

*August 13, 2019*

## **Agenda**

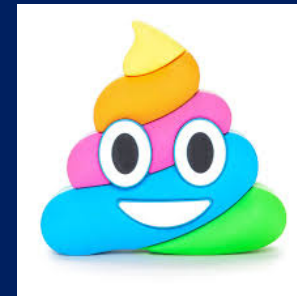
- Didactic: *The Power of Poop: Updates in C. difficile infections*
- Case Discussions



# UW TASP

tele-antimicrobial stewardship program

## The Power of Poop: Updates In *C. difficile*



**Zahra Kassamali Escobar, PharmD, BCIDP**

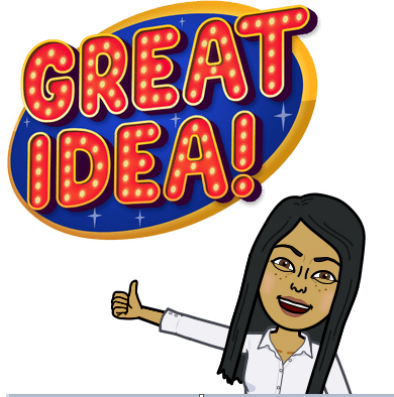
- UW Medicine | Valley Medical Center
- [zescobar@uw.edu](mailto:zescobar@uw.edu)

August 13, 2019

*This presentation is intended for educational use only, and does not in any way constitute medical consultation or advice related to any specific patient.*



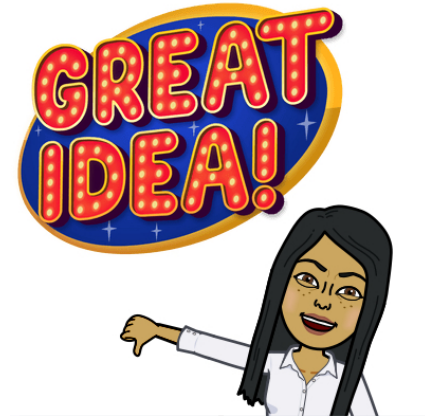
# Agenda



✓ Recommended Treatment

✓ Bile Acids

✓ Fecal Transplant and  
Microbiome health



✗ Diagnosis: Which test to use

✗ Colonization vs. Infection

✗ Prophylaxis



Jeannie Chan,  
PharmD



# Recommended Treatment (Mar 2018)

- Discontinue therapy with inciting antibiotic(s)  
*STRONG recommendation, MODERATE quality evidence*
- 1<sup>st</sup> Episode: PO vancomycin OR fidaxomicin  
preferred over metronidazole  
*STRONG recommendation, HIGH quality evidence*
- Recurrent CDI:  
Vancomycin + taper or fidaxomicin  
*WEAK recommendation, LOW quality evidence*
- Multiply Recurrent CDI:  
Stool transplant  
*STRONG recommendation, MODERATE quality evidence*



# Metronidazole is OUT

**Multicenter, Randomized, Double-Dummy, Double-Blind**

**2005 - 2007**

91 sites in US & Canada

109 sites in Europe, Australia, Canada

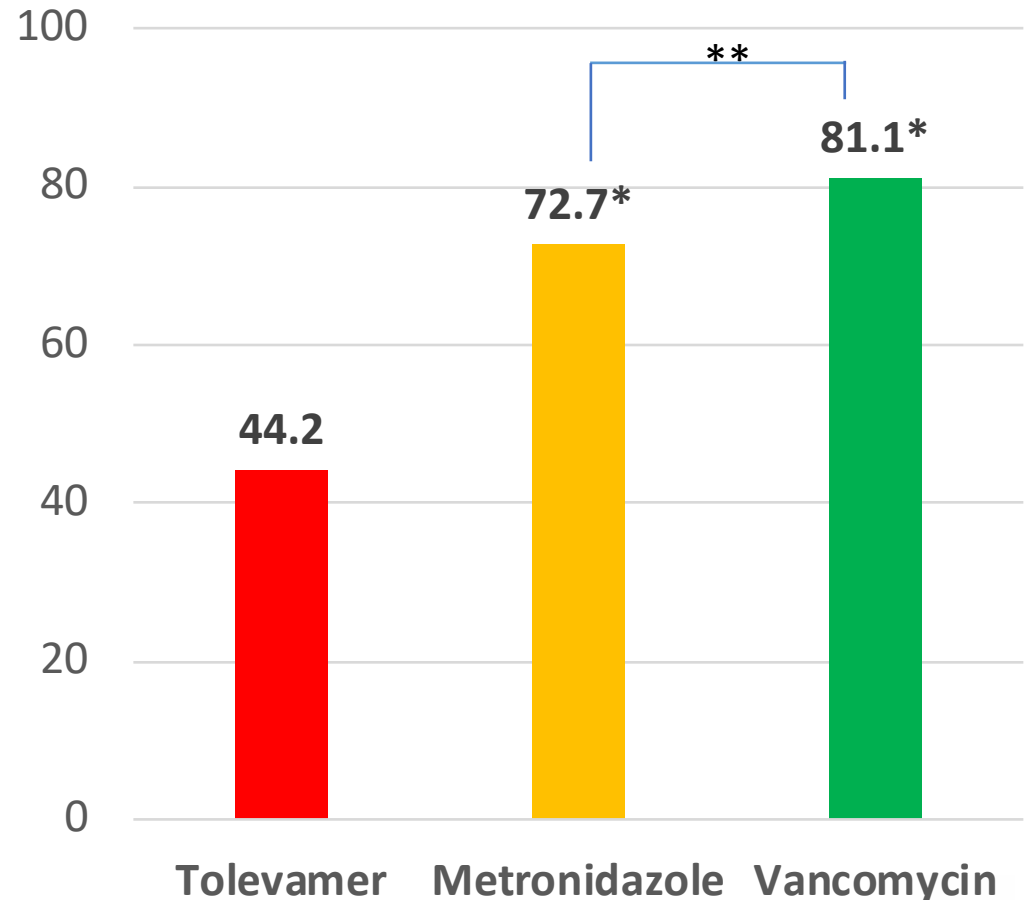
**Tolevamer**  
**N = 563**

14 days

**Metronidazole**  
**375mg q6h**  
**N = 289**

10 days

**Vancomycin**  
**125 PO q6h**  
**N = 266**

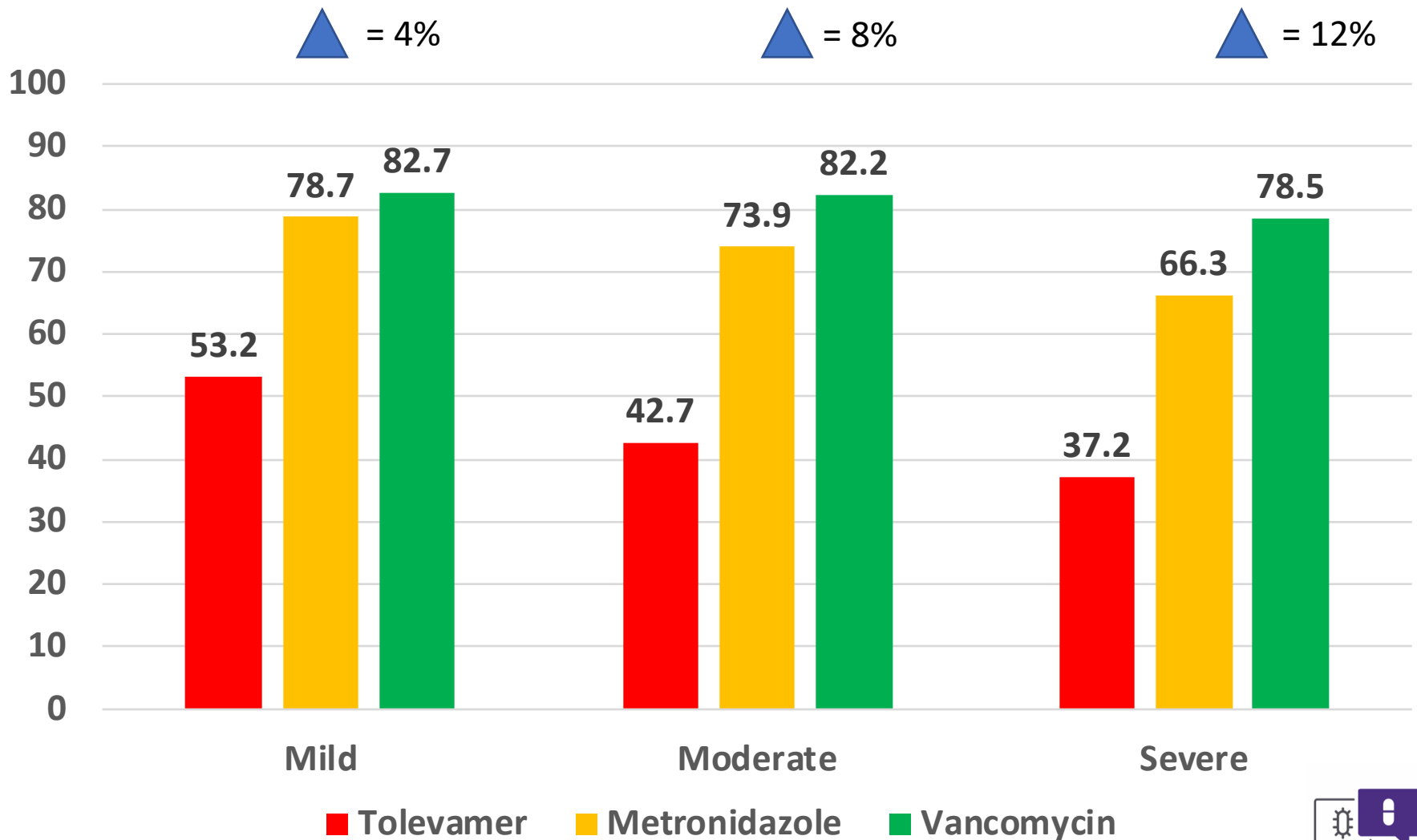


Clin Infect Dis 2014;59(3):345-54.



# Is Metronidazole EVER appropriate?

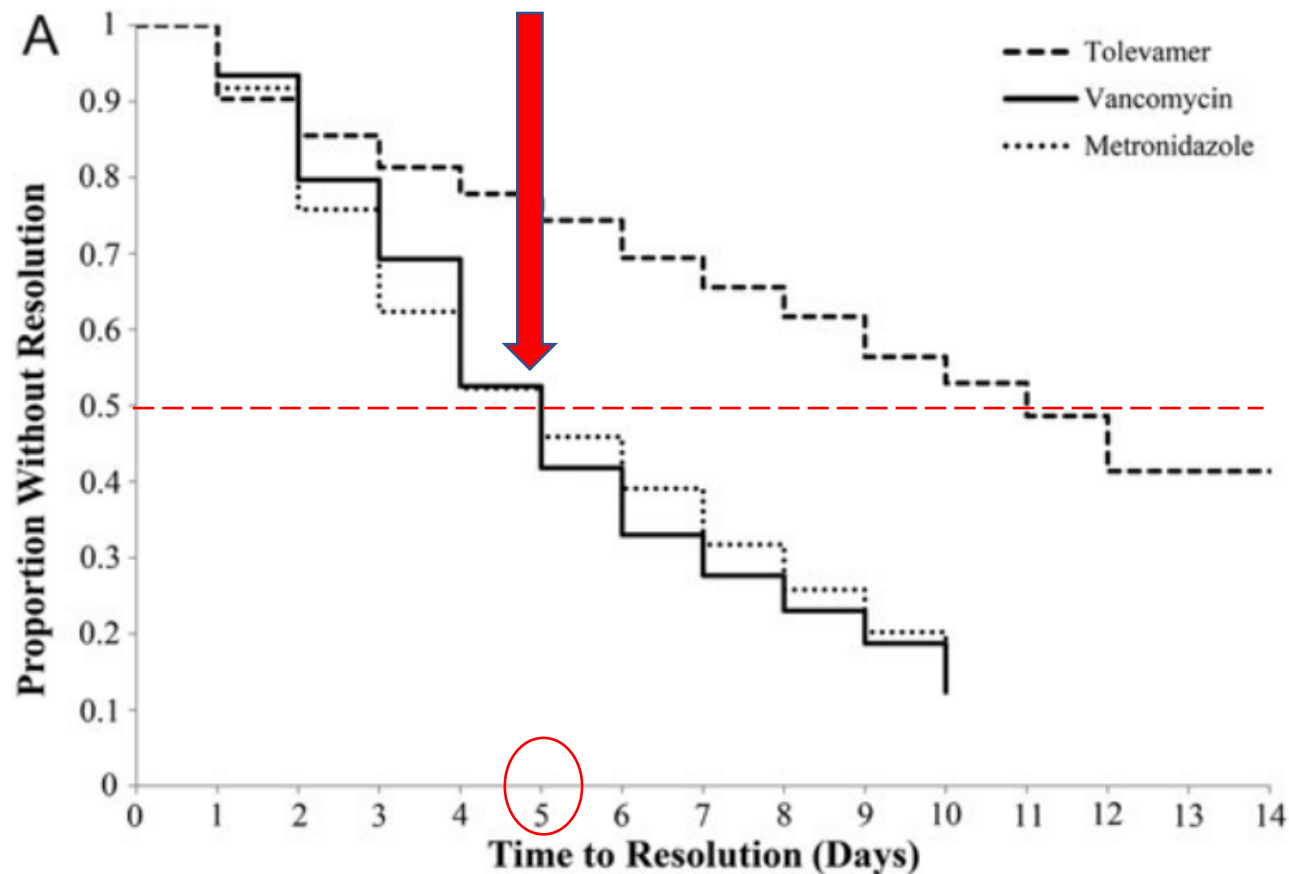
May consider for mild cases when vancomycin unavailable



# Learning Points from the Best C. Diff Trial We'll Ever Have:

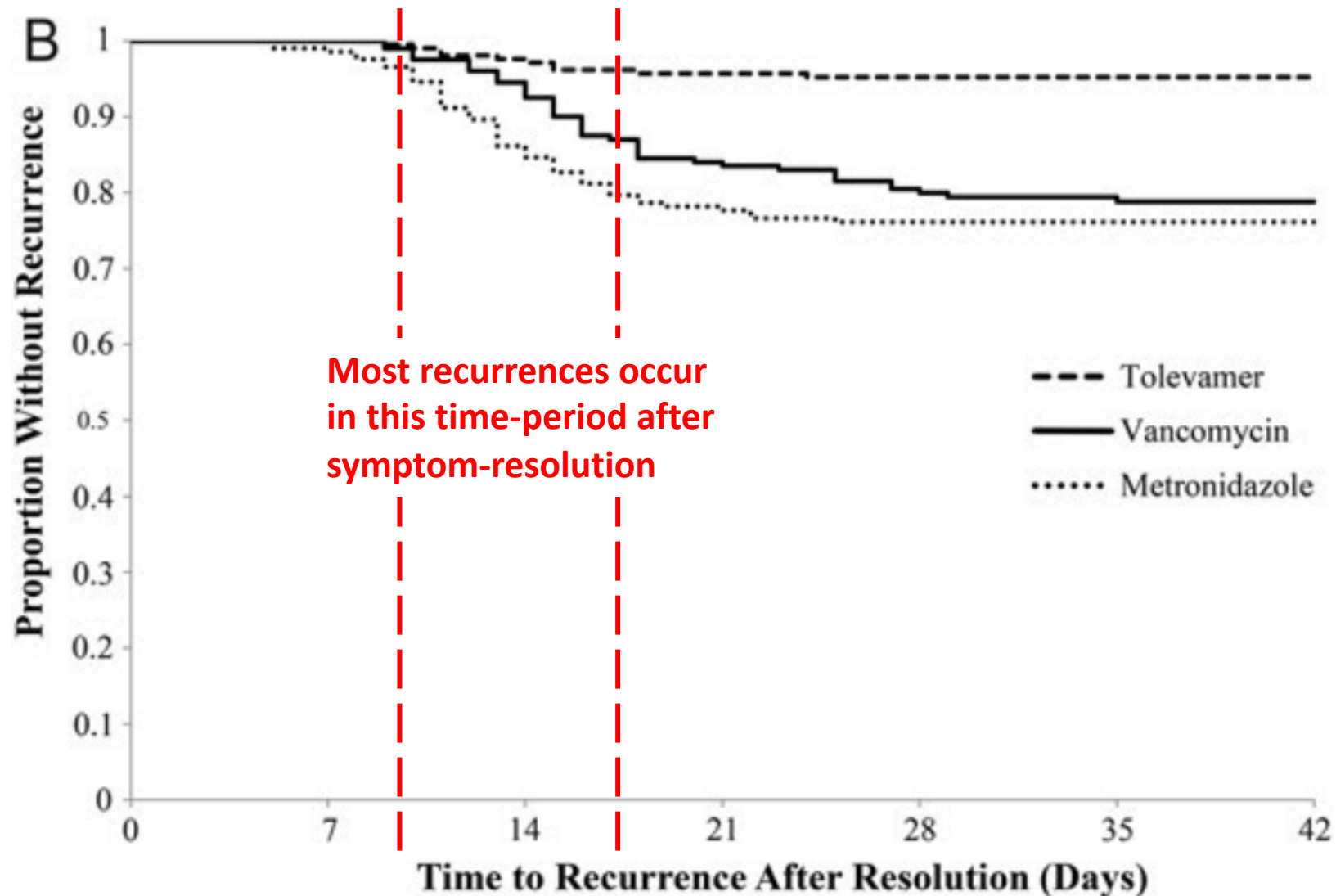
## Symptoms generally resolve within 5-7 days

Half of the patients saw their symptoms resolve within 5 days into therapy



# Learning Points from the Best C. Diff Trial We'll Ever Have:

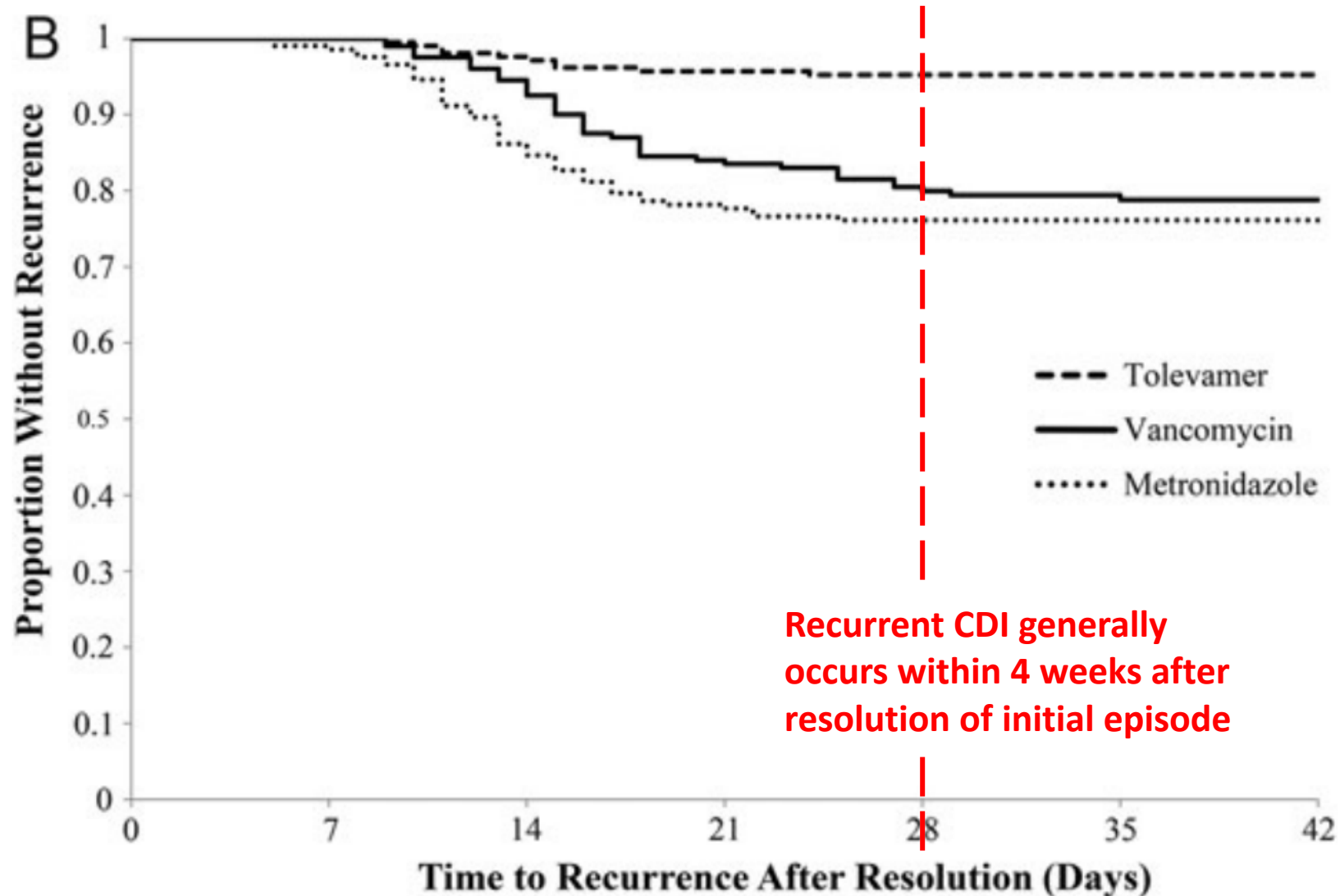
## Recurrences most often occur 10-15 days after initial episode





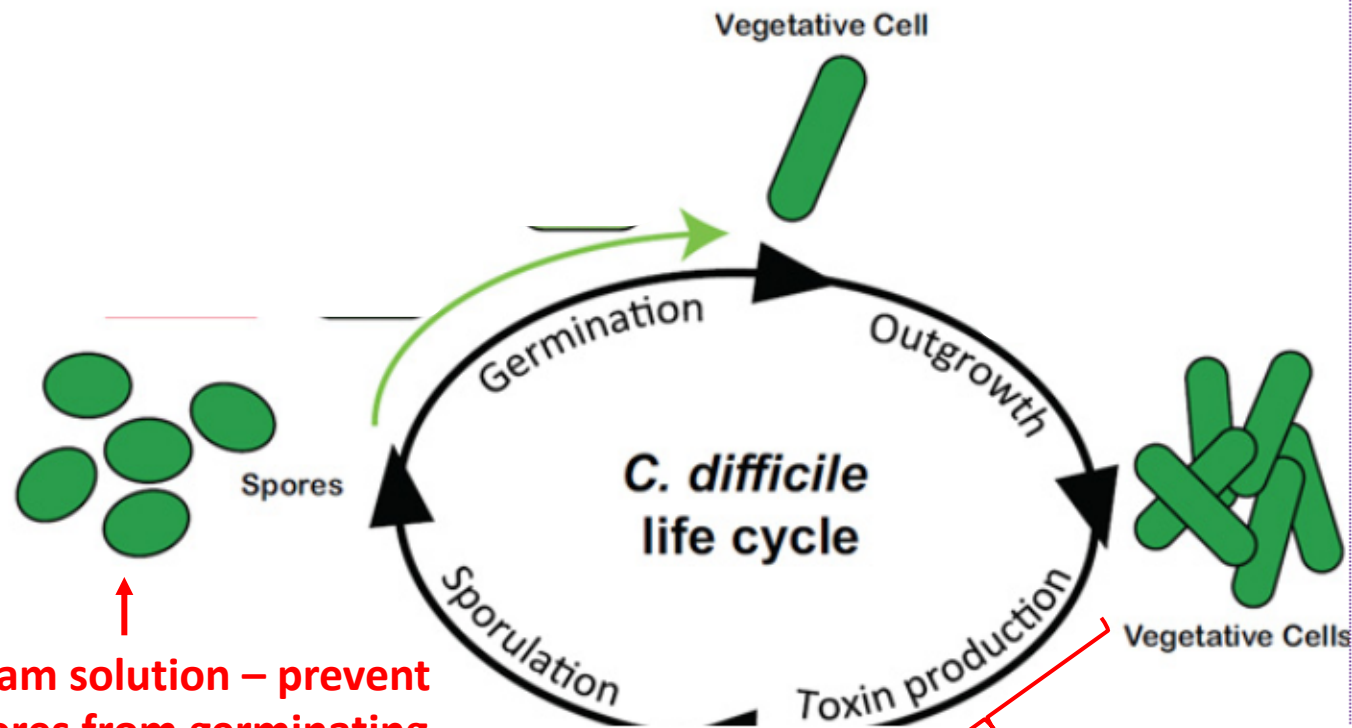
# Learning Points from the Best C. Diff Trial We'll Ever Have:

## In the clear 4 weeks after initial symptom resolution

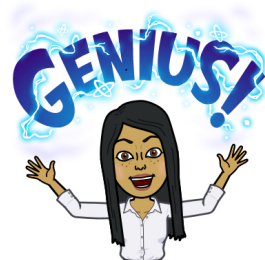


# Why Look at Tolevamer in the First Place?

## Tolevamer binds C. diff toxin



Upstream solution – prevent the spores from germinating in the first place

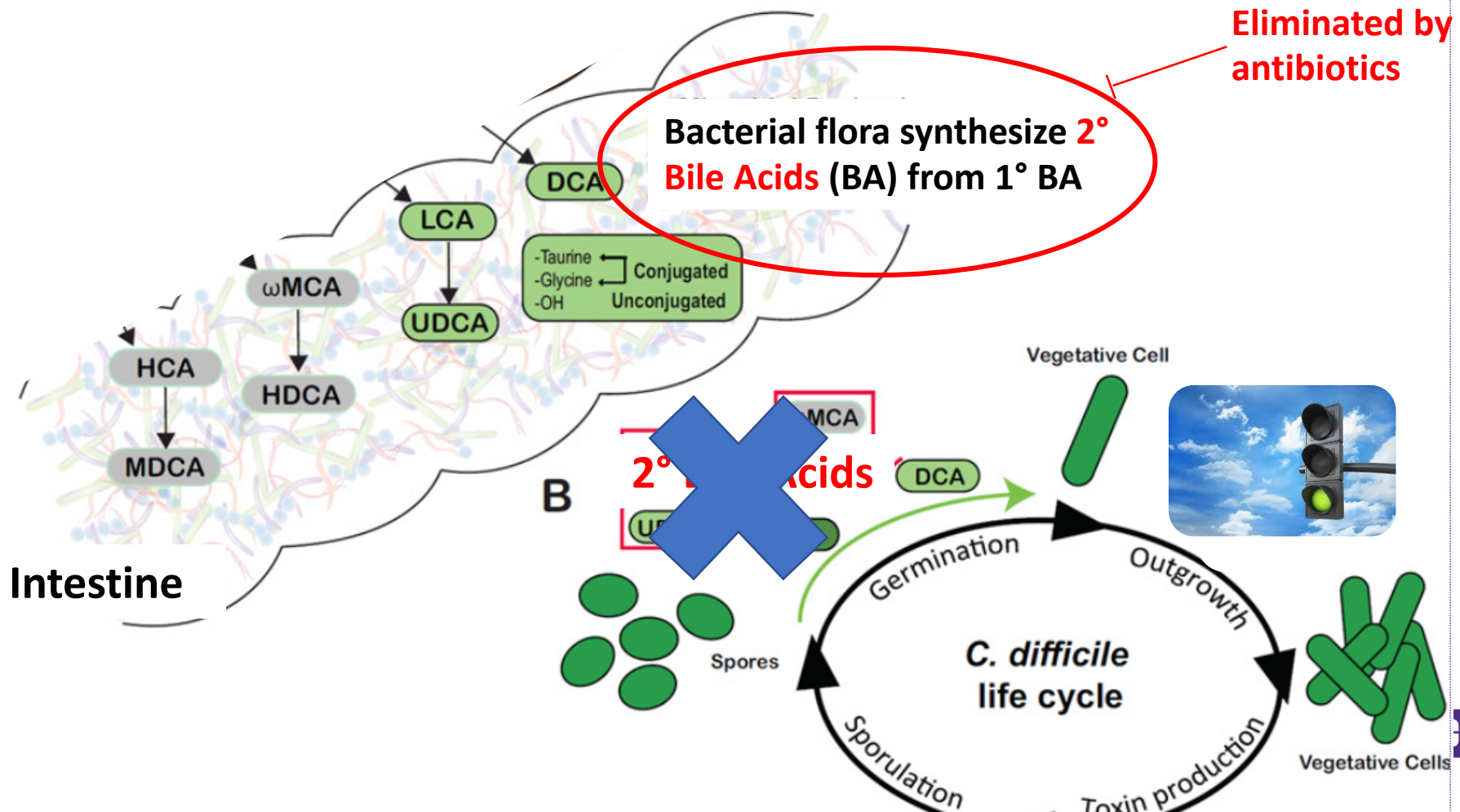


Tolevamer is a non-antibiotic polymer that binds C. diff toxin

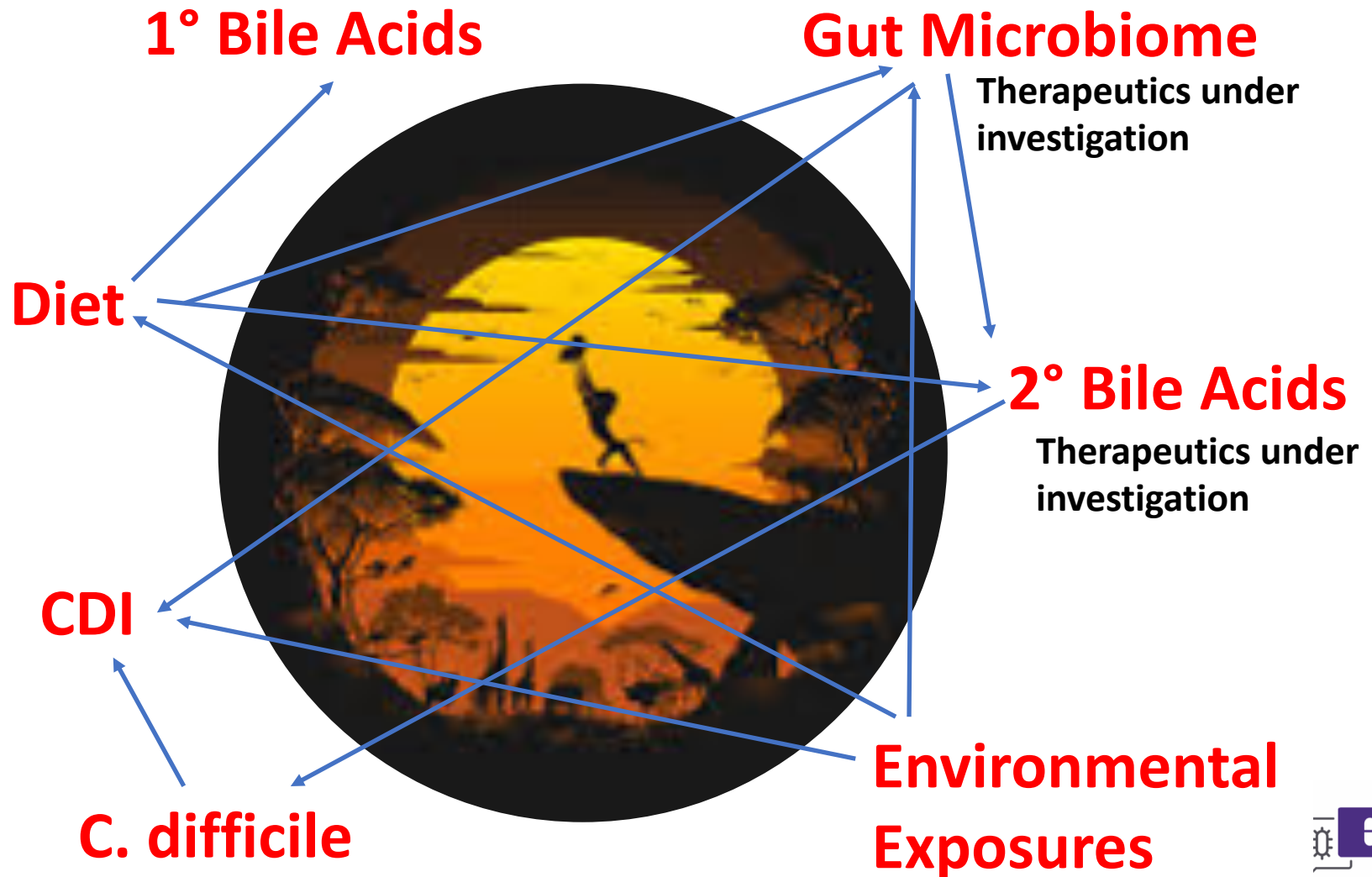


# Bile Acids, the New Magic Bullet?

## 2° Bile Acids Inhibit *C. diff* spore germination



# Everything is connected



## Impact of microbial derived secondary bile acids on colonization resistance against *Clostridium difficile* in the gastrointestinal tract.

Winston JA<sup>1</sup>, Theriot CM<sup>2</sup>.



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
## Inhibiting the Initiation of *Clostridium difficile* Spore Germination using Analogs of Chenodeoxycholic Acid, a Bile Acid

Joseph A. Sorg, Abraham L. Sone

DOI: 10.1128/JB.00610-10

ARTICLE | VOLUME 26, ISSUE 1, P27-34.E4, JANUARY 17, 2019

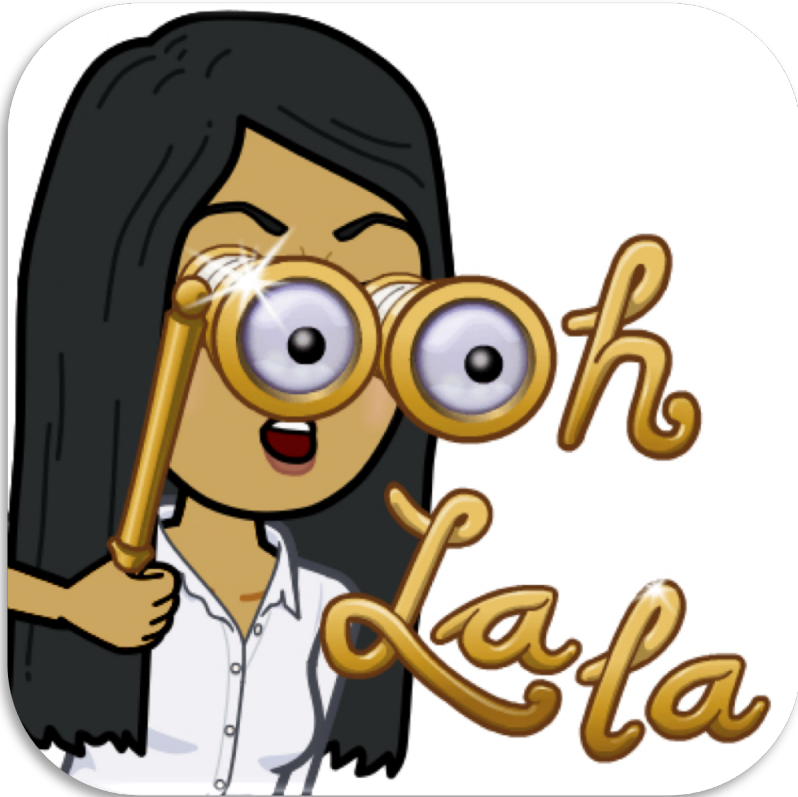
### Bile Acid 7 $\alpha$ -Dehydroxylating Gut Bacteria Secrete Antibiotics that Inhibit *Clostridium difficile*: Role of Secondary Bile Acids

Jason D. Kang • Christopher J. Myers • Spencer C. Harris • ... Jasmohan S. Bajaj • Huiping Zhou •  
Phillip B. Hylemon   • [Show all authors](#) • [Show footnotes](#)

Published: October 25, 2018 • DOI: <https://doi.org/10.1016/j.chembiol.2018.10.003> •



# Why try to recreate the magic when it already exists: **Fecal Transplant**





# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

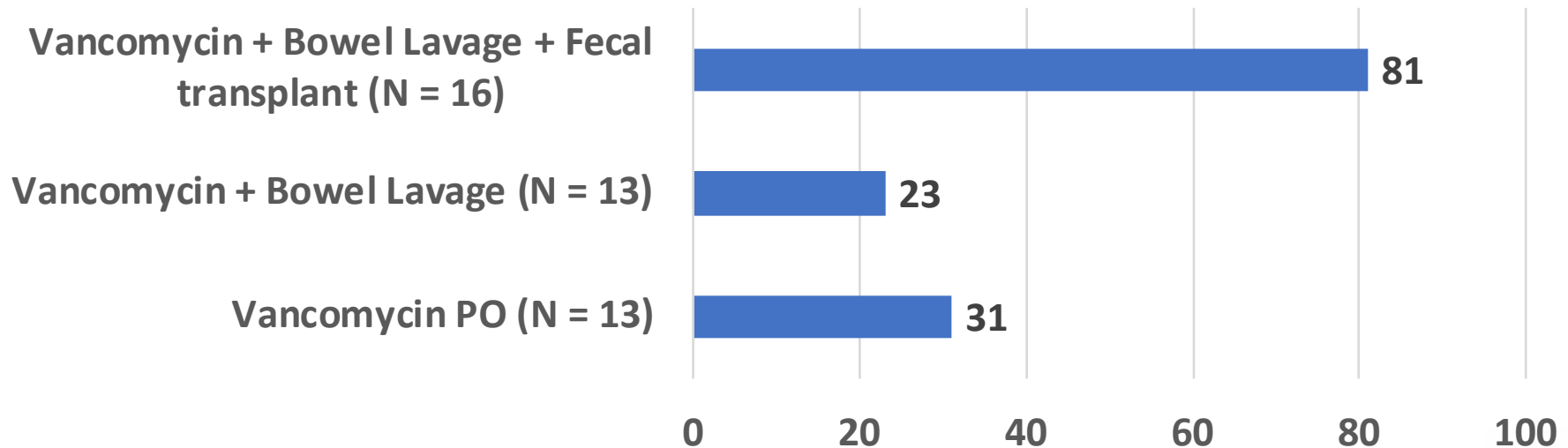
JANUARY 31, 2013

VOL. 368 NO. 5

## Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susan J. van der Meulen, M.D.,  
Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Pieter J. van der  
Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter J. van der Sloot, M.D., Ph.D.,  
Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D.

**Trial stopped early**

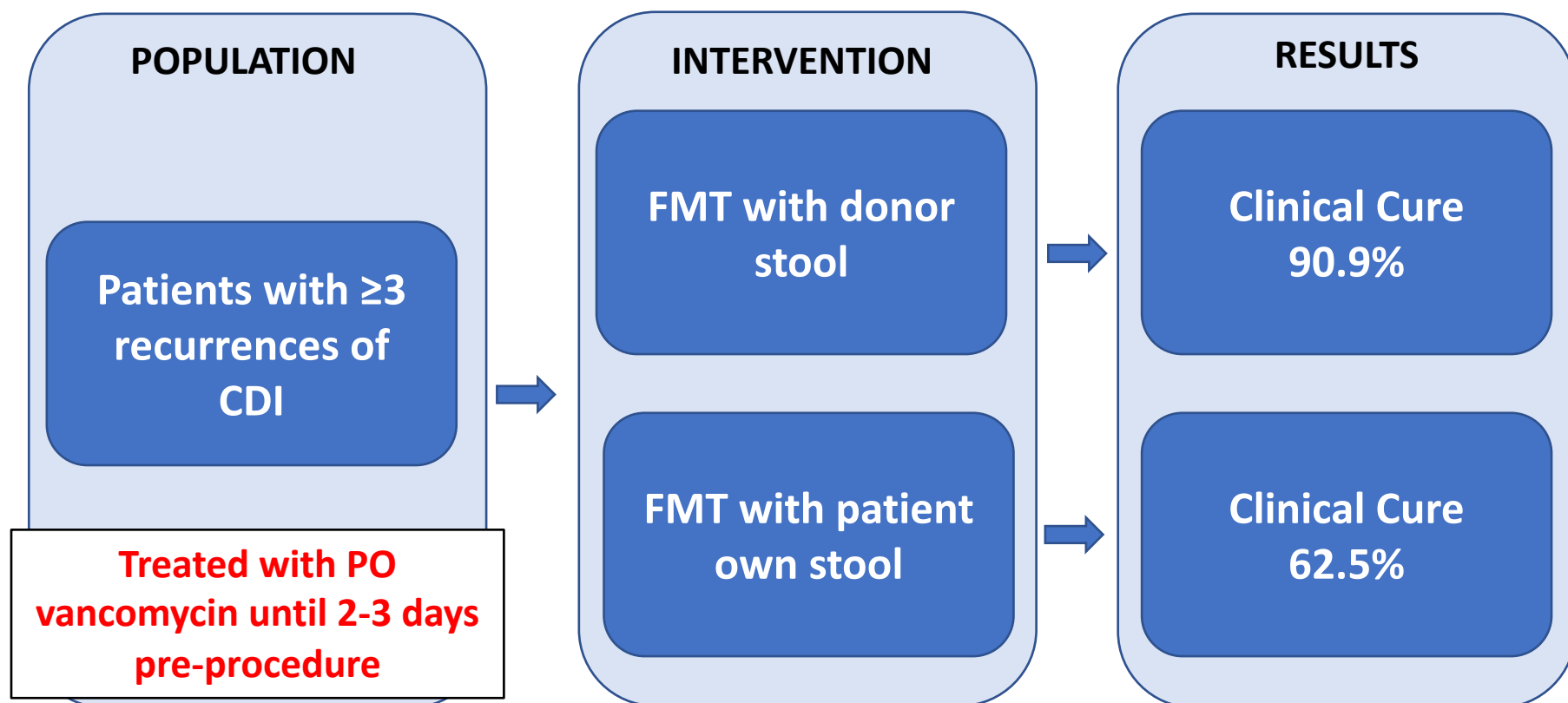


**% of Patients with Resolution of CDI without relapse after 10 weeks**



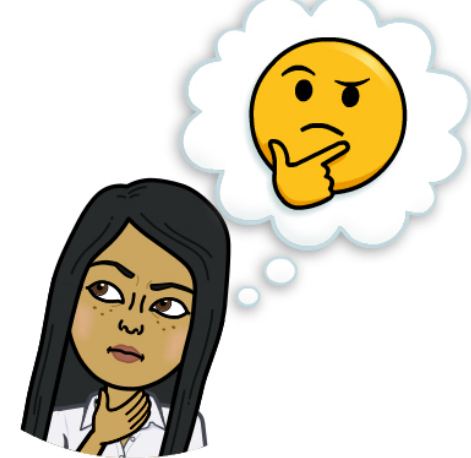
# Effect of Fecal Microbiota Transplantation on Recurrence in Multiply Recurrent *Clostridium difficile* Infection:

## A Randomized Trial





# Why Was Transplant with Diseased Stool Effective in 2/3 of Patients?



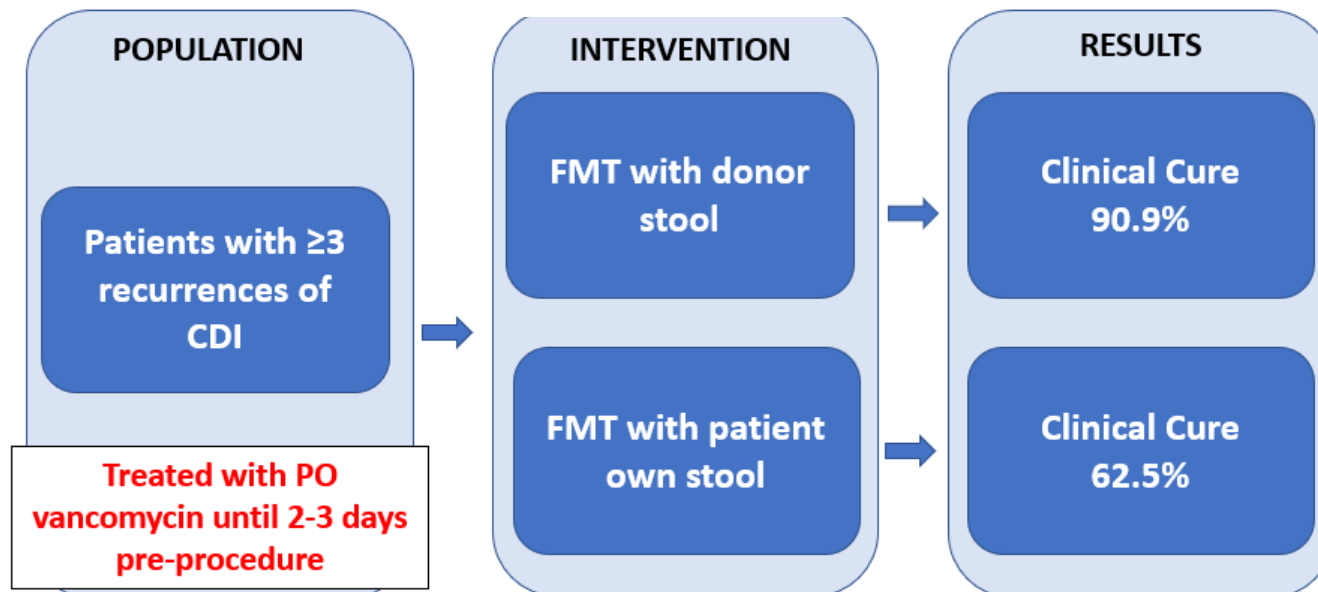
Published in final edited form as:

*Ann Intern Med.* 2016 November 01; 165(9): 609–616. doi:10.7326/M16-0271.

## Effect of Fecal Microbiota Transplantation on Recurrence in Multiply Recurrent Clostridium difficile Infection:

A Randomized Trial

**Placebo effect?**



# Summary

**Recommended Treatment**



**PO Vancomycin is 1<sup>st</sup> Line for All**

PO Metronidazole may be considered in cases of mild disease

**Bile Acids**



**Bile Acids** are a target for new CDI therapeutics. They are **directly impacted by diet, microbiome, antibiotic usage**

**Fecal Transplant  
Microbiome health**



**Fecal Transplants are Effective.** Does prolonged PO vancomycin make them less effective?

