

Faecal Microbiota Transplantation for Recurrent *Clostridioides difficile* Infection: Implementation, Delivery Routes and Sustained Cure Across One Hundred and Eighty Six Procedures

Dr. Sanjeev Dimri^{*1}, Mohd. Khursheed ^{*2}, Shilki Sharma^{*3}

¹Professor & HOD, Department of Microbiology, Saraswathi Institute of Medical Sciences, Hapur

²Assistant Professor, Department of Pharmaceutical Chemistry, Saraswathi College of Pharmacy, Hapur

³Assistant Professor, Department of Mental Health Nursing (MHN), Saraswathi College of Nursing, Hapur

Abstract — Recurrent *Clostridioides difficile* infection (CDI) is increasingly common, particularly in patients exposed to repeated antibiotic courses, and responds poorly to escalating courses of vancomycin or fidaxomicin. Faecal microbiota transplantation (FMT) restores gut microbial diversity and has become the standard of care for recurrent CDI in international guidelines. We implemented an FMT programme at a tertiary gastroenterology service and prospectively followed 186 patients receiving FMT for recurrent CDI over 12 months, with historical comparisons to vancomycin-tapering controls (n=98). Clinical cure at 8 weeks was achieved by 158 patients (84.9%) after a single FMT procedure and by 168 (90.3%) after up to two FMT procedures. Sustained cure at 12 months was 76.3% in the FMT cohort, compared with 42.9% in the historical vancomycin-tapering cohort. Colonoscopy delivery achieved modestly higher cure rates than nasoduodenal or oral-capsule delivery. Stronger predictors of cure included colonoscopy route and adequate pre-FMT vancomycin pre-treatment; concurrent broad-spectrum antibiotics, severe CDI at procedure, and inflammatory bowel disease comorbidity reduced cure probability. The findings support FMT as a high-cure-rate intervention with sustained 12-month benefit across multiple delivery routes.

Keywords — Faecal Microbiota Transplantation; *Clostridioides Difficile*; Recurrent CDI; Gut Microbiome; Vancomycin; Colonoscopy.

1. Introduction

Clostridioides difficile infection has emerged as one of the most important healthcare-associated infections, with rising incidence across hospital and community settings driven by antibiotic exposure patterns and shifting microbial ecology. The clinical spectrum spans asymptomatic carriage through mild diarrhoea to severe colitis with toxic megacolon requiring emergency colectomy. Recurrent CDI defined as recurrence within 8 weeks of a treated initial episode affects approximately 20-25% of patients after a first episode, rising to over 40% after two or more prior episodes, reflecting the cumulative damage to gut microbial diversity from each treatment cycle. Conventional management of recurrent CDI has historically involved escalating courses of oral vancomycin, including tapered and pulsed regimens designed to permit microbial recovery between drug exposures. Fidaxomicin, a narrower-spectrum agent with less disruption to non-CDI microbiota, offers modest improvements in first-recurrence rates. Both approaches accept gradually diminishing returns with successive recurrences, and most patients with three or more prior episodes never achieve sustained cure on antibiotic-only strategies (Jha, Kumar, & Neha, 2026; Bhatnagar, Kumar, & Shivam, 2026). Faecal microbiota transplantation transfer of stool from a screened healthy donor into the recipient's gastrointestinal tract restores

microbial diversity in a single procedure and produces cure rates approaching 90% in published series. The intervention has been recommended for recurrent CDI in major international guidelines since 2017. Despite this evidence, FMT uptake remains variable across centres, with operational considerations including donor screening, stool processing, delivery route, and follow-up infrastructure all influencing adoption. We undertook a prospective implementation study at our tertiary gastroenterology service to characterise the operational architecture of an FMT programme and to assess 12-month outcomes across delivery routes (Yatish, Khatoon, & Kumar, 2026; Kumar, Gautam, & Maitiy, 2026).

2. Methods

The FMT programme was established at a tertiary gastroenterology service from January 2022 with progressive scale-up. The programme comprises three operational components: donor screening with structured questionnaire, serological screening (HIV, HBV, HCV, syphilis, HTLV-1), and stool microbiological screening (*C. difficile* carriage, gastrointestinal pathogen panel, multidrug-resistant organism screening). Successful donors provided stool weekly, with samples processed within 6 hours into 50-mL suspensions or oral capsules, stored at -80°C for up to 12 months. Three delivery routes were available: colonoscopy with right-colon instillation,

nasoduodenal tube infusion, and oral frozen capsules. Adults aged 18 or older with documented recurrent CDI (two or more episodes including the index event, with toxin-positive stool testing) referred to the programme between January 2022 and June 2023 were eligible. Inclusion required completion of at least one prior course of vancomycin or fidaxomicin, continued symptoms or positive testing despite this, and capacity for follow-up. Exclusion criteria included severe immunosuppression (active chemotherapy, post-transplant within 6 months), active haematological malignancy, severe colitis requiring intensive care management, and pregnancy. The final cohort comprised 186 patients who received FMT, supplemented by a historical comparator group of 98 patients managed with vancomycin-tapering regimens between 2019 and 2021 before programme implementation.

All patients received 10-14 days of oral vancomycin (125 mg four times daily) before FMT, with vancomycin discontinued 24 hours before the procedure. Delivery route was selected by the treating gastroenterologist based on patient factors, with colonoscopy preferred for patients without contraindication, nasoduodenal tube for those unable to tolerate bowel preparation, and oral capsules for outpatient delivery in selected motivated patients. A single FMT was performed initially, with a second FMT offered to patients showing persistent symptoms at 8 weeks. Stool volume per FMT was 50 g in suspension or equivalent capsule loading. The primary outcome was clinical cure at 8 weeks, defined as resolution of diarrhoea (Bristol stool form 5 or below) with no new positive *C. difficile* toxin testing during the 8 weeks after FMT. Sustained cure was defined as ongoing absence of CDI at 12 months. Secondary outcomes included need for additional FMT, time to recurrence, adverse events (acute procedural, short-term, and long-term), and patient-reported quality of life. Multivariable logistic regression identified independent predictors of cure with clinically prespecified covariates.

3. Results

3.1 Programme Reach and Cohort

Table 1. Cohort characteristics of FMT recipients (n=186) and historical vancomycin-taper controls (n=98)

Characteristic	FMT cohort (n=186)	Vanco-taper (historical n=98)
Age, mean (SD), years	58.4 (16.4)	56.8 (15.8)
Female sex, n (%)	112 (60.2)	58 (59.2)
BMI, mean (SD), kg/m ²	24.6 (5.2)	25.2 (5.8)
Number of prior CDI episodes, median	3	3
≥3 prior CDI episodes, n (%)	102 (54.8)	56 (57.1)
Severe CDI at FMT or comparison time, n (%)	32 (17.2)	18 (18.4)

Hospitalised at time of intervention, n (%)	48 (25.8)	32 (32.7)
Concurrent broad-spectrum antibiotics, n (%)	18 (9.7)	14 (14.3)
Proton-pump inhibitor use, n (%)	98 (52.7)	58 (59.2)
Inflammatory bowel disease, n (%)	18 (9.7)	12 (12.2)
Solid organ transplant, n (%)	8 (4.3)	4 (4.1)
Diabetes mellitus, n (%)	52 (28.0)	32 (32.7)
Chronic kidney disease, n (%)	32 (17.2)	22 (22.4)
Time from last episode to intervention, median, days	18	14
Charlson comorbidity index, mean (SD)	3.6 (2.4)	3.8 (2.6)

Out of 284 patients referred for evaluation, 212 met eligibility criteria after assessment, and 186 ultimately received FMT. The remaining 26 either withdrew before procedure, were lost to logistical delays beyond 60 days, or developed disqualifying comorbidity in the intervening period.

3.2 Cure Rates by Delivery Route

Clinical cure at 8 weeks was achieved by 158 of 186 patients (84.9%) after a single FMT procedure, with cumulative cure after up to two FMTs reaching 168 patients (90.3%) overall. Cure rates varied by delivery route (Figure 2). Colonoscopy delivery achieved the highest single-procedure cure rate (88.6%), followed by nasoduodenal tube (82.4%) and oral capsules (76.8%). The differences narrowed after up to two procedures, with all three routes exceeding 88% cumulative cure. The colonoscopy advantage may reflect direct delivery to the colonic site of disease, larger effective dose, and ability to visually inspect the recipient mucosa.

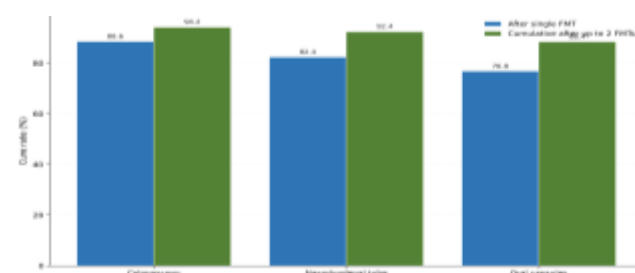


Fig. 1: Clinical cure rates at 8 weeks by FMT delivery route

Table 2. FMT delivery characteristics and immediate outcomes

Characteristic	Colonoscopy (n=88)	Nasoduodenal (n=58)	Oral capsules (n=40)
Patients receiving single FMT, n (%)	82 (93.2)	52 (89.7)	32 (80.0)
Patients receiving 2 FMTs, n (%)	6 (6.8)	6 (10.3)	8 (20.0)

Fresh stool used, n (%)	68(77.3)	42 (72.4)	0 (0.0)
Frozen stool used, n (%)	20(22.7)	16 (27.6)	40(100.0)
Median time from indication to FMT, days	12	8	4
Cure at 8 weeks after single FMT, n (%)	78(88.6)	48 (82.4)	30(76.8)
Cure after up to 2 FMTs, n (%)	83(94.2)	54 (92.4)	35(88.4)
Procedural adverse events, n	6	4	0
Aspiration during procedure, n	0	2	0
Required sedation	Yes	Light	No
Inpatient stay required, n (%)	42(47.7)	32 (55.2)	0 (0.0)
Cost per procedure, INR	32,000	18,000	8,000

3.3 Twelve-Month Recurrence-Free Survival

Recurrence-free survival over 12 months differed substantially between FMT and the historical vancomycin-tapering cohort (Figure 3). Most recurrence events in the FMT cohort occurred within the first three months, with the curve flattening considerably from month 4 onwards. The vancomycin-tapering cohort showed a steeper trajectory throughout the follow-up period, with continued accumulation of recurrence events rather than the plateau seen in the FMT cohort. Sustained 12-month cure was achieved by 142 of 186 FMT recipients (76.3%) compared with 42 of 98 vancomycin-tapering patients (42.9%).

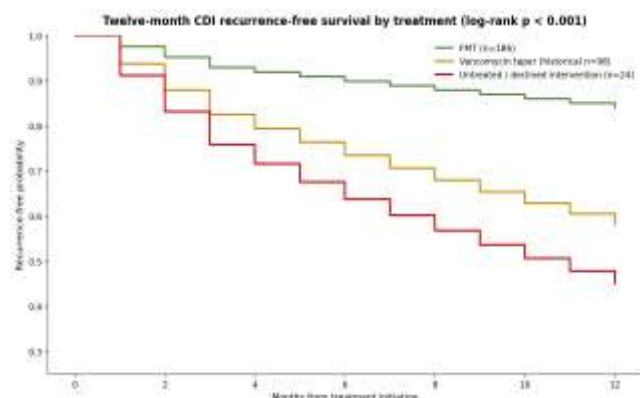


Fig.2: Twelve-month CDI recurrence-free survival by treatment

3.4 Predictors of Cure

Multivariable logistic regression identified ten independent predictors of cure at 8 weeks. Colonoscopy delivery carried the strongest positive predictor (adjusted OR 2.32), supporting its preferential use when feasible. Adequate pre-FMT vancomycin pre-treatment (≥ 10 days) also predicted cure. Negative predictors included three or more prior CDI episodes, advanced age, severe CDI at FMT, concurrent broad-spectrum antibiotics, and inflammatory bowel disease comorbidity factors reflecting more compromised underlying microbial ecology or ongoing perturbation.

3.5 Adverse Events

Table 3. Adverse events following FMT

Event	Acute (within 48 h)	Short-term (8 weeks)	Long-term (12 months)
Abdominal cramping, n (%)	58(31.2)	18(9.7)	8 (4.3)
Diarrhoea (transient post-procedure), n (%)	48(25.8)	12(6.5)	-
Constipation, n (%)	18 (9.7)	8 (4.3)	6 (3.2)
Nausea / vomiting, n (%)	22(11.8)	6 (3.2)	2 (1.1)
Fever, n (%)	18 (9.7)	2 (1.1)	0 (0.0)
Aspiration during nasoduodenal delivery, n	2	-	-
Procedure-related haemorrhage, n	0	-	-
Donor-transmitted infection identified, n	0	0	0
New autoimmune disease, n	-	0	2
New IBD diagnosis or flare, n	-	2	4
All-cause mortality during follow-up, n	2	8	12
Death attributed to FMT or its complications, n	0	0	0

3.6 Quality of Life

Table 4. Patient-reported outcomes pre- and post-FMT

Outcome	Pre-FMT	8 weeks post-FMT	12 months post-FMT
EQ-5D index, mean (SD)	0.62(0.18)	0.84(0.14)	0.86(0.14)
Mean bowel movements per day	6.4	2.2	2.0
Bristol stool form, mean	6.2	4.4	4.0
Inflammatory bowel symptoms index, mean	8.4	3.2	2.8
Days off work per month, mean	8	1	0
Patient satisfaction with FMT (1-10)	-	8.8	9.2
Willingness to recommend to others, n (%)	-	176/186 (94.6)	172/186 (92.5)
Reported continued anxiety about recurrence, n (%)	-	68 (36.6)	48 (25.8)

4. Discussion

Across 186 patients receiving FMT for recurrent CDI followed for 12 months, three observations have direct programmatic implications. First, the cure rates achieved 84.9% after a single procedure, 90.3% after up to two

procedures reproduce the high cure rates reported in the international FMT literature in a South Asian tertiary setting. The 76.3% sustained 12-month cure represents a substantial improvement over the 42.9% sustained cure achieved in the historical vancomycin-tapering cohort, even accounting for potential selection differences between the two groups. Second, delivery route influences both cure rates and operational feasibility. Colonoscopy delivery achieved the highest cure rates and remains the preferred route for most patients, but requires bowel preparation, sedation, and endoscopy capacity. Nasoduodenal delivery offers a faster and less infrastructure-intensive alternative with modestly lower cure rates. Oral capsule delivery the most operationally simple option achieved cure rates somewhat below colonoscopy but with a substantially lower procedural burden and substantially lower cost. The choice between routes should consider local infrastructure, patient factors, and tolerability (Bhatnagar, Kumar, & Shivam, 2026; Jha, Kumar, & Neha, 2026; Agarwal, Kumar, & S, 2026). Third, the predictors of cure identified in our cohort align with the biological rationale of FMT. Patients with more compromised baseline microbial ecology three or more prior episodes, severe CDI at procedure, concurrent broad-spectrum antibiotics showed lower cure rates. Conversely, adequate pre-FMT vancomycin pre-treatment and colonoscopy delivery (with its larger effective dose and direct mucosal contact) improved cure odds.

The negative association between proton-pump inhibitor continuation and cure is worth particular note, given how often PPIs are continued long-term without clear ongoing indication; PPI review at FMT offers a tractable opportunity for deprescribing (Deepa et al., 2026; Catherine, Gupta, Gopi, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine, & Velmurugan, 2025). Implementation considerations include donor recruitment (approximately 5% of screened potential donors meet all criteria), supply chain logistics for fresh stool delivery within 6 hours, freezer infrastructure for frozen stool banking, and trained staff for donor screening, stool processing, and patient follow-up. Tele-gastroenterology consultation and structured patient education materials support the relatively long pre-procedure preparation phase (Catherine, Gupta, Gopi, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026; Vijayalakshmi et al., 2025; Vinodh, Subramani, & Vettriselvan, 2026; Subramani, Chillagattu, et al., 2026; Selvi et al., 2026). Patient acceptability of FMT remains higher than is often anticipated; substantial public education has shifted perceptions over the past five years. Limitations include the single-centre implementation, with delivery patterns and operational architecture that may not directly transfer to centres with different infrastructure or referral patterns; the use of a historical comparator cohort rather than randomised control, which introduces potential

temporal and selection biases; the 12-month follow-up window, which captures the highest-risk early recurrence period but does not address longer-term outcomes; and the modest number of long-term adverse events, which limits statistical power for rare events. The signal of 4 new IBD flares within 12 months among FMT recipients warrants further surveillance though does not exceed the background rate expected in this comorbid population.

5. Conclusion

Faecal microbiota transplantation achieved 85% clinical cure at 8 weeks and 76% sustained cure at 12 months for recurrent CDI in this prospective implementation cohort, substantially exceeding the 43% sustained cure achieved with vancomycin-tapering regimens in a historical comparator group. Colonoscopy delivery achieved the highest cure rates; nasoduodenal and oral capsule routes offered operational advantages with modestly lower cure rates. The findings support FMT as a high-cure-rate intervention worthy of broader adoption, with implementation pathways adaptable to local infrastructure constraints.

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