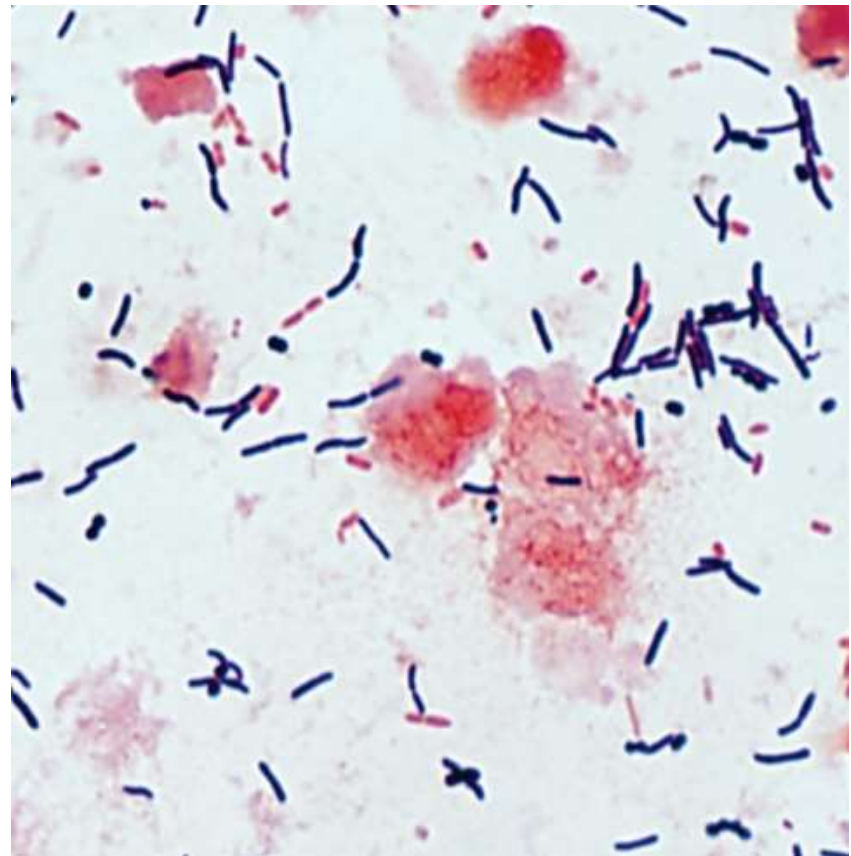
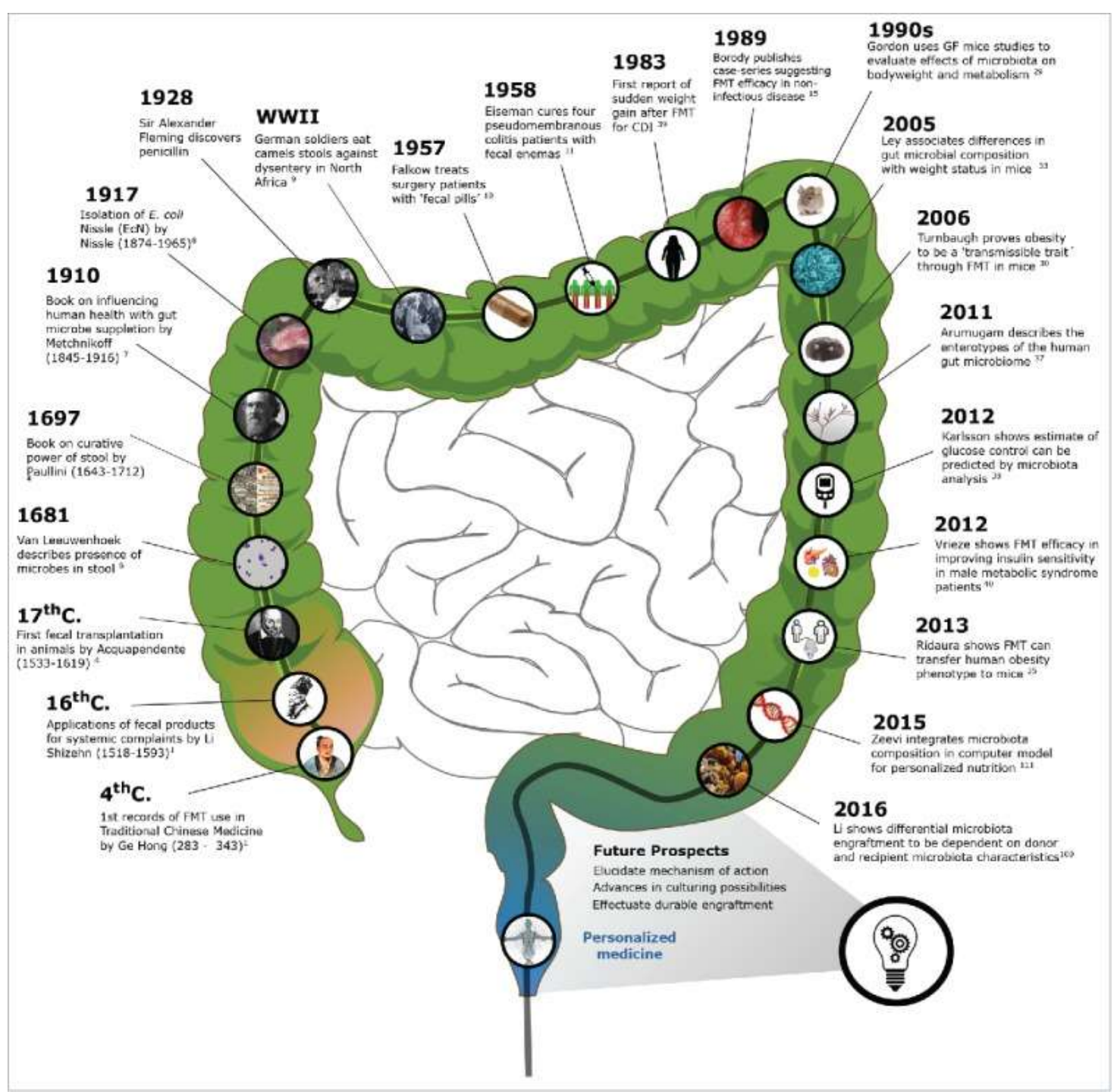


FMT at JHH

Dr Tom Goodsall
Gastroenterology
December 2024
Newcastle, NSW

Disclaimer- BiomeBank association





Why FMT?

- Antibiotics => Decreased phylogenetic diversity
- Antibiotic therapy does not eliminate spores and also destroys competitive microbiome leading to recurrence
- FMT can restore balance in microbiota and diversity
- Secondary bile acids?
- Cost

Antibiotics and the microbiome

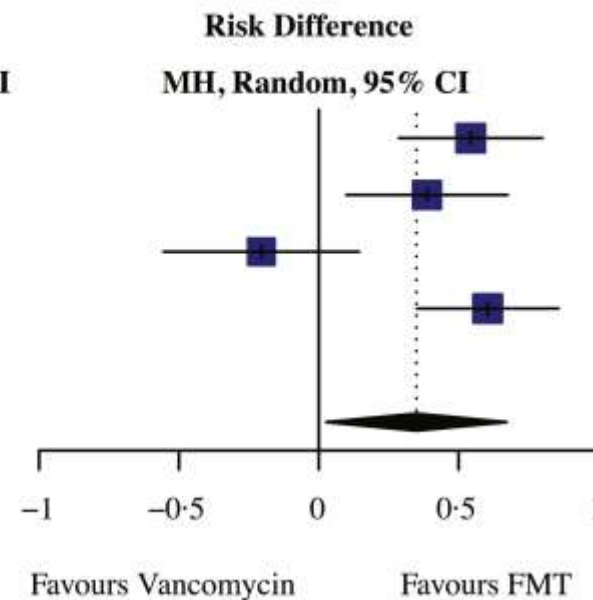


a) Single FMT versus vancomycin

	Single FMT	Vancomycin		
Study	(n/N)	(n/N)	Weight	MH, Random, 95% CI
van Nood, 2013	13/16	7/26	26.0%	0.54 [0.29, 0.80]
Cammarota, 2015	13/20	5/19	25.0%	0.39 [0.10, 0.67]
Hota, 2017	7/16	9/14	22.8%	-0.21 [-0.55, 0.14]
Hvas, 2019	22/24	5/16	26.2%	0.60 [0.35, 0.86]
Total (95% CI)	55/76	26/75	100.0%	0.35 [0.03, 0.67]

Heterogeneity: $\text{Tau}^2 = 0.09$; $\text{Chi}^2 = 15.55$, $\text{df} = 3$ ($P < 0.01$) ; $I^2 = 81\%$

Test for overall effect: $Z = 2.12$ ($P = 0.03$)



NNT=1.5

Baunwall et al. Lancet
2020

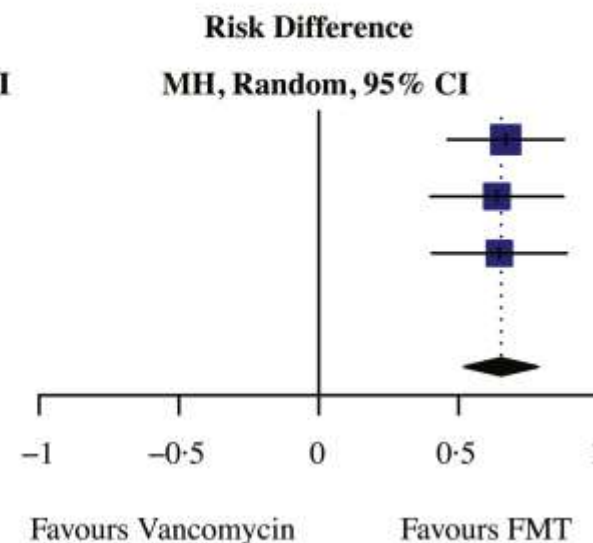
<https://doi.org/10.1016/j.eclim.2020.100642>

b) Repeat FMT versus vancomycin

	Repeat FMT	Vancomycin		
Study	(n/N)	(n/N)	Weight	MH, Random, 95% CI
van Nood, 2013	15/16	7/26	39.9%	0.67 [0.46, 0.88]
Cammarota, 2015	18/20	5/19	30.5%	0.64 [0.40, 0.87]
Hvas, 2019	23/24	5/16	29.7%	0.65 [0.41, 0.89]
Total (95% CI)	56/60	17/61	100.0%	0.65 [0.52, 0.78]

Heterogeneity: $\text{Tau}^2 = 0$; $\text{Chi}^2 = 0.04$, $\text{df} = 2$ ($P = 0.98$) ; $I^2 = 0\%$

Test for overall effect: $Z = 9.74$ ($P < 0.01$)



Therapeutic Guidelines, Australia

Treatment for second and subsequent recurrences or ongoing refractory disease

In addition to the following recommendations, [rehydration](#) is important when treating *C. difficile* infection.

Seek expert advice for all patients with **severe disease** (eg any of: leucocytosis, severe abdominal pain, elevated serum creatinine, elevated blood lactate, low serum albumin, high fever, or organ dysfunction). See [Severe *Clostridioides difficile* infection](#) for recommendations.

Faecal microbiota transplantation (FMT) or 'stool transplant' is an effective therapy for *C. difficile* infection, and is the preferred treatment for adults with second and subsequent recurrences or ongoing refractory *C. difficile* disease.

Faecal microbiota transplantation given through a nasoduodenal tube is superior to vancomycin in patients with recurrent *C. difficile* infection [\[Note 11\]](#). Faecal microbiota transplantation has also been administered via colonoscopy and using frozen stool in oral capsules.

Although faecal microbiota transplantation is not approved by the Australian Therapeutic Goods Administration (TGA) at the time of writing, it is increasingly being undertaken at specialist centres in Australia. Safety and ethical concerns are managed at a local level. There are considerable logistical issues to consider (including consent, donor screening, processing, dosing, and method and route of administration). At the time of writing, there are no long-term safety data available. Seek expert advice.

In adults, faecal microbiota transplantation is the preferred treatment for second and subsequent recurrences or ongoing refractory disease.

In **adults**, faecal microbiota transplantation is the preferred treatment for second and subsequent recurrences of *C. difficile* infection or ongoing refractory disease. If faecal microbiota transplantation is not available, use:

2 vancomycin 125 mg orally or enterally, 6-hourly for 14 days [\[Note 12\]](#) [\[Note 13\]](#)



OR

3 fidaxomicin 200 mg orally, 12-hourly for 10 days [\[Note 14\]](#).



Methods

STEP 1

- Clinical need (including local audit)
- Efficacy and safety comparison
- Cost Analysis

STEP 2

- Quality Use of Medicines Committee
- New Interventional Procedures Committee

STEP 3

- Equipment and product supply
- Structured supervision and accreditation program

STEP 4

- Implementation
- Data collection
- Follow-up

- Efficacy and safety data
- TGA approved stool
- Quality Use of Medicines approval for TGA approved third party donor stool
- Cost analysis
- Local expertise to provide FMT
- Model for safe longterm storage



Efficacy and Cost Analysis Examples

	Antibiotic Therapy	FMT
Initial cure rate	90%	92%
Rate of recurrence following 28 days	Up to 30%	12%
Colectomy rate for severe <i>C. Difficile</i> colitis	6.8%	2.7%
Mortality severe refractory <i>C. Difficile</i> colitis	43.2%	12.1%

Single FMT vs Vancomycin had a 35% gain in absolute treatment effect (NNT 2.9) (Lancet 2020)

Baunwall, S. (2020). Faecal microbiota transplantation for recurrent *Clostridioides difficile* infection: an updated systematic review and meta-analysis. *EClinicalMedicine*, 29.

Cheng, Y. W. (2020). Fecal microbiota transplant decreases mortality in patients with refractory severe or fulminant *Clostridioides difficile* infection. *Clinical Gastroenterology and Hepatology*, 18(10), 2234-2243.

	FMT	Vancomycin	Fidaxomicin
Average dose per day	1	125mg QID	200mg BD
Average treatment duration	1 dose	14 days	10 days
Cost per dosage unit	\$4000	\$5	\$99
Cost per course	\$4000	\$280	\$1986
Additional costs per patient (average LOS following treatment initiation)	\$0	\$7424	\$7424
Expected number of patients/ year	5	5	5
Annual cost	\$20,000	\$38,520	\$47,050
Annual difference		\$18,520	\$27,050



Preparing FMT



Delivering FMT

Colonoscopic delivery

1. Remove Biomictra packet from -80°C freezer and thaw for 4 hours at room temperature (or 10 hours at 4°C) prior to procedure.
2. Record FMT batch number and date of production in patient's medical record.
3. Record patient's name, UR number, date of birth, date of first CDI, number of relapses in prospective database (if established)
4. Prior to positioning patient for procedure, ideally place a sliding sheet under the normal sheet to assist rolling the patient during the procedure.
5. All proceduralists and assistants should be wearing a mask and splash shield or protective eyewear prior to FMT administration.
6. During the colonoscopy, suction as much residual stool and fluid as possible from the colon on entry.
7. Once the scope reaches the caecum, using the sliding sheet roll the patient onto their right side.
8. Cover patient, bed rails and any nearby surfaces with towels or absorbent sheets to contain any spillage.
9. Delivering Biomictra:
 - Remove the colonoscopy biopsy valve and insert the syringe into the biopsy port
 - Flush the FMT into the channel
 - Once syringe is empty, place finger over biopsy port while swapping syringes to prevent spillage
 - Repeat until all syringes have been used
 - Using one of the empty syringes, draw up 30 mL of sterile water for injection and flush the biopsy channel
10. Withdraw the scope without suctioning
11. Patient to remain in right lateral position for at least 1-hour post FMT administration before getting up
12. Encourage high fibre diet and inform patient that antibiotics pose a risk of relapse of CDI in future

Protocol provided by BiomeBank-
colonoscopic preparation and delivery

Our Results

- 24 months, 17 patients, total of 21 FMT procedures
- Complete remission in 15/17 patients (88%) following 1st FMT
- 92% achieved sustained clinical outcomes
- 3 patients with IBD (one diagnosed at time of FMT)
- 2 colectomies: 1 in a patient with resolved *C. difficile* but severe flare of Crohns colitis
1 patient with megacolon, initial FMT for *C. difficile* colitis with SIRS underwent subsequent push enteroscopy FMT but did not respond.
- 47% FMT performed as outpatients

Outcome from total 17 patients		N (%)
Female		11 (65%)
Median age (Range)		67 (27-84)
Number of FMT procedures	1	14 (82%)
	2	2 (12%)
	3	1 (6%)
Colitis or systemic inflammatory response present		7 (41%)
Inpatient		9 (53%)
Prior antibiotic exposure identified		17 (100%)
Primary response		15 (88%)
30 day outcome	Primary cure	15 (88%)
	Recurrence	2 (12%)
IBD	Crohn's	2 (12%)
	Ulcerative proctitis	1 (6%)
Morbidity	Two colectomies, one subsequent duodenal neuroendocrine tumour	3 (18%)
Mortality	One massive PE after colectomy, One death from unrelated sepsis	2 (12%)

C Kelly et al. FMT is highly effective in real-world practice: Initial results from the FMT national registry. Gastroenterology 2021

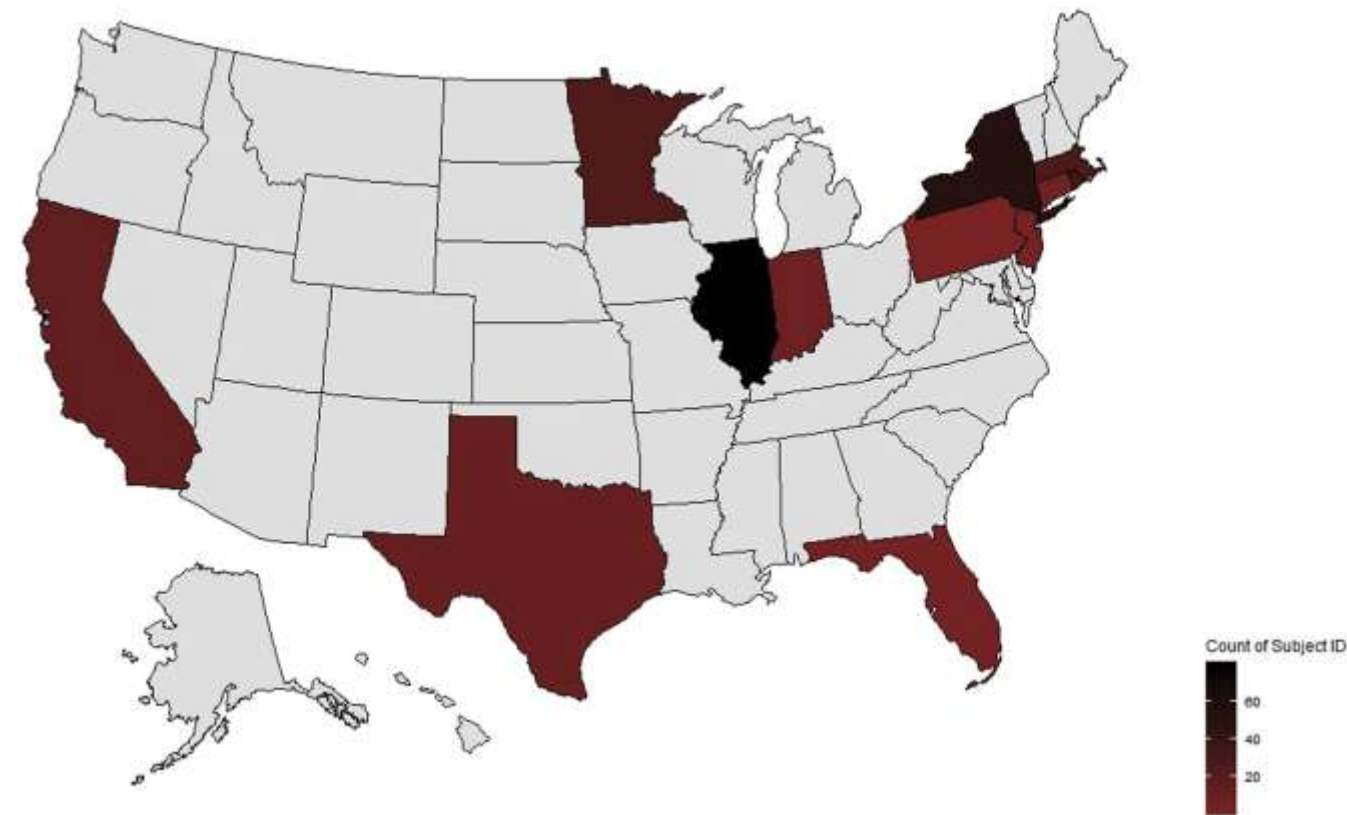
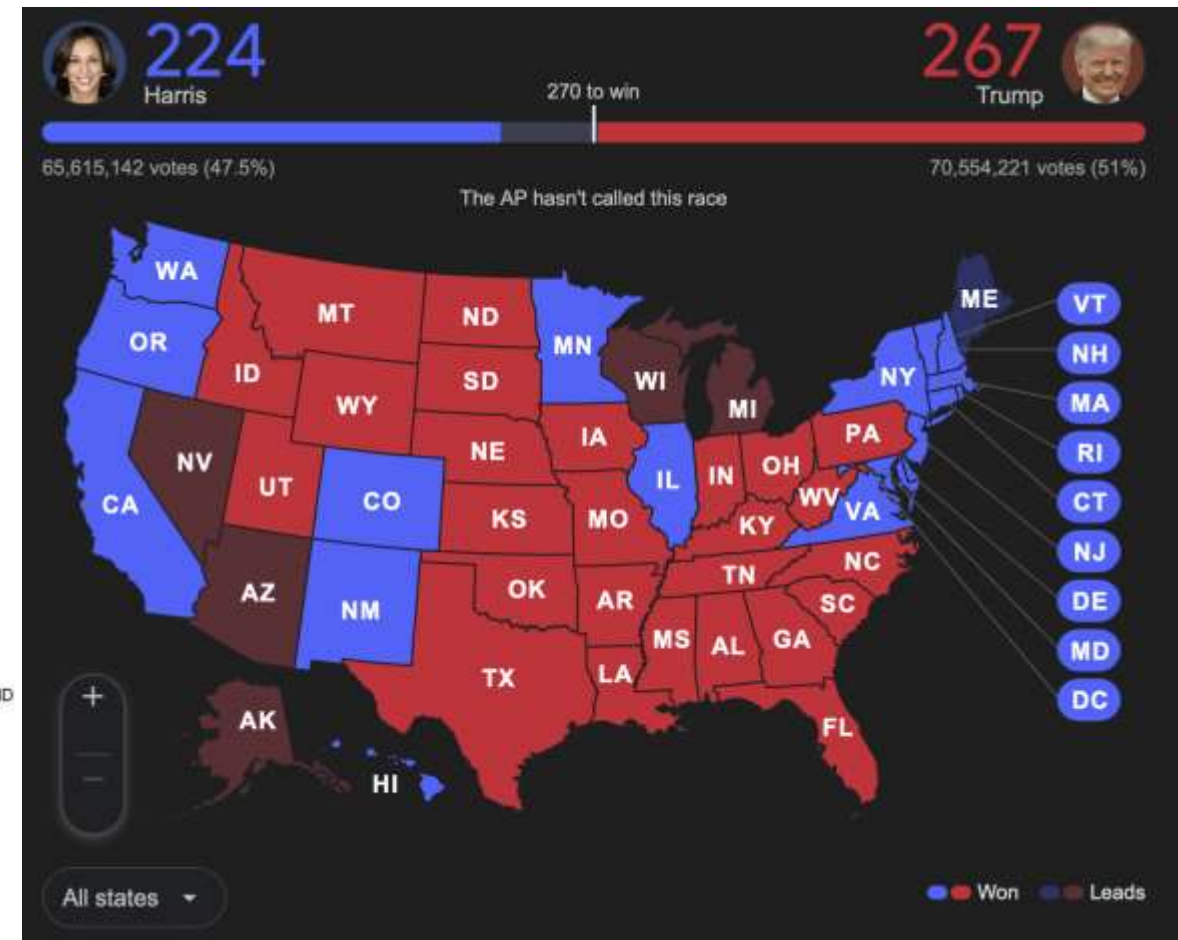


Figure 1. Distribution of registry sites by total number of subjects enrolled.



Kelly et al. Gastroenterology 2021

- P: Prospective national FMT registry for patients undergoing FMT for CDI
- I: FMT
- O: 30 day CDI cure (resolution of diarrhoea without need for additional therapy)

Table 1. Demographics Characteristics of Participants

Characteristic	n (%)
Age	
<18 y	20 (8)
18–55 y	77 (29)
>55 y	162 (63)
Sex	
Female	171 (66)
Male	88 (34)
Race	
White	238 (92)
Black/African American	5 (2)
Asian	3 (1)
Other	4 (2)
Unknown	9 (3)
Ethnicity	
Not Hispanic/Latino	246 (95)
Hispanic/Latino	11 (4)
Not reported	2 (1)
Region	
US Northeast	117 (45)
US Midwest	111 (43)
US South	18 (7)
US West	13 (5)
Comorbidities at baseline (≥5% prevalence) ^a	
Hypertension	82 (32)
Hyperlipidemia	70 (27)
Anxiety	48 (19)
IBD	45 (17)
Ulcerative colitis	24 (9)
Crohn’s disease	19 (7)
Indeterminate colitis	2 (1)
Depression	40 (15)
Cancer	35 (14)
Hypothyroidism	32 (12)
Cardiovascular disease	31 (12)
Irritable bowel syndrome	30 (12)
Type 2 diabetes	28 (11)
Asthma or allergic/atopic conditions	15 (6)

Table 2. Fecal Microbiota Transplantation Indication and Related Characteristics

Characteristics	n (%)
FMT indication	
CDI	259 (100)
Method of CDI diagnosis	
Symptoms and PCR	163 (63)
Symptoms and EIA	54 (21)
Symptoms, EIA and PCR	20 (8)
Symptoms only	12 (5)
PCR only	8 (3)
EIA only	1 (<1)
Not reported	1 (<1)
CDI severity	
Mild	92 (36)
Moderate	115 (44)
Severe	48 (19)
Severe-complicated	2 (1)
Not reported	2 (1)
CDI duration	
<1 mo	14 (5)
1–6 mo	149 (58)
7–12 mo	61 (24)
13–24 mo	17 (7)
>24 mo	16 (6)
Not reported	2 (1)
No. of prior CDI episodes	
1	15 (6)
2	34 (13)
3	110 (42)
4	56 (22)
5 or more	42 (16)
Not reported	2 (1)
Prior treatments for CDI	
Vancomycin	236 (91)
Vancomycin taper/pulse	141 (54)
Metronidazole	104 (40)
Fidaxomicin	73 (28)
Probiotics	44 (17)
Other treatments	14 (5)
No prior treatments	5 (2)

Kelly et al. Gastroenterology 2021

Outcomes:

- 200/222 (90%) cured at 30 days
 - 197/200 (98%) required only one FMT

Table 3. Summary of Fecal Microbiota Transplantation Methodology

Variable	n (%)
Stool donor type	
Unknown donor	249 (96)
OpenBiome	167 (67)
Other stool bank	73 (29)
Source not reported	9 (4)
Known donor	8 (3)
Not reported	2 (1)
Primary method of FMT delivery	
Colonoscopy	221 (85)
Upper endoscopy	15 (6)
Oral capsule	8 (3)
Sigmoidoscopy	2 (1)
Naso-intestinal tube	2 (1)
Colonoscopy and upper endoscopy (same procedure date)	2 (1)
Other	3 (1)
Not reported	6 (2)

Kelly et al. Gastroenterology 2021

Table 4. Adverse Events Reported Up to 1 Month After Fecal Microbiota Transplantation

Adverse event	n (%)
Common symptoms of any severity with >2% prevalence	
Diarrhea	69 (30)
Abdominal pain	39 (17)
Bloating	34 (15)
Constipation	24 (10)
Nausea and/or vomiting	15 (6)
Severe symptoms	
Diarrhea	5 (2)
Abdominal pain	4 (2)
Bloating	1 (<1)
Constipation	1 (<1)
Other	2 (1)
New infections	
None	219 (95)
Unrelated to FMT	9 (4)
Possibly related to FMT	2 (1)
<i>Bacteroides fragilis</i>	1 (<1)
Enteropathogenic <i>Escherichia coli</i>	1 (<1)
Not reported	1 (<1)
Hospitalizations	
None	204 (88)
Unrelated to FMT	24 (10)
Possibly related to FMT	3 (1)
Perforation	1 (<1)
Ulcerative colitis flare	1 (<1)
Diarrhea, abdominal pain, fever	1 (<1)

Table 5. Adverse Events Reported Between 1 and 6 Months After Fecal Microbiota Transplantation

Adverse event	n (%)
New diagnoses	
No	125 (80)
Yes ^a	21 (13)
Irritable bowel syndrome, diarrhea	2 (1)
Ulcerative colitis	2 (1)
Other ^b	22 (14)
Not reported	10 (6)
Serious infections	
No	140 (90)
Yes ^a	6 (4)
Pneumonia	1 (<1)
UTI	1 (<1)
<i>Campylobacter</i> infection	1 (<1)
Cellulitis	1 (<1)
Infected AV fistula/MRSA bacteremia	1 (<1)
Streptococcus pharyngitis	1 (<1)
Pneumonia/acute kidney injury with or without aspiration pneumonia/UTI	1 (<1)
Not reported	10 (6)
Hospitalizations	
No	126 (81)
Yes ^a	30 (19)
Infection other than CDI	8 (6)
CDI recurrence	3 (2)
Other ^c	30 (20)
Deaths	
Unrelated to FMT	4 (3)
Related to FMT	0 (0)

Shogbesan et al. A systematic review of the safety and efficacy of FMT in immunocompromised patients. Can J Gas Hep. 2018.

- 44 studies, 303 patients
 - Immunosuppressant 77.2%
 - Solid organ transplant 18.2%
 - Malignancy including haematologic 16.2%
 - SCT 2.5%
 - HIV/AIDs 2.1%
- 206/234 clinical resolution (87.7%) after first FMT, 93% after 2 or more FMTs.
- Safety: 2 deaths (pneumonitis day 1 and pneumonia 2 weeks), 2 colectomies, 5 episodes infection, 10 hospitalisations)

Case 1

Male, 26 - Background History: *Cerebral palsy, epilepsy, cholecystectomy*

Risk Factors

- Hospitalisation
- Multiple inpatient antibiotic courses

Pathway to FMT

- Admitted with gangrenous gall bladder
- PEG inserted for malnutrition complicated by abscess
- Refractory *C. Difficile* diarrhea
- Treated with Vancomycin, Fidaxomicin (total LOS >8 weeks), recurrence following long taper within 5 days

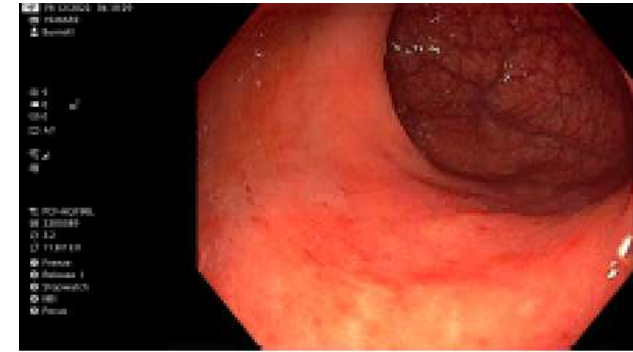
Response to FMT

- Discharged on day after FMT
- Improvement in diarrhea from day of FMT

Follow Up

- 6 week follow-up: complete resolution of symptoms
- 4 month follow-up:
 - Needing Movicol every 2 days for bowel habit, rarely using PEG, improved nutrition
- No further recurrence or need for antibiotics

Case 2



Female, 34 - Background History: *Iron deficiency anaemia*

Risk Factors

- Antibiotics for cystitis

Pathway to FMT

- Multiple ED presentations (abdominal pain + diarrhoea)
- Initial treatment with metronidazole
- Subsequent treatment with Vancomycin
- Further recurrence → referred as outpatient

Response to FMT

- Day procedure
- Ulcerative proctitis diagnosed at time of FMT
- Early response

Follow Up

- 6 weeks: acute symptoms resolved
- 1 year follow-up complete clinical and histological remission

Costello et. al JAMA 2019

Case 3

Female, 80 - Background History: *Gallbladder cancer, Ischaemic heart disease, depression*

Risk Factors

- Age >65yo
- Hospitalisations
- Multiple antibiotic courses

Pathway to FMT

- *C. difficile* diagnosed in Coffs Harbour, recent antibiotic use
- Recurrent *C. difficile* colitis despite Metronidazole, Vancomycin, Fidaxomicin
- CRP 169 with fevers on transfer to JHH

Response to FMT

- Endoscopy confirmed *C. difficile* colitis
- Sustained response

Follow Up

- Complete response with no recurrence

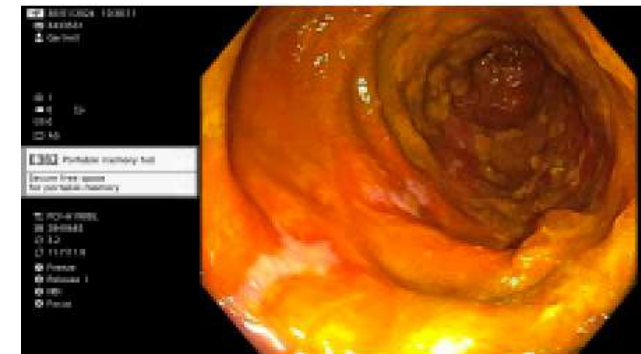
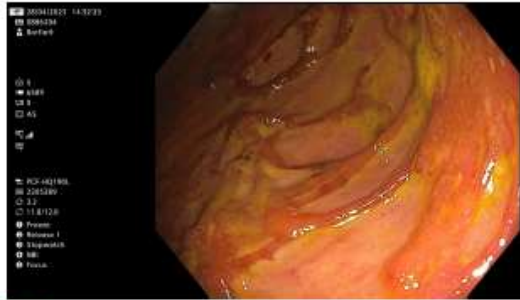


Table 1. FMT patient demographics and outcomes.

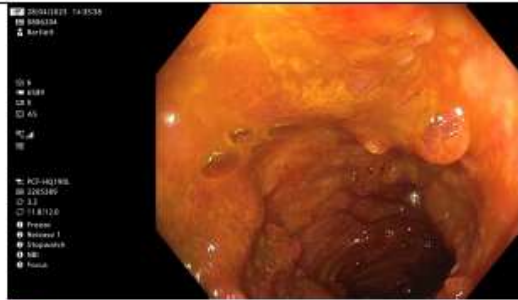
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Colectomy CB 60F

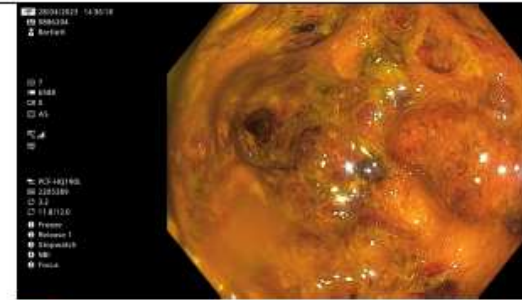
- Initial presentation with weeks of bloody diarrhoea and fevers, C-diff positive on stool Managed with vancomycin. Returned to referring hospital with ongoing bloody diarrhoea and CRP 177.
- Return to JHH with SIRS
- FMT Day 10



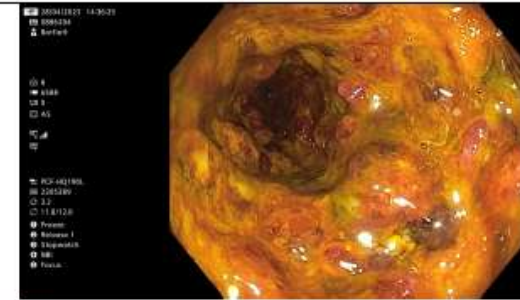
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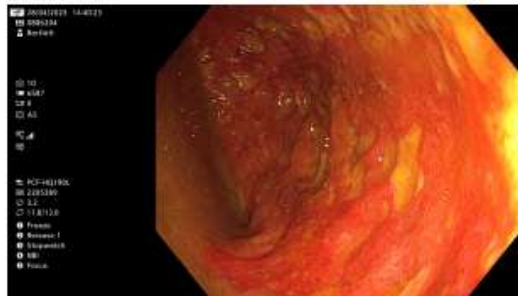
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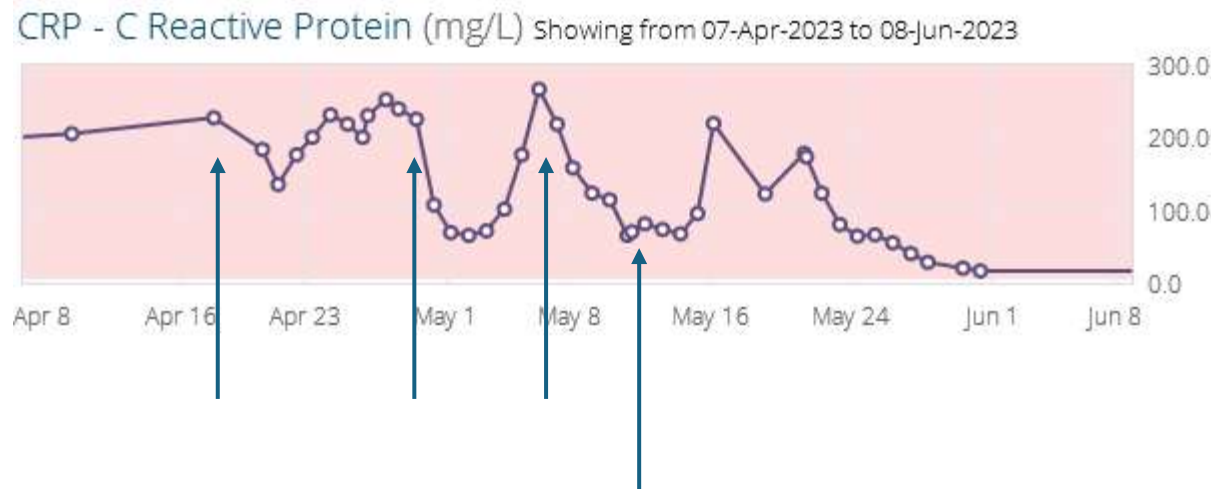


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Colectomy CB 60F

- Initial response then refractory Crohn's colitis failing steroids and infliximab
- Proceeded to colectomy. CD PCR negative and no C-diff identified on colectomy specimen.



Colectomy VS 62F

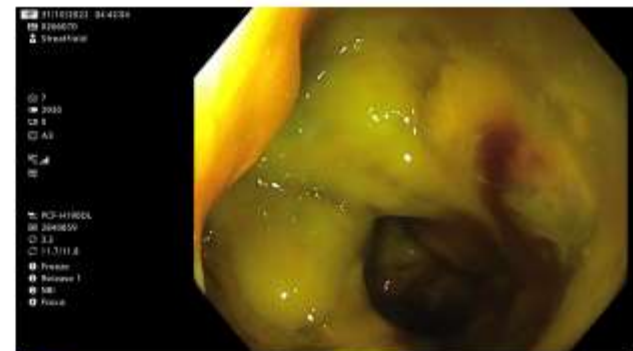
- Severe CDI with SIRS 6 weeks after cephazolin for elective orthopaedic procedure.
- Vanc and fidax non-responsive, CRP 181→127
- FMT performed, severe pseudomembranous colitis



1 Transverse Colon



2 Transverse Colon



3 Transverse Colon

Colectomy VS 62F

- Persistent severe CDI with repeat FMT delivered endoscopically to the jejunum (unsafe for colonoscopy, abdo pain significant)
- Post FMT improvement with subsequent recurrence 3 days later developing megacolon and requiring urgent colectomy.
- Died frontal lobe ICH 9 months later.

Summary

- FMT is effective and safe for the treatment of recurrent and refractory CDI
- Safety and efficacy demonstrated in immunocompromised populations
- Capsule is in phase 2 and 3 trials in Australia – will make endoscopic delivery obsolete