香港中文大學
The Chinese University of Hong Kong

香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong

40th Anniversary 四十週年

Role of Gut Microbiota in the Pathogenesis and Therapeutics of CDI

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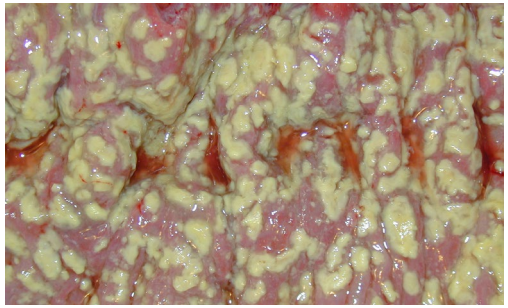
Microbiota I-Center (MagIC)
Chinese University of Hong Kong

What is *C. diff*?



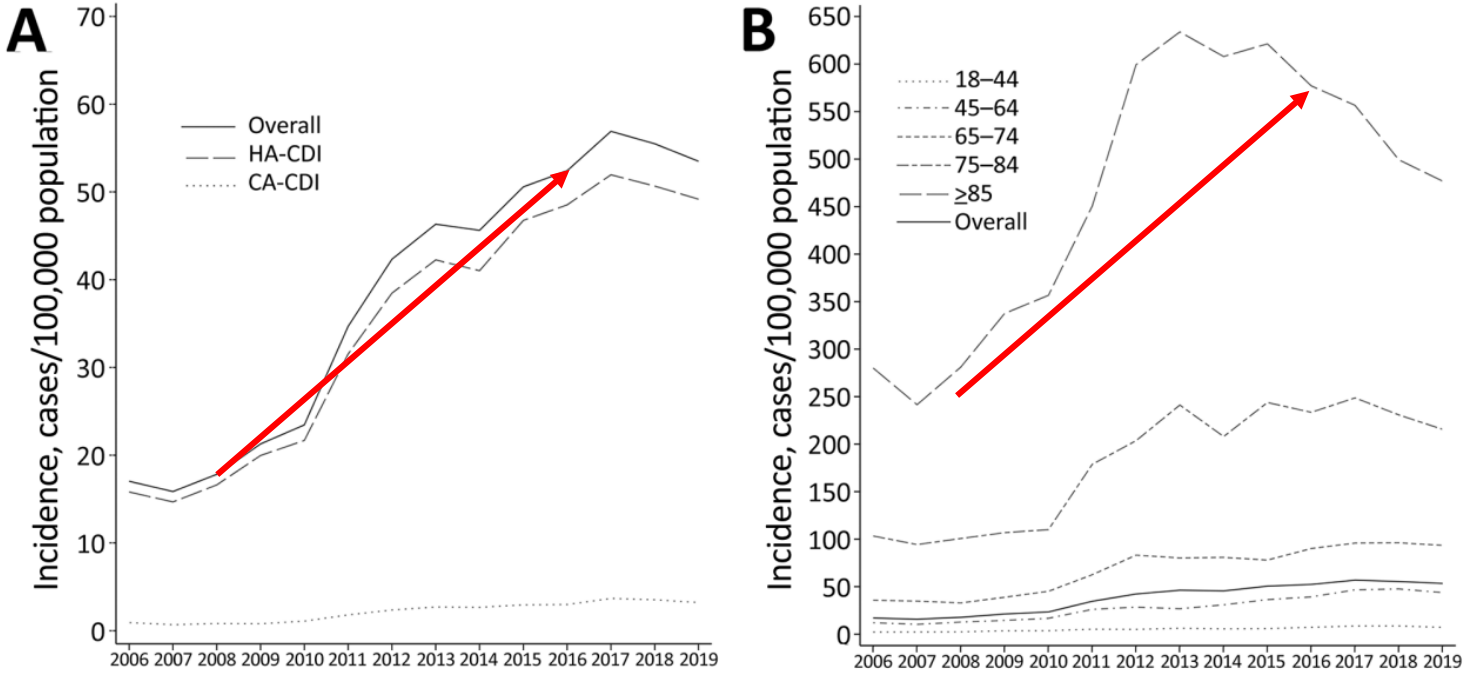
C. diff (also known as *Clostridioides difficile* or *C. difficile*) is a germ (bacterium) that enter the human body through the mouth. They can begin reproducing in the small intestine. When they reach the part of the large intestine, the colon, the bacteria can release toxins which damage tissues.

Outside the colon, the bacteria are not active, but can live for a long time in places such as:

- Human or animal feces.
- Surfaces in a room.
- Unwashed hands.
- Soil.
- Water.
- Food, including meat.

https://www.cdc.gov/cdiff/what-is.html

Prevalence of *C. diff*



Nowadays, *C. diffi* has become a leading cause of hospital-acquired infections and CDI represents a major health problem. The epidemiology of CDI has changed dramatically over the last 20 years.

Risk Factors for *C. diff*

C. diff can affect anyone. Most cases of *C. diff* occur when you've been taking antibiotics or not long after you've finished taking antibiotics.

- Being 65 or older
- Recent stay at a hospital or nursing home
- A weakened immune system, such as people with HIV/AIDS, cancer, or organ transplant patients taking immunosuppressive drugs
- Previous infection with *C. diff* or known exposure to the germs

https://www.cdc.gov/cdiff/what-is.html

Symptoms of *C. diff*

Symptoms might develop within a few days after you begin taking antibiotics.

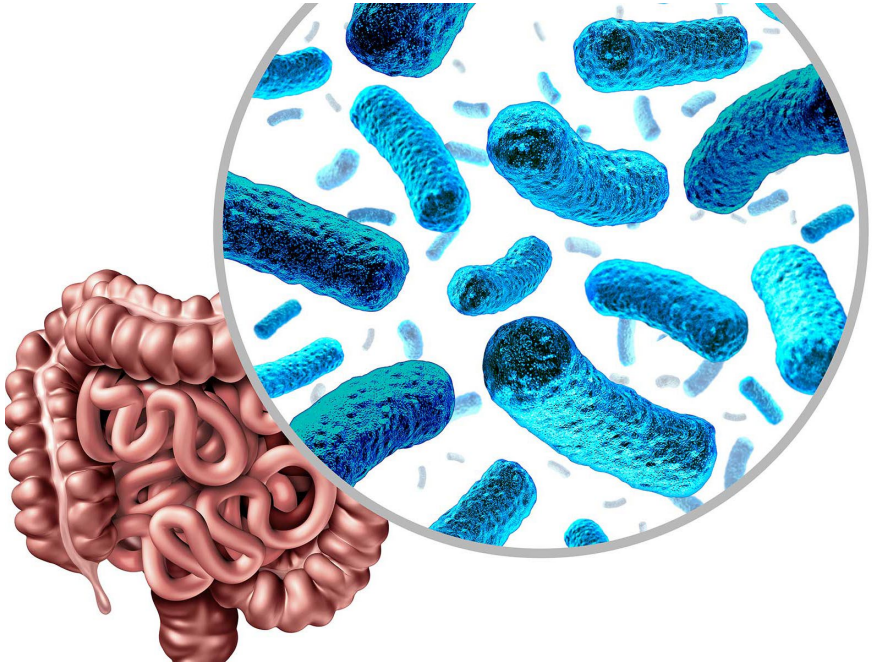
- Watery diarrhea as often as 10 to 15 times a day
- Fever
- Stomach tenderness or pain
- Loss of appetite
- Nausea

About **1 in 6 patients** who get *C. diff* will get it again in the subsequent 2-8 weeks.

One in 11 people over age 65 diagnosed with a healthcare-associated *C. diff* infection die within one month.

https://www.cdc.gov/cdiff/what-is.html

Why antibiotics trigger *C. diff*

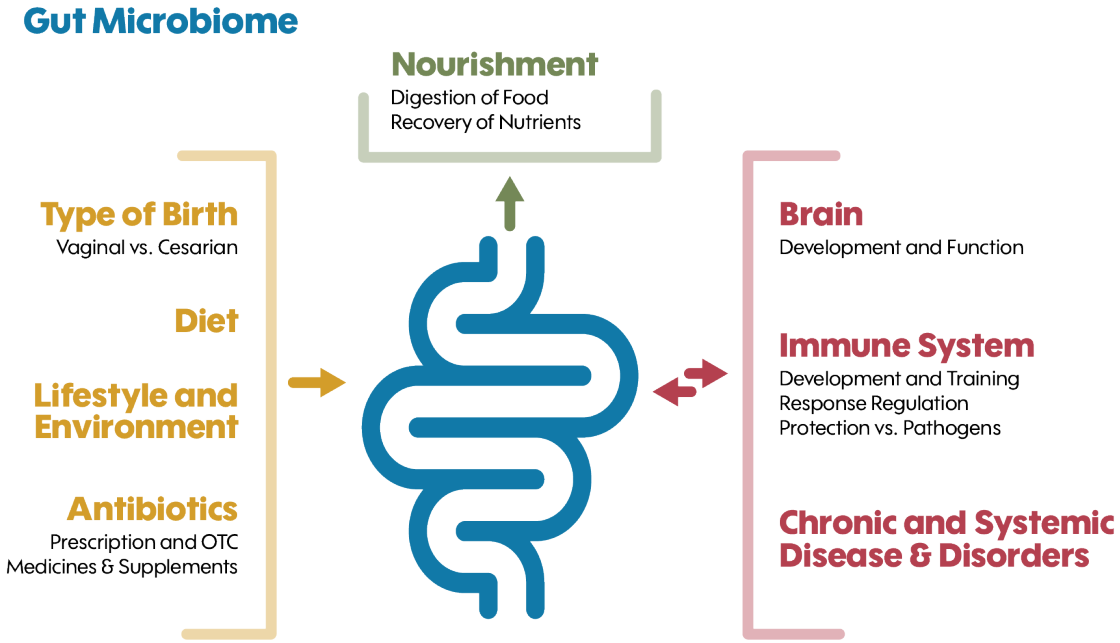


The microbiota of the gastrointestinal tract is estimated to consist of 100 trillion of microorganisms.

The diverse gastrointestinal microbiota is predominantly composed of bacteria from two major phyla, *Firmicutes* and *Bacteroidetes*.

This diverse and complex microbiome serves as a functional expansion of host genomes and is estimated to harbor 50- to 100-fold more genes compared to the host.

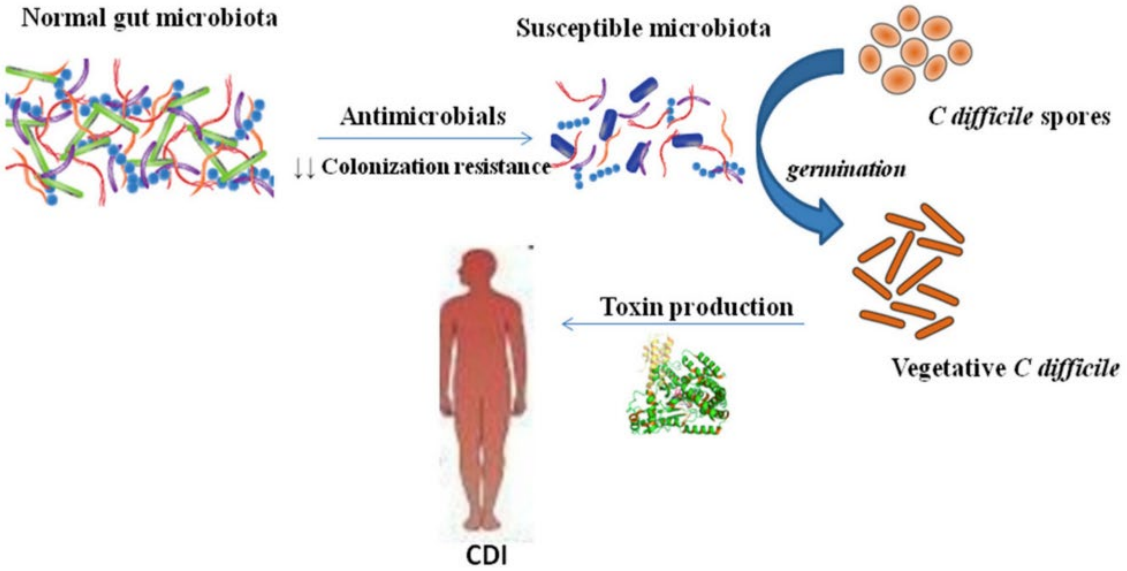
Why antibiotics trigger *C. diff*



The human gut microbiota is involved in many functions of the host, such as food processing, adjustment of the gut epithelium development, the synthesis of essential vitamins, and pathogen protection.

The role of gut microbiota and their unique metabolites is crucial in conferring the host defense against invading pathogens, colonization.

Why antibiotics trigger *C. diff*



Antibiotics that treat an infection tend to destroy most of the helpful bacteria in the body as well as the bacteria causing the infection.

Without enough helpful bacteria, C. difficile can grow out of control quickly.

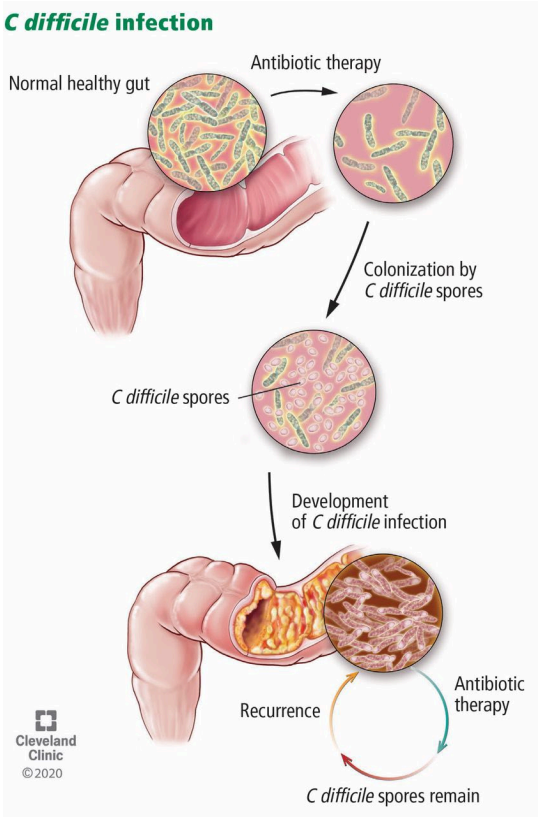
Treatment of *C. diff*

If *C. difficile* infection is related to an antibiotic, a health care provider will likely stop its use. Often, however, an antibiotic is needed to treat another infectious condition. A switch to another antibiotic might be less likely to cause diarrhea related to C. difficile infection.

Antibiotics are the main treatment for C. difficile infection. Commonly used antibiotics include:

- Vancomycin
- Fidaxomicin

Treatment of *C. diff*



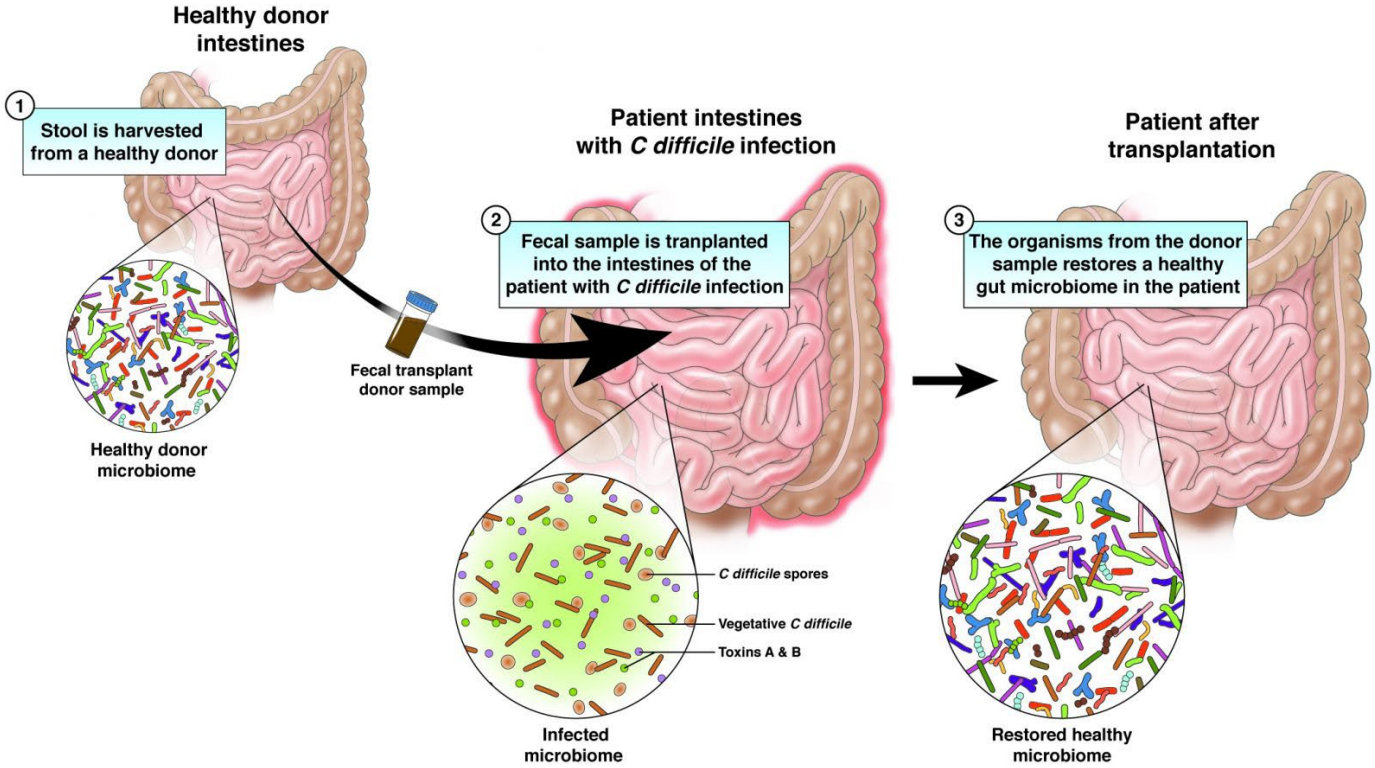
About 25% of people treated for *C. difficile* infection get sick again.

The reason might be that the first infection never went away or that bacteria cause a new infection.

The risk increases with each *C. difficile* infection. After three or more infections, the risk of another infection is greater than 50%.

Treatment for repeat infections may involve one or more courses of an antibiotic. The antibiotic is often different from the one used at first. Antibiotic therapy works less well each time the infection comes back.

Fecal Microbiota Transplantation



History of FMT


葛洪

Though new to the Western medical world, FMT has been described 1700 years ago.

It was an ancient Chinese researcher of the fourth century, by the name of Ge Hong, who first used what he called ‘yellow soup’ to treat his patients with severe diarrhea.

The ‘soup’ was administered orally, possibly accounting for the failure of the technique to become widely known.

https://www.news-medical.net/health/History-of-Fecal-Transplant.aspx

History of FMT

Camel stool was also used by German soldiers to treat bacterial dysentery during World War II.

History of FMT

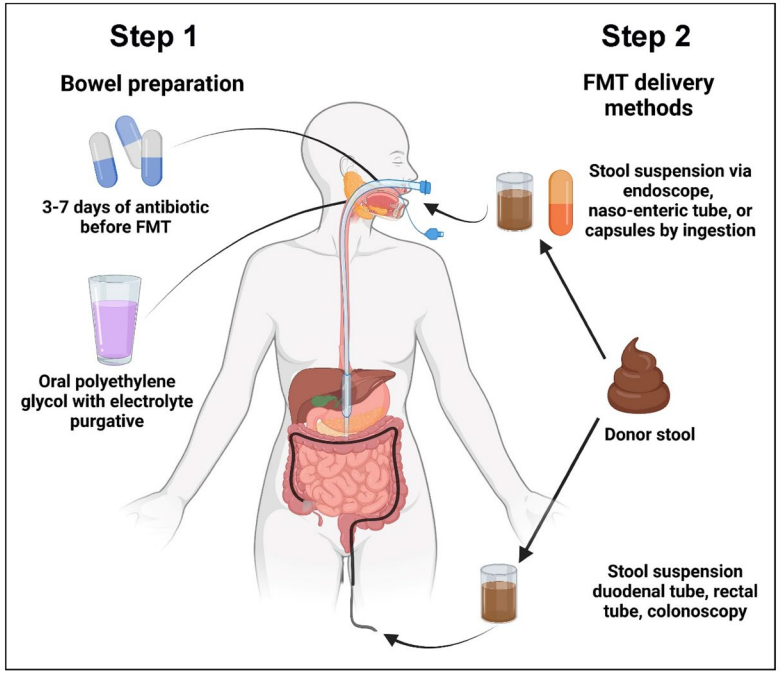
Surgery. 1958 Nov;44(5):854-9.

Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis

B EISEMAN, W SILEN, G S BASCOM, A J KAUVAR

PMID: 13592638

FMT came to attention this century after it was published by Eiseman et al., in a report on his treatment of patients with antibiotic-associated diarrhea with FMT via retention enemas. The patients recovered promptly and well from the diarrhea. This was in 1958.

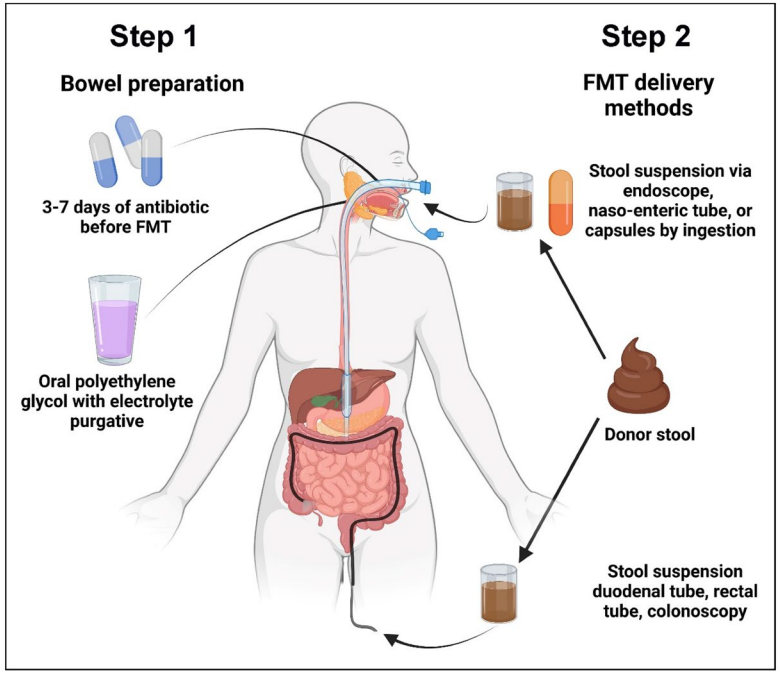


History of FMT

ANTIBIOTIC-ASSOCIATED PSEUDOMEMBRANOUS COLITIS DUE TO TOXIN-PRODUCING CLOSTRIDIA

John G. Bartlett, M.D., Te Wen Chang, M.D., Marc Gurwith, M.D., Sherwood L. Gorbach, M.D., and Andrew B. Onderdonk, Ph.D.

Abstract A substance producing cytotoxicity in tissue culture was detected in stool specimens from all of four patients with pseudomembranous colitis due to antibiotics and in one of 54 with antibiotic-associated diarrhea. These stools also caused enterocolitis when injected intracecally into hamsters. On each occasion, cytotoxicity in tissue culture and enterocolitis in hamsters were neutralized by pretreatment with gas-gangrene antitoxin. The toxicity in both tissue cultures and hamsters could be reproduced with broth cultures of clostridia strains isolated from four of the five stools. These results suggest that toxin-producing clostridia are responsible for antibiotic-associated pseudomembranous colitis. (N Engl J Med 298:531-534, 1978)



Despite the volume of empirical evidence, however, it was only in 1978 that the value of FMT was widely recognized when CDI was identified as the primary cause of antibiotic-related diarrhea.

RCT of FMT on recurrent CDI

The NEW ENGLAND JOURNAL of MEDICINE

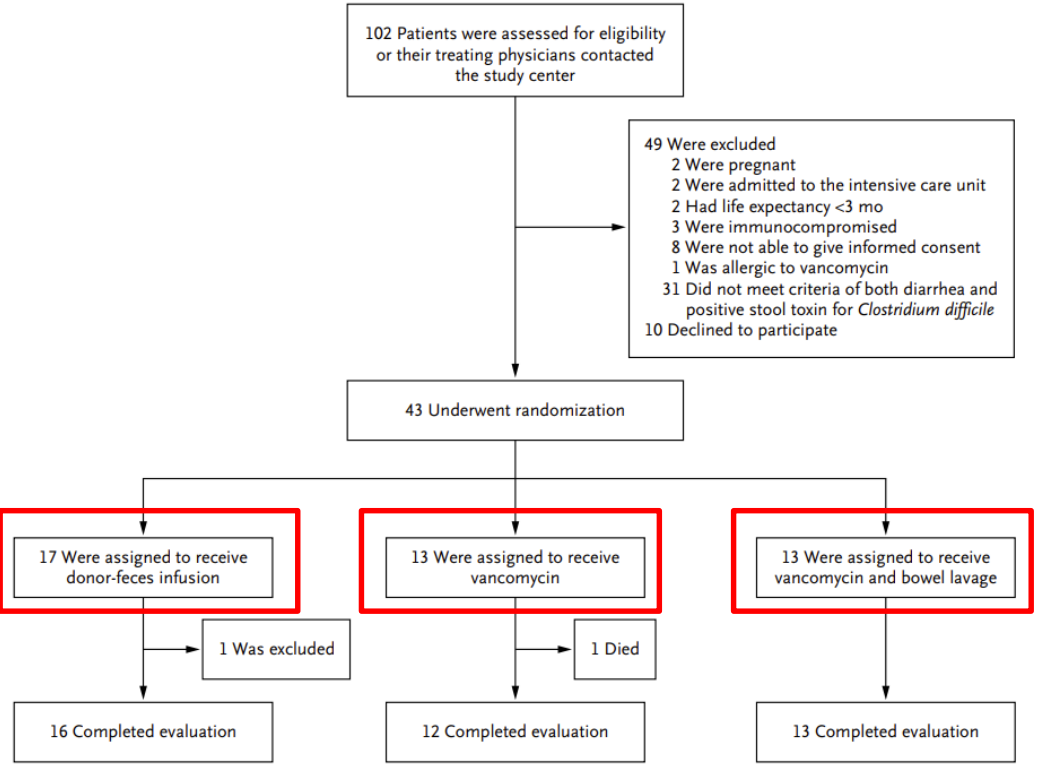
ESTABLISHED IN 1812 JANUARY 31, 2013 VOL. 368 NO. 5

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.

The first randomized, controlled clinical trial (RCT) of FMT for recurrent CDI was reported in 2013.

RCT of FMT on recurrent CDI



Inclusion criteria

patients who were at least 18 years of age and who had a life expectancy of at least 3 months and a relapse of C. difficile infection after at least one course of adequate antibiotic therapy.

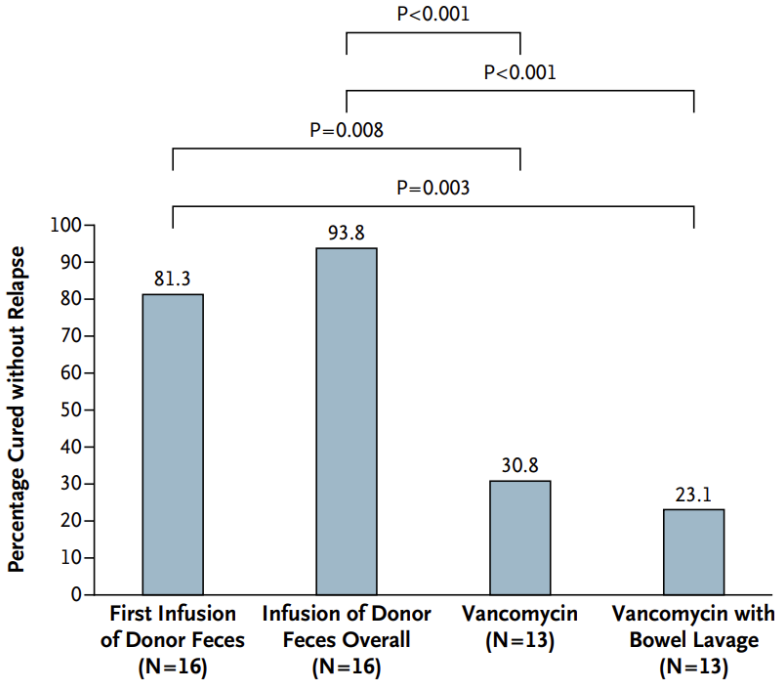
Exclusion criteria

e prolonged compromised immunity because of recent chemotherapy, the presence of human immunodeficiency virus (HIV), or prolonged use of prednisolone; pregnancy; use of antibiotics other than for treatment of C. difficile infection at baseline; admission to an intensive care unit; or need for vasopressor medication.

RCT of FMT on recurrent CDI

Table 1. Baseline Demographic and Clinical Characteristics of the Patients.*

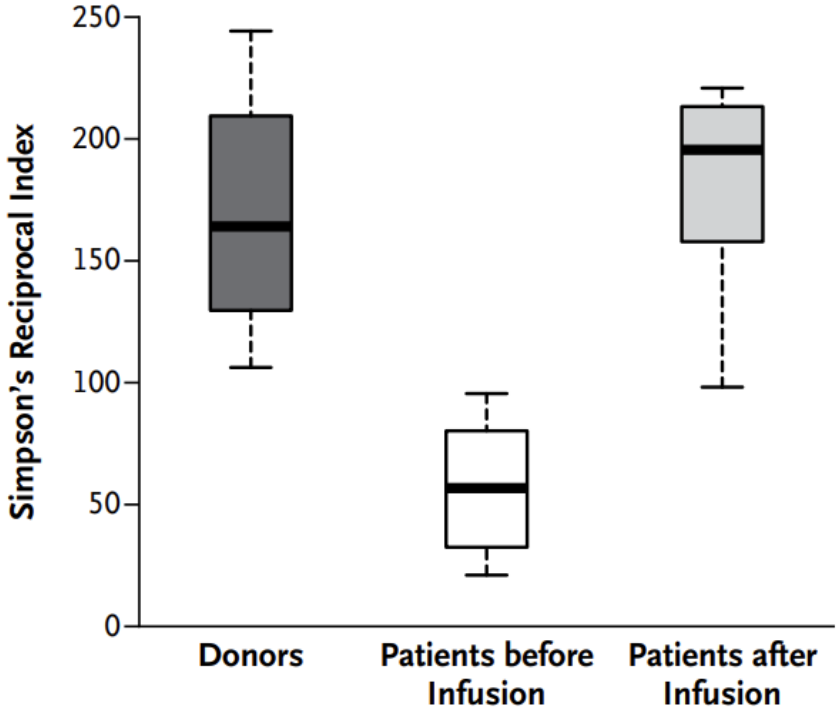
Characteristic	Donor-Feces Infusion (N=16)	Vancomycin Only (N=13)	Vancomycin and Bowel Lavage (N=13)	P Value†
Age — yr	73±13	66±14	69±16	0.39
Body-mass index‡	22±3	22±4	24±4	0.41
Female sex — no. (%)	8 (50)	7 (54)	3 (23)	0.22
Karnofsky performance status§	50±18	50±17	56±21	0.62
Median Charlson comorbidity index (range) — score¶	3 (0–4)	1 (0–8)	1 (0–6)	0.53
Median recurrences of CDI (range) — no.	3 (1–5)	3 (1–4)	2 (1–9)	0.69
Previous failure of tapered vancomycin therapy — no. (%)	10 (62)	8 (62)	6 (46)	0.63
Reported antibiotic use before CDI — no. (%)	16 (100)	12 (92)	13 (100)	0.62
Hospital-acquired CDI infection — no. (%)	10 (62)	6 (46)	10 (77)	0.27
Admitted to a hospital at study inclusion — no. (%)	5 (31)	4 (31)	4 (31)	1.00
Days of antibiotic use for CDI since first diagnosis — no.	63±41	51±27	49±38	0.56
Use of proton-pump inhibitor — no. (%)	13 (81)	10 (77)	11 (85)	0.88
ICU admission in preceding month — no. (%)	1 (6)	0	1 (8)	1.00
Feeding tube present — no. (%)	3 (19)	2 (15)	2 (15)	0.96
Median stool frequency per 24 hr (range) — no.	5 (3–20)	5 (3–12)	5 (3–10)	0.72
Leukocyte count — per mm³**				
Median	8000	8100	6500	0.39
Range	4000–15,000	4000–23,000	3000–14,000	
Albumin — g/dl**	3.7±0.7	3.8±0.7	3.9±0.8	0.66
Median creatinine (range) — mg/dl**	1.3 (0.6–10.3)	1.0 (0.5–1.8)	0.9 (0.6–5.2)	0.26
Ribotype 027 in first sample — no. (%)††	3 (23)	1 (11)	0	0.28



RCT of FMT on recurrent CDI

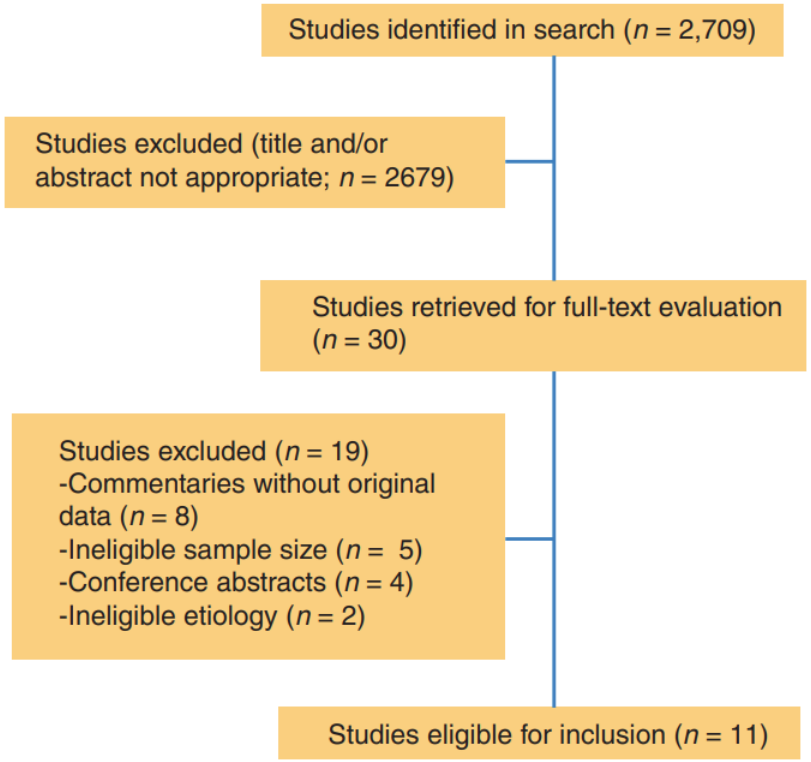
Table 2. Adverse Events in 16 Patients in the Infusion Group.*

Adverse Event	On Day of Infusion of Donor Feces	During Follow-up
	no. of events	
Belching	3	0
Nausea	1	0
Vomiting	0	0
Abdominal cramps	5	0
Diarrhea	15	0
Constipation	0	3
Abdominal pain	2 (associated with cramping)	0
Infection	0	2†
Hospital admission	NA	1‡
Death	0	0
Other adverse event	1§	1‡



This study for the first time confirmed the efficiency and safety of FMT in treating recurrent CDI.

RCT of FMT on recurrent CDI



Author (reference)	Sample size	Patient type (in-patient, out-patient, mixed)	CDI type (recurrent, refractory, both)	Donor (patient selected, anonymous, both)	Delivery modality	Stool sample dose/solution	Follow-up data	Total NICE score
Kassam *et al.* (47)	27	Mixed	Both	Anonymous	Enema	150 g Stool/300 ml sterile water	Mean "427.3 days"	4
Mattila *et al.* (37)	70	Mixed	Both	Both	Colonoscopy	20–30 ml Stool/ 100 ml water	3 Month and 12 month	5
Kelly *et al.* (43)	26	Out-patient	Recurrent	Patient selected	Colonoscopy	6–8 Tablespoon stool/ 1,000 ml sterile water or saline; total aliquoted dose 500–960 ml	Mean "10.7 months (range 2–30 months)"	4
Polak *et al.* (44)	15	NR	Recurrent	Patient selected	Nasojejunal tube	20–50 g Stool/dilute in 50 ml saline	NR	2
Mellows *et al.* (39)	13	Mixed	Both	Patient selected	Colonoscopy	Stool amount NR/saline (amount NR); Total aliquoted dose 300–600cc	Mean "5 months (range 1–10 months)"	4
Garborg *et al.* (40)	40	Mixed	Recurrent	Patient selected	Gastroscopy, Colonoscopy	50–100 g Stool/ 250 ml saline; total aliquoted dose ~200 ml	NR	1
Rohlke *et al.* (38)	19	Out-patient	Recurrent	Patient selected	Colonoscopy	Variable (full quantity-"several ounces")/ saline (amount: NR); total aliquoted dose 200–300cc	Mean "27.2 months (range 6–65 months)"	5
Yoon *et al.* (45)	12	NR	Both	Patient selected	Colonoscopy	Stool amount NR/1,000 ml saline; total aliquoted dose ~250–400cc	Mean NR; range "3 weeks to 8 years"	5
MacConnachie *et al.* (41)	15	Mixed	Recurrent	Patient selected	Nasogastric tube	30 g Stool/150 ml saline; total aliquoted dose 30 ml	Mean NR; median 16 weeks (range 4–24 weeks)	2
Aas *et al.* (46)	18	Mixed	Recurrent	Both	Nasogastric tube	30 g Stool/50–70 ml saline; total aliquoted dose 25 ml	90 Days	5
Lund-Tonnesen *et al.* (42)	18	In-patient	Unclear	Anonymous	Colonoscopy, Gastrostomy tube	5–10 g Stool/milk (amount: NR)	"2–3 Weeks"	2

NICE, National Institute of Clinical Excellence; NR, not reported.

Kassam et al., 2020

FDA approved FMT for CDI

Rebyota is approved for the prevention of recurrence of Clostridioides difficile infection (CDI) in individuals 18 years of age and older. It is for use after an individual has completed antibiotic treatment for recurrent CDI.

https://www.rebyota.com/

FDA approved FMT for CDI

Efficacy and Safety of RBX2660 in PUNCH CD3, a Phase III, Randomized, Double-Blind, Placebo-Controlled Trial with a Bayesian Primary Analysis for the Prevention of Recurrent *Clostridioides difficile* Infection

Sahil Khanna[1] · Maha Assi[2] · Christine Lee[3] · David Yoho[4] · Thomas Louie[5] · Whitfield Knapple[6] · Humberto Aguilar[7] · Julia Garcia-Diaz[8] · Gary P. Wang[9] · Scott M. Berry[10] · Joe Marion[10] · Xin Su[11] · Tricia Braun[11] · Lindy Bancke[12] · Paul Feuerstadt[13,14]

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Abstract

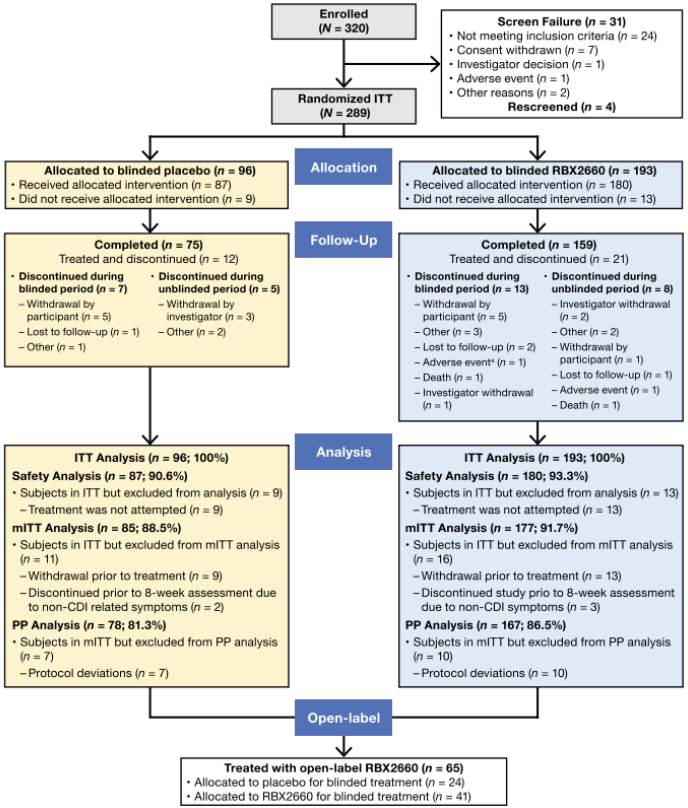
Background Recurrent *Clostridioides difficile* infection, associated with dysbiosis of gut microbiota, has substantial disease burden in the USA. RBX2660 is a live biotherapeutic product consisting of a broad consortium of microbes prepared from human stool that is under investigation for the reduction of recurrent *C. difficile* infection.

Methods A randomized, double-blind, placebo-controlled, phase III study, with a Bayesian primary analysis integrating data from a previous phase IIb study, was conducted. Adults who had one or more *C. difficile* infection recurrences with a positive stool assay for *C. difficile* and who were previously treated with standard-of-care antibiotics were randomly assigned 2:1 to receive a subsequent blinded, single-dose enema of RBX2660 or placebo. The primary endpoint was treatment success, defined as the absence of *C. difficile* infection diarrhea within 8 weeks of study treatment.

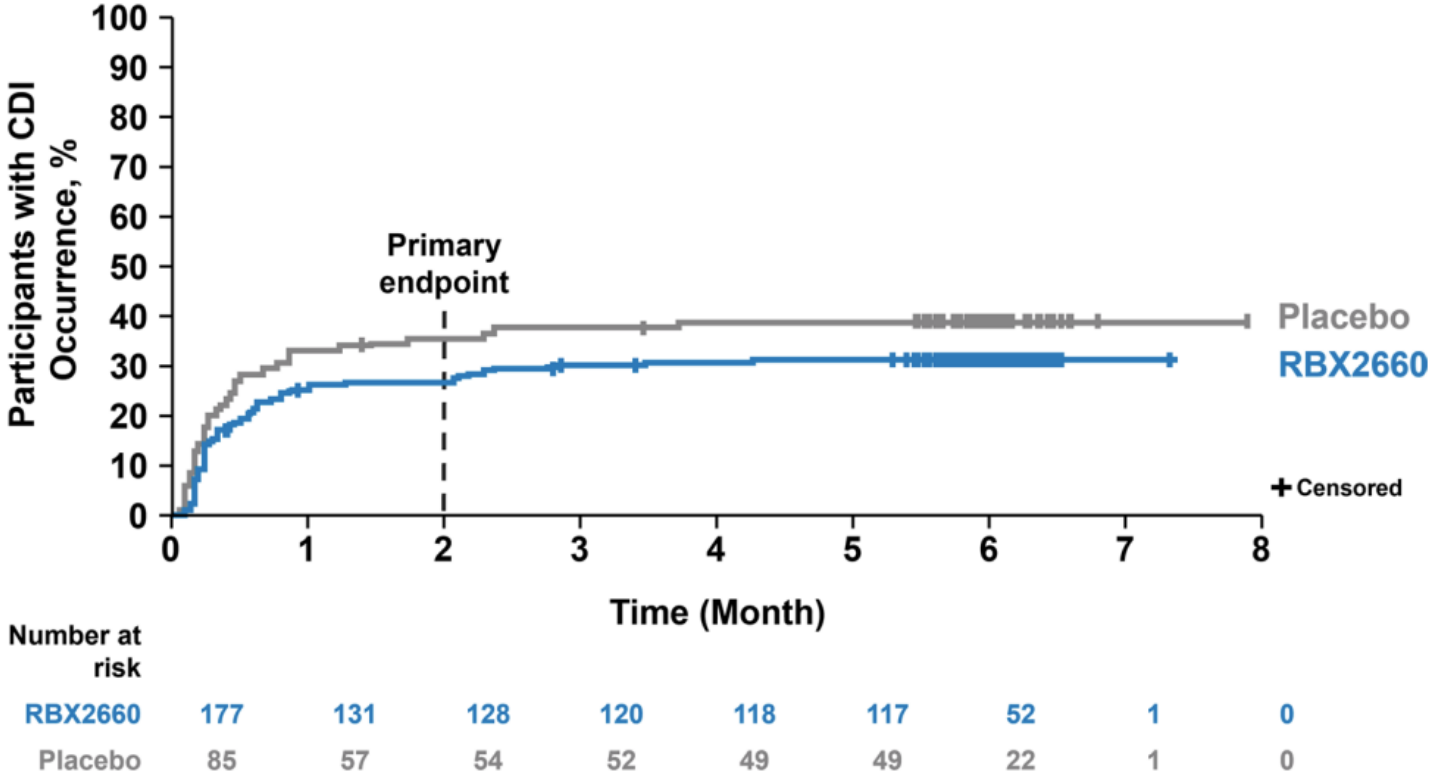
Results Of the 320 patients screened, 289 were randomly assigned and 267 received blinded treatment ($n = 180$, RBX2660; $n = 87$, placebo). Original model estimates of treatment success were 70.4% versus 58.1% with RBX2660 and placebo, respectively. However, after aligning the data to improve the exchangeability and interpretability of the Bayesian analysis, the model-estimated treatment success rate was 70.6% with RBX2660 versus 57.5% with placebo, with an estimated treatment effect of 13.1% and a posterior probability of superiority of 0.991. More than 90% of the participants who achieved treatment success at 8 weeks had sustained response through 6 months in both the RBX2660 and the placebo groups. Overall, RBX2660 was well tolerated, with manageable adverse events. The incidence of treatment-emergent adverse events was higher in RBX2660 recipients compared with placebo and was mostly driven by a higher incidence of mild gastrointestinal events.

Conclusions RBX2660 is a safe and effective treatment to reduce recurrent *C. difficile* infection following standard-of-care antibiotics with a sustained response through 6 months.

Clinical Trial Registration NCT03244644; 9 August, 2017.



FDA approved FMT for CDI



FDA approved FMT for CDI

Table 3 Summary of AEs over the full study period (PUNCH CD3 safety population; $N = 267$)

	Through 6 months after blinded treatment[a]		Through 6 months after open-label treatment	
	Blinded placebo ($n = 87$)	Blinded RBX2660 ($n = 180$)	Blinded placebo, open-label RBX2660 ($n = 24$)	Blinded RBX2660, open-label RBX2660 ($n = 41$)
All AEs, *n* (%)	39 (44.8)	100 (55.6)	14 (58.3)	24 (58.5)
AEs by maximum severity[b]				
Mild	9 (10.3)	42 (23.3)	6 (25.0)	8 (19.5)
Moderate	25 (28.7)	47 (26.1)	6 (25.0)	10 (24.4)
Severe	5 (5.7)	10 (5.6)	1 (4.2)	5 (12.2)
Potentially life threatening	0	1 (0.6)[c]	1 (4.2)	1 (2.4)
Discontinued because of AE	0	1 (0.6)[c]	0	2 (4.9)
Serious AEs	2 (2.3)	7 (3.9)	1 (4.2)	5 (12.2)
Deaths	0	1 (0.6)[c]	0	1 (2.4)

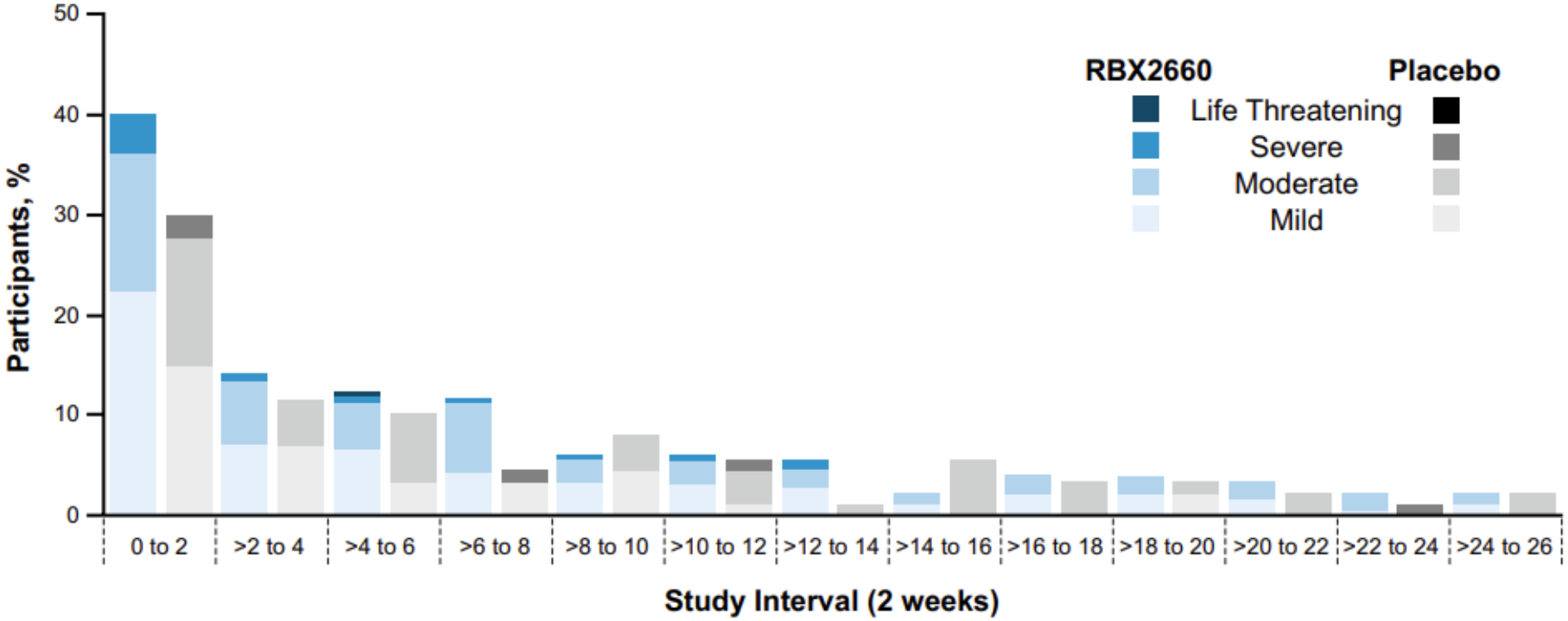
AE adverse event, *CDI Clostridioides difficile* infection, *IP* investigational product

[a]Treatment failures are censored at the time of CDI recurrence

[b]AEs reported by maximum severity as assessed by investigator using Common Terminology Criteria for Adverse Events (CTCAE) criteria

[c]Same participant represented in each category

FDA approved FMT for CDI



FMT on CDI in Hong Kong

Long-Term Safety Outcomes of Fecal Microbiota Transplantation: Real-World Data Over 8 Years From the Hong Kong FMT Registry

Yuk Kam Yau,[1,2,3,4] Louis Ho Shing Lau,[2,3,4] Rashid Nok Shun Lui,[2,3,4] Sunny Hei Wong,[5] Cosmos Liutao Guo,[2] Joyce Wing Yan Mak,[2,3,4] Jessica Yuet Ling Ching,[2,3,4] Margaret Ip,[3,6] Michael A. Kamm,[7,8] David T. Rubin,[9] Paul Kay Sheung Chan,[3,6] Francis Ka Leung Chan,[1,2,3,4] and Siew Chien Ng[1,2,3,4]

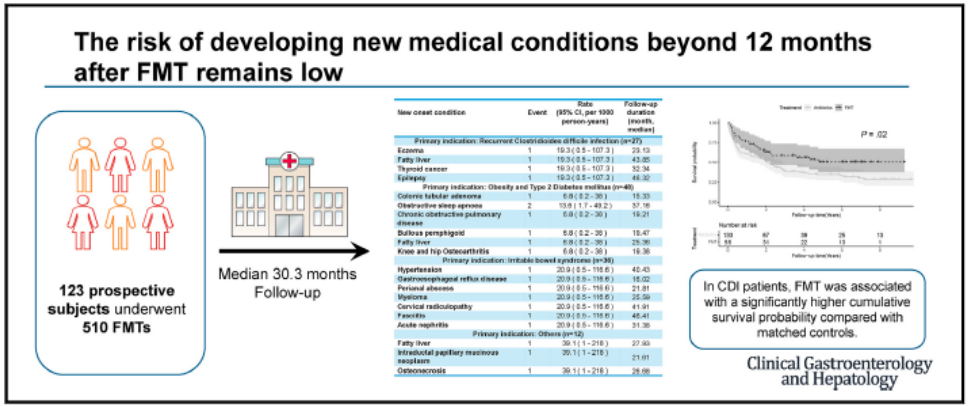
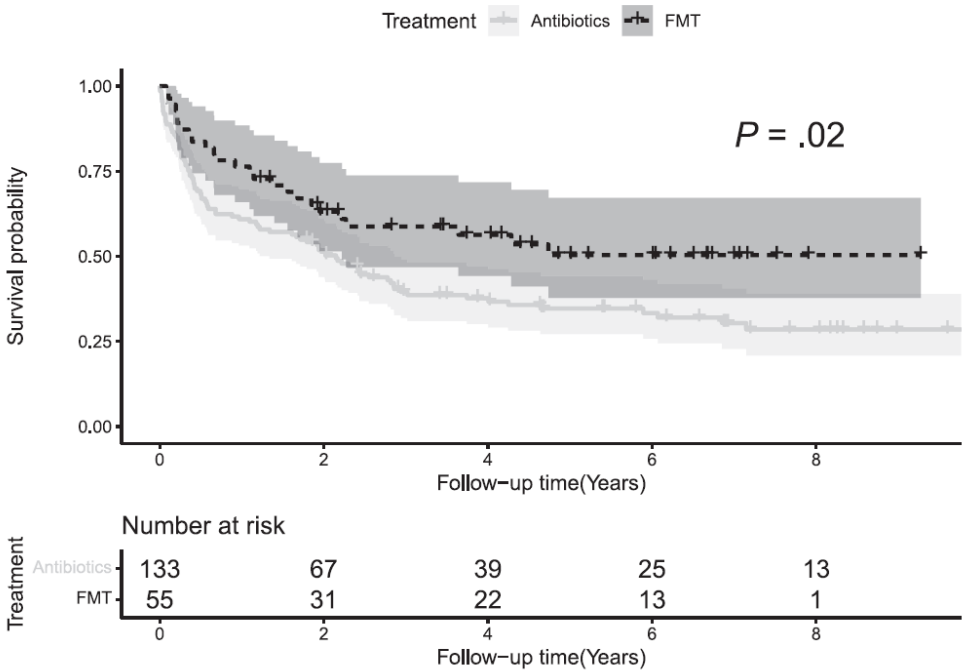


Table 2. Adverse Events Reported in the Short Term (Within 1 Month) and Medium Term (1–12 Months) After FMT

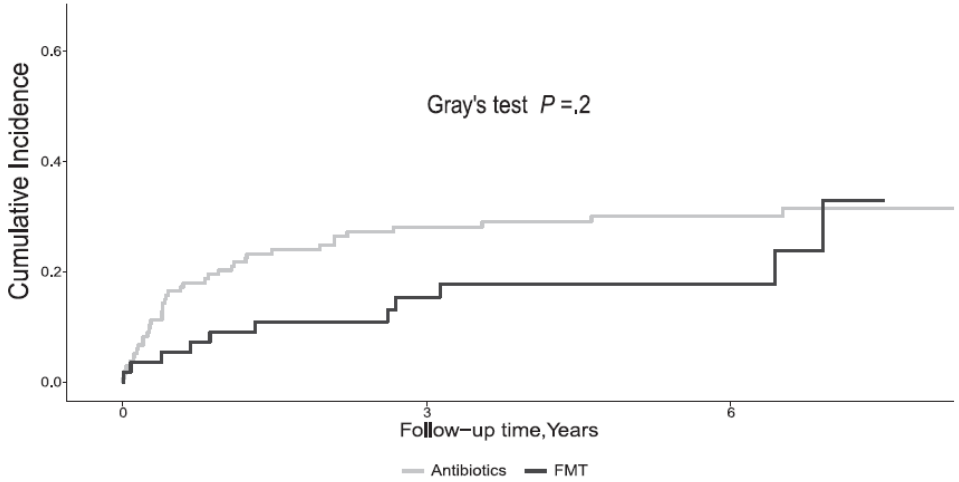
Adverse Event	Within 1 mo	1–6 mo	6–12 mo
Primary indication: recurrent *Clostridioides difficile* infection (n = 27)			
GI symptom	10 (40.0)	12 (60.0)	5 (27.8)
Diarrhea	6 (24.0)	9 (45.0)	2 (11.1)
Constipation	0	0	1 (5.6)
Abdominal pain	6 (24.0)	5 (25.0)	3 (16.7)
Abdominal bloating	1 (4)	2 (10.0)	0
Nausea and vomiting	1 (4)	2 (10.0)	1 (5.6)
IBD flare	0	4 (20.0)	2 (11.1)
Septicemia	0	1 (5.0)[a]	1 (5.6)
Death	0	2 (10.0)[b]	1 (5.6)[c]
Related to FMT	0	0	0
Not related to FMT	0	2	1

FMT on CDI in Hong Kong



A total of 55 patients who received FMT for CDI (FMT group) were matched with 133 patients treated with standard antibiotic therapy (control group) by age, sex, and Charlson Comorbidity Index. Median follow-up durations were comparable in both groups (FMT group: 27.6 months, control group: 24.5 months; p=0.13). The FMT group was associated with a significantly higher cumulative survival probability during the follow-up period compared with the control group, which received standard antibiotic therapy (p=0.02)

FMT on CDI in Hong Kong



Antibiotics			
Number at Risk	133	36	23
Cumulative Events	0	37	39
FMT			
Number at Risk	55	22	10
Cumulative Events	0	8	9

No significant difference was observed in the cumulative incidence of all (Figure 2) new-onset medical diagnoses between both groups.

FMT donors in Hong Kong

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DOI: 10.1002/ueg2.12160

ORIGINAL ARTICLE

ueg journal WILEY

High prevalence of extended-spectrum beta-lactamase organisms and the COVID-19 pandemic impact on donor recruitment for fecal microbiota transplantation in Hong Kong

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FMT donors in Hong Kong

Potential donors will be excluded from donation if they:	
Basic information	• Aged <18 or >50 years • Body mass index <18 or >23 kg/m^2 • On regular medications
Risk of infectious diseases	• History of hepatitis B, hepatitis C, tuberculosis, or HTLV • History of anonymous sexual behavior, sexual activity with someone who uses intravenous drugs, sexual contact with a man who might have had oral or anal sex with another man or male-to-male sex or been a sex worker or engaged in sexual activity with sex worker • History of acquiring a sexually transmittable disease • Had sexual contact with someone who turned out to be infected with human immunodeficiency virus, HTLV, hepatitis B or C, or syphilis • Incarcerated or held in a lock-up or detention center • Had a tattoo or piercing/earrings in the past 6 months • Had acupuncture in the past 6 months • Received bovine insulin injection since 1 Jan 1980 • Received blood products or transplantation within 1 year • Travel history to endemic regions with a high risk acquiring infectious pathogens within the past 6 months, including India, Pakistan, and Africa

FMT donors in Hong Kong

Bowel habits and bowel diseases	• History of celiac disease, IBD, irritable bowel syndrome, idiopathic chronic constipation or chronic diarrhea, gastrointestinal malignancy or known polyposis • Have ever had blood in stool • Have ever received gastrointestinal surgery • First-degree relative diagnosed with IBD or colorectal cancer under the age of 55 • Do not have regular bowel movements • Have difficulty defecating or have abdominal cramps frequently (regularly more than once a week)
Medical history and medications	• History of malaria, trypanosomiasis, intestinal infestation (worms, parasites), systemic autoimmunity diseases, atopic diseases, cardiovascular or metabolic syndrome, neuro-logical diseases, chronic pain syndromes, congenital, chronic liver disease or any malignancy • History of depression, bipolar disorder, schizophrenia or delusional disorder, eating disorder or other psychiatric illnesses • Took antibiotics or probiotics within 3 months • Took proton pump inhibitor or drugs for gastric problems regularly • Took experimental medicine or experimental vaccine within 6 months • Received live vaccine within 6 months • Took immunosuppressive agents or drugs including growth hormone

FMT donors in Hong Kong

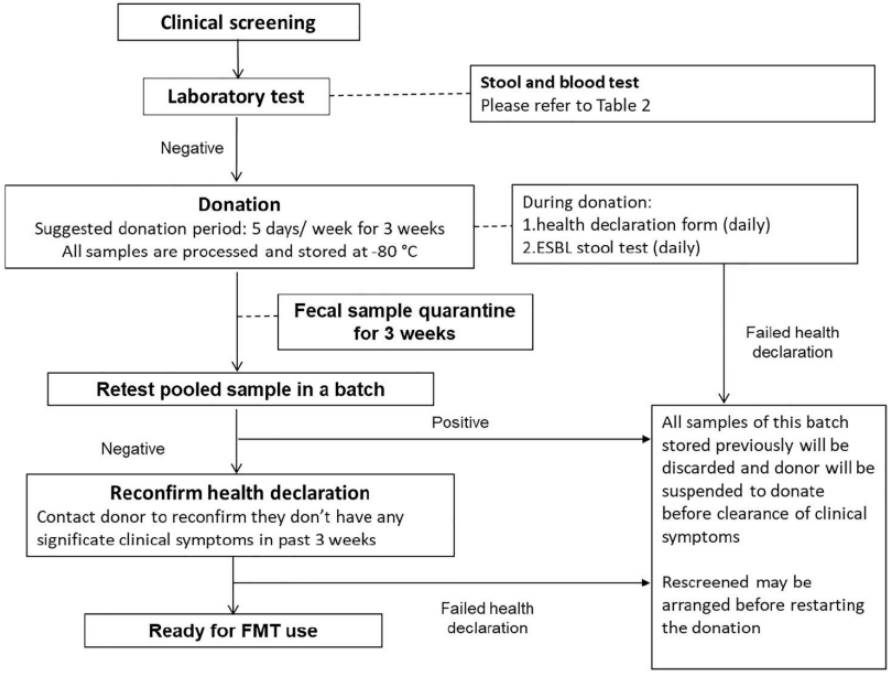
Travel history	• Have spent 5 or more years in Europe between 1 Jan 1980 till present • Have spent 3 or more months in the United Kingdom from 1 Jan 1980 to 31 Dec 1996 • Have received blood transfusion in the United Kingdom or France between 1 Jan 1980 till present • Have worked or lived for 6 or more months at United States Military bases in Europe from 1 Jan to 31 Dec 1996
Others	• Pregnant or lactating • Current/past smoker or current heavy drinker • Regular contact with patients or clinical specimens or animals • Strict vegetarian (refrain from animal products, eggs, dairy products, etc.) • Have history of using drugs intravenously which were not prescribed by a clinician, sniffed drugs, use of recreational drugs or taken illicit drugs

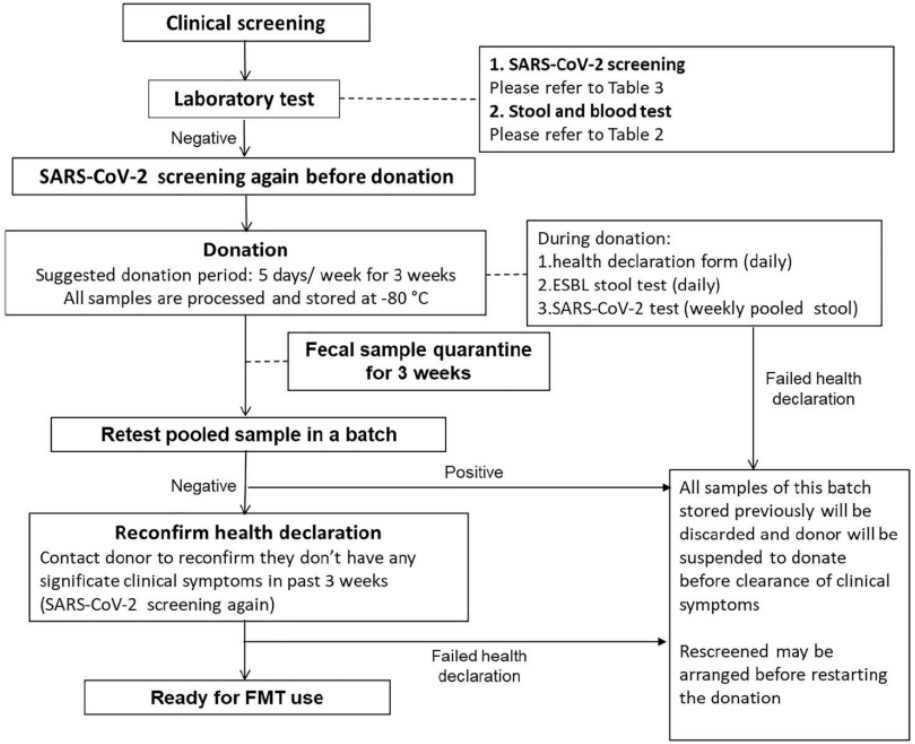
FMT donors in Hong Kong

TABLE 2 Blood and stool screening tests for potential FMT donors

Blood tests	Stool tests
• Liver and renal function	• Norovirus (RNA PCR)
• Fasting lipid profile	• Rotavirus (antigen detection)
• C-reactive protein	• Bacterial (*Escherichia coli* O157, *Shigella*, *Vibrio*, *Campylobacter*)
• Complete blood count	
• Hemoglobin Alc	• *Clostridioides difficile* (GDH + PCR)
• Erythrocyte sedimentation rate	
• Hepatitis A virus (Anti-HAV IgM)	• Multidrug-resistant organisms (MDRA, MRSA, ESBL, CRE, VRE)
• Hepatitis B virus (HBs Ag or Anti HBc)	
• Hepatitis C virus (Anti-HCV)	
• Hepatitis E virus (Anti-HEV IgM)	
• Human immunodeficiency virus (Anti-HIV)	• Parasites including: *Clonorchis*, *Crytosporidium parvum*, *Giardia*, *Entamoeba histolytica*, Microsporidia, *Cyclospora*, *Isospora*
• Human T-lymphotropic virus (Anti-HTLV 1)	
• Syphilis (VDRL)	• *Helicobacter pylori* antigen
• *H. pylori* (Anti-*H. pylori* IgG)	

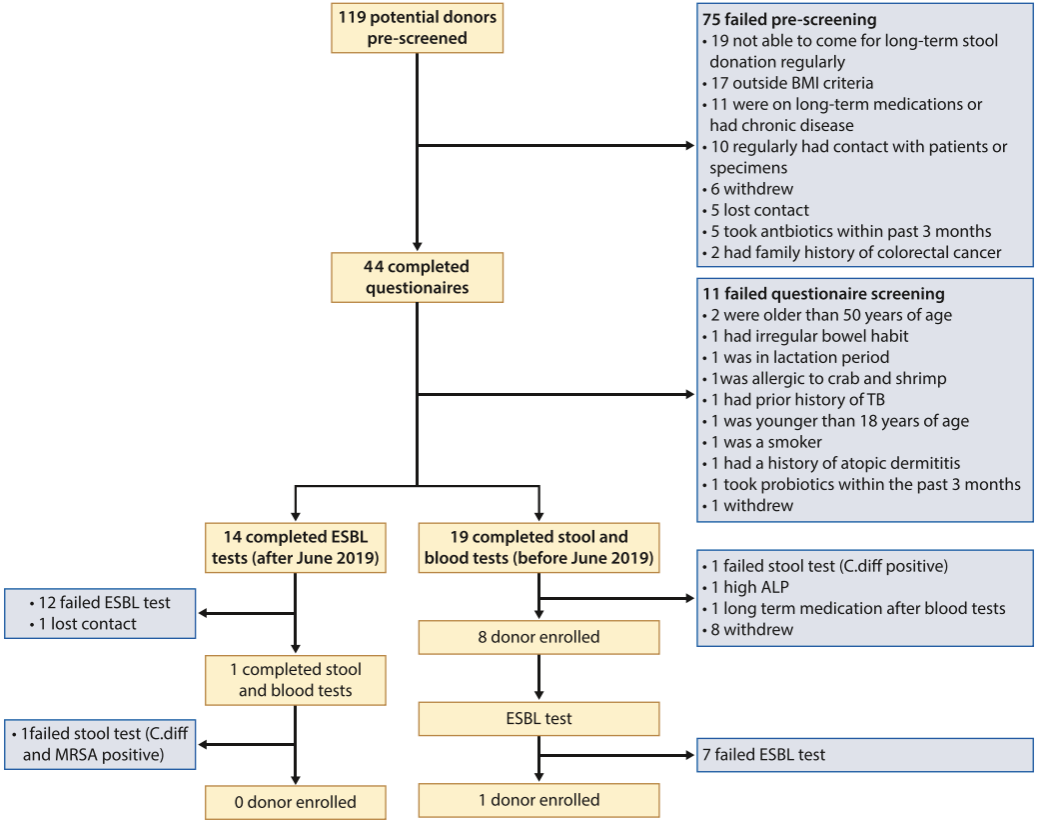
FMT donors in Hong Kong





Screening procedure flow chart (a: before COVID-19 era; b: after COVID-19 era)

FMT donors in Hong Kong



Alternative of FMT for CDI

Vowst (SER-109) is an investigational oral microbiome therapeutic composed of live purified Firmicutes bacterial spores, was developed to reduce the risk of C. difficile infection recurrence.

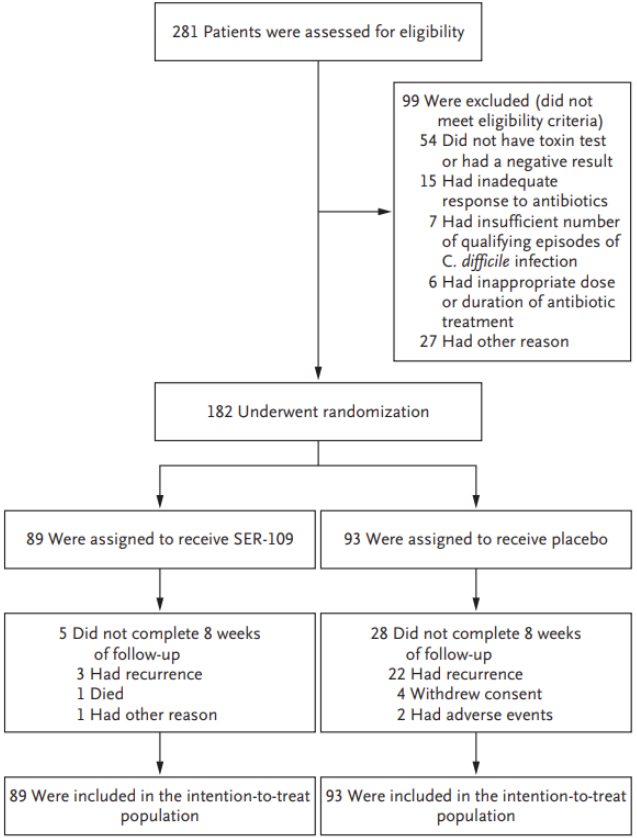
Alternative of FMT for CDI

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.



Alternative of FMT for CDI

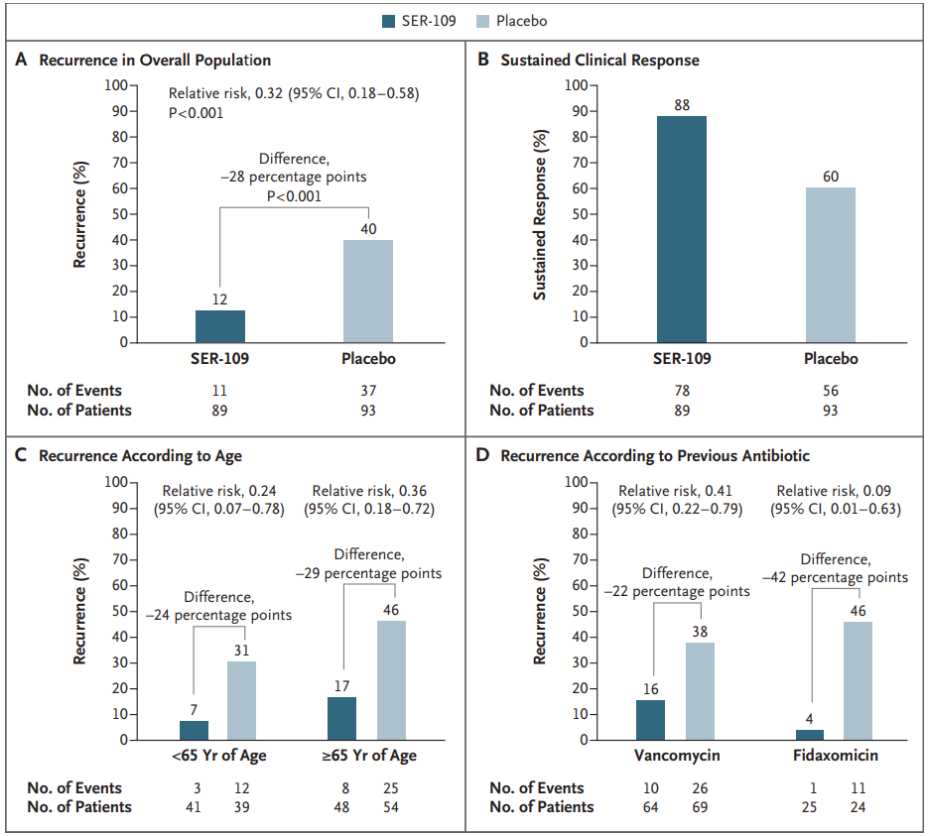
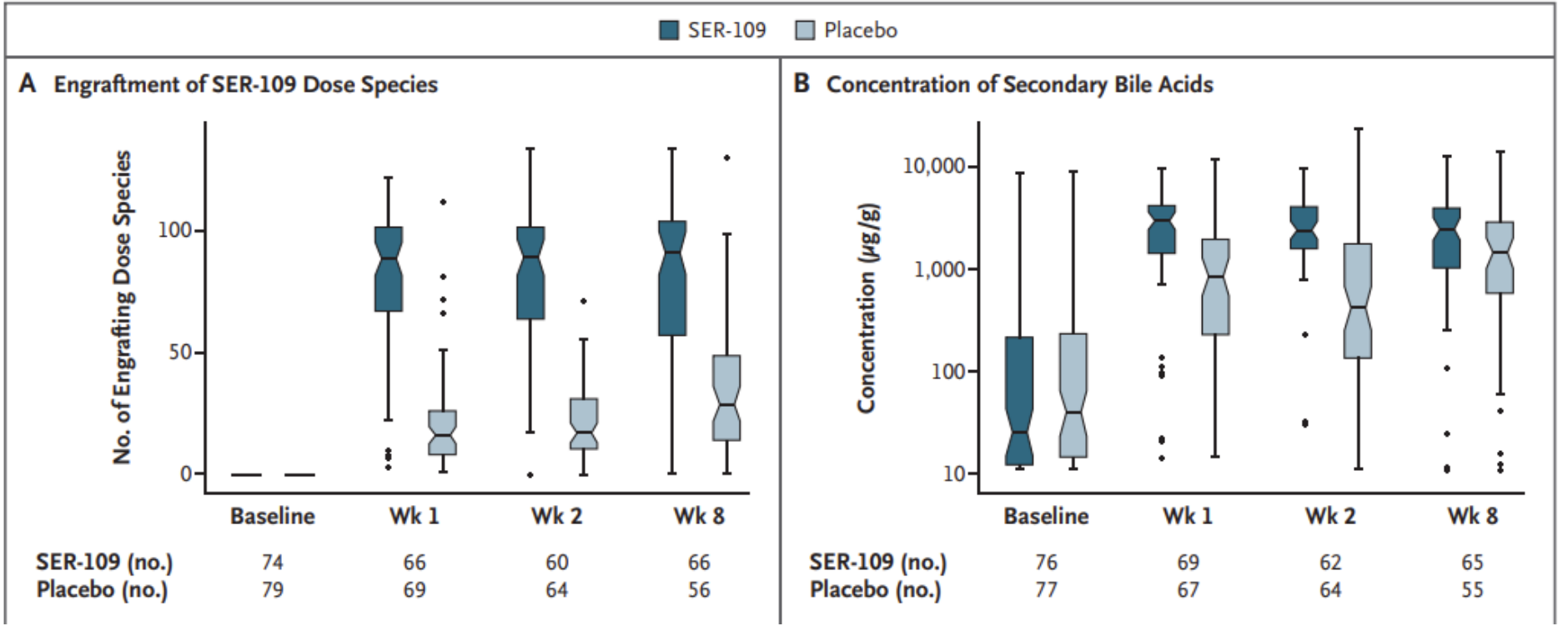


Table 2. Adverse Events through 8 Weeks (Safety Population).*

Adverse Event	SER-109 (N=90)	Placebo (N=92)
	no. of patients (%)	
Any adverse event	84 (93)	84 (91)
Adverse event related or possibly related to SER-109 or placebo	46 (51)	48 (52)
Serious adverse event†	7 (8)	15 (16)
Adverse event of special interest that occurred or worsened after initiation of SER-109 or placebo	1 (1)	1 (1)
Serious adverse event or an adverse event of special interest that occurred or worsened after initiation of SER-109 or placebo and was related or possibly related to SER-109 or placebo	0	0
Serious adverse event leading to withdrawal from the trial	0	1 (1)
Adverse event leading to death‡	2 (2)	0
Adverse events reported in ≥5% of patients		
Gastrointestinal disorders	79 (88)	80 (87)
Flatulence	63 (70)	70 (76)
Abdominal distension	49 (54)	49 (53)
Abdominal pain	46 (51)	56 (61)
Constipation	28 (31)	22 (24)
Diarrhea	22 (24)	20 (22)
Nausea	16 (18)	30 (33)
Vomiting	3 (3)	10 (11)
General disorders and administration site conditions	57 (63)	65 (71)
Fatigue	53 (59)	58 (63)
Chills	21 (23)	22 (24)
Metabolism and nutrition disorders	28 (31)	36 (39)
Decreased appetite	26 (29)	34 (37)

Alternative of FMT for CDI



Non-bacteria microbes in FMT

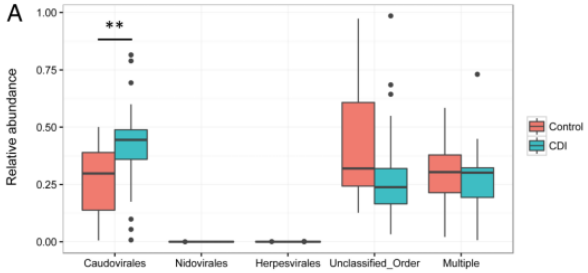
Gut microbiota

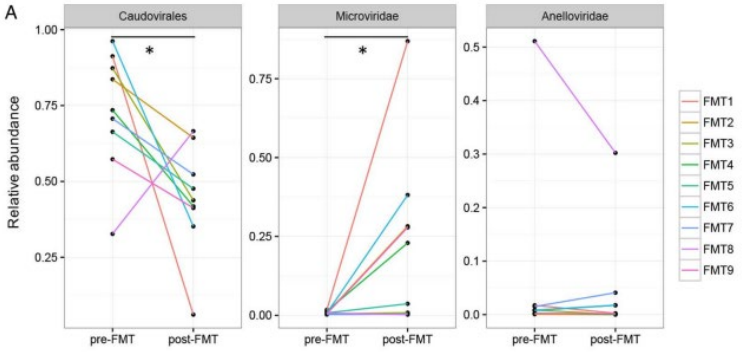
OPEN ACCESS

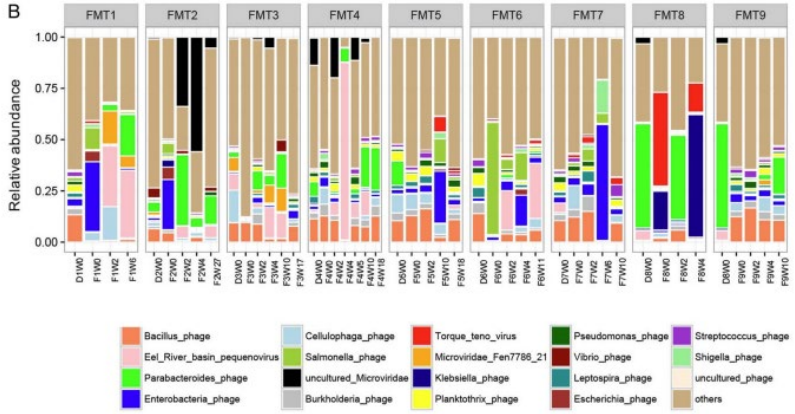
ORIGINAL ARTICLE

Bacteriophage transfer during faecal microbiota transplantation in *Clostridium difficile* infection is associated with treatment outcome

Tao Zuo,[1,2] Sunny H Wong,[1,2] Kelvin Lam,[1] Rashid Lui,[1] Kitty Cheung,[1] Whitney Tang,[1] Jessica Y L Ching,[1] Paul K S Chan,[3] Martin C W Chan,[3] Justin C Y Wu,[1,2] Francis K L Chan,[1,2] Jun Yu,[1,2] Joseph J Y Sung,[1,2] Siew C Ng[1,2]







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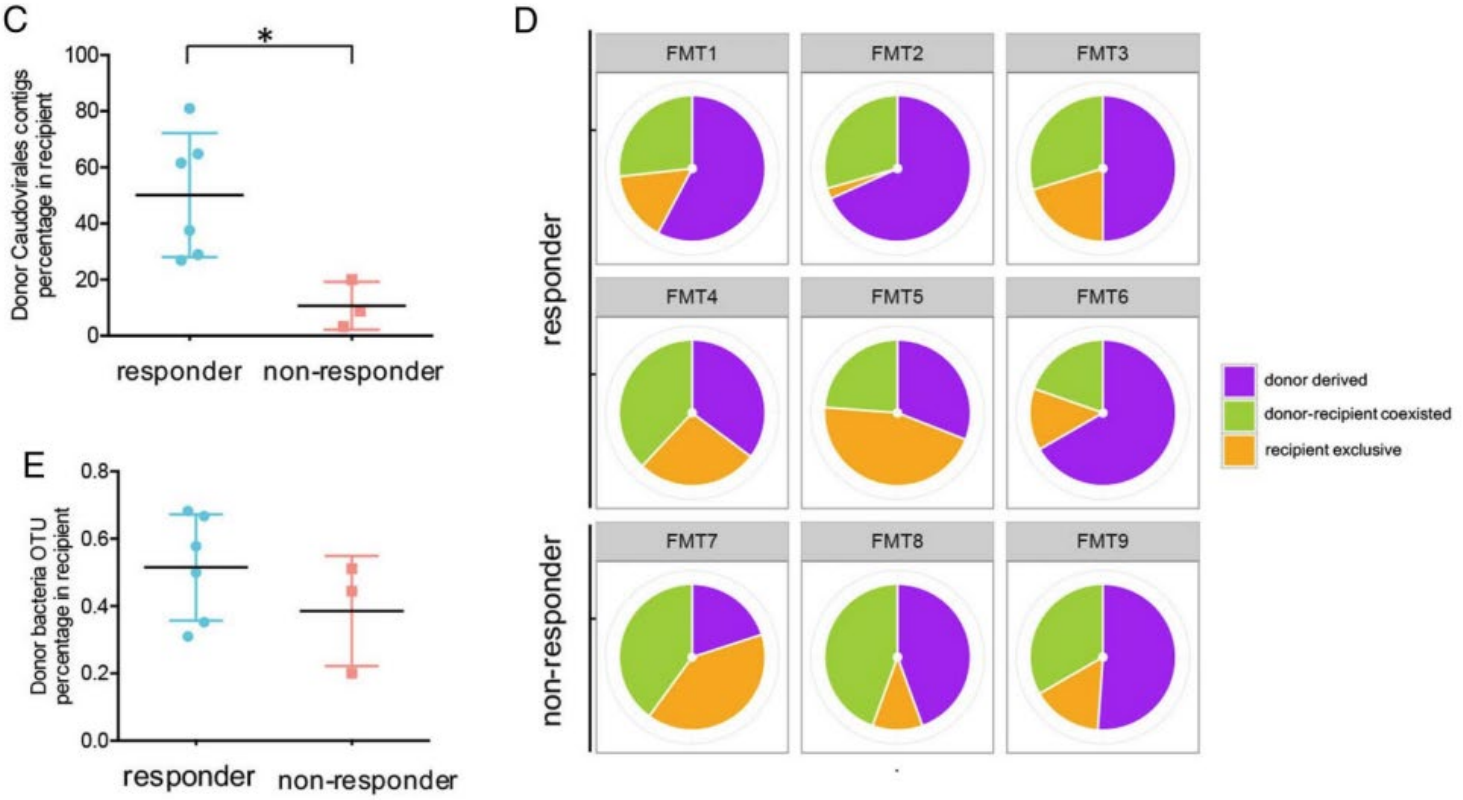
Non-bacteria microbes in FMT



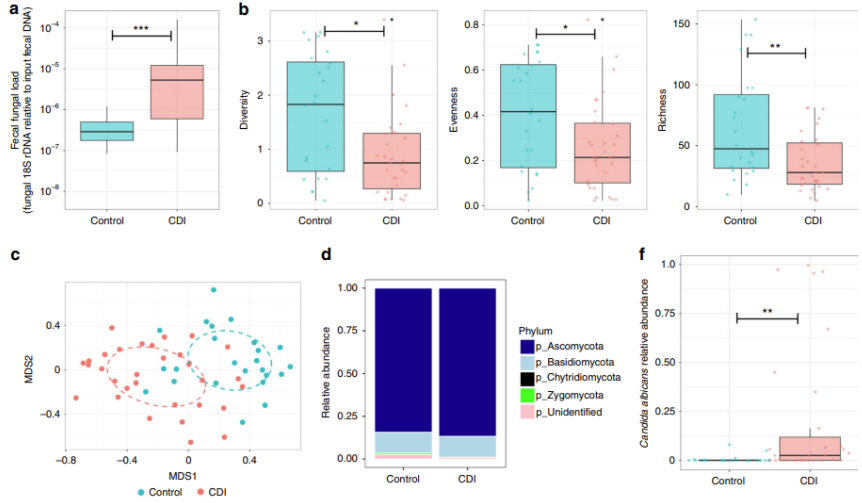
Non-bacteria microbes in FMT

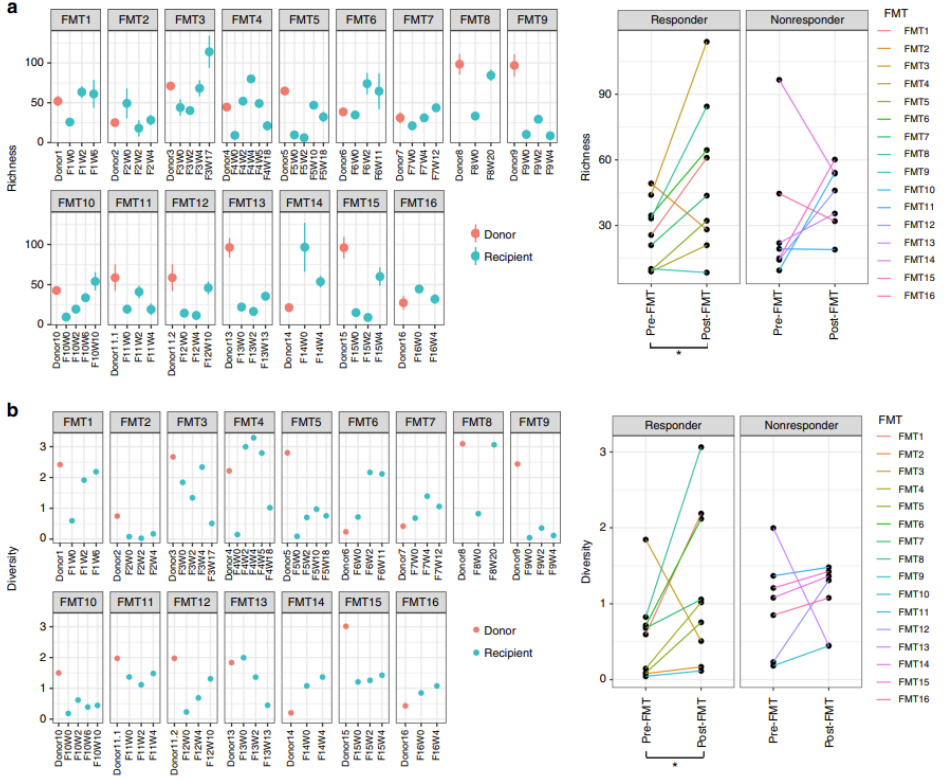
ARTICLE

DOI: 10.1038/s41467-018-06103-6 OPEN

Gut fungal dysbiosis correlates with reduced efficacy of fecal microbiota transplantation in *Clostridium difficile* infection

Tao Zuo[1,2], Sunny H. Wong[1,2,3], Chun Pan Cheung[1], Kelvin Lam[1], Rashid Lui[1], Kitty Cheung[1], Fen Zhang[4], Whitney Tang[1], Jessica Y.L. Ching[1], Justin C.Y. Wu[1,2], Paul K.S. Chan[3,5], Joseph J.Y. Sung[1,2], Jun Yu[1,2,3], Francis K.L. Chan[1,2,3] & Siew C. Ng[1,2,3]





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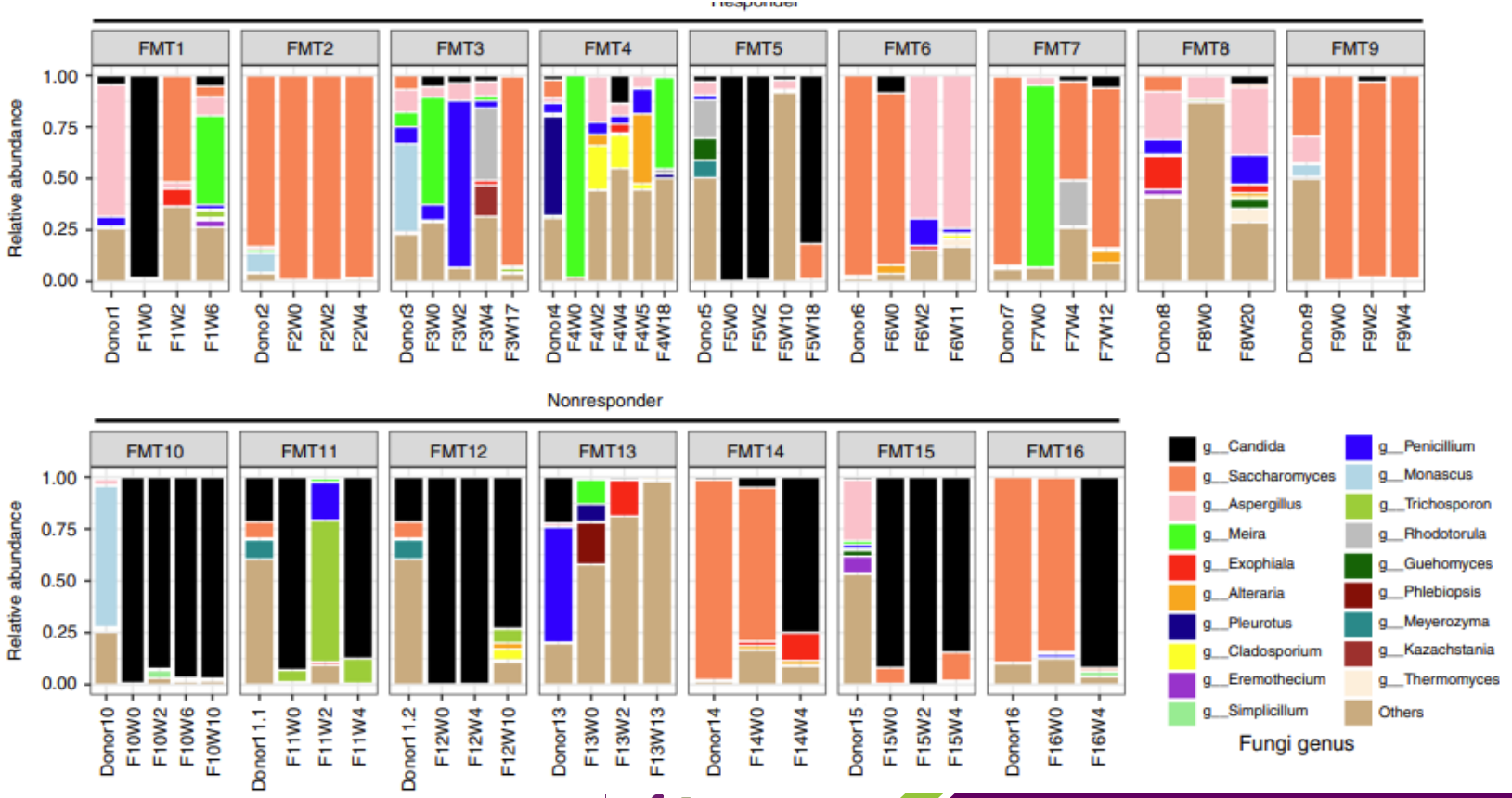
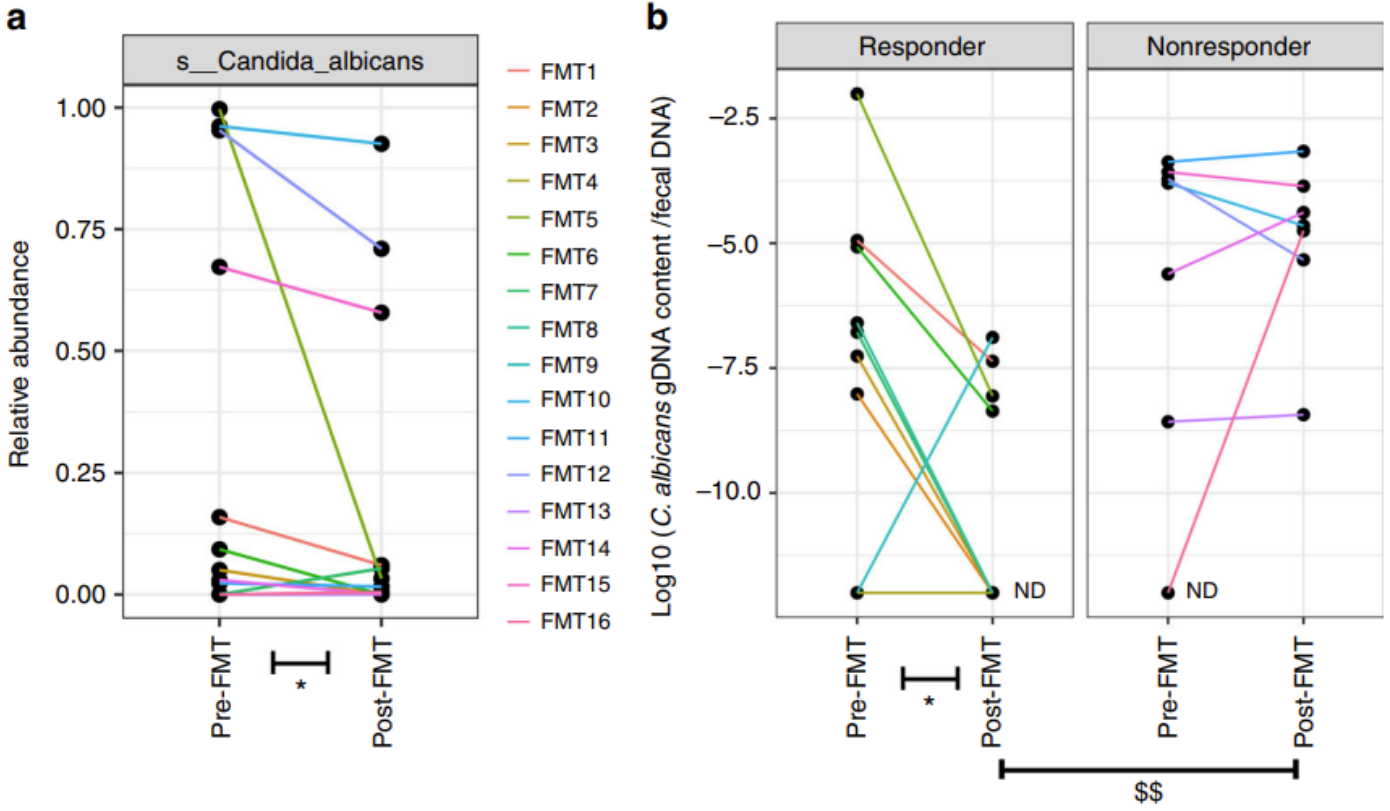
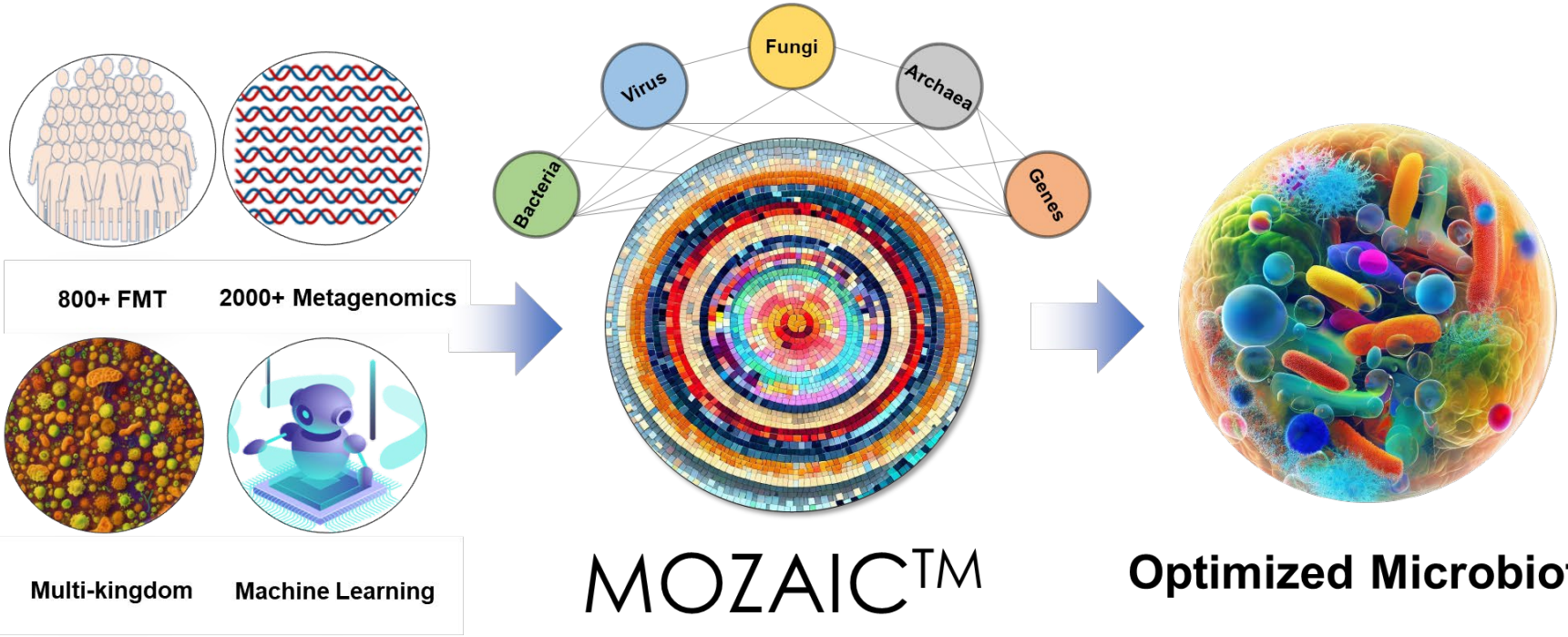
Non-bacteria microbes in FMT



Non-bacteria microbes in FMT



Next Generation of FMT



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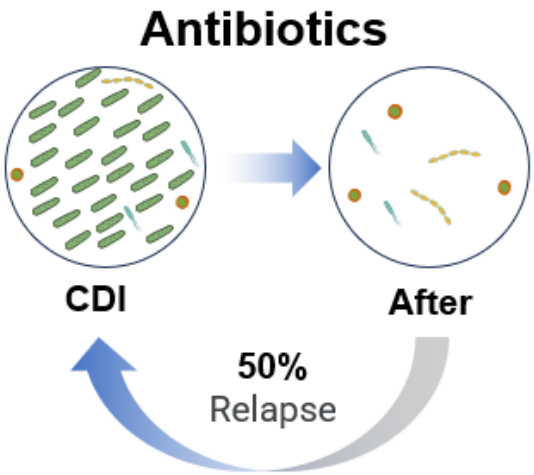

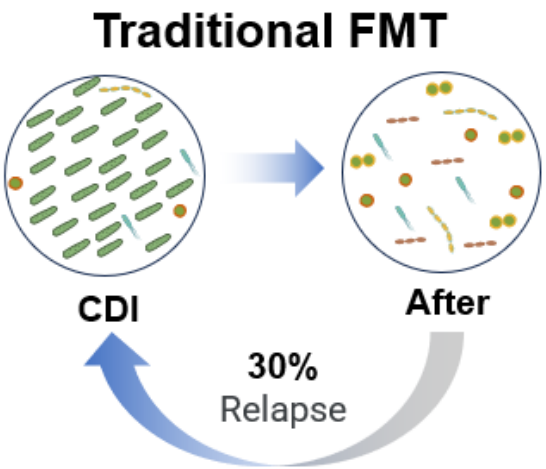

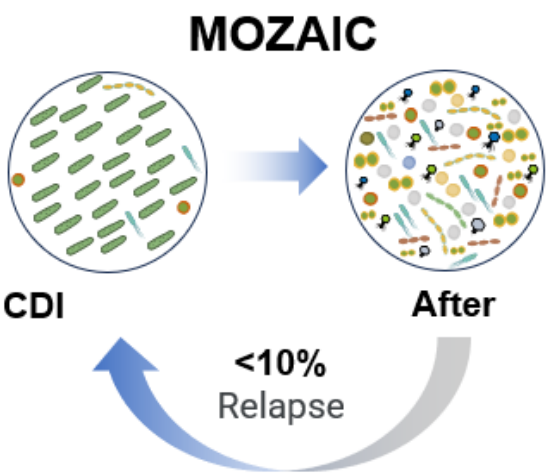

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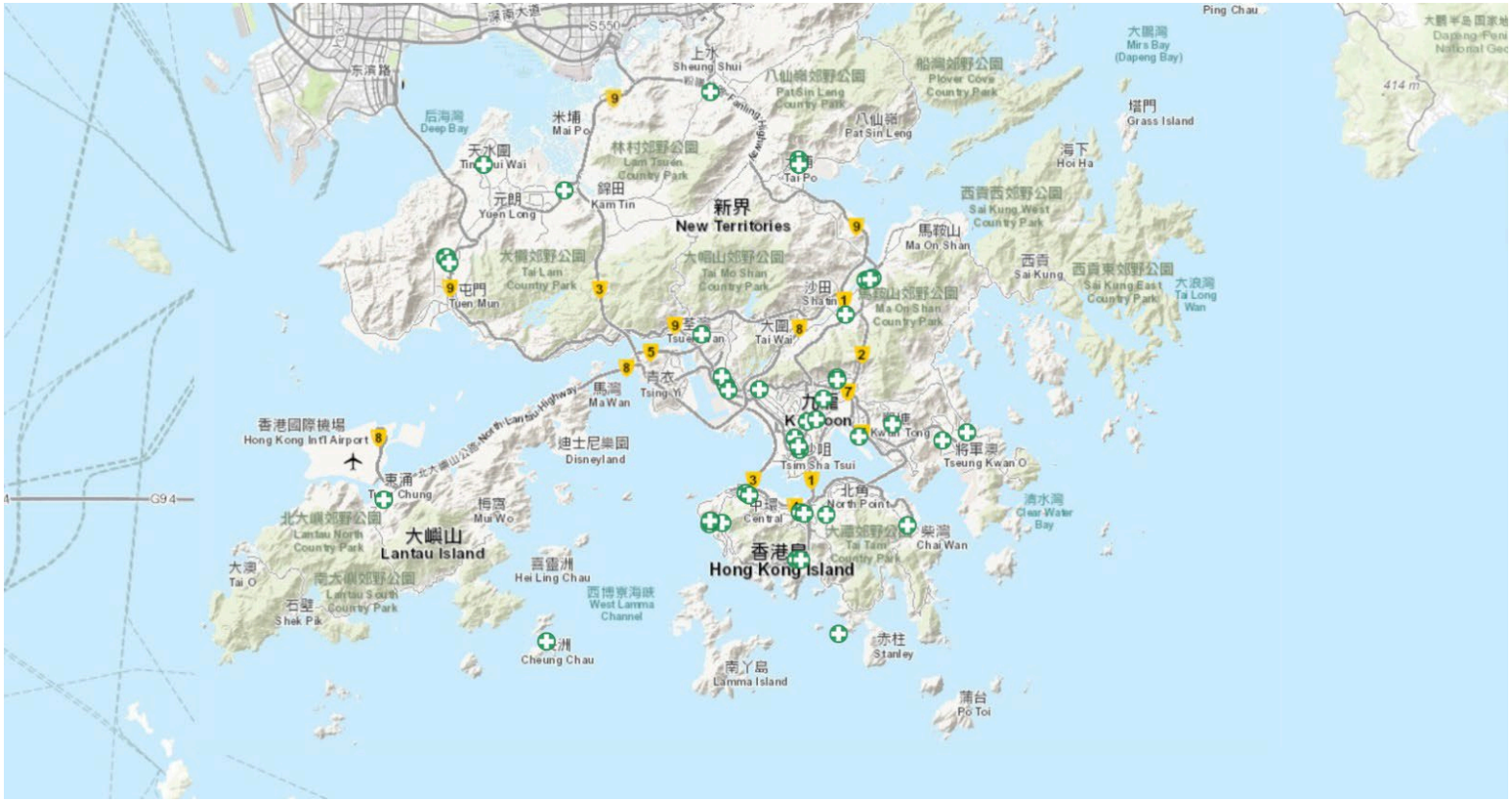

Take-home message

- Antibiotic-induced gut dysbiosis is a major risk factor for CDI
- FMT is an effective and safe method to treat CDI
- In addition to bacteria, non-bacterial archaea, viruses, and fungi are also related to the efficiency of FMT in treating CDI

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40th Anniversary 四十週年

Thank you