



# FMT: Just another “crap” shoot?

Ted Steiner, M.D.

2016 PICNet meeting

March 4, 2016

# CONFLICT OF INTEREST DISCLOSURE SLIDE

| | |
|---|---|
| **In the past 2 years I have been an employee of:** | |
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| **I agree to disclose approved and non-approved indications for medications in this presentation:** | **YES** |
| **I agree to use generic names of medications in this presentation:** | **YES** |

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stool transplant

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**Fecal** bacteriotherapy - Wikipedia, the free encyclopedia
en.wikipedia.org/wiki/**Fecal**_bacteriotherapy
Fecal microbiota transplantation (FMT) also known as a **stool transplant** is the process of transplantation of fecal bacteria from a healthy individual into a ...
Procedure - History - In animals - Theoretical basis

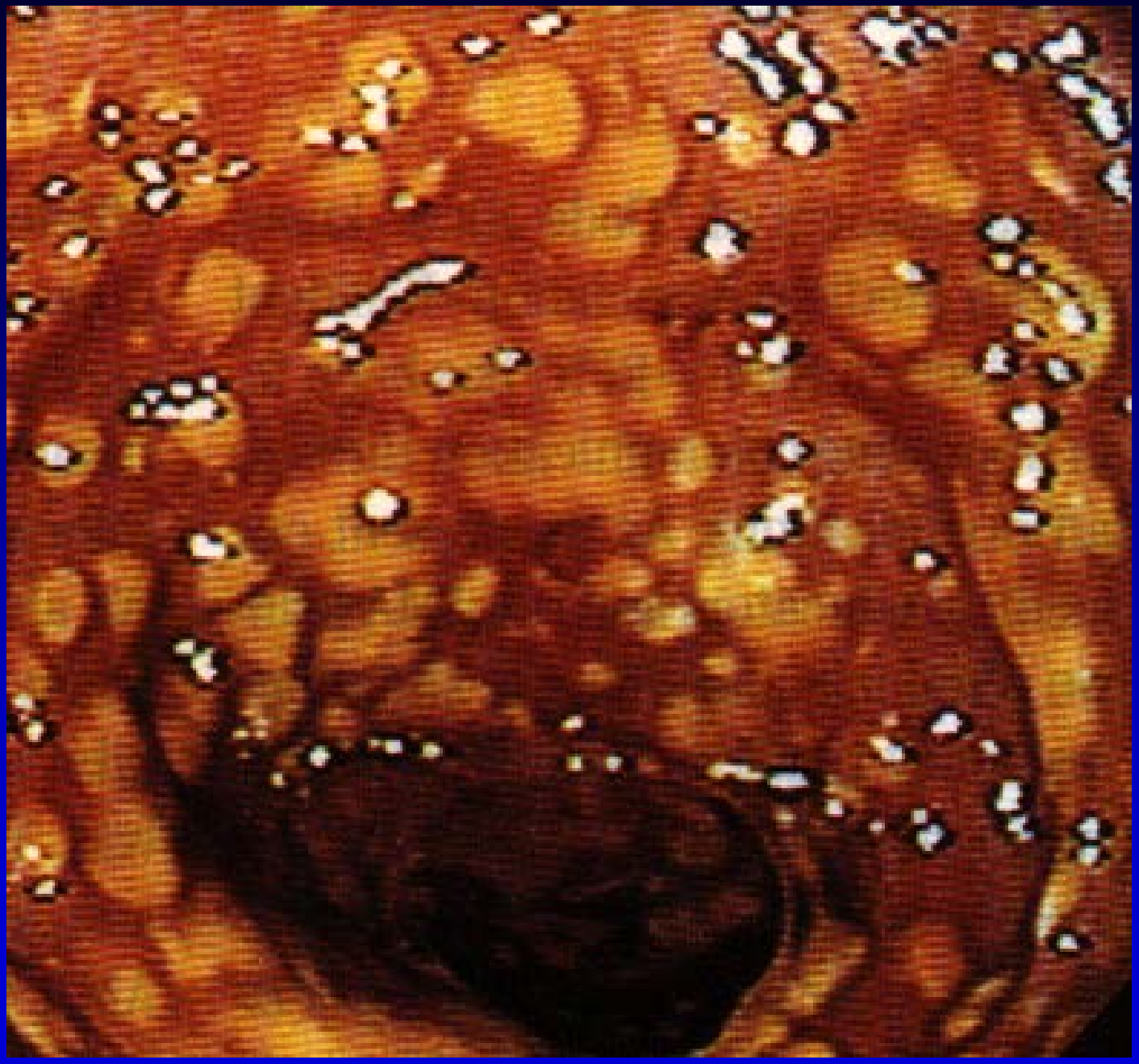
Quick, inexpensive and a 90 percent cure rate - For Medical ...
www.mayoclinic.org/medical.../quick-inexpensive-90-percent-cure-rate
But, he says, one therapy — fecal microbiota transplantation (FMT or **fecal transplantation**) — has proved highly effective at eradicating C. difficile infection and ...

HowStuffWorks "How **Fecal Transplants** Work"

health.howstuffworks.com/medicine/.../**fecal-transplant**.htm
by Nicholas Gerbis
**Fecal transplants** might just be the next big thing in medicine. Learn about the advantages and challenges of **fecal transplants**.

How to Safely do a **Fecal Transplant** at Home - DIY Instructi...
thepowerof**poop**.com/epatients/**fecal-transplant**-instructions/
Everything you want to know about **fecal transplant** at home, but were afraid to ask, including DIY Instructions, testing protocols and FAQs.


http://2.bp.blogspot.com/-EPw7VzDBDWw/TkGcgq0Ht_I/AAAAAAAAH20/QOFeQPP8giM/s1600/diarrhea+cartoon.jpeg



# What is FMT?

Instillation of (products derived from)
donor feces for treatment of a disease of condition

AKA “fecal microbial transplantation”, “stool transplant”, “Human biotherapy”

Proven indications:

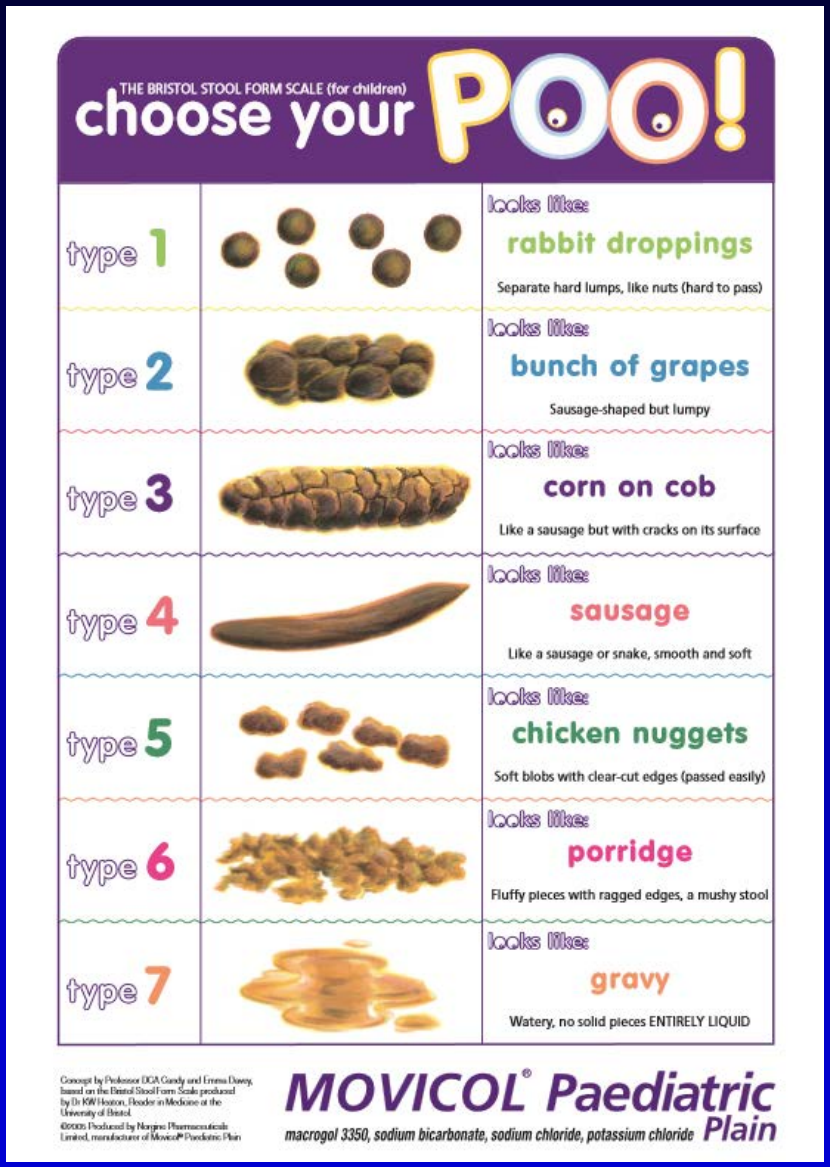
- Relapsing or refractory CDI

Under investigation:

- IBD
- Metabolic syndrome
- MDR organism decolonization

# What is a CDI relapse

- Depends on the case definition!
- Most studies define as a recurrence of diarrhea with a positive stool assay
  - What is diarrhea?
  - Fecal shedding can persist
  - PCR lacks specificity for colonization v dz
- Relapse vs. reinfection difficult to determine


THE BRISTOL STOOL FORM SCALE (for children)
choose your POO!
type 1
looks like:
rabbit droppings
Separate hard lumps, like nuts (hard to pass)
type 2
looks like:
bunch of grapes
Sausage-shaped but lumpy
type 3
looks like:
corn on cob
Like a sausage but with cracks on its surface
type 4
looks like:
sausage
Like a sausage or snake, smooth and soft
type 5
looks like:
chicken nuggets
Soft blobs with clear-cut edges (passed easily)
type 6
looks like:
porridge
Fluffy pieces with ragged edges, a mushy stool
type 7
looks like:
gravy
Watery, no solid pieces ENTIRELY LIQUID
Concept by Professor DCA Cundy and Emma Davey, based on the Bristol Stool Form Scale produced by Dr KW Heaton, Reader in Medicine at the University of Bristol.
©2005 Produced by Norgine Pharmaceuticals Limited, manufacturer of Movicol® Paediatric Plain
MOVICOL® Paediatric Plain
macrogol 3350, sodium bicarbonate, sodium chloride, potassium chloride


THE BRISTOL STOOL TART
1
2
3
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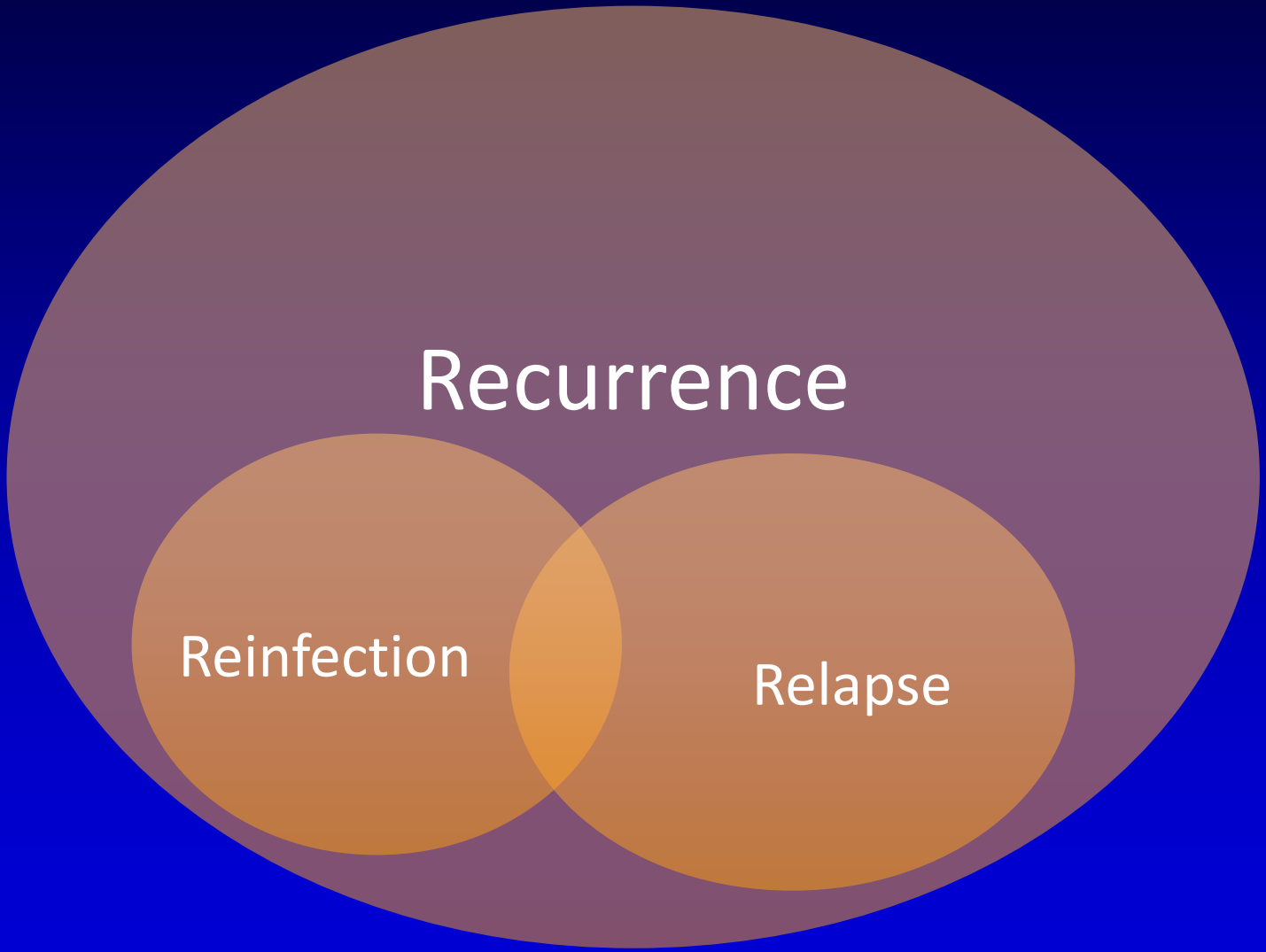
7

# CDI recurrences



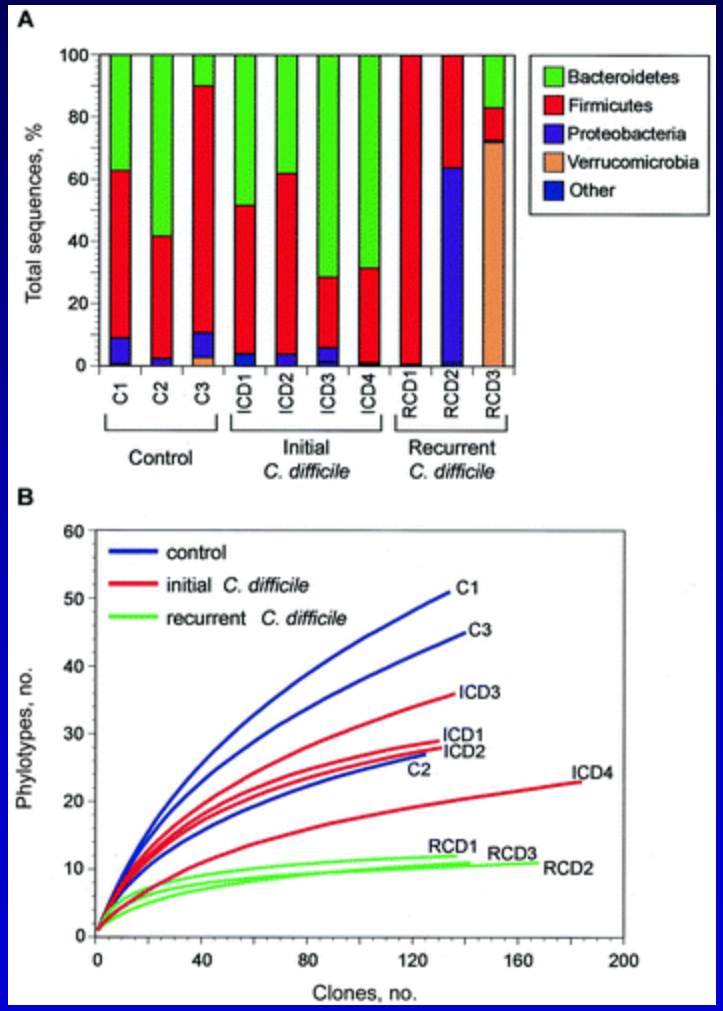
# Why do we care about recurrences?

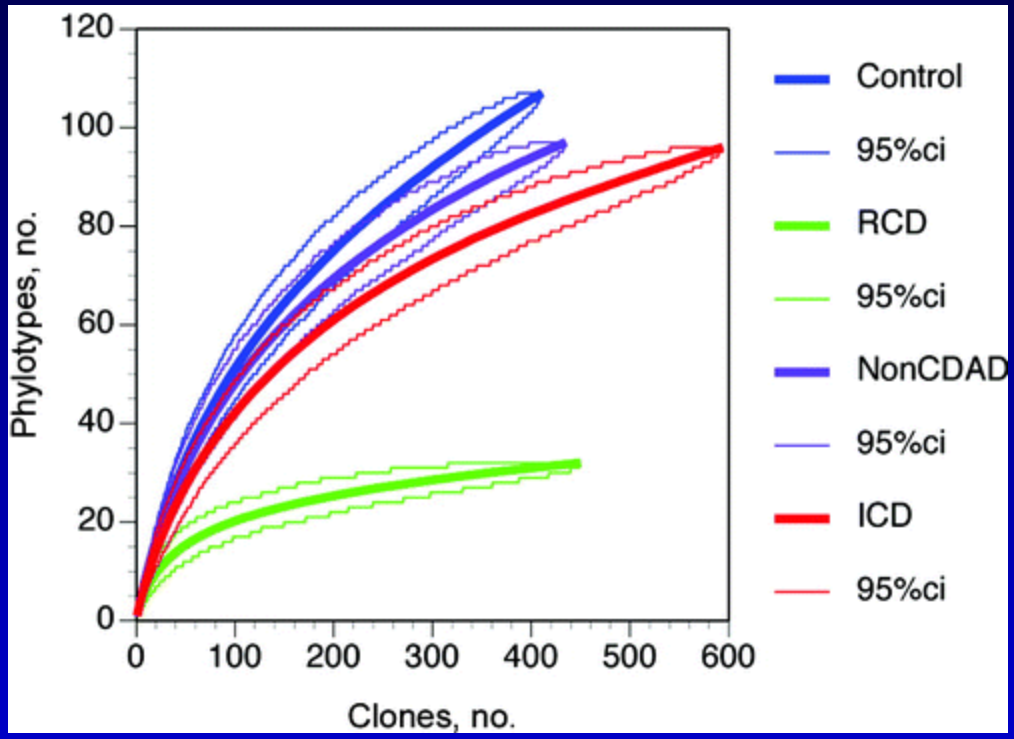
- Morbidity/mortality
  - 26% 6 mo mortality (1.33 HR vs no relapse)( Clin Microbiol Infect. 2015 Feb;21(2):164-70)
  - 85% readmission risk in 6 mos (vs. 41% with no relapse) (Am J Infect Control. 2015 Apr 1;43(4):318-22)
- $$$
  - Average cost of recurrence $11,000 in US (Infect Control Hosp Epidemiol. 2014 Nov;35(11):1400-7)
  - Recurrences account for $65M in Canada (out of total $281M) (Open Forum Infect Dis. 2015 Jun 3;2(3))
- Infection control issues

# Who gets a CDI relapse?

- Multiple studies reported, with frequently inconsistent results
- Consistent risk factors
  - Antibiotics
  - Acid suppression
  - Age
  - Severity of presentation
- Unknown/inconsistent factors: immune status, antibody response, other host factors

# Reduced fecal bacterial diversity in recurrent CDI




JY Chang et al, J. Infect. Dis. 2008, 197:435

# BC recommendations for treatment of recurrent CDI

- First recurrence: treat as initial epidose
- Second recurrence: vancomycin 125 mg QID x 14 d
  - “Consider” taper
  - refer to ID or GI for multiple recurrences
- What then?

# Treatment of CDI relapses

- Vancomycin taper or pulse?
- Probiotics?
- FMT
- Other options

# Does vancomycin taper/pulse work?

**Table 3.** Description of Vancomycin Taper and Pulsed Antibiotic Regimens

| Taper (beginning dose to ending dose) | Recurrence (n = 9) | Cure (n = 20) | |
|---|---|---|---|
| 500–125 | 1 (20%) | 4 | |
| 750–375 | 1 (50%) | 1 | |
| 1000–125 | 2 (22%) | 7 | |
| 2000–250 | 5 (42%) | 7 | |
| 3000–750 | 0 (0%) | 1 | |
| Total tapered | 9 (31%) | 20 | $p = 0.01$* |
| Mean days of taper | 25.4 ± 13.3 | 19.5 ± 8.0 | $U = 107$, ns* |
| No. of tapers followed by pulses | 2 (20%) | 8 | |
| Mean days of pulses | 3.0 ± 0 | 6 ± 4.2 | $t = 0.97$, ns* |
| Pulse only | n = 1 | n = 6 | |
| 500-mg pulse | 0 | 4 | |
| 250-mg pulse | 1 | 1 | |
| 125-mg pulse | 0 | 1 | |
| Total pulsed only | 1 (14.3%) | 6 | $p = 0.02$* |
| Mean days pulsed | 9 ± 0 | 20.3 ± 11 | $t = 0.95$, ns* |

* Recurrence *vs* cure.

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PII S0002-9270(02)04195-3

Breaking the Cycle: Treatment Strategies for 163 Cases of Recurrent *Clostridium difficile* Disease

Lynne V. McFarland, Ph.D., Gary W. Elmer, Ph.D., and Christina M. Surawicz, M.D., F.A.C.G.

# Probiotics

- Not recommended in IDSA guidelines (C-III)
- Based on limited data and risk of bloodstream infection
- Some experts still use *Saccharomyces boulardii* (Florastor) in relapsing patients undergoing stool transplant
- My experience—they just don’t work

# What about kefir?

- Case series of 25 patients with recurrent CDI treated with vancomycin pulsing plus TID kefir
- 21/25 free of diarrhea at 9 months
- 4 relapses cured with vanco + rifaximin
- RCT needed

**Protocol utilizing a staggered and tapered antibiotic treatment regimen for the treatment of recurrent Clostridium difficile infection that has failed to respond to standard antibiotic therapy.**

| Antibiotic<br>Time Course | Metronidazole<br>Dose/Frequency | | Vancomycin<br>Dose/Frequency | | Kefir |
|---|---|---|---|---|---|
| Weeks 1-2 | 250 mg Q 6h | | 125 mg Q 6h | | 150 mL TID |
| Weeks 3-4 | 750 mg Q 72h | | 375 mg Q 72h | | 150 mL TID |
| Weeks 5-6 | 500 mg Q 72h | **OR** | 250 mg Q 72h | **PLUS** | 150 mL TID |
| Weeks 7-8 | 250 mg Q 72h | | 125 mg Q 72h | | 150 mL TID |
| Weeks 9-15 | | | | | 150 mL TID |

Johan S. Bakken Clin Infect Dis. 2014;59:858-861



Clinical Infectious Diseases

# Fecal microbial therapy (FMT)

- 28 case series reported since 1994
- 3 RCTs
- Overall success generally very high, and very few adverse events reported
  - No infections transmitted by FMT
  - Several complications of delivery method
  - Reports of IBD flares
  - One case report of weight gain

Annals of Internal Medicine
Established in 1927 by the American College of Physicians

# From: Fecal Microbiota Transplantation for Clostridium difficile Infection: A Systematic Review

Ann Intern Med. 2015;162(9):630-638. doi:10.7326/M14-2693

*Table 2.* Summary Results for Reported Resolution of Symptoms After Initial FMT for Recurrent CDI, Overall and by FMT Method

| FMT Method | Patients With Resolution of Symptoms Without Recurrence, %* | Studies/Total Studies Analyzed, *n/N* |
|---|---|---|
| Upper GI tract | 77 | 7/187† |
| Colonoscopy | 90 | 11/257† |
| Enema | 78 | 5/45 |
| Upper GI tract and colonoscopy | 100 | 1/27 |
| All methods | 85 | 23/516‡ |

CDI = *Clostridium difficile* infection; FMT = fecal microbiota transplantation; GI = gastrointestinal.
* Because of small sample sizes and the abundance of data from case-series studies, 95% CIs were considered to be unreliable and were not calculated.
† Includes 10 patients from reference 18.
‡ Total number of studies is 1 less than the sum of individual rows.

# Weight Gain After Fecal Microbiota Transplantation

**Neha Alang[1] and Colleen R. Kelly[2]**

[1]Department of Internal Medicine, Newport Hospital, and [2]Division of Gastroenterology, Center for Women's Gastrointestinal Medicine at the Women's Medicine Collaborative, The Miriam Hospital, Warren Alpert School of Brown University, Providence, Rhode Island

**Fecal microbiota transplantation (FMT) is a promising treatment for recurrent *Clostridium difficile* infection. We report a case of a woman successfully treated with FMT who developed new-onset obesity after receiving stool from a healthy but overweight donor. This case may stimulate further studies on the mechanisms of the nutritional-neural-microbiota axis and reports of outcomes in patients who have used non-ideal donors for FMT.**

- 32 yo woman, BMI 26 pre-transplant
- Received stool from 16 yo daughter (BMI 26.4)
- 16 mos post FMT, unintentional weight gain (BMI 34.5)

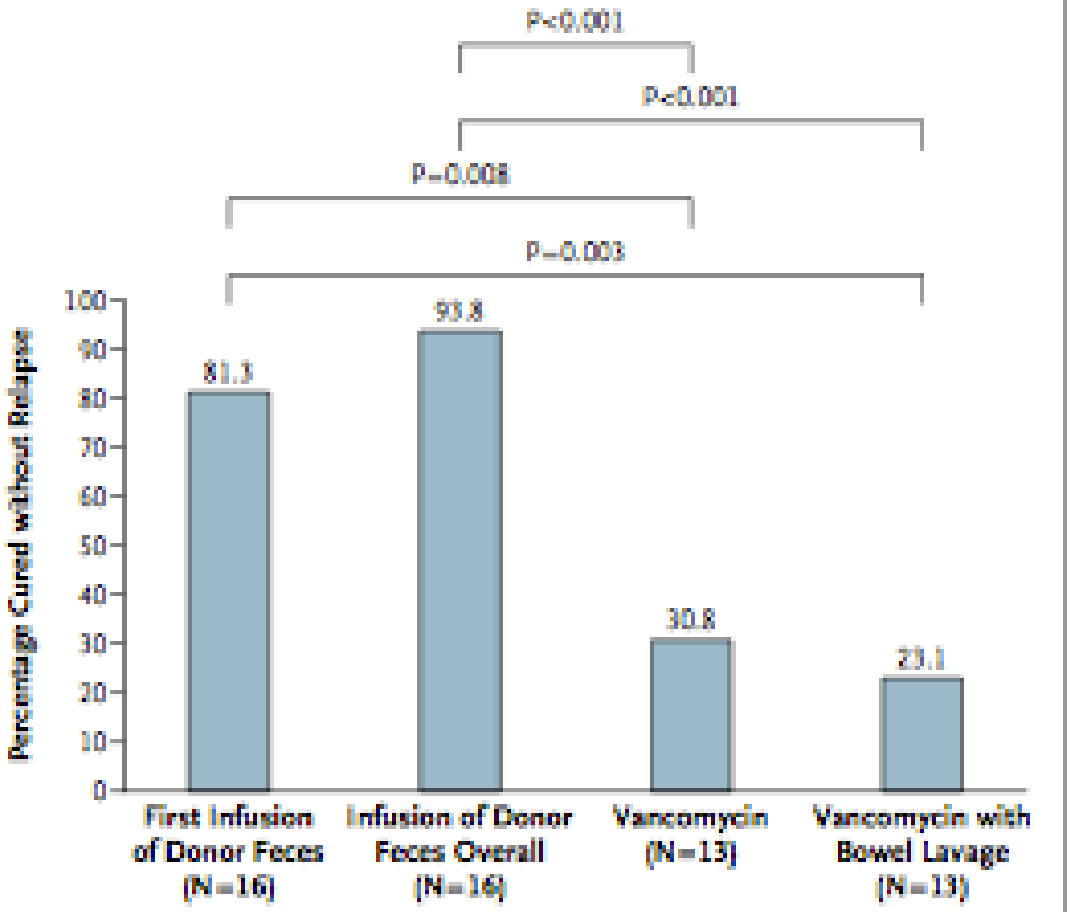



**Figure 2. Rates of Cure without Relapse for Recurrent *Clostridium difficile* Infection.**

Shown are the proportions of patients who were cured by the infusion of donor feces (first infusion and overall results), by standard vancomycin therapy, and by standard vancomycin therapy plus bowel lavage.

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., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

http://www.npr.org/blogs/health/2014/10/11/355126926/frozen-poop-pills-fight-life-threatening-infections

# From: **Oral, Capsulized, Frozen Fecal Microbiota Transplantation for Relapsing Clostridium difficile Infection**

JAMA. Published online October 11, 2014. doi:10.1001/jama.2014.13875

**Table 1. Baseline Characteristics of Study Participants**

| Patient No. | Sex | Age, y | Prior CDI, No.[a] | Previous Vancomycin Taper | Previous Fidaxomycin Treatment | Maximal No. of BM per Day During Current CDI | Type of CDI[b] | Pretreatment: Overall Health Score[c] | Pretreatment: GI Health Score[c] | Pretreatment: BM per Day, No. | Donor No. | Diarrhea Resolution After 1 Treatment[d] | Overall Diarrhea Resolution[e] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 69 | 3 | Yes | No | 20 | Refractory | 2 | 2 | 8 | 1 | No | Yes |
| 2 | M | 55 | 4 | Yes | Yes | 15 | Recurrent | 6 | 3 | 5 | 1 | Yes | Yes |
| 3 | M | 79 | 2 | Yes | Yes | 6 | Recurrent | 5 | 3 | 3 | 1 | Yes | Yes |
| 4 | M | 62 | 3 | Yes | No | 10 | Recurrent | 9 | 7 | 6 | 1 | Yes | Yes |
| 5 | M | 70 | 3 | No | Yes | 10 | Recurrent | 5 | 5 | 6 | 1 | No | Yes |
| 6 | M | 65 | 6 | Yes | Yes | 8 | Recurrent | 7 | 7 | 4 | 2 | Yes | Yes |
| 7 | F | 84 | 5 | Yes | No | 6 | Recurrent | 4 | 4 | 3 | 1 | Yes | Yes |
| 8 | M | 53 | 2 | Yes | No | 10 | Recurrent | 6 | 3 | 2 | 1 | Yes | Yes |
| 9 | F | 89 | 3 | Yes | Yes | 6 | Recurrent | 7 | 6 | 4 | 2 | Yes | Yes |
| 10 | M | 74 | 6 | Yes | No | | Refractory | 5 | 3 | 6 | 2 | No | No |
| 11 | F | 76 | 5 | Yes | No | 15 | Recurrent | 7 | 6 | 3 | 2 | Yes | Yes |
| 12 | F | 17 | 6 | Yes | Yes | | Recurrent | 5 | 7 | 3 | 3 | No | Yes |
| 13 | M | 49 | 3 | Yes | Yes | 30 | Recurrent | 8 | 4 | 4 | 3 | Yes | Yes |
| 14 | F | 37 | 3 | Yes | No | 14 | Recurrent | 5 | 7 | 3 | 3 | Yes | Yes |
| 15 | M | 61 | 3 | Yes | No | 10 | Recurrent | 7 | 7 | 2 | 2 | Yes | Yes |
| 16 | F | 82 | 2 | Yes | No | 8 | Refractory | 3 | 3 | 6 | 3 | No | No |
| 17 | F | 56 | 3 | Yes | No | 12 | Recurrent | 9 | 8 | 2 | 3 | Yes | Yes |
| 18 | M | 89 | 4 | Yes | No | 10 | Recurrent | 4 | 3 | 1 | 2 | Yes | Yes |
| 19 | F | 11 | 5 | Yes | Yes | 15 | Recurrent | 5 | 3 | 2 | 4 | No | Yes |
| 20 | M | 64 | 5 | Yes | Yes | 15 | Refractory | 5 | 5 | 6 | 2 | Yes | Yes |
| Median (IQR) [range] | | 64.5 (53.5-78.3) [11-89] | 3 (3-5) [2-6] | | | 10 (8-15) [6-30] | | 5 (5-7) [2-9] | 4.5 (3-7) [2-8] | 3.5 (2.3-6) [1-8] | | | |
| Total No. (%) | Female, 9 (45) | | | 19 (95) | 9 (45) | | Recurrent, 16 (80) | | | | | 14 (70) | 19 (90) |

Abbreviations: BM, bowel movements; CDI, *Clostridium difficile* infection; GI, gastrointestinal; IQR, interquartile range.

[a] Documented number of previous episodes of CDI.

[b] Refractory CDI was considered when fecal microbiota transplantation was performed in a patient who was clinically unresponsive to standard treatment. Recurrent CDI was considered when a patient responded to standard treatment but relapsed at least twice when treatment was discontinued. In all cases, patients had proof of active CDI consisting of compatible symptoms and recent positive stool test results.

[c] Self-reported health ranking on a scale of 1 to 10, with 1 being the least well and 10 being "best possible health for you."

[d] One treatment denotes administration of 15 capsules on 2 consecutive days (total of 30 capsules). Diarrhea resolution is defined as being symptom free and not receiving anti-CDI treatment at 8 weeks.

[e] Overall diarrhea resolution includes patients who responded to initial treatment with 30 capsules over 2 consecutive days in addition to patients who were retreated with a second inoculum of 15 capsules on 2 consecutive days (total of 60 capsules; n = 6). Diarrhea resolution is defined as being symptom free and not receiving anti-CDI treatment at 8 weeks after time of second inoculum.

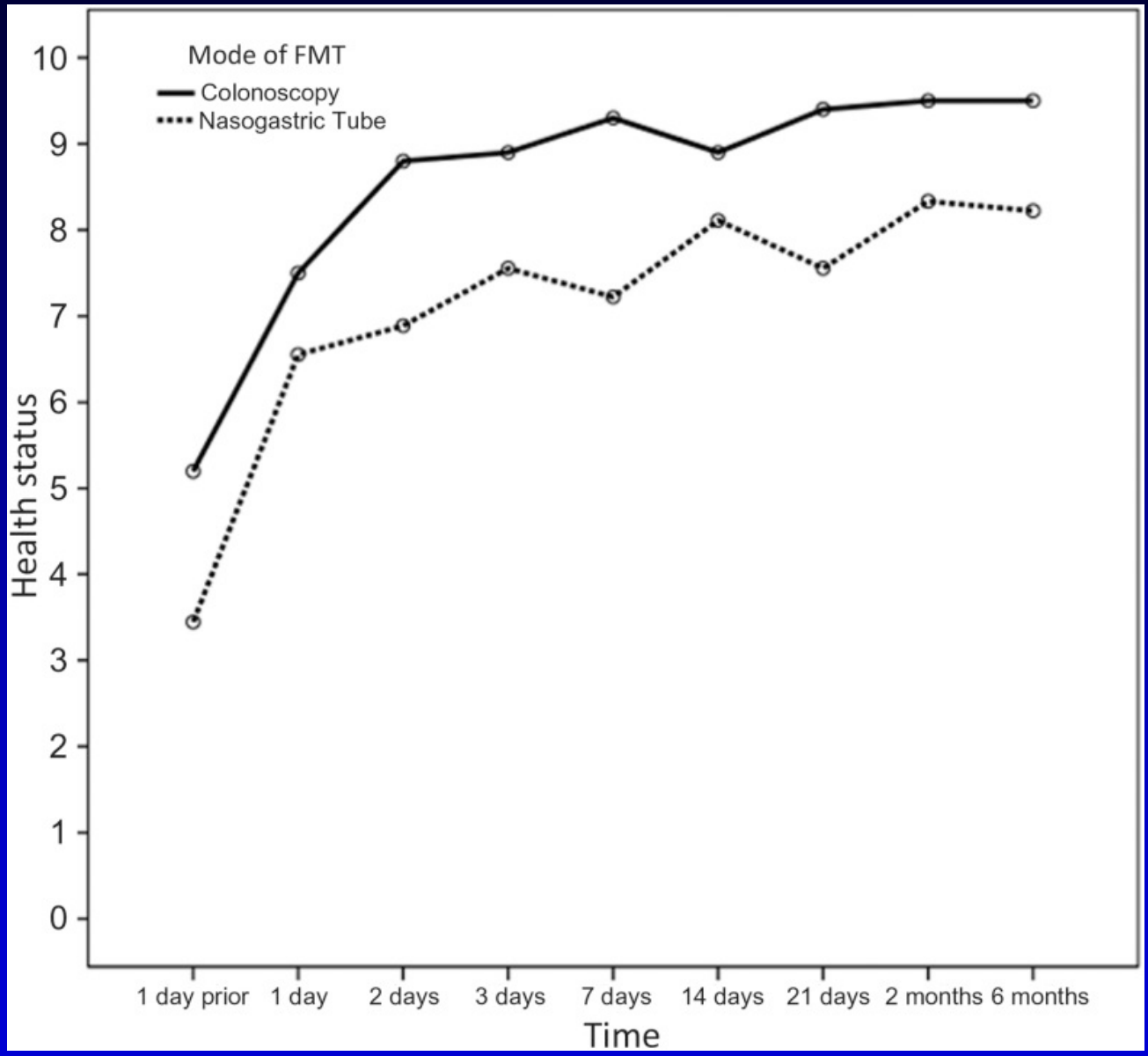
**Figure Legend:**

Baseline Characteristics of Study Participants

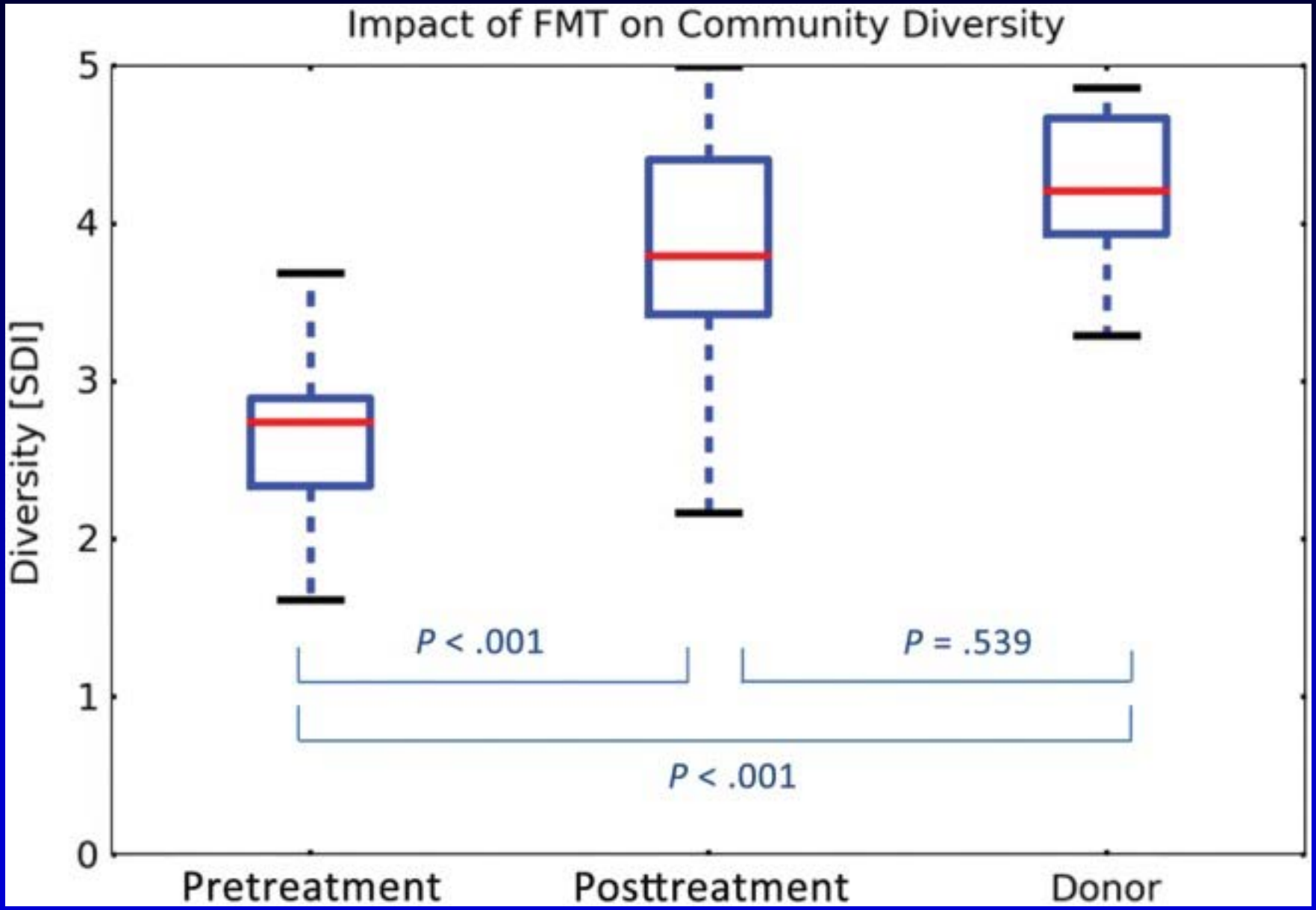
# RCT of NG vs colonoscopy

- Pilot study of 20 patients
- Cure rate 70/90% after 1/2 doses
- No difference between routes
- Microbiota analyzed before and after treatment
- 1 of the 2 failures cured himself with daily FMT enemas from his roommate

Clin Infect Dis. 2014 Jun 1; 58(11): 1515–1522.
**Fecal Microbiota Transplant for Relapsing *Clostridium difficile* Infection Using a Frozen Inoculum From Unrelated Donors: A Randomized, Open-Label, Controlled Pilot Study**




Clin Infect Dis. 2014 Jun 1; 58(11): 1515–1522.




Clin Infect Dis. 2014 Jun 1; 58(11): 1515–1522.

# RCT of fresh vs frozen stool

- Subjects with recurrent (>3) or refractory CDI
- Stratified based on age, mode of acquisition, number of relapses
- 1:1 fresh stool vs. frozen-and-thawed by 50 ml concentrated, filtered enema
- 219 subjects enrolled, 178 treated per-protocol

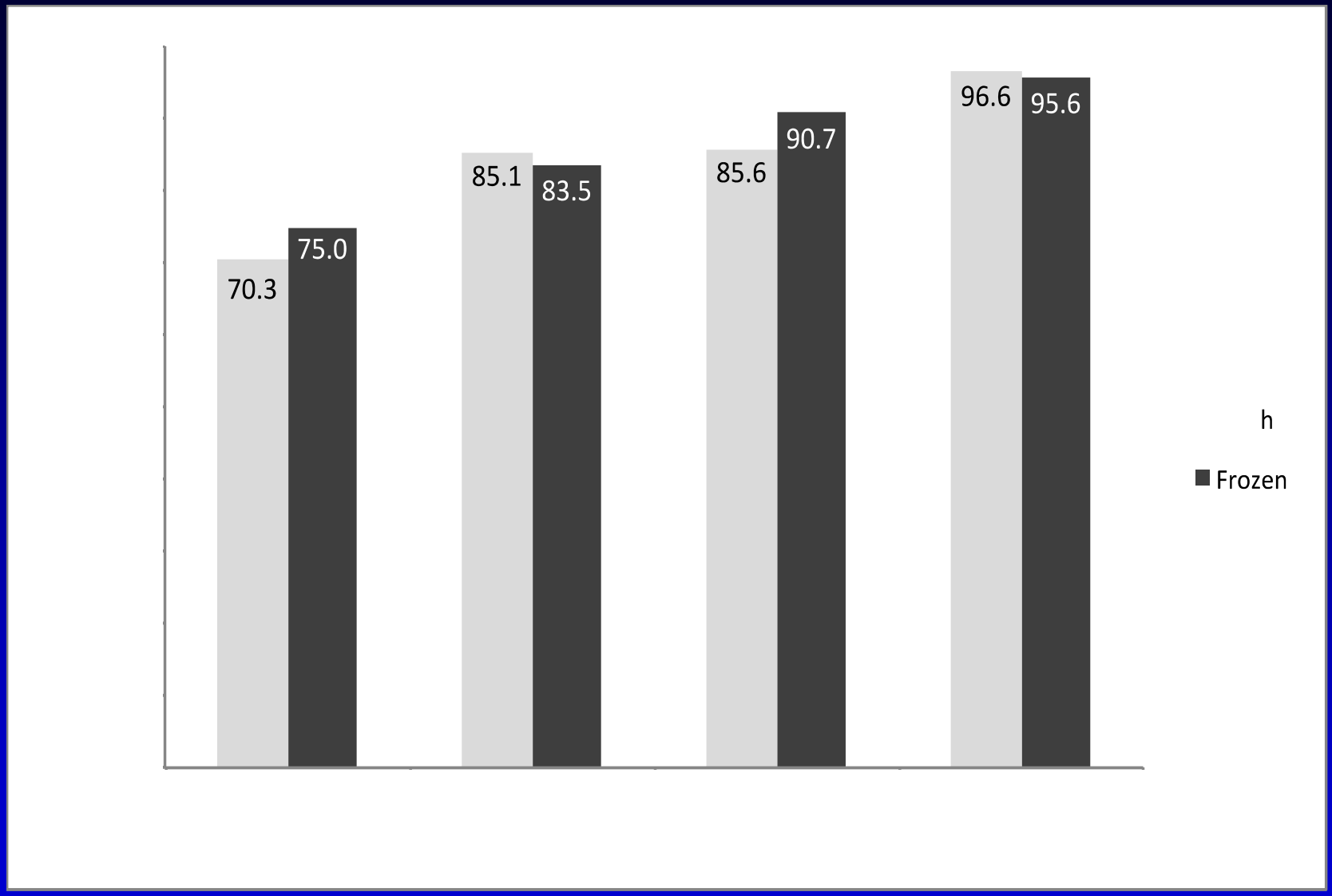
From: **Frozen vs Fresh Fecal Microbiota Transplantation and Clinical Resolution of Diarrhea in Patients With Recurrent Clostridium difficile Infection: A Randomized Clinical Trial**

JAMA. 2016;315(2):142-149. doi:10.1001/jama.2015.18098

Table 2. Number of Fecal Microbiota Transplantations and the Proportion With Clinical Resolution at 13 Weeks After Last Transplantation

| | No. (%) With Clinical Resolution | | | |
|---|---|---|---|---|
| | mITT Population | | Per-Protocol Population | |
| No. of FMTs | Frozen (n = 108) | Fresh (n = 111) | Frozen (n = 91) | Fresh (n = 87) |
| 1 | 57 (52.8) | 56 (50.5) | 57 (62.7) | 54 (62.1) |
| 2 | 24 (75.0) | 22 (70.3) | 19 (83.5) | 20 (85.1) |
| 3-5 | 13 (87.0) | 12 (81.1 | 9 (93.4) | 9 (95.4) |
| >5 | 4 (90.7) | 5 (85.6) | 2 (95.6) | 1 (96.6) |
| **Total** | **98**/108 (90.7) | **95**/111 (85.6) | **87**/91 (95.6) | **84**/87 (96.6) |

Abbreviations: FMT, fecal microbiota transplantation; mITT, modified intention-to-treat.




C. Lee et al, JAMA 2016

# What is the current status of FMT in BC?

- As of March 1, only readily available by clinical trial
  - Prospective, open-label frozen-and-thawed enema (C. Lee et al)
  - Punch CD2 (Rebiotix)
- Provincial guidelines under review

# FMT as approved therapy

- Will only be for CDI
  - Recurrent or refractory
- Donor testing per guidelines
  - Can be family member, acquaintance, or stranger but must be traceable
- Goal: to have local infrastructure for donor testing and stool prep
  - Or a central testing/prep facility and shipping
- Will need billing infrastructure and HCP training

# Donor testing

- Same as for blood donors
- Also test for stool pathogens
- Controversies: Hp, enteric viruses, HTLV I/II, Hep A, ESBL, CPE
- Exclude donors with malignancy, IBD, immunosuppression, recent Abx, IBS, systemic autoimmune disease
- Caution with morbid obesity or psychiatric condition

# What is my experience with FMT?

- Fresh-vs-frozen trial—results published
- Frozen and thawed trial
  - 20 patients treated, 9 completed 3 mo f/u
  - 6 success, 3 failure
  - 2 failures in severe IBD
  - 1 elderly patient with late relapses
- 3 deaths/55 patients (none related to C. diff)

# Challenges with FMT

- Is it really CDI?
- If it is, are all the symptoms due to CDI?
- If not, will eliminating C. diff/restoring microbiota make the symptoms better?
- What if it doesn’t work?

# Is it really relapsing CDI?

- Stool PCR can stay positive for months after successful treatment (and can be negative quickly on treatment)
- PCR+EIA+ samples more likely to be true positives in acute disease, but no data on relapses (JAMA Intern Med. 2015 Nov;175(11):1792-801)
- The smell and color of stool are not helpful (Clin Infect Dis. 2013 Feb 15; 56(4): 615–616) and can mislead patients (but not dogs!)

# Is CDI really causing the symptoms?

- Post-infectious IBS common after repeated episodes
- Chronic abdominal pain conditions can follow repeated infections or can be slow to resolve

# Example case 1

- 59 yo woman with multiple recurrences with disabling abdominal pain
- Psychiatric comorbidities (anxiety, somatization d/o, PTSD)
- Treated with FMT but ongoing abdominal pain, dizziness, occas. loose stools for months
- No recurrence of diarrhea
- 6 mos post FMT—ER visit with Abd pain, high CRP/WBC—stool neg for TcdB
- No subsequent relapses

# What about co-morbid GI illness?

- FMT safe in immune-compromised (Am J Gastroenterol. 2014 Jul;109(7):1065-71 )
- FMT in IBD patients very complicated
  - Role of medications?
  - How to tell IBD flare from CDI?
  - Risk of disease exacerbation after FMT (14% in study above)

# Recurrent CDI in IBD—case 2

- 25 yo man with UC dx in 2009 (after receiving Abx)
- Ongoing activity on 5-ASA
- Stool tested + for C. diff in 2011—response to MTZ/vanco several times but sxs recurred off abx with bloody diarrhea, pain
- Admitted to SPH—scope showed only mild colitis: put on prednisone and vancomycin

# Case 2 (cont.)

- Sxs gone on vancomycin + prednisone—returned after both tapered off, so restarted on both
- Vanco stopped but prednisone continued (30 mg with taper). FMT 2 doses 1 wk apart, but sxs returned d10.
- 2 more doses FMT plus cholestyramine, but no improvement—back on vanco and prednisone, and sxs settled
- Slowly tapered off prednisone, and stable on low-dose vanco
- Will plan to re-treat with FMT

# CDI in IBD—case 3

- 21 yo man with ?crohn's colitis dx in 2006
- Failed several biologics (including anti-TNF, investigational agenst)
- Found C. diff + in 2012 and responded to MTZ
- CDI recurred in 2013—put on vanco with resolution and maintained on OD-BID for 2 years
- Referred for FMT on vanco but no meds for IBD

# CDI in IBD—case 3 (cont)

- Received 1 dose FMT—well for 3 weeks
- Loose stools returned, + cramps, 0 blood
- Given dose #2, but next day sxs worse so self-started on vancomycin
- 1 wk later, no better; stool – for TcdB; self-stopped vancomycin—advised to go to hospital. Was started on prednisone
- 1 wk later presented to hospital with no improvement; required emergency colectomy

# What if FMT fails?

- Exclude other causes of sxs (e.g. other infections, IBS, microscopic colitis)
- Try again
- Cholestyramine
- Try again (different donor?)
- Try again
- Try again

# Case 4

- 74 yo woman, previously healthy, h/o mild IBS
- Several episodes of CDI since 2011 without relapse
- Relapsing CDI since early 2014—completely well on vancomycin; hospitalized within days of stopping each time

# Case 4 (cont)

- FMT#1: did well for 2 weeks, then relapse
- FMT#2: did well for 3 weeks, then relapse (PCR+)
- Fidaxomicin x 10 d then FMT#3: relapsed again after 3 weeks, back on vanco
- FMT#4: relapse after 1 week, back on vanco for 1 month
- FMT#5: did well, then abrupt onset N/V, then typical diarrhea

# Case 4 (cont)

- FMT#5, did well, then relapse within a month
- FMT#6,7 4 days apart: improving but still some sxs at 1 wk
- FMT#8: 5 d later, in ER, back on vanco
- FMT#9-11 in 1 week: relapsed in 1 month
- FMT#12-16 within 10 days
- Has remained well since then; still on cholestyramine!!

# Case 4 (cont)

- Pt agreed to give blood for measurement of T cell responses to TcdA/B
- PDF: “the CD4 percentage was really low”
- Sent blood to clinical lab: CD4=280 (HIV neg)

- No reports of CDI in idiopathic CD4 lymphopenia

# Future of FMT

- Oral capsule delivery
  - Stool
  - Bacterial pellet
  - Lyophilized stool
- Stool-free systems
  - SERES
  - RePOOPulate

# Alternatives to FMT

- Vancomycin pulse with kefir (case series)
- Fidaxomicin “chaser” (case series) (Open Forum Infect Dis. 2014 Aug 25;1(2)
- Rifaximin “chaser” (several case series)
- Chronic vancomycin suppression
- Bezlotoxumab ?
  - Not yet available

# Actoxumab/bezlotoxumab

- Humanized mAbs against TxA and TxB
- Given I.V. as single dose
- Phase II trial:  70% reduction in recurrence rate vs placebo (p=0.0004)
- Trend towards less severe disease after treatment (p =0.06)
- Phase III trials recently completed

Lowy et al, DDW 2009, 751b

# Actox/Bezlo Phase III results

Efficacy and Safety of Bezlotoxumab (BEZ) alone and with Actoxumab (ACT) for Prevention of Recurrent *C. difficile* Infection (rCDI) in Patients on Standard of Care (SoC) Antibiotics (MODIFY II)

| | ACT+BEZ | | BEZ alone | | Placebo | |
|---|---|---|---|---|---|---|
| | n/N | (%) | n/N | (%) | n/N | (%) |
| rCDI[†] | 58/390 | (14.9) | 62/395 | (15.7) | 97/378 | (25.7) |
| Global Cure[‡] | 224/390 | (57.4) | 264/395 | (66.8) | 197/378 | (52.1) |
| rCDI by Subgroup | | | | | | |
| Metronidazole | 28/191 | (14.7) | 24/189 | (12.7) | 42/182 | (23.1) |
| Vancomycin | 29/187 | (15.5) | 36/190 | (18.9) | 51/184 | (27.7) |
| Fidaxomicin | 1/12 | ( 8.3) | 2/16 | (12.5) | 4/12 | (33.3) |
| Inpatient | 35/269 | (13.0) | 33/273 | (12.1) | 54/259 | (20.8) |
| Outpatient | 23/121 | (19.0) | 29/122 | (23.8) | 43/119 | (36.1) |
| History of CDI in past 6 months | 21/104 | (20.2) | 27/113 | (23.9) | 47/110 | (42.7) |
| Infected with 027 Ribotype | 5/37 | (13.5) | 9/40 | (22.5) | 19/58 | (32.8) |
| Severe CDI at study entry | 9/80 | (11.3) | 6/55 | (10.9) | 13/65 | (20.0) |
| Age ≥ 65 years | 42/241 | (17.4) | 32/205 | (15.6) | 61/206 | (29.6) |
| Immunocompromised | 11/75 | (14.7) | 11/82 | (13.4) | 15/53 | (28.3) |

# Conclusions

- FMT is a very safe and effective treatment for relapsing CDI
- Real world success lower than in case series
  - Reporting bias
  - Inconsistent definitions
- No major safety concerns yet
  - Exercise caution in IBD patients
  - Ensure proper donor screening