Sep 12;71(6):1472-1478.

Should I treat a patient with PCR+/EIA- *C. difficile* testing (discordant)?

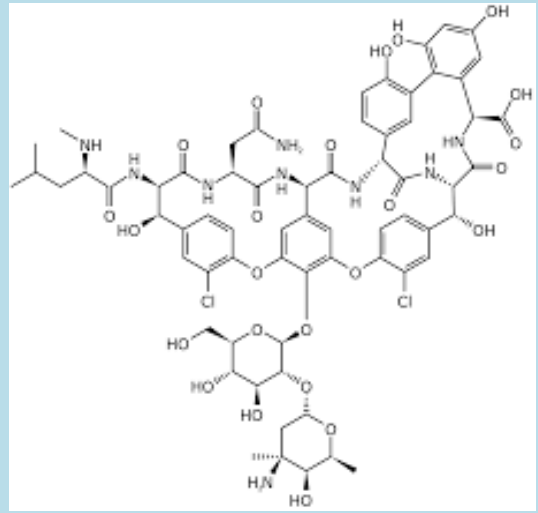
The clinical laboratory can place the perpetrator (*C. difficile*) and weapon (toxin B) at the scene of the crime, but only the clinician can establish whether a crime (CDI) has taken place.

--Ferric Fang

J Clin Microbiol. 2010 Dec; 48(12): 4347–4353



(fidaxomicin)
tablets 200 mg
oral suspension 200 mg/5 ml



"What's in your (inpatient pharmacy's) wallet?"

What is the preferred medical management for CDI?

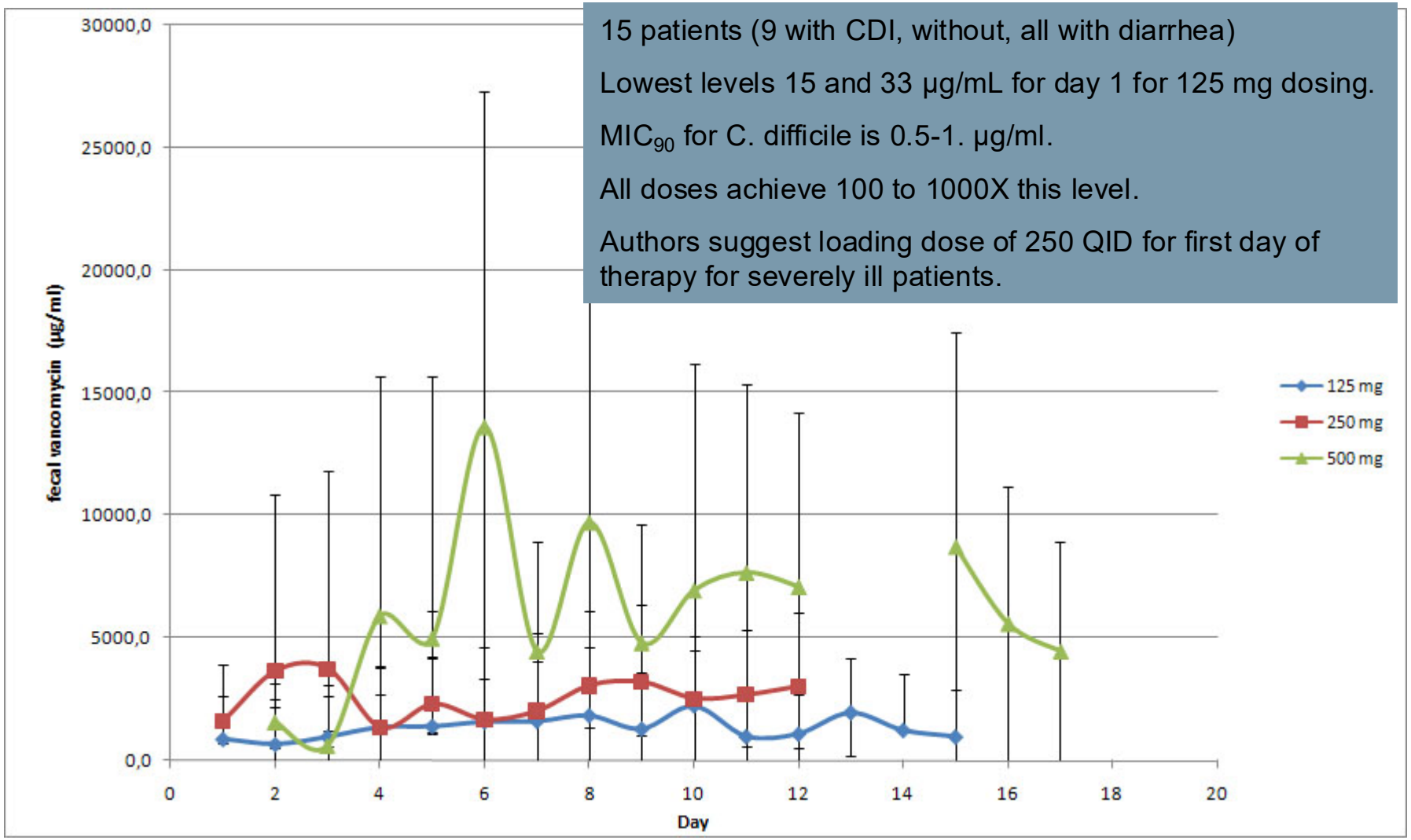
Available antimicrobial treatments 2026

Drug (brand)	FDA Indication	Adult Dosing	Target	Cost per course
vancomycin (Vancocin) (Firvanq)	CDI	125 mg PO QID x 10 days	Cell wall	$37 (capsules) $140 (liquid)
fidaxomicin (Dificid)	CDI	200 mg PO BID x 10 days	RNA polymerase	$2,425
Metronidazole (off-label)	Anaerobic infections	500 mg PO TID (IV in severe dz)	Prodrug→ Bacterial DNA	$8.70 (generic PO)

2026 cost differential per course in US dollars vancomycin : fidaxomicin 1 : 65

Prices as of 5/1/2026 on goodrx.com

Fecal levels with vancomycin: > 125 mg PO QID = $$$ down the toilet



15 patients (9 with CDI, without, all with diarrhea)

Lowest levels 15 and 33 µg/mL for day 1 for 125 mg dosing.

MIC_{90} for C. difficile is 0.5-1. µg/ml.

All doses achieve 100 to 1000X this level.

Authors suggest loading dose of 250 QID for first day of therapy for severely ill patients.

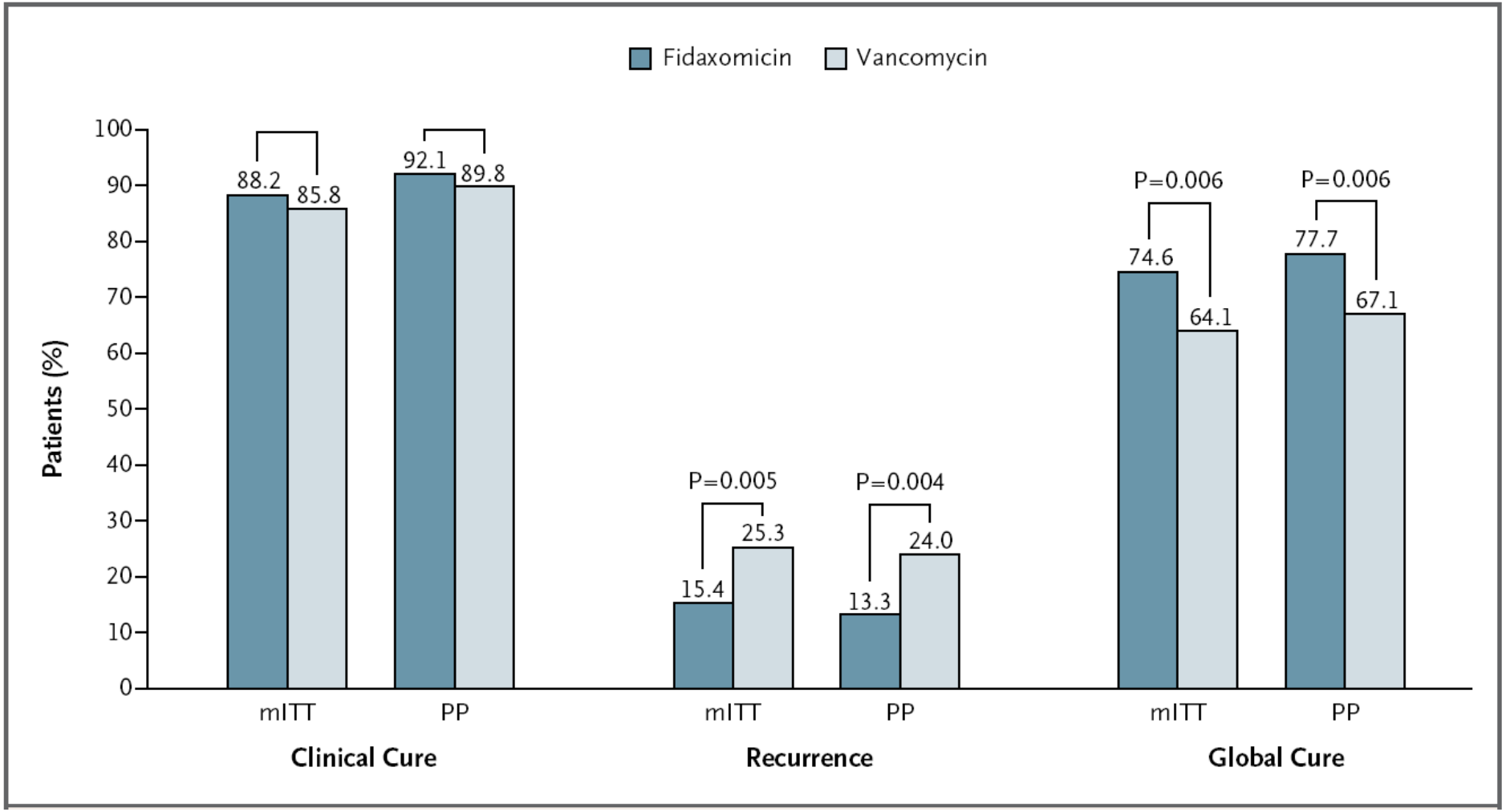
Gonazales M et al. *BMC Infect Dis* 2010. 10:363

The Evolution of IDSA/SHEA Treatment Guidelines

	2018 Guidelines	2021 Focused Guideline Update
Initial episode, non-severe	• Vancomycin 125 QID x 10 days • Fidaxomicin 200 BID x 10 days	• Fidaxomicin 200 BID x 10 days • Vancomycin 125 QID x 10 days
Initial episode, severe	• Vancomycin 125 QID x 10 days • Fidaxomicin 200 BID x 10 days	
Initial episode, fulminant	• Vancomycin 500 QID + • IV metronidazole 500 Q8+ • Rectal vancomycin	
1st recurrence	• Pulsed or tapered vancomycin • Fidaxomicin 200 BID x 10 days	• Fidaxomicin 200 BID x 10 days or 200 BID x 5 days followed by QOD x 20 days • Tapered or pulsed vancomycin • Adjunctive bezlotoxumab
2nd or subsequent recurrence	• Pulsed or tapered vancomycin • Vancomycin 125 QID x 10 days followed by rifaximin 400 TID x 20 days • Fidaxomicin 200 BID x 10 days • Fecal microbiota transplantation	Above + • Vancomycin 125 QID x 10 days followed by rifaximin 400 TID x 20 days • Fecal microbiota transplantation

McDonald LC, Gerding DN et al. *Clin Inf Dis* 2018; 66(7):e1-e48
https://www.idsociety.org/globalassets/idsa/practice-guidelines/cdi-2021-focused-update.pdf

Recurrence observed with fidaxomicin therapy (28 days from end of tx)



Louie et al. *N Engl J Med* 364 (5):422-431, 2011.

Do relapses stop at 4 weeks?

TABLE 3 Median time interval between 117 recurrent CDI episodes for 82 patients

Episode type	No. (%) of patients	Interval (days)	Range (days)	*P* value
Single recurrence				
Relapse ($n = 36$)	36 (69.2)	48	19–402	0.01
Reinfection ($n = 16$)	16 (30.8)	108	23–1,260	
Multiple recurrence				
Relapse ($n = 23$)	11 (36.7)	30	15–319	0.03
Reinfection ($n = 17$)	8 (26.6)	40	17–325	
Relapse + reinfection ($n = 25$)	11 (36.7)	78	17–778	

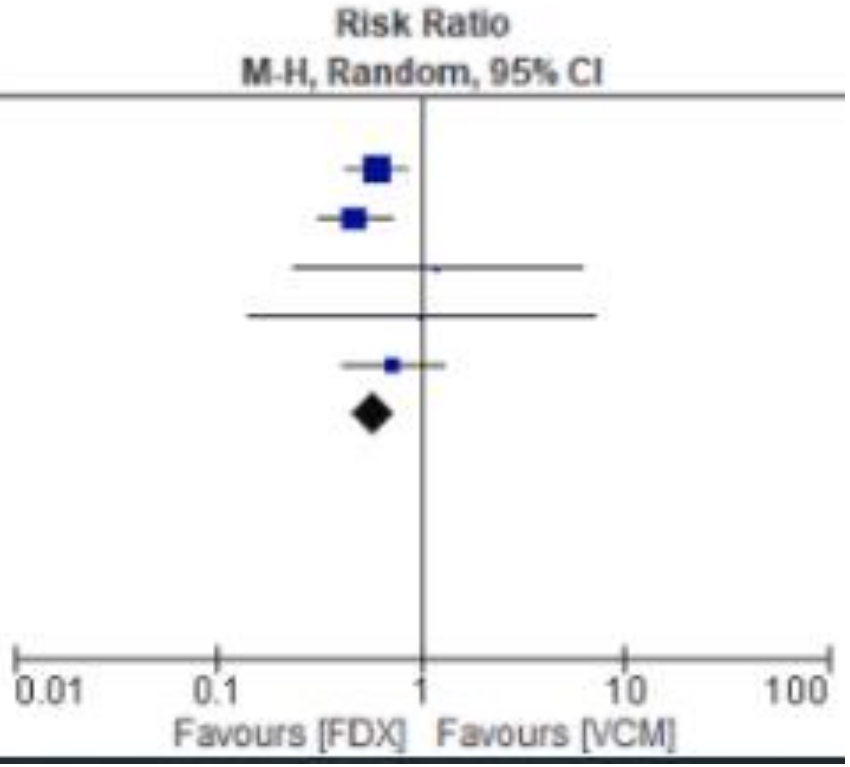
Marsh JW et al. *J Clin Microbiol.* 2012 Dec; 50 (12): 4078-82.

Small reproducible effect for fidaxomicin vs 4-week recurrence endpoint

Study or Subgroup	FDX Events	FDX Total	VCM Events	VCM Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
All CDI							
Louie 2011	39	253	67	265	44.7%	0.61 [0.43, 0.87]	2011
Cornely 2012	28	221	60	223	33.8%	0.47 [0.31, 0.71]	2012
Housman 2016	3	15	2	12	2.1%	1.20 [0.24, 6.06]	2016
Thabit 2016	2	6	1	3	1.5%	1.00 [0.14, 7.10]	2016
Mikamo 2018	16	86	24	95	17.9%	0.74 [0.42, 1.29]	2018
Subtotal (95% CI)		**581**		**598**	**100.0%**	**0.59 [0.47, 0.75]**	
Total events	88		154				

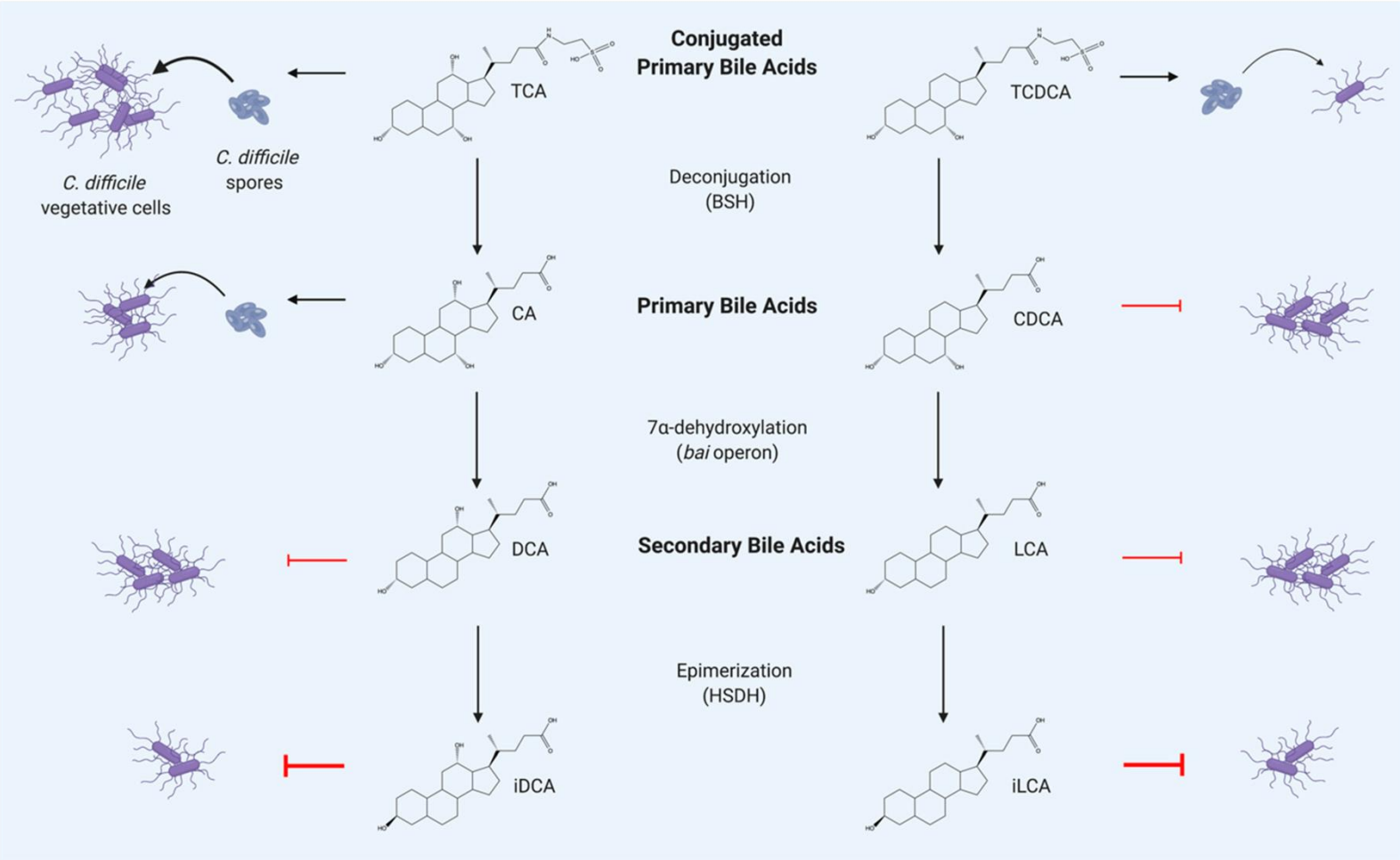
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.82$, $df = 4$ ($P = 0.59$); $I^2 = 0\%$

Test for overall effect: $Z = 4.35$ ($P < 0.0001$)



Tashiro S, Mihara T et al. *J Infect Chemother*. 2022 Nov;28(11):1536-1545

Pathogenesis updates: Bile acids and CDI



Host resistance to CDI and the paradox of CDI treatment:

1. Collateral flora responsible for deconjugation and dehydroxylation of bile acid are highly antibiotic-susceptible
2. Antibiotics active against CDI also disrupt #1

Reed AD and Theriot CM. *Microorganisms* 2021, 9(2), 371

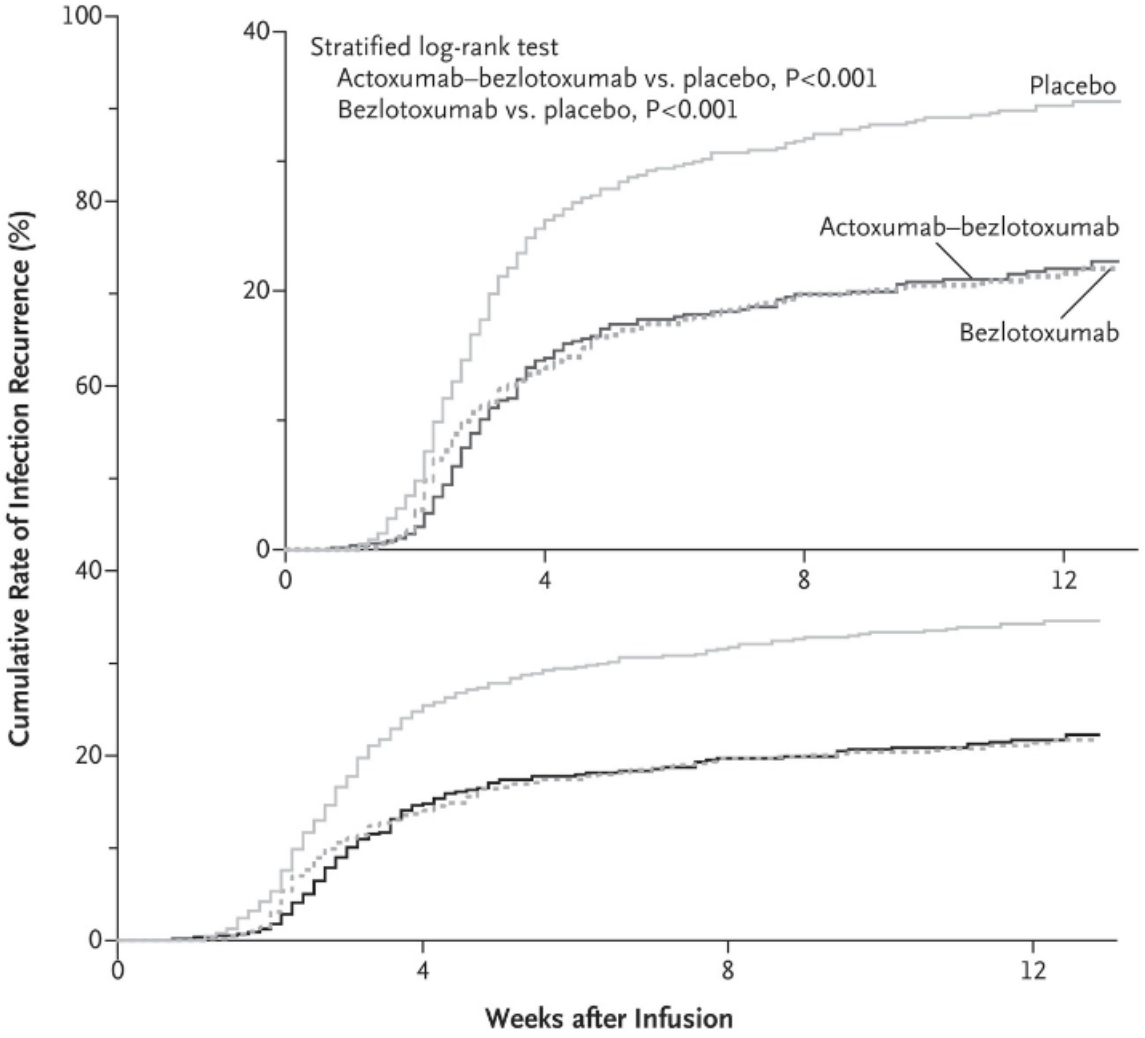
WHO NEEDS IT, AND HOW?

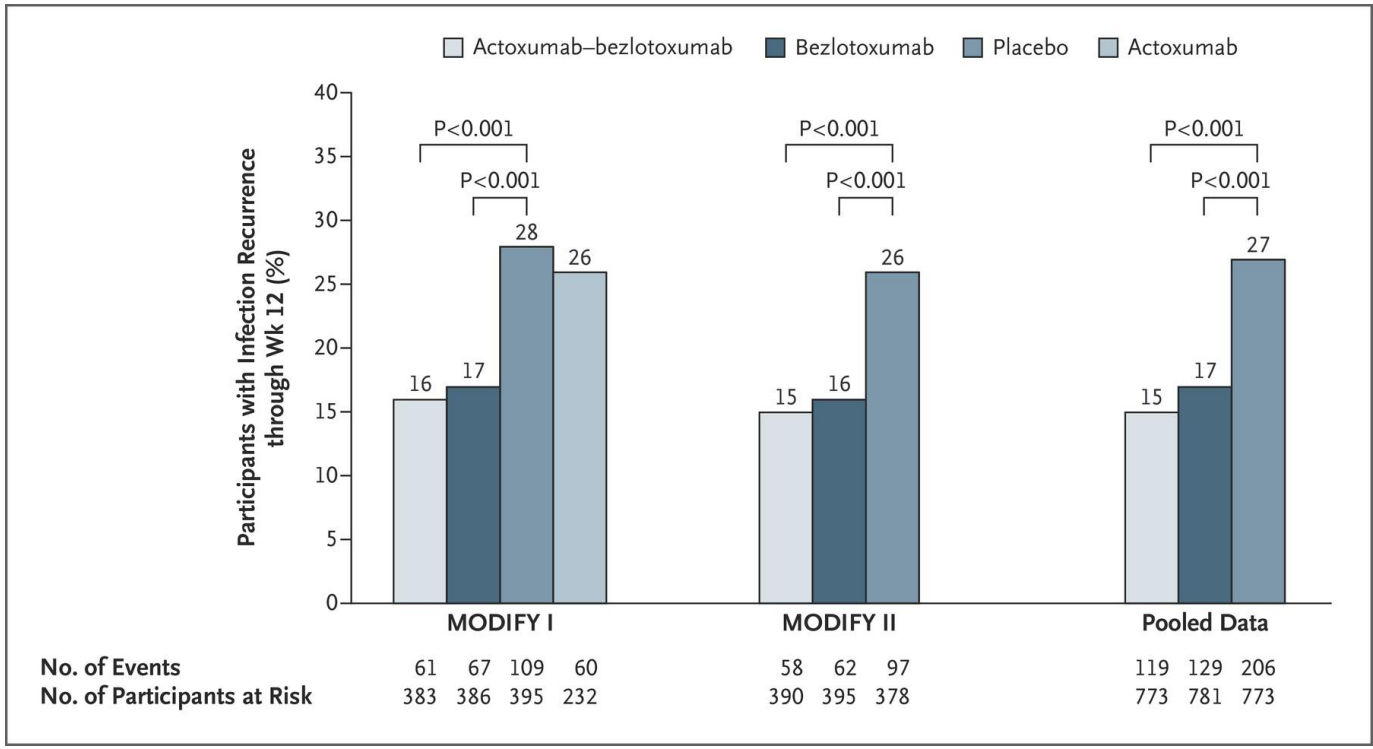
Management of recurrent CDI: FMT and monoclonals

Products approved by FDA for recurrent CDI as of 2026

Drug (brand)	FDA Indication	Adult Dosing	Target	Cost per course	Timing
~~**bezlotoxumab (Zinplava™)**~~ **Discontinued Jan 2025**	~~rCDI (Oct 2016)~~	~~10 mg/kg IV x 1 dose~~	~~Toxin B~~	~~$ 4010 (100 kg)~~	~~Anytime during standard therapy~~
Fecal microbiota, live-jslm REBYOTA®	rCDI (Nov 2022)	100 ml enema x 1	unknown	$9,220 (goodrx.com)	1-2 days following standard antibiotics
Fecal microbiota spores, live-brpk VOWST®	rCDI (Apr 2023)	4 capsules PO daily x 3 days	unknown	$17,500 (WAC)	2-4 days after standard antibiotics

Can we reduce recurrences with monoclonal antibodies?

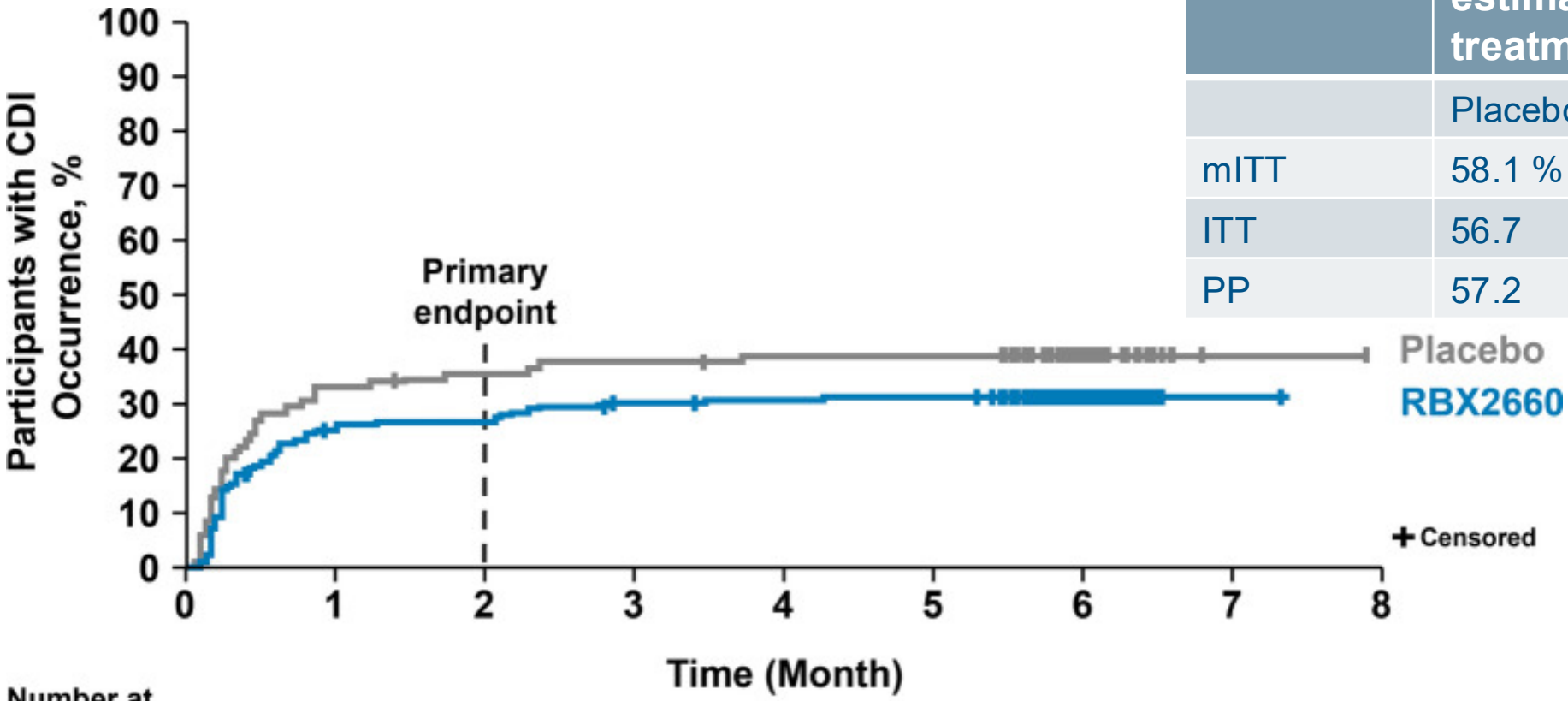




Wilcox MH, Gerding DN, et al. *N Engl J Med*. 2017 Jan 26;376(4):305-317

PUNCH CD3 Trial of FMT for *C. difficile* infection (REBYOTA)

Population	Modeled estimated treatment success		Treatment effect [95% CI]
	Placebo	RBX2660	
mITT	58.1 %	70.4 %	12.3 [1.4-23.3]
ITT	56.7	69.1	12.5 [1.6-23.3]
PP	57.2	70.9	13.7 [2.4-25.1]

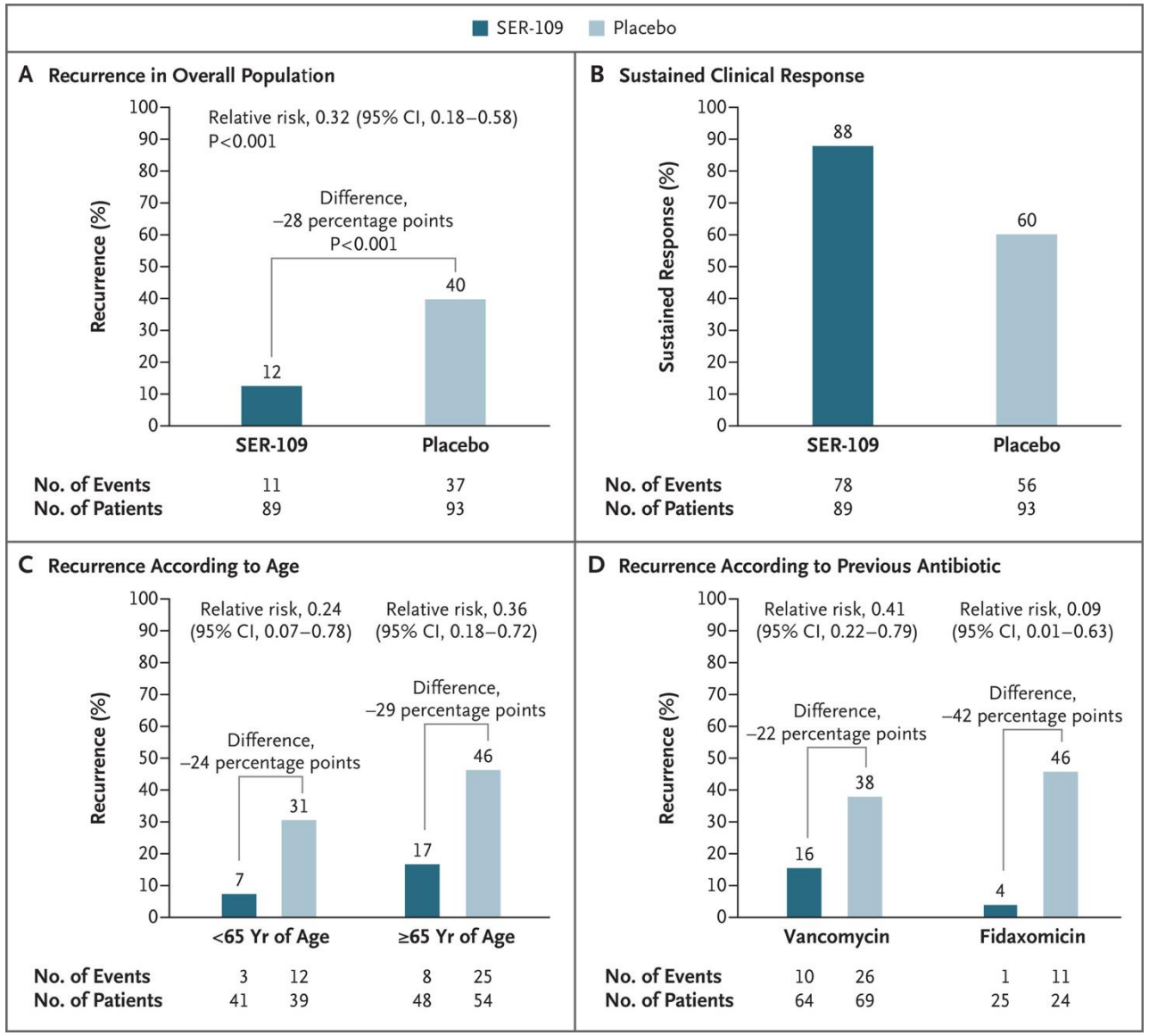


Number at risk

RBX2660	177	131	128	120	118	117	52	1	0
Placebo	85	57	54	52	49	49	22	1	0

Khanna S, Assi M, et al. *Drugs*. 2022; 82(15): 1527–1538

SER-109: an Oral Microbiome Therapy for recurrent CDI (Vowst)

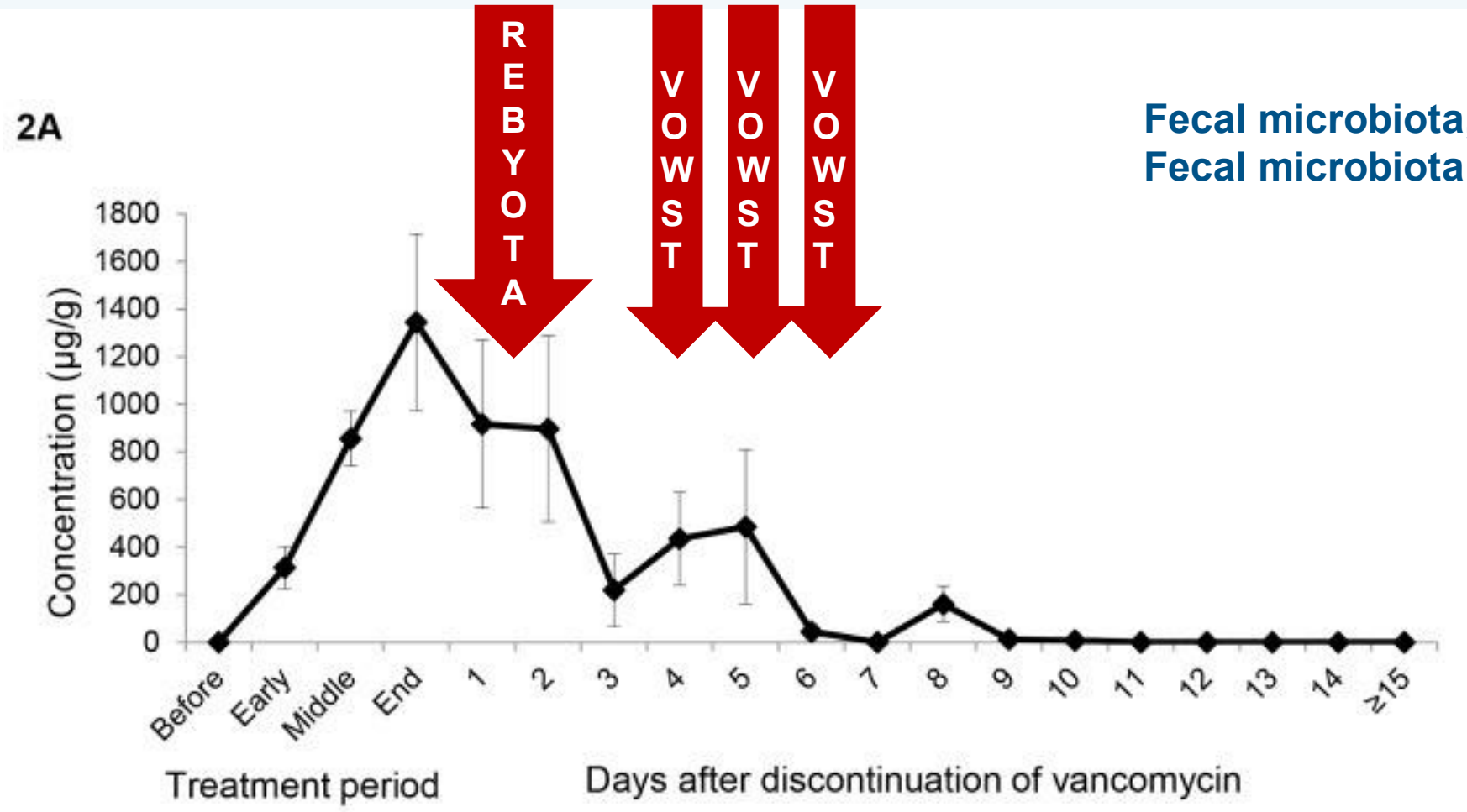


- 4 capsules daily x 3 days
- 40% rCDI in placebo group
- 12% in SER-109 group
- SER-109 species detected week 1 (CD-inhibiting bile acid profiles)
- 4 donors, well-described purification process
- All participants had 3+ rCDI
- All on standard therapy 10-21 days
- 8-week recurrence endpoint

NOTE:
Vancomycin recurrences:
36/133 = 27.1%
Fidaxamycin recurrences:
12/49 = 24.5 %

Feuerstadt P, Louie TJ et al. *N Engl J Med* 2022; 386:220-22

Key Challenge in FMT: Engraftment & Time off CDI Therapy



Fecal microbiota, live-jslm (REBYOTA®)
Fecal microbiota spores, live-brpk (VOWST®)

Abujamel T et al. *PLoS One*. 2013 Oct 2;8(10):e76269.

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FMT has been reported inferior to extended vancomycin

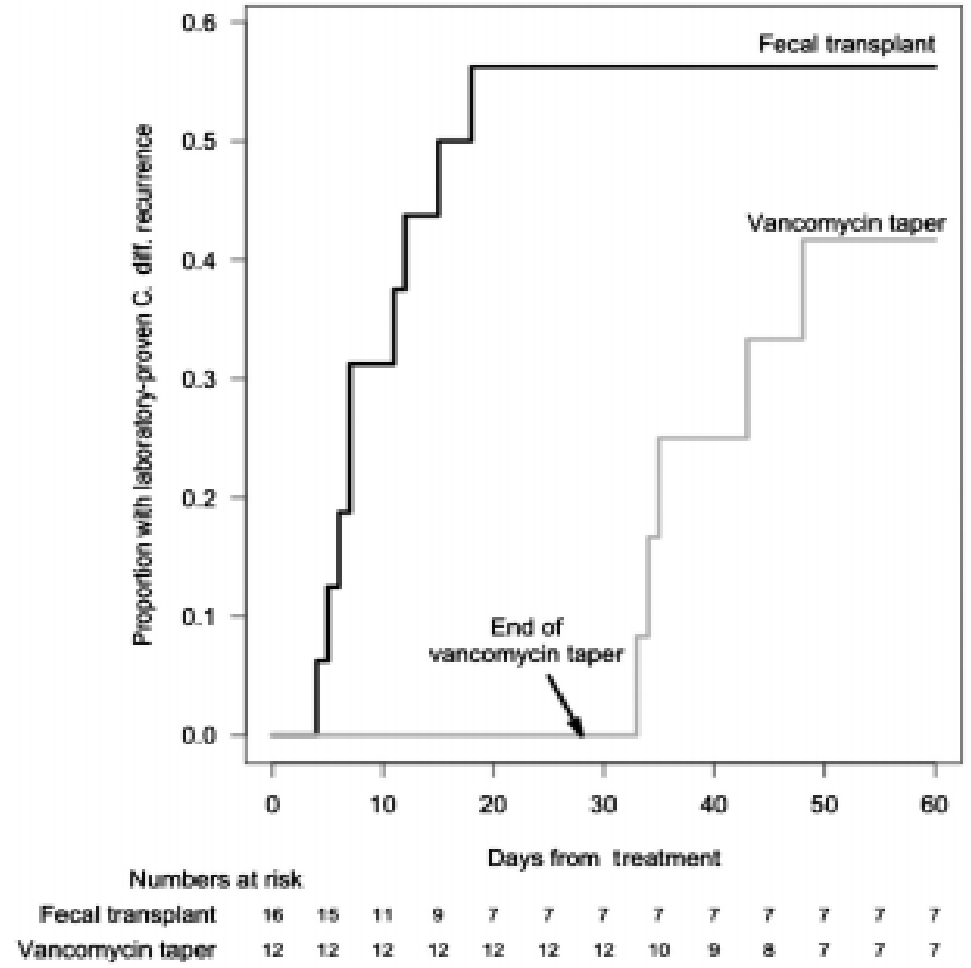


Figure 2. Cumulative incidence of *Clostridium difficile* infection recurrence by treatment group over 120 days. Day 0 indicates day of fecal transplant for fecal transplant group and first day of tapering protocol for vancomycin taper group. Although follow-up continued for 120 days, the y-axis ends at 60 days as there were no recurrences beyond this timepoint.

9/16 (56%) FMT patients recurred

5/12 (42%) vanco taper patients recurred

ARR= 42-56= -14%

Median time-to-recurrence
9 days after FMT

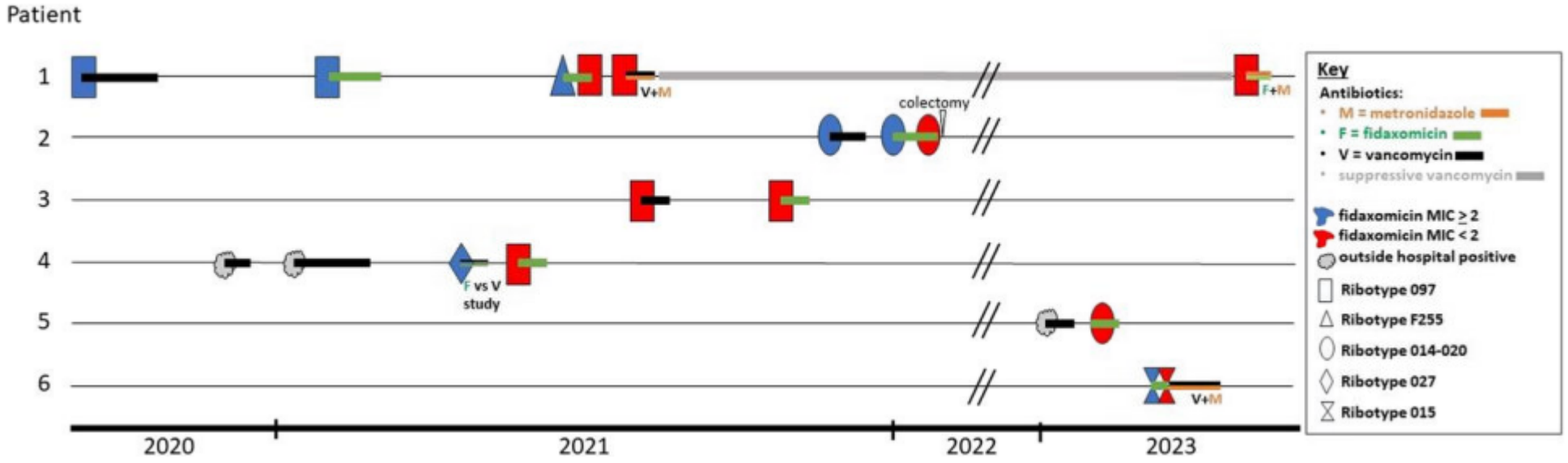
Hota SS et al. *Clin Infect Dis.* 2017 Feb 1;64(3):265-271. PMID: 28011612

Who can and cannot benefit from FMT

DO NOT PERFORM	Benefits unproved & unlikely	Benefits unproved but likely	Proved benefit but risks for donor-derived infection should be discussed with patient	Proved benefits likely outweigh the risks
Neutropenia (current or expected)	Equivocal CDI diagnosis	CDI not yet on antibiotics	Pediatric patients	>65 yo with recurrent CDI responsive to anti-CDI antibiotics, not currently ON anti-CDI antibiotics
	No response to prior CDI antibiotics		Patients ages 18-65	
	Currently on antibiotics (CDI or otherwise)		Severely immunosuppressed patients	

It is unlikely that ANY inpatient will benefit from FMT as currently formulated and studied.

Fidaxomicin-resistant *C. difficile*!



108 fidaxomicin-treated patients

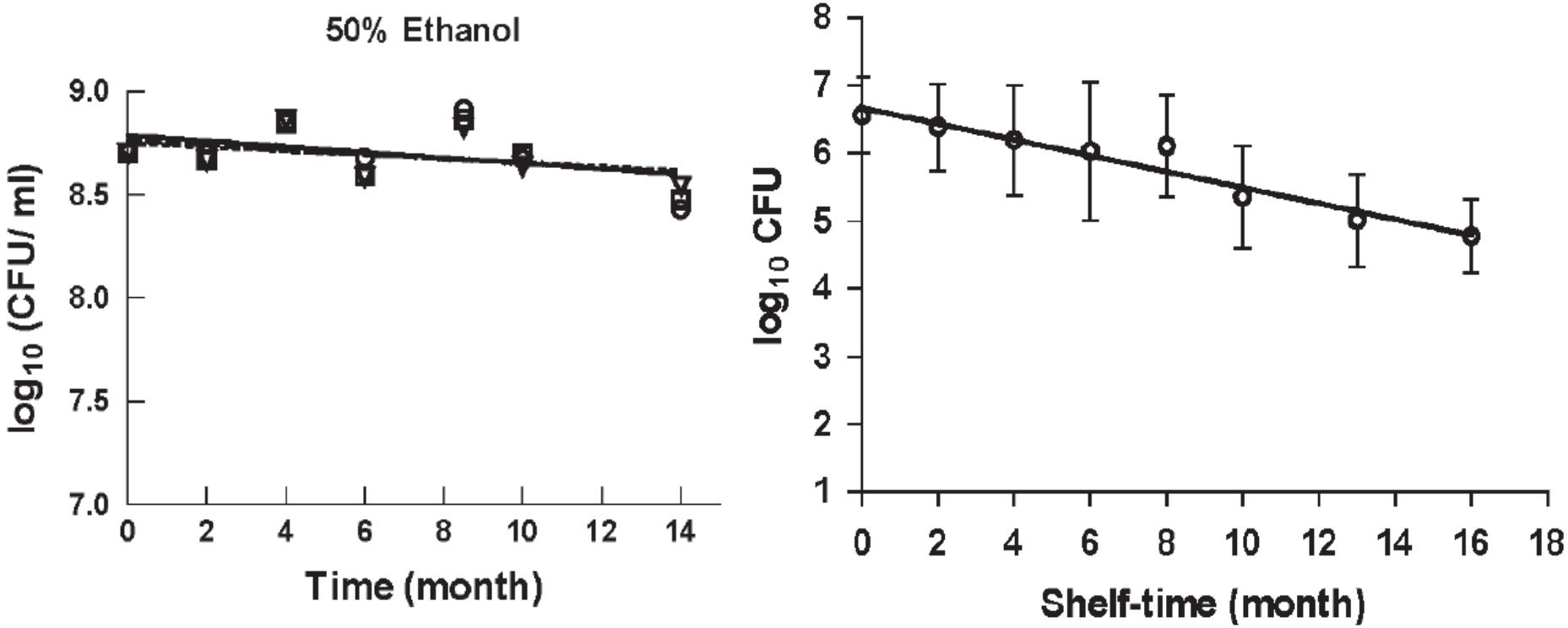
- 6 (5.6%) infected with MICs 8-32
- 3 had clinical failure after initially susceptible isolates
- 3 were infected with fidaxomicin isolates with high MICs at baseline
- Only two (2) patients had to be switched to alternative therapy (vancomycin)

Redmond SN, Cadnum JL, et al. *Clin Infect Dis*. 2025 Jun 4;80(5):984-991. PMID: 40036727

To Screen or Not To Screen: Pre-emptive Strategies to Address Colonization with *Clostridioides difficile*

Photos provided by faculty

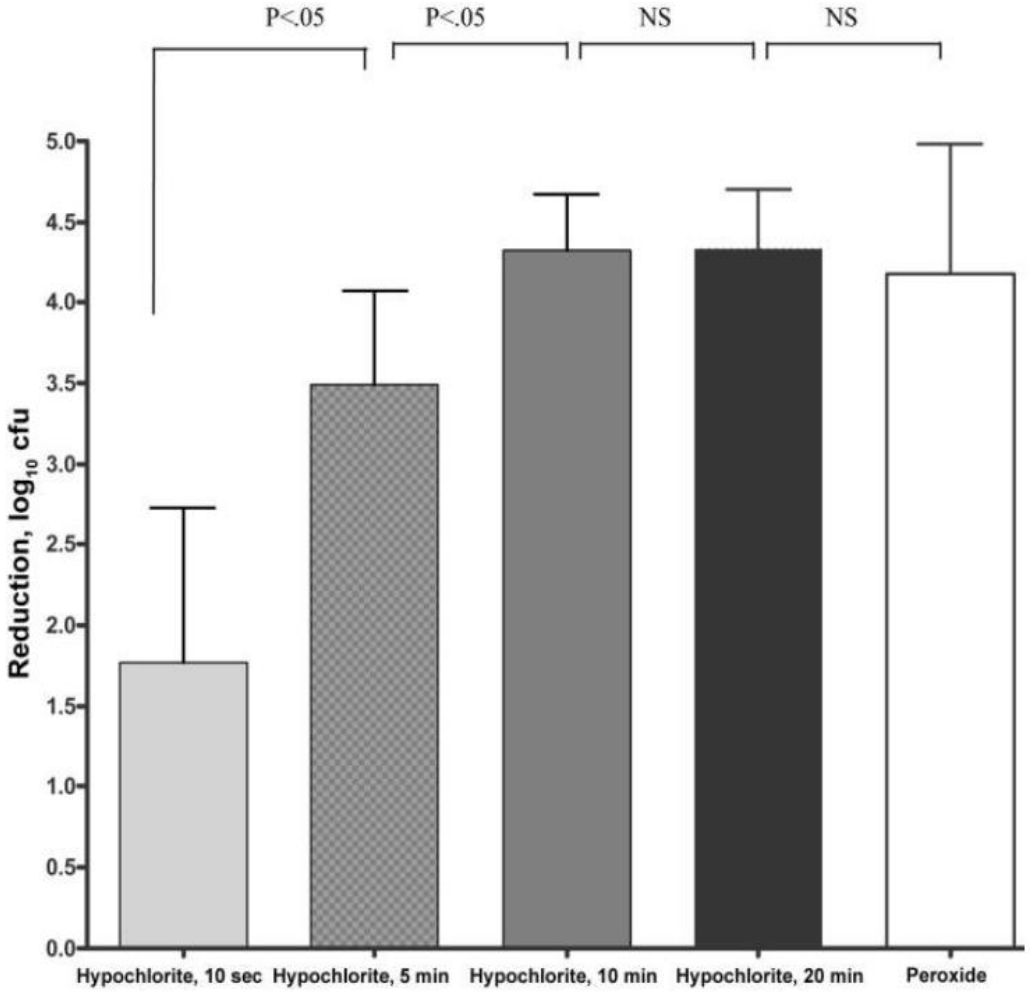
Longevity of *C. difficile* spores



Viability of *C. difficile* spores stored in 50% ethanol (left) or dried on metal disks (right).

Perez *et al*. *J AOAC Int* 94(2): 618-626, 2011.

C. difficile is tough to kill



Standard hospital disinfectants (NH3)

Isopropyl alcohol 70%

Ethanol 80%

INEFFECTIVE

Strong oxidizing agents:

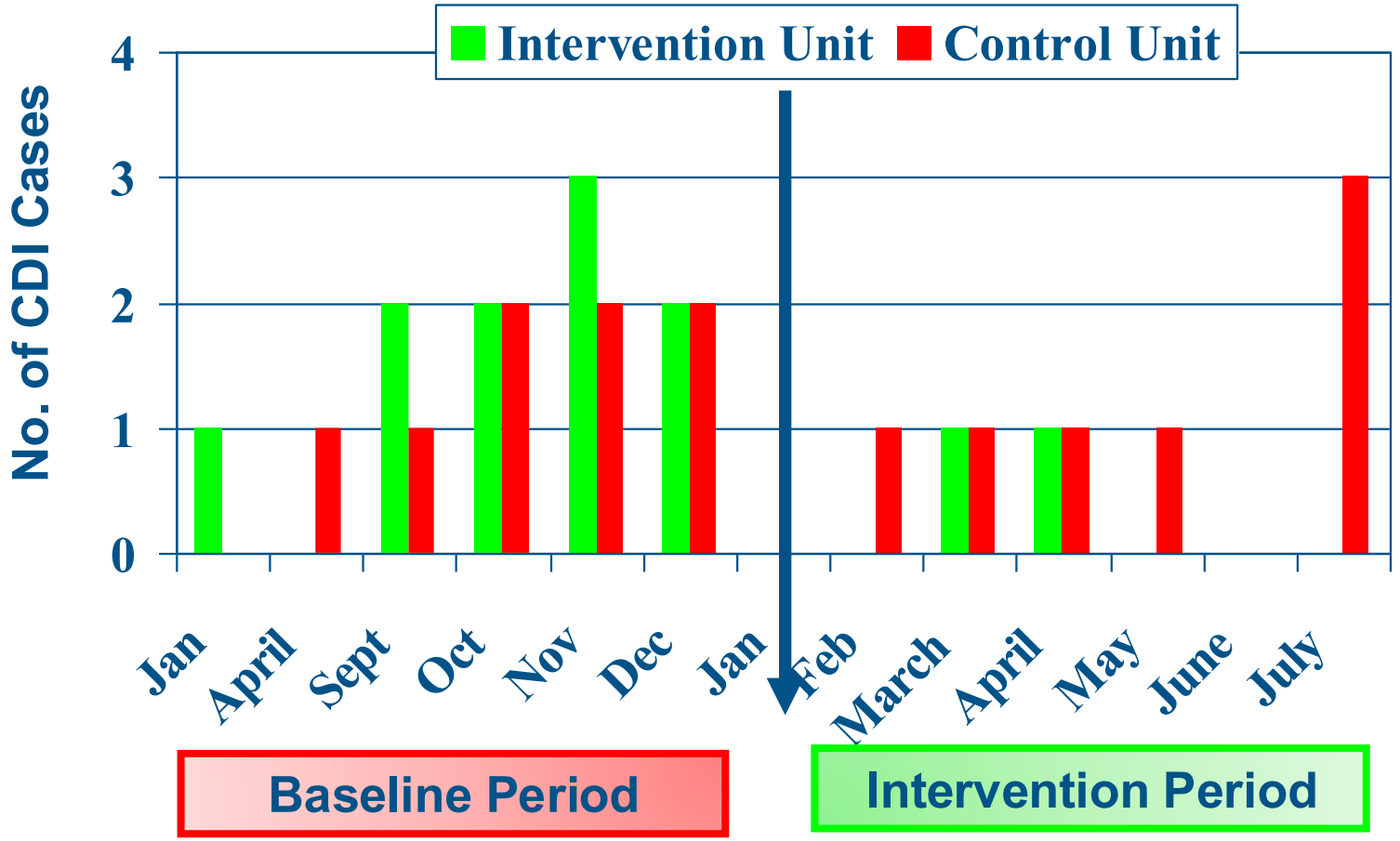
H_2O_2 10%

5000 ppm bleach

Prolonged contact time (10 minutes)

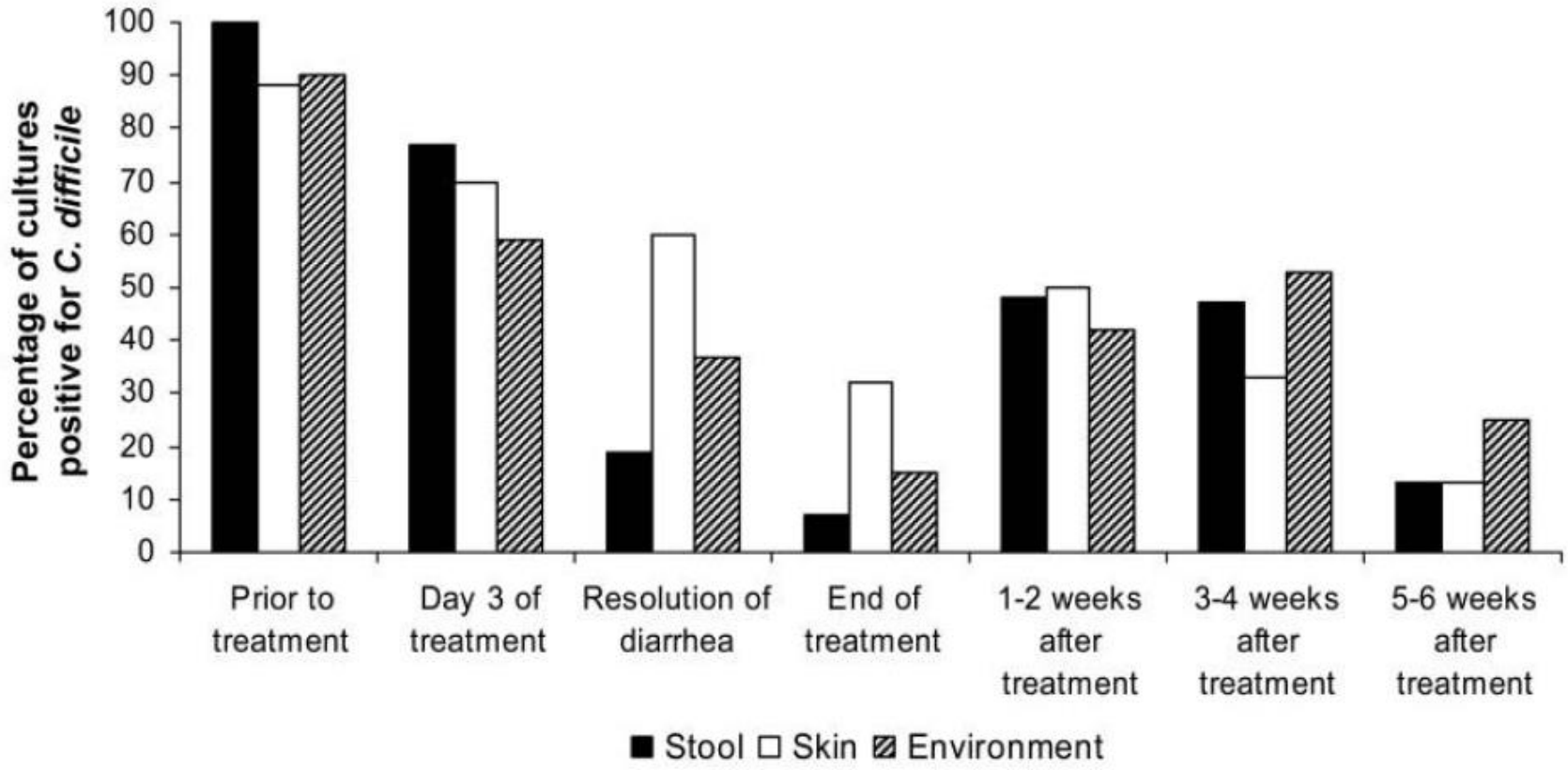
Wilcox et al, ICHE 28 (8): 921-25, 2008.

Effect of Glove-Wearing by Personnel on 2 Wards vs 2 Control Wards



Johnson S, et al. *Am J Med.* 1990;88:137-140.

Persistence of *C. difficile* in stool, skin, & environment in CDI patients

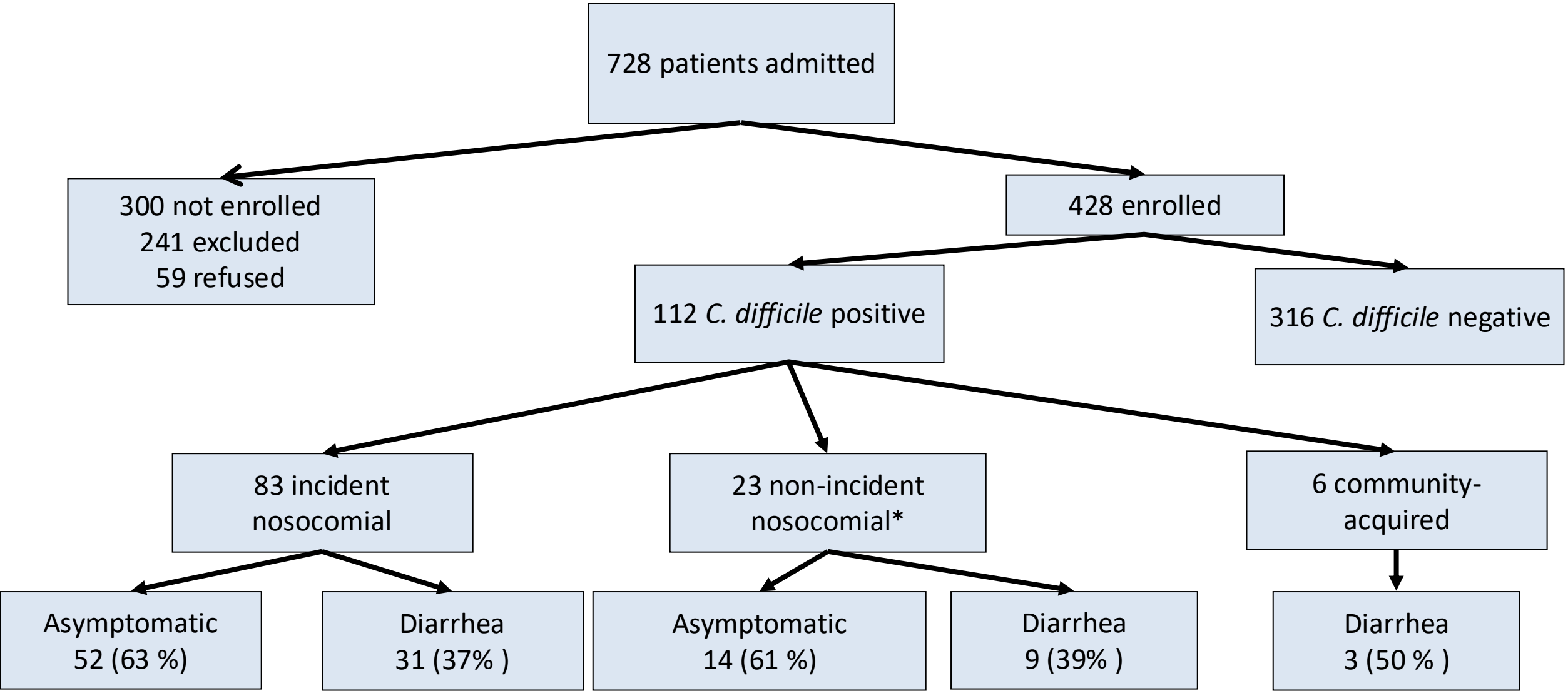


Sethi AK et al. *Infect Control Hosp Epidemiol*. 2010 Jan;31(1):21-7.

Key infection-prevention strategies available for CDI

- Glove use during CDI (+/- 60 days after CDI)
- Gown use during CDI (+/- 60 days after CDI)
- Dedicated patient equipment during CDI (thermometers, BP cuffs)
- Use of sporicidal agents for terminal disinfection / daily cleaning of CDI rooms
- Use of sporicidal agents for terminal disinfection / daily cleaning of all rooms
- Addition of other disinfection technologies for continuous or terminal cleaning
  - UVC
  - Hydrogen peroxide vapor
- Screening for carriers of *C. difficile* ???

Asymptomatic carriers of *C. difficile* outnumber patients with CDI

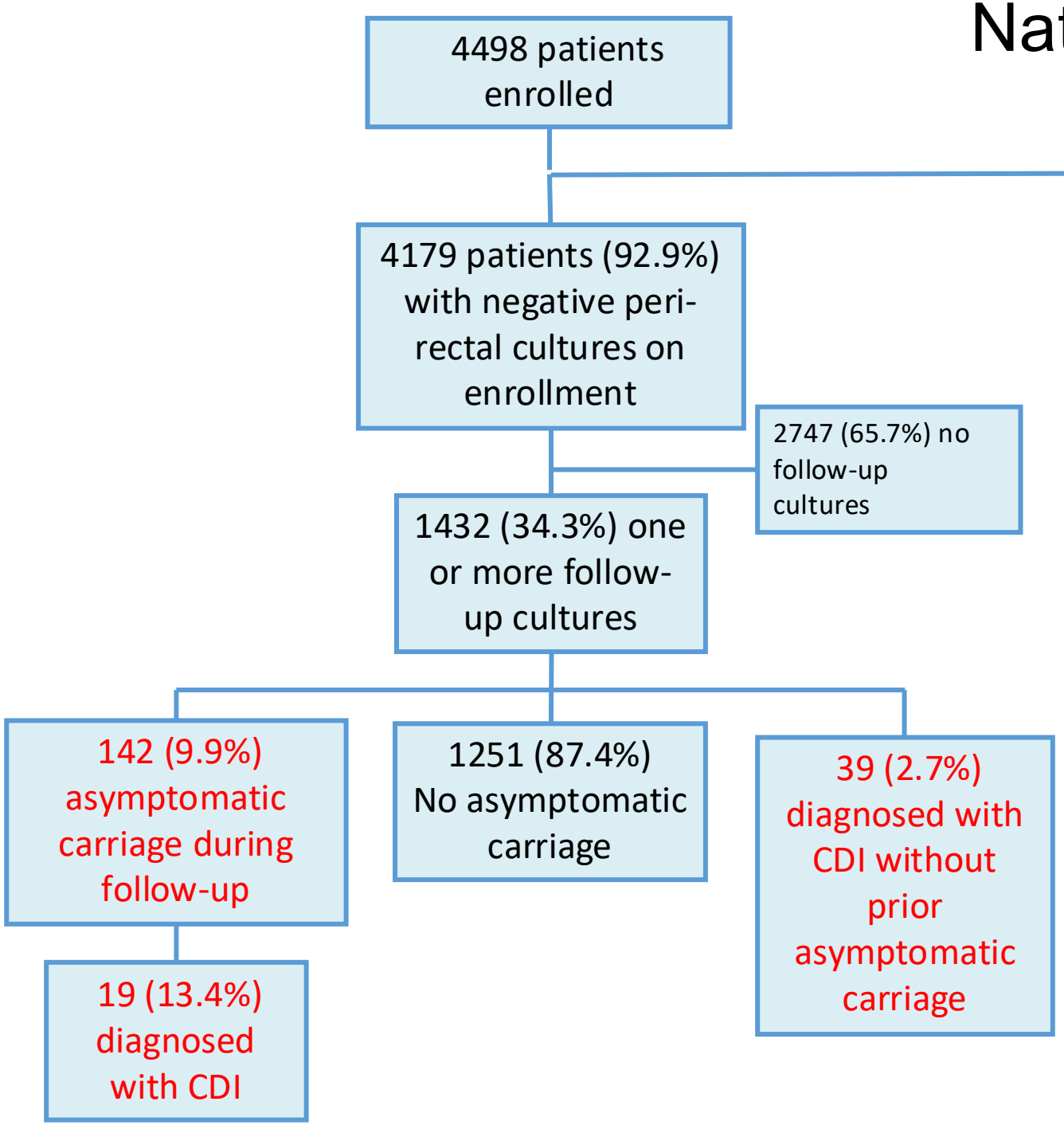


McFarland *et al*. *N Engl J Med* 320 (4): 204-210, 1989.

Who is colonized with *C. difficile:* Not So Simple

Definition	References	Comment
Patients with diarrhea and *C. difficile* test ordered by clinician is PCR+/EIA-	Polage CR 2015 Warren BG 2022	Clinical definition under scrutiny Not useful for infection control unless results used for isolation decisions.
Patients with formed stool sampled by perirectal or rectal swab positive for *C. difficile* by anaerobic culture	McFarland LV 1987 Cadnum JL 2014	Sensitivity varies widely by research methodology. LOD = 10 cfu / gram stool
Patients with formed stool positive by modified PCR from rectal/perirectal swab for *C. difficile*.	Donskey CJ 2014 Curry SR 2011	Not FDA-cleared indication for any commercially available NAAT. LOD= $4\log_{10}$ cfu

Natural history of *C. difficile* colonized patients



- Most carriers are never diagnosed with CDI (>85%)
- Only 32/142 carriers were persistent

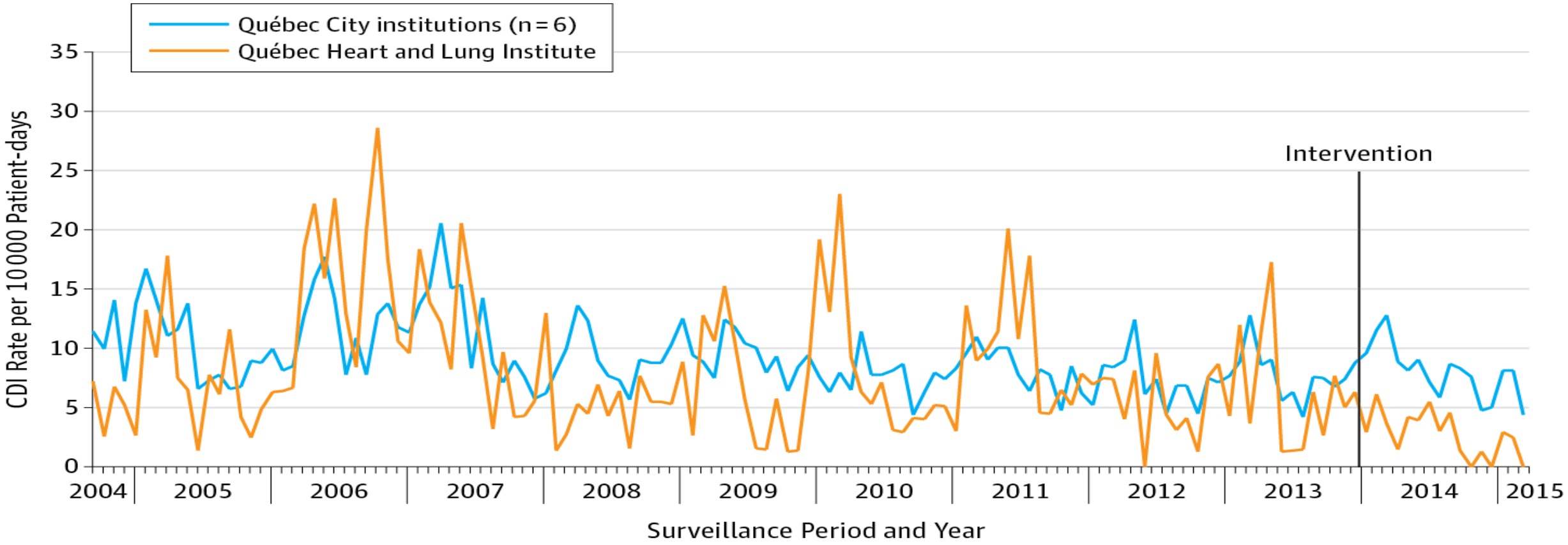
Curry SR, Hecker MT et al. *Clin Infect Dis*. 2023 PMID: 36905149.

Patients with *C. difficile* colonization are an important source of incident CDI

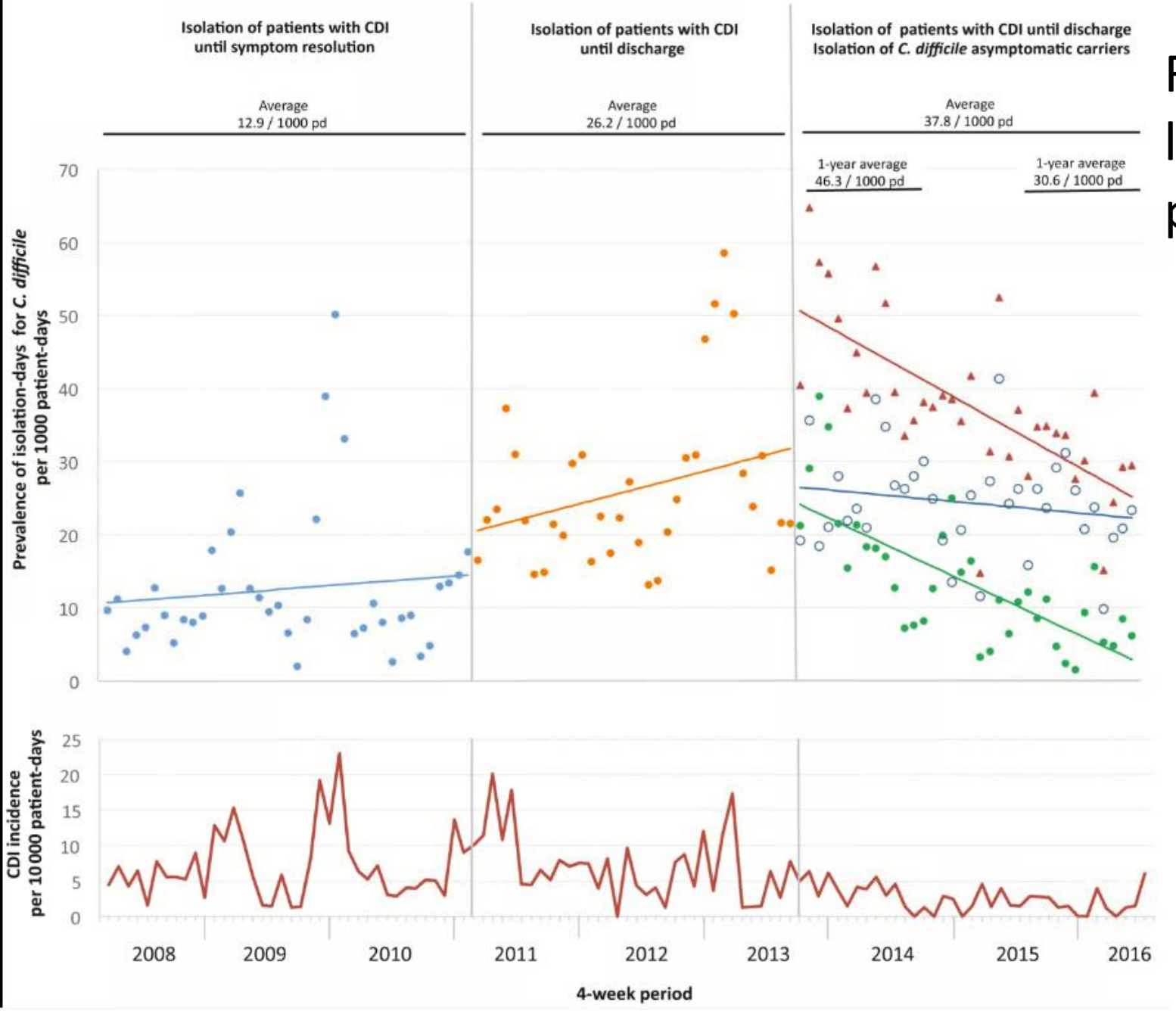
- Eyre et al. using whole genome sequencing over 3 years in UK
  - Only 38% of hospital-onset CDI could be linked to another CDI case
  - 45% of cases over 3 years were genetically unlike all prior CDI cases
- Curry et al. using MLVA genotyping over 117 days in Pittsburgh, PA
  - Using rectal swabs for VRE surveillance (~25% of the inpatient population)
  - 16/56 (29%) HO-CDI patients were linked to asymptomatic carriers
  - 17/56 (30%) HO-CDI patients were linked to other CDI patients

Eyre DW, Cule ML, et al. *N Engl J Med* 369:1195–1205, 2013.
Curry SR, Muto CA, et al. *Clin Infect Dis* **57**:1094–1102, 2013.

Active surveillance for *C. difficile* associated with 62% reduction in HO-CDI in quasi-interventional study



Longtin Y. *JAMA Intern Med*. 2016 Jun 1;176(6):796-804



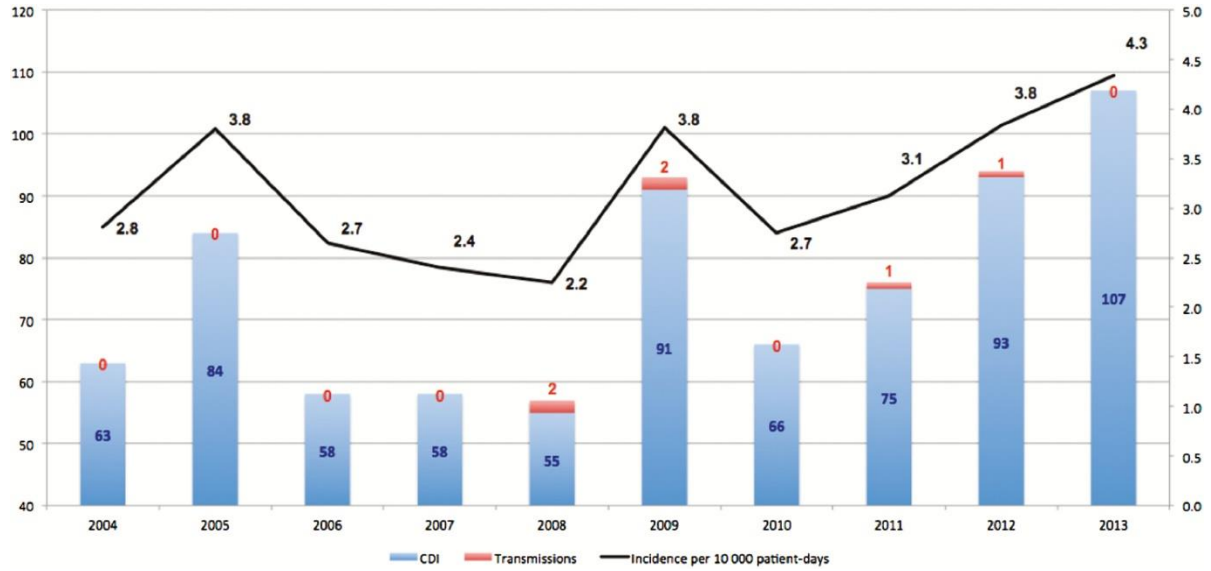
Follow-up data shows sustained low rates in the hospital performing AST for *C. difficile*

- 92% of inpatient admissions screened
- Perirectal swabs used on modified PCR
- + patients placed on modified contact precautions
- Gloves
- Semi-private rooms

- Total isolation days go up
- CDI isolation days go down

Xiao Y, Paquet-Bolduc B, et al. *Clin Infect Dis*. 2018 Apr 17;66(9):1377-1382. PMID: 29149279

Counterfactual: No transmission of *C. difficile* In a Hospital Not Mandating Contact Isolation



- 10-year study in single Swiss hospital
- Standard precautions for CDI (except when incontinent)
- Sporicidal disinfectants only for CDI
- 493 exposed contacts of 279 index cases
  - 27 + toxigenic *C. difficile*

Important limitations:

- The HO-CDI rate went UP over the course of the study
- Very low rates of environmental sample recovery from 16 index patients (3/128 samples, 2.3%)

Widmer AF, Frei R, et al. *Clin Infect Dis.* 2017 Feb 15;64(4):393-400. PMID: 28172613.

Open questions regarding AST for *C. difficile*

Question	Comments
How will NHSN categorize a positive test not done for the purposes of diagnosing CDI?	1. Risk to inflate CO-HCFA CDI rates if these tests are considered + labID events. 2. Risk to miss HO-CDI events if CDC patients become CDI patients with empiric treatment
How much empiric therapy will result for patients who screen positive?	Two randomized trials have shown harms result from treating CDC (Fishbein 2021, Johnson 1992)
What horizontal controls are already in place in centers that adopt AST?	Universal use of sporicidal terminal disinfectant Surveillance for environmental cleaning effectiveness Hand hygiene compliance Use of sensitive *C. difficile* diagnostics
Who pays for the AST?	What prevents this from being CMS abuse if charged to the patient?
What infection prevention interventions are needed for patients with *C. difficile* colonization?	Just gloves?
Should patients with *C. difficile* colonization be re-screened?	At what interval? How many for good NPV?

You may consider AST for *C. difficile* if your facility meets the following conditions

Condition	
1	HO-CDI rate is consistently <10 cases / 10,000 patient-days
2	Terminal disinfectant active against *C. difficile* spores is used for all patient rooms
3	Hand hygiene measured by a reliable method is consistently >95%
4	Standard precautions for care of patients incontinent of stool is consistent
5	Contact isolation precautions used for CDI patients for *at least* the duration of symptoms
6	Environmental disinfection auditing shows effective deployment of #2
7	High-sensitivity testing for CDI in place with a policy that addresses infection prevention for colonized patients

Everyone else needs a randomized cluster trial.

Key features of future trials of AST for *C. difficile*

Feature	Rationale
Rates of HO-CDI before/after intervention are well-defined	Primary endpoint
High-sensitivity, rapid turn-around method (PCR) for AST should be used	Research methods / culture would result in critical delays. Less likely to identify low-burden transient carriers.
Compliance with horizontal control features is described in detail	Needed to assess validity in facilities with strong vs weak infection prevention programs.
Conditions for patient re-screening are identified	Need to account for persistent vs transiently colonized.
Effect of patient-days in isolation are quantified as well as associated harms (codes)	Credible acknowledgment of harms of isolation
Screening of >90% of admissions is achieved	Negative studies are likely to result if most sources are not identified.
Molecular epidemiology of CDI cases and colonized patients is performed	Biological plausibility that existing controls are working
Patient days of *C. difficile*-active treatment before and after intervention are described	Need to account for possible over-treatment of identified carriers and/or empiric CDI treatment without testing.

Avoiding the Top 10 Management Missteps in CDI

1.	**If a patient isn't better by day 7 of CDI antibiotic therapy, they have something else!* -- (don't ask for fidaxomicin if vancomycin isn't working * think about fidaxomicin-R CDI if vice versa)**
2.	Regardless of guidelines, the best therapy for CDI is the therapy the patient will fill.
3.	For extended vancomycin therapy use pulse dosing, not tapers.
4.	When prescribing outpatient vancomycin for CDI, never, ever prescribe more than 125 mg
5.	Do not prescribe probiotics for primary or secondary prevention of CDI.
6.	FMT and FMT-like biotherapeutics should be considered for recurrent CDI, but they won't work A. If standard of care antibiotics did not work (see #1 above) B. While you are still on standard of care antibiotics
7.	Fidaxomicin should only be preferred for vancomycin for treatment of the first episode likely only cost-effective if the price is no greater than ~10% more than vancomycin —generic fidaxomicin is reducing prices!
8.	FMT and FMT-like biotherapeutics have no place on an inpatient formulary (see #6)
9.	Patients with vancomycin allergies (red man etc) can safely receive enteral vancomycin.
10.	Do not use metronidazole for CDI (side effects, efficacy issues) except for fulminant disease where parenteral agents may be needed.


Questions