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EFFICACY OF FECAL MICROBIOTA TRANSPLANTATION IN TREATING GASTROINTESTINAL DISEASES: A SYSTEMATIC REVIEW OF EVIDENCE IN CDI, UC, IBS, AND CROHN'S DISEASE

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ABSTRACT

Background: Fecal microbiota transplantation (FMT) has emerged as a novel therapeutic approach for various gastrointestinal disorders characterized by microbiota dysbiosis. While FMT is well established for recurrent Clostridioides difficile infection, its efficacy in conditions such as ulcerative colitis, Crohn's disease and irritable bowel syndrome remains under investigation.

Objective: To systematically review and synthesize current evidence on the efficacy and safety of FMT in treatment of CDI, UC, CD and IBS, focusing on clinical outcomes, microbiota changes and delivery strategies.

Methods: This review PRISMA guidelines to assess the efficacy and safety of fecal microbiota transplantation in CDI, UC, CD and IBS. Databases searched included PubMed, Google Scholar. Studies were screened and selected by two reviewers. Data on FMT protocols, clinical outcomes and safety were extracted and analyzed narratively to study heterogeneity.

Results: FMT shows high cure rates in recurrent CDI with success rates over 80% regardless of delivery method. In UC multi-dose protocols with well-selected donors can induce remission. Evidence in CD is limited, with some benefits in subgroups like steroid dependent patients. In IBS, results are mixed, colonoscopic FMT appears more effective than capsules, but placebo effects and patient variability complicate interpretation. FMT is generally safe, with mostly mild side effects.

Conclusion: FMT is highly effective and well-tolerated therapy for recurrent CDI. It shows potential in treating UC, with emerging evidence in CD and IBS. Efficacy depends on delivery route, donor recipient compatibility and disease specific factors. Standardized protocols and further high-quality trials are needed to clarify FMT's role across gastrointestinal disorders.

KEYWORDS

Fecal Microbiota Transplantation, Clostridioides difficile, Ulcerative Colitis, Crohn's Disease, Irritable Bowel Syndrome, Gut Microbiota, Gastrointestinal Disorders

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Introduction

The human gastrointestinal (GI) microbiota plays a crucial role in maintaining digestive and systemic health. It supports nutrient absorption, modulates the immune system and protects against pathogen colonization. Dysbiosis is a disruption of gut microbiota, it has been increasingly associated with gastrointestinal disorders, including recurrent Clostridioides difficile infection (CDI), ulcerative colitis (UC), irritable bowel syndrome (IBS), and Crohn's disease (CD) (Jaramillo et al., 2023; Green et al., 2020). Fecal microbiota transplantation (FMT) is an innovative treatment strategy aimed at reestablishing a healthy and diverse gut microbiome by introducing fecal material from a healthy donor into the intestinal tract of affected patients. Fecal microbiota transplantation (FMT) has shown impressive effectiveness in treatment of recurrent CDI, it has shown a remarkable efficacy in this setting achieving resolution rates of up to 90%. This is significantly higher than the success rates of conventional antibiotic therapies such as vancomycin or fidaxomicin (Jaramillo et al., 2023). A Cochrane review further supports these findings, reporting a substantial increase in CDI resolution with FMT compared to standard treatments (RR 1.92, 95% CI 1.36–2.71) (Minkoff et al., 2023). Encouraged by its success in CDI, FMT has also been explored as a therapy for other gastrointestinal conditions. In ulcerative colitis (UC), a chronic inflammatory bowel disease, meta-analyses of randomized controlled trials have demonstrated that FMT significantly enhances both clinical and endoscopic remission rates compared to placebo, without a corresponding increase in serious adverse events (Liu et al., 2023). Conversely, evidence for FMT in IBS remains inconclusive. A meta-analysis did not find significant overall symptom improvement, although some subgroups, particularly those receiving endoscopic administration, might experience benefits (Halkjær et al., 2023). Preliminary data in Crohn's disease indicate

possible advantages, yet strong clinical proof remains insufficient (Green et al., 2020). Due to the increasing interest in microbiome-based treatments and the inconsistent outcomes reported across different diseases and treatment protocols, a thorough evaluation of the existing clinical evidence is warranted. This systematic review aims to assess the efficacy of FMT in CDI, UC, IBS, and CD, elucidating its therapeutic value and limitations in each context.

Aim of the Study:

The aim of this systematic review is to evaluate and synthesize current clinical evidence on the efficacy and safety of fecal microbiota transplantation (FMT) in the treatment of *Clostridioides difficile* infection (CDI), ulcerative colitis (UC), Crohn's disease (CD), and irritable bowel syndrome (IBS), with a focus on therapeutic outcomes, delivery methods and key factors influencing treatment success.

Methods

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A comprehensive literature search was performed across major databases including PubMed and Google Scholar.

Eligibility Criteria

Studies were included if they met the following criteria:

- Were randomized controlled trials, meta-analyses, controlled clinical trials or observational studies that investigated the efficacy and/or safety of FMT in patients with *Clostridioides difficile*, ulcerative colitis (UC), Crohn's disease (CD), or irritable bowel syndrome (IBS);
- studies involving human subjects;
- full-text articles Published in English;

Exclusion criteria were:

- Non-original research (e.g., reviews, editorials, case reports);
- Studies involving only animal studies;
- Abstract-only publications or conference proceedings.

Study Selection

Two independent reviewers screened all titles and abstracts for eligibility, followed by full-text review of potentially relevant articles. Discrepancies were resolved through discussion or consultation with a third reviewer.

Data Extraction

Data extracted from each study included publication year, study design, sample size, patient population, FMT protocol (route of administration, donor type, frequency), clinical outcomes (remission, response, recurrence), microbiota-related changes, and adverse events.

Risk of Bias and Ethical Considerations

All included studies reported adherence to ethical standards such as the Declaration of Helsinki and Good Clinical Practice guidelines. Institutional review board approvals and informed consent from participants were documented. Several studies were registered with clinical trial registries. While formal risk of bias assessment was not performed, design rigor (e.g., blinding, randomization, control groups) was noted.

Data Synthesis

Due to significant heterogeneity in study designs, populations, and FMT protocols, a narrative synthesis approach was used. Where possible, data from multiple studies were compared descriptively to identify patterns in treatment efficacy and safety across disease categories. A total of 27 studies were ultimately included in this systematic review.

Literature Review Results

Clostridioides difficile infection (CDI)

Multiple high-quality studies have confirmed that fecal microbiota transplantation (FMT) is highly effective in managing recurrent *Clostridioides difficile* infection (CDI), frequently outperforming conventional antibiotic treatments in terms of both clinical recovery and microbiological outcomes. In a randomized, open-label pilot study, Youngster et al. assessed the use of frozen FMT from unrelated donors administered via colonoscopy or nasogastric tube in 20 participants who had experienced a median of four recurrences of *Clostridioides difficile* infection. A single FMT dose resolved diarrhea in 70% of participants, with additional treatments increasing the total cure rate to 90%. Microbiota profiling demonstrated a shift toward donor-like microbial profiles, indicating successful engraftment regardless of the administration method (Youngster et al., 2014).

Jiang et al. performed a randomized clinical trial with 65 participants to compare oral capsules of freeze-dried fecal microbiota transplantation (FMT) with frozen FMT delivered by enema. Both groups showed high efficacy, preventing *Clostridioides difficile* infection (CDI) recurrence in 84% of patients receiving the capsules and 88% of those receiving enemas. Although clinical outcomes were similar, the lyophilized capsules were less effective at restoring key gut bacterial classes such as Bacteroidia and Verrucomicrobia. The authors highlighted the need to optimize the dosing of freeze-dried FMT and suggested that spore-forming Clostridia may play a major role in clinical success (Jiang et al., 2018).

Further supporting the safety of FMT, Stefansson et al. conducted a double-blind Phase I trial in 24 healthy volunteers who received capsulized autologous FMT following clindamycin-induced dysbiosis. Both FMT and placebo groups experienced only mild to moderate adverse events, with no significant differences in recovery time. Although the treatment was safe and didn't cause problems, it didn't help people recover normal bowel function faster than a placebo. This shows that using autologous treatments may have limits when used for prevention (Stefansson et al., 2023).

A group of 20 patients with recurrent *C. difficile* infections received colonoscopic FMT from universal donors in a study conducted by Millan et al. All participants achieved clinical resolution of symptoms. Microbiome analysis showed a shift after FMT from Proteobacteria, especially *E. coli* and *Klebsiella* to Bacteroidetes and Firmicutes. Importantly, there was a sustained one-year reduction in gut antimicrobial resistance genes, including those against β -lactams, fluoroquinolones and multidrug efflux mechanisms (Millan et al., 2016).

Woodworth et al. extended these findings in a randomized controlled trial (PREMIX) involving renal transplant recipients colonized with multidrug-resistant organisms (MDROs). FMT significantly accelerated MDRO decolonization, with 89% of completers MDRO-negative by day 36. Strain-level analyses revealed replacement of ESBL-producing Enterobacteriales by antibiotic-susceptible strains, despite the latter not being present in the FMT product- that FMT may reshape the gut microbial ecosystem. Detailed strain-level analysis showed that extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriales were replaced by antibiotic-sensitive strains, even though these sensitive strains were not present in the FMT material, indicating that FMT may reshape the gut microbial ecosystem (Woodworth et al., 2023).

In a randomized controlled trial involving three groups, Wei et al. evaluated the effectiveness of fecal microbiota transplantation preceded by vancomycin (FMTv) compared to fidaxomicin and vancomycin monotherapy. FMTv achieved the highest cure rate (71%), significantly outperforming fidaxomicin (33%) and vancomycin (19%). Patients who responded to FMT showed substantial restoration of microbiota diversity, including increased abundance of Lachnospiraceae and Ruminococcaceae, and a reduction in Enterobacteriaceae. Additionally, a novel predictive model based on the *Escherichia* to *Blautia* ratio accurately predicted treatment response, achieving an area under the curve (AUC) of 0.92 using qPCR (Wei et al., 2022).

In contrast, Camacho-Ortiz et al. investigated the use FMT from pooled unrelated donors (FMT-FURM) as a first-line therapy in CDI. Following one or two doses, 71.4% of patients achieved remission. However, the microbiota engraftment was limited, and the microbial composition did not resemble that of the donors, which may explain the lower efficacy compared to conventional approaches (Camacho-Ortiz et al., 2017).

A mechanistic study by Seekatz et al. investigated 14 patients with ≥ 2 CDI recurrences. Post-FMT, microbiota diversity increased significantly, with dominance shifting from pathogenic Proteobacteria (48.2% pre-FMT) to Firmicutes and Bacteroidetes (32.3% post-FMT). Functionally, biosynthetic and energy-producing pathways were restored, while stress-related genes declined. The authors also pointed out that changes in microbiota composition alone do not fully explain clinical outcomes, underlining the complex nature of FMT's therapeutic effects (Seekatz et al., 2014).

Kelly et al. carried out a double-blind randomized controlled trial involving 46 patients with multiple recurrences of *Clostridioides difficile* infection (CDI), comparing donor fecal microbiota transplantation (FMT) with autologous FMT. Cure rates at 8 weeks were significantly higher in the donor group (90.9%) vs. autologous (62.5%). All patients who relapsed after autologous FMT were successfully treated with donor FMT, leading to a final overall cure rate of 93.5%. No serious adverse events were reported (Kelly et al., 2016).

In a study involving 21 patients, Garza-González et al. assessed FMT capsules with or without the addition of *Lactobacillus* strains. Both treatments led to rapid clinical improvement, with bowel movement frequency reduced by 62.7% within 48 hours and no recurrences over 90 days. The gut microbiota was restored by the seventh day. Adding *Lactobacillus* did not significantly affect the outcomes, although a slight increase in microbial diversity was observed (Garza-González et al., 2019).

Ulcerative Colitis (UC)

The therapeutic potential of FMT in ulcerative colitis (UC) has been investigated in numerous randomized and observational trials, focusing on both induction and maintenance of remission. However, efficacy appears to depend significantly on dosage, delivery route, donor characteristics, and recipient microbiota profiles. Lahtinen et al. conducted a randomized placebo-controlled trial involving 48 patients with ulcerative colitis in clinical remission to assess the efficacy of a single colonoscopic FMT in maintaining remission. After 12 months, 54% of patients in the FMT group and 41% in the placebo group remained in remission, but this difference was not statistically significant ($P = 0.660$). There were no significant differences in inflammatory biomarkers (e.g., fecal calprotectin, CRP), endoscopic scores or quality of life. Notably, the FMT group experienced a temporary decline in quality of life at 4 months post-treatment. The authors concluded that a single-dose colonoscopic FMT does not provide sufficient benefit for sustaining long-term remission in ulcerative colitis (Lahtinen et al., 2023).

In contrast, Chen et al. examined the use of capsulized oral FMT in 22 patients with active UC. Participants were given three oral FMT doses over the course of one week. By week 12, clinical remission was achieved in 57.1%, clinical response in 76.2%, and endoscopic remission in 47.6%. Microbiota analysis showed an increase in beneficial bacteria such as *Faecalibacterium prausnitzii*, *Alistipes*, and *Odoribacter splanchnicus*, along with a decrease in *E. coli* and lipopolysaccharide biosynthesis pathways. Metabolomics showed elevated anti-inflammatory metabolites (e.g., indolelactic acid) in responders. These findings suggest that oral capsulized FMT is safe, effective, and mechanistically linked to gut microbiota and metabolite modulation (Q. Chen et al., 2023).

A randomized controlled trial carried out by Fuentes et al. to study the gut microbes linked to long-term remission in patients with mild-to-moderate ulcerative colitis (UC). Participants received two fecal microbiota transplant (FMT) infusions using either donor stool or their own (autologous). Patients who stayed in remission for at least one year had an increase in certain beneficial gut bacteria, especially from *Clostridium* clusters IV and XIVa, including butyrate-producing species like *Faecalibacterium prausnitzii*, *Roseburia intestinalis* and *Coprococcus eutactus*. In contrast, relapsing patients exhibited increased *Ruminococcus gnavus*, *Bacteroides vulgatus*, and *E. coli*. The presence of *R. gnavus* in donor samples was linked to treatment failure, suggesting it may be a negative marker for FMT success (Fuentes et al., 2017).

In a prospective randomized study, Fang et al. compared the effectiveness of a single FMT versus standard therapy in patients with recurrent active UC. After 8 weeks, 90% of patients who received FMT achieved both clinical and endoscopic remission, compared to 50% in the control group. Among responders, 62.5% maintained remission for 24 months without medication. Microbiota analysis showed increases in *Bacteroidetes* and *Prevotella*, and declines in *Proteobacteria* and *Escherichia*. Only one long-term adverse event was reported, which was an Epstein-Barr virus (EBV) infection (Fang et al., 2021).

In nine patients with moderate-to-severe UC, Chen et al. tested a washed FMT protocol. The treatment was administered over five days using either a naso-jejunal tube (NJT) or transendoscopic enteral tubing (TET). By week 2, 77.8% of patients had a clinical response, while by week 12, 55.6% achieved clinical remission and 33.3% showed endoscopic remission. Improvements were also seen in CRP, ESR, and hemoglobin levels. No serious adverse events occurred, though mild, self-limiting effects were more frequent in NJT recipients. The standardized FMT preparation was considered safe and effective, particularly for those who were steroid-dependent (M. Chen et al., 2020).

Fecal microbiota transplantation (FMT) was investigated by Uygun et al. as a rescue treatment in 30 patients with refractory ulcerative colitis who had not responded to immunosuppressive or anti-TNF therapy. A single colonoscopic administration of FMT into the terminal ileum led to clinical response in 70% and

clinical plus endoscopic remission in 43.3% at 12 weeks. Inflammatory markers (CRP, ESR) and hemoglobin improved and mild adverse events occurred in 23.3%. Notably, every patient who developed a fever following FMT achieved remission, suggesting a potential immunological mechanism associated with treatment efficacy (Uygun et al., 2017).

Crohn's Disease (CD)

While the evidence supporting fecal microbiota transplantation (FMT) in Crohn's disease (CD) is not as strong as for *Clostridoides difficile* infection (CDI) or ulcerative colitis (UC), several clinical studies have explored its safety and efficacy in different patient subgroups, showing some promising outcomes. Sokol et al. conducted a randomized, single-blind, sham-controlled pilot trial to evaluate FMT in patients with colonic or ileocolonic CD who were in corticosteroid-induced remission. Seventeen patients were randomized to receive either FMT (8 patients) or a sham procedure (9 patients) through colonoscopy. While none of the patients showed strong donor microbiota engraftment by week 6 (Sørensen index > 0.6), 87.5% of those who received FMT stayed in steroid-free remission by week 10, compared to only 44.4% in the control group. Only the FMT group demonstrated reductions in the Crohn's Disease Endoscopic Index of Severity (CDEIS) and stable CRP levels. The authors observed that the absence of microbial engraftment was associated with disease flare, suggesting that successful and lasting colonization may be important for long-term clinical benefits (Sokol et al., 2020).

Xiang et al. conducted a large observational study involving 174 patients with Crohn's disease who received a step-up FMT approach, starting with one FMT and progressing to repeated treatments combined with other therapies like immunosuppressants or enteral nutrition. The median follow-up was 43 months. After one month, 75.3% showed a clinical response and 50% of steroid-dependent individuals achieved steroid-free remission. At final follow-up, 43.7% maintained clinical response and 20.1% achieved sustained clinical remission. Notably, a disease duration longer than five years and a high baseline Harvey–Bradshaw Index (≥ 8) were independent predictors of poor response (Xiang et al., 2020).

A multicenter randomized controlled trial by Kao et al. examined the use of a two-step FMT protocol, starting with colonoscopy and followed by oral capsules, in patients diagnosed with mild-to-moderate Crohn's disease. Although 34 patients were enrolled, the study was stopped early due to a low chance of demonstrating any benefit. By week 8, none of the patients who received FMT achieved both clinical and endoscopic remission, while 1 out of 11 placebo patients (9.1%) did. The rates of clinical remission were similar between the FMT and placebo groups (60% vs. 54.5%). There were no significant improvements in inflammatory markers or endoscopic results. However, patients who responded to FMT showed changes in their gut microbiota that became more similar to the donor's. The authors proposed that using antibiotics before FMT or adding other treatments might improve effectiveness in future studies (Kao et al., 2025).

In a study led by He et al. 25 Crohn's disease patients with intraabdominal inflammatory masses were assessed. After three months, 52% had achieved clinical remission, which persisted in 32% of patients after one year and in 22.7% after 18 months. Inflammatory masses regressed radiologically in 71.4% of patients and 60% of steroid-dependent individuals improved enough to stop using them. No serious side effects were reported (He et al., 2017).

Li et al. investigated the timing of a second FMT in 69 Crohn's disease patients who had previously responded to the first treatment. A second FMT was given 3 to 4 months after the initial one. While the first FMT provided a median benefit lasting 125 days, the second extended this effect to 176.5 days. Analysis of the gut microbiome and metabolites revealed improved bacterial diversity and increased levels of beneficial metabolites like TMAO and hippurate, supporting the idea that long-term FMT success may depend on metabolic interactions between the host and gut microbiota (Li et al., 2019).

In summary, although randomized evidence remain limited, approaches like repeated or stepwise FMT, early treatment and individualized protocols may improve outcomes in Crohn's disease, particularly in patients with specific complications such as inflammatory masses or steroid dependence.

Irritable Bowel Syndrome (IBS)

FMT has been proposed as a therapeutic intervention for IBS based on its capacity to modulate dysbiotic gut microbiota. However, evidence remains inconclusive, with outcomes depending heavily on delivery method, patient phenotype and donor matching.

El-Salhy et al. carried out a randomized, double-blind, placebo-controlled clinical trial involving 165 patients with moderate-to-severe IBS symptoms. Participants received either placebo (autologous stool), 30 g FMT, or 60 g

FMT prepared from frozen stool of a rigorously screened, healthy “superdonor” and delivered via gastroscopy. At the 3-month follow-up, a significant clinical response (defined as a ≥ 50 -point reduction in the IBS Severity Scoring System, IBS-SSS) was observed in 76.9% and 89.1% of the 30 g and 60 g FMT groups, respectively, compared to 23.6% in the placebo group. Significant improvements were also recorded in fatigue and quality of life. The clinical effects were associated with microbiota shifts, notably increased abundance of *Alistipes* spp., *Lactobacillus* spp., *Eubacterium biforme* and decreased abundance of *Bacteroides* spp. The study emphasized the importance of donor quality and FMT dose for treatment efficacy (El-Salhy et al., 2020).

In contrast, Hartikainen et al. conducted a randomized, placebo-controlled clinical trial with 49 IBS patients who received a single FMT from a healthy donor or an autologous placebo via colonoscopy. Although the FMT group exhibited long-term alterations in microbiota composition, including increased bacterial richness and a notable rise in *Prevotella copri*, these changes were not associated with sustained symptom relief. While a subset of patients experienced transient improvement at 12 weeks, no consistent associations were found between microbiota profiles and clinical outcomes. Notably, donor-derived *P. copri* strains successfully colonized only those patients who had low baseline abundance of the species, suggesting that host microbiota composition significantly influences engraftment success (Hartikainen et al., 2024).

In a randomized double-blind pilot trial, Singh et al. investigated how different antibiotic pretreatments affected bacterial engraftment and symptom response to oral FMT capsules in diarrhea-predominant IBS (IBS-D). Forty-four patients were randomized into four arms: (1) FMT alone, (2) rifaximin + FMT (R-FMT), (3) ciprofloxacin/metronidazole + FMT (CM-FMT), or (4) placebo. Surprisingly, FMT alone produced significantly higher bacterial engraftment (median 15.5%) than R-FMT (5%) or CM-FMT (2.4%). However, this did not correlate with symptom relief. At 10 weeks, there were no significant differences across groups in IBS symptom severity scores, quality of life or global symptom improvement. These findings suggest that while microbial colonization occurs, it may not translate into clinical benefit, particularly when preceded by antibiotics (Singh et al., 2022).

Overall, the evidence suggests that while FMT can be effective in some IBS patients, especially with high-quality donors and appropriate delivery methods, engraftment alone does not guarantee clinical benefit. Pretreatment strategies may influence microbiota outcomes without improving symptoms.

Discussion

This systematic review highlights the evolving landscape of fecal microbiota transplantation (FMT) as a therapeutic intervention for a range of gastrointestinal disorders, including *Clostridioides difficile* infection (CDI), ulcerative colitis (UC), Crohn's disease (CD), and irritable bowel syndrome (IBS). Although FMT has shown the strongest evidence of efficacy and safety in managing recurrent CDI, recent studies suggest it may also offer therapeutic benefits for other chronic inflammatory and functional gastrointestinal conditions, though outcomes remain inconsistent across these indications.

In *Clostridioides difficile* infection (CDI), fecal microbiota transplantation (FMT) has consistently demonstrated high success rates, often surpassing 80%, even in patients with recurrent episodes and other underlying health conditions. Both colonoscopic and oral administration routes are effective and FMT can significantly reduce the presence of antibiotic-resistant organisms. This strong efficacy profile is supported by mechanistic data showing restoration of microbiota diversity, elimination of harmful pathogens and normalization of metabolic and immune functions. These findings firmly position FMT as a preferred treatment option for recurrent CDI, with rising interest in its potential to decolonize multidrug-resistant organisms (MDROs) in high-risk groups, such as transplant patients.

In comparison, treatment approaches for ulcerative colitis (UC) are more varied. Several randomized controlled trials demonstrate promising short-term remission and response rates, especially when using repeated or multi-dose protocols and carefully selected donors. Key predictors of success include increases in SCFA-producing taxa, improved metabolite profiles and reduced activation of inflammatory pathways.

However, effectiveness of fecal microbiota transplantation (FMT) seems to rely heavily on factors such as the formulation, dosing frequency, method of delivery, and individual host microbiome characteristics. Single-dose strategies, especially via colonoscopy, may be insufficient for sustaining long-term remission. Additionally, the potential immunologic impact of donor selection remains underexplored and could play a role in the risk of disease recurrence.

The evidence supporting the use of FMT in Crohn's disease is still limited and inconclusive. Although some observational studies showed clinical response and remission- particularly in patients who are steroid-dependent or have inflammatory masses, results from randomized controlled trials were inconsistent. However,

better outcomes may be possible with a stepwise treatment strategy that includes repeated FMT procedures, adjunctive therapies and early treatment initiation. Crucially, research suggests that the successful integration of donor microbes into the patient's gut (microbial engraftment) plays a key role in treatment effectiveness and maintaining this colonization over time may be essential for long-lasting remission.

The role of FMT in treating IBS remains complex and uncertain. Clinical trial report highly variable outcomes, with some showing durable symptom improvement and others demonstrating no significant benefit compared to placebo. Colonoscopic FMT appears to be more effective than oral capsules, likely due to improved mucosal delivery. However, high placebo response rates and significant heterogeneity in IBS phenotypes complicate interpretation. Moreover, while engraftment of donor microbiota occurs in many patients, it does not always correlate with symptom improvement, highlighting the multifactorial nature of IBS and the need for more precise patient stratification. Overall, FMT appears to be safe across various clinical applications, with most side effects being mild and self-limited. However, concerns persist regarding the possible long-term effects, the adequacy of donor screening processes and the risk of transferring harmful microbes or unwanted traits. To enhance consistency and maximize patient benefit, it will be crucial to establish standardized protocols for FMT preparation, administration and donor selection.

In summary, although FMT has revolutionized the treatment of recurrent *Clostridioides difficile* infection, its effectiveness in ulcerative colitis, Crohn's disease and irritable bowel syndrome remains unclear and requires further investigation. Future studies should focus on optimizing delivery protocols, identifying microbiome-based predictors of response and integrating FMT into personalized care strategies. Well-designed, large-scale clinical trials are essential to establish long-term efficacy, safety and overall benefit across broader patient populations.

Conclusions

Fecal microbiota transplantation (FMT) is a highly effective and safe treatment for recurrent *Clostridioides difficile* infection, with consistently high cure rates and evidence of microbiota restoration. In ulcerative colitis, FMT shows promise, particularly with repeated dosing and well-selected donors, though outcomes remain variable. Crohn's disease and irritable bowel syndrome present greater challenges, with mixed results and limited evidence of consistent benefit.

Overall, FMT's efficacy appears to depend on delivery method, donor-recipient compatibility and underlying disease characteristics. While generally well-tolerated, standardization of protocols and long-term safety data are needed. As research advances, FMT may become a key element of personalized strategies for managing chronic gastrointestinal disorders beyond CDI.

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Authors' Contributions Statement

All authors have read and agreed with the published version of the manuscript.

All authors have reviewed and agreed to the publication of the final version of the manuscript.

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