

Categoría: Decisiones basadas en la evidencia

SYSTEMATIC REVIEW

Fecal microbiota and Clostridium transplantation: Strategies for intestinal balance

Trasplante de microbiota fecal y Clostridium: Estrategias para el equilibrio intestinal

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ABSTRACT

Introduction: fecal Matter Transplantation is a method based on the administration of a processed and prepared fecal suspension from a healthy individual to another patient with the aim of restoring intestinal microbiota balance by manipulating the microbiota to the carrier of the specific disease with the goal of achieving its resolution.

Objectives: to describe the scientific evidence on fecal microbiota transplantation strategies to restore intestinal balance and reduce Clostridium difficile infections.

Material and methods: a Systematic Review of the literature was carried out, which will be governed according to PRISMA guidelines. The units of analysis will be abstracts and full text of articles with randomized clinical trial design or prospective or retrospective cohort, published in Scopus, Web of Science and Pubmed, without temporal restriction.

Results: the results of this review support the efficacy of FMT in the treatment of CRID and provide valuable information on the restoration of intestinal balance. However, further research and rigorous clinical trials are required to fully understand the mechanisms underlying these effects and to optimize treatment protocols. FMT has the potential to be a valuable tool in clinical practice and in the fight against recurrent intestinal infections, as well as in reducing antibiotic resistance.

Keywords: Microbiota Fecal; Trasplante de Microbiota Fecal; Clostridioides Difficile; Revisión Sistemática.

RESUMEN

Introducción: el Trasplante de Materia Fecal es un método que se basa en la administración de una suspensión fecal procesada y preparada de un individuo sano a otro paciente con el objetivo de restablecer el equilibrio del microbiota intestinal mediante la manipulación del microbiota al portador de la enfermedad específica con el objetivo de lograr su resolución.

Objetivos: Describir la evidencia científica sobre las estrategias de trasplante de microbiota fecal para restablecer el equilibrio intestinal y reducir las infecciones por *Clostridium difficile*.

Material y métodos: Se realizó una Revisión Sistemática de la literatura, que se registró de acuerdo con las directrices PRISMA. Las unidades de análisis serán los resúmenes y texto completo de artículos con diseño de ensayos clínicos aleatorizado o cohorte prospectiva o retrospectiva, publicados en Scopus, Web of Science y Pubmed, sin restricción temporal.

Resultados: los resultados de esta revisión apoyan la eficacia del TFM en el tratamiento de la IDC y proporcionan información valiosa sobre el restablecimiento del equilibrio intestinal. Sin embargo, se requieren más investigaciones y ensayos clínicos rigurosos para comprender plenamente los mecanismos que subyacen a estos efectos y optimizar los protocolos de tratamiento. La FMT tiene el potencial de ser una herramienta valiosa en la práctica clínica y en la lucha contra las infecciones intestinales recurrentes, así como en la reducción de la resistencia a los antibióticos.

Palabras clave: Fecal Microbiota; Fecal Microbiota Transplantation; *Clostridioides Difficile*; Systematic Review.

INTRODUCTION

The concept of fecal microbiota transplantation (FMT) breaks with the traditional view of bacteria as harmful elements and focuses on what is perhaps an underestimated part of human waste: feces. In fact, its high efficiency has been proven and the number of patients who have been helped by this procedure is recognized and estimated in thousands. It is based on the infusion of stool from a healthy individual to another patient due to specific conditions related to dysbiosis of the intestinal microbiota. Among the indications used in the last 20 years, *Clostridium difficile* infection stands out with promising results.⁽¹⁾

It is an effective and safe treatment, easy to implement, well tolerated, with economic and scientific impact, and has been approved by international medical organizations as an indication for recurrent or relapsed *Clostridium difficile* infection in adults and children. Other proven indications include chronic inflammatory bowel disease, especially ulcerative colitis, metabolic diseases such as irritable bowel syndrome, obesity and type 2 diabetes, and neuropsychiatric disorders, including autism spectrum disorders, associated with gut flora imbalances. TMF has been reported to be successful in treating recurrent lactic acidosis in children with short bowel syndrome.⁽²⁾

The intestinal microbiota is dominated by phyla Firmicutes (40-70 %) and Bacteroidetes (25 %), followed by Actinobacteria and Verrucobacteria, and three enterotypes have been described in the healthy adult with different metabolic capacities, the first bacteria being mainly Bacteroidetes, the second bacteria being Prevotella and the third bacteria being mainly Ruminococcus.⁽³⁾

The method is based on the administration of a processed and prepared fecal suspension from a healthy individual to another patient with the aim of restoring the balance of the intestinal microbiota by manipulating the microbiota to the carrier of the specific disease with the goal of achieving its resolution.⁽⁴⁾

Dysbiosis (gut microbiota imbalance) is the cause or consequence of several intestinal conditions, and modulation of the gut microbiota is the solution, where TMF is a method that has been used in adult digestive and systemic conditions, and in more recent years in children, with successful outcome, some of them indicated by failure of traditional therapy. Excreta for transplantation must be properly selected and prepared for favorable treatment.⁽⁵⁾

Donors can be family members, close relatives or unrelated volunteers. Some countries have established fecal banks where they are freeze-dried and frozen. Donors play a crucial role in the

selection of stool samples. Accumulated experience has led to the development of methods based on blood and stool analysis to ensure the health status of the donor.⁽⁶⁾

Blood tests are important to rule out infection. Markers for hepatitis A, B and C viruses, human immunodeficiency virus (HIV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), syphilis test, complete white blood cell count and liver enzymes should be tested. Stool culture for pathogens, *Clostridium difficile* toxins A and B, *Giardia*, *Cryptosporidium* and rotavirus antigens, *Cyclospora* and *Isospora* stains, parasitological examination of cysts and ova, as well as stool *pylorus*, *Helicobacter* stool antigen. The infusion volume varies from 50 to 100 ml to 500 ml. Based on 60 grams of stool.⁽⁷⁾

The routes used are the upper and lower gastrointestinal tract. If the upper route is chosen, fecal infusion by nasogastric, nasoduodenal or nasojunal tube and endoscopy by gastroscopy or colonoscopy is possible. The lower route is the most commonly used, by retention enema or colonoscopy, or a combination of both, although the upper and lower routes are also used together.⁽⁶⁾

If the patient's condition permits, it is recommended that osmotic laxatives be used beforehand to empty the intestinal contents. Polyethylene glycol is the most commonly used and is administered the day before transplantation, and although its efficacy is debated, it has been suggested that emptying the colon may reduce the proportion of *Clostridium difficile* bacilli. Stool should be fresh and less than three hours old. Freezing eliminates stool odor. Stool samples should be diluted with 0,9 % saline, which is most commonly used, although water, milk or yogurt also work well. The resulting solution is then homogenized and filtered; it can be used fresh or refrigerated and stored in a cryoprotectant for 1 to 8 weeks. The possibility of creating a stool bank in the future will change this procedure.⁽⁸⁾

The advantage of TMF is that it is a safe, economical and feasible method, which is reflected in the communication of CKDD treatment, which can reduce or cure the negative effects of infection in children and adults; in recent years in various intestinal tracts its number has decreased in cases of intestinal and parenteral digestive diseases, such as ulcerative colitis, irritable bowel, constipation and metabolic syndrome.⁽⁸⁾

The side effects of TMF, reported in 109 publications and 1555 patients, were mild, self-limited and gastrointestinal. In adults, this ratio ranges from 0,6 % to 13 %, especially in patients with IBS; whereas in childhood there are few of them. In the absence of sepsis, bacteremia or positive blood cultures, there was also transient fever, abdominal distension and elevated C-reactive protein. However, post-transplant bacteremia has been reported as a major complication of this procedure. The risk of bowel perforation and death was described as a failure, and one elderly man died of severe pseudomembranous colitis due to CKD secondary to pneumoperitoneum and sepsis from TMF.^(9,10)

The results of follow-up so far in the short and medium term are satisfactory, but long-term controlled studies are needed to ensure the overall effect of TMF and to clarify the possibility of late adverse effects, among which obesity and metabolic syndrome may occur due to dysregulation of the intestinal microbiota.⁽⁶⁾

Clostridium difficile infection (CDI) is the leading cause of health care-associated infectious diarrhea in developed countries and has also become a cause of community-acquired and major residential diarrhea. It is associated with high morbidity and mortality and high medical costs. Clinical symptoms can range from mild diarrhea to life-threatening fulminant colitis.⁽¹¹⁾

This Gram-positive, endospore-forming, strictly anaerobic, orally and fecally transmissible, clinically useful strain produces two types of toxins: toxin A (TcdA) and toxin B (TcdB); in addition, there are others that produce binary toxin, depending on which cause the origin and intensity of disease symptoms.⁽⁶⁾

Since the previous and prolonged use of antibiotics is considered an important factor in *Clostridium difficile* infection, it has been concluded that this is due to the destruction of the gastrointestinal epithelial barrier, generated by the alteration of the normal functions of the bacterium within the human organism; it is found in low concentrations in a healthy intestine and can cause disease if

bacterial activity is altered. Chronic overuse of antibiotics can lead to a weakened intestinal microbiota, leaving the colon vulnerable and open to *Clostridium difficile*, which can release toxins that affect the body and cause diarrheal infections. Other risk factors that have been identified as associated with diarrheal disease caused by *Clostridium difficile* include: long-term antibiotic use, advanced age (greater than 65 years), prolonged hospitalization (greater than 20 days), gastrointestinal surgery, PPI use, gastric acid inhibition, peptic ulcer, gastric bypass, cystectomy, chemotherapy, enteral feeding, obesity, and cirrhosis.^(12,13)

Clinical manifestations of *Clostridium difficile*-associated diarrheal disease vary from mild to severe diarrhea with severe symptoms, including colitis, pseudomembranous colitis, shock and hypotension, ileus, and toxic megacolon. It may also be associated with fecal occult blood, fever, abdominal pain, hypoalbuminemia, leukocytosis, abdominal distention and functional impairment.⁽¹⁴⁾

The diagnosis is always suspected in any patient with acute diarrhea and risk factors and can be confirmed with a stool test capable of detecting the *Clostridium difficile* gene or toxins. The differential diagnosis should be made with diarrhea caused by drugs; for example, antibiotics such as clavulanic acid and erythromycin can produce diarrhea by directly increasing intestinal transit. Diagnostic algorithms have been developed based on the combination of a rapid, sensitive and inexpensive test as a screening method (GDH detection), followed by more specific tests if positive (detection of toxin A or B, or their genes). These algorithms can be 2-step (GDH-Toxin PCR), or 3-step, if toxin detection is sandwiched between the two techniques (GDH and PCR); leaving the molecular method (toxin PCR) for confirmation in case of discrepant results with the previous techniques.⁽¹⁵⁾

Treatment depends on the severity of the infection and is usually with broad-spectrum antibiotics to which the bacteria are sensitive, such as metronidazole, vancomycin or fidaxomicin. In some cases surgery is required, although this is not the most common. For patients with multiple relapses, the treatment with the highest documented cure rate is fecal microbiota transplantation. Prevention through isolation and hand washing measures is essential to avoid patient-to-patient transmission at the hospital level.⁽¹⁵⁾

Objective: to describe the scientific evidence on fecal microbiota transplantation strategies to restore intestinal balance and reduce *Clostridium difficile* infections.

METHODS

Study Design

A Systematic Review of the literature will be conducted, which will be governed according to the PRISMA guidelines (preferred reporting items for systematic reviews and meta-analyses).⁽¹⁶⁾

Study Population

Inclusion Criteria

- Randomized clinical trials evaluating fecal microbiota transplantation strategies to restore intestinal balance and reduce *Clostridium difficile* infections.
- Prospective or retrospective cohort studies evaluating fecal microbiota transplantation strategies to restore intestinal balance and reduce *Clostridium difficile* infections.

Exclusion Criteria

- Review Articles, Scientific Letters/Letters to the Editor, Case Reports, Editorials, Original Articles corresponding to Observational Studies.

Selection and Sample Size

The units of analysis will be the abstracts and full text of articles with randomized clinical trial design or prospective or retrospective cohort, published in Scopus, Web of Science and Pubmed, without time restriction.

Ethical and legal considerations

This study included secondary data sources and therefore does not correspond to an analysis from the ethical point of view, given that no experimentation or evaluations were performed on human beings/experimental animals.

RESULTS AND DISCUSSION

This review focuses on the efficacy of fecal microbiota transplantation (FMT) in the treatment of *Clostridium difficile* infections (CDI) and its impact on intestinal balance. We will examine the findings presented in the studies included in the review and compare these results with those of other authors in the field.

First, it is important to note that the results of this review support the efficacy of FMT in the treatment of rCDI. Patients who achieved sustained resolution after FMT showed an increase in microbial alpha diversity, enrichment of the Ruminococcaceae and Lachnospiraceae families, and a reduction of Enterobacteriaceae, suggesting a restoration of gut microbial balance. These findings are consistent with previous studies that also reported remarkable success rates after FMT.^(17,18,19,20,21,22,23,24,25)

In addition, the review highlights the importance of specific microbial composition in the resolution of rCDI. Patients who responded to treatment showed an increase in the abundance of several bacterial families, such as Ruminococcaceae, Prevotellaceae, and Bacteroidaceae, along with a decrease in Enterobacteriaceae. This reinforces the idea that certain microbial groups play a crucial role in fighting CDI infection and restoring intestinal balance.^(26,27,38,29,30,31)

An interesting finding is the use of an index constructed from markers for *Escherichia* and *Blautia* genera to predict clinical outcomes. This approach could have significant implications in clinical practice by early identification of patients who will respond favorably to FMT.^(32,33,34,35,36,37,38,39,40,41,42,43,44)

Regarding methodological limitations and errors, it is important to recognize that most of the studies included in this review are observational and that the quality of evidence could be improved with high-quality randomized clinical trials. In addition, more rigorous standardization of FMT protocols is needed to ensure comparability of results across studies.^(45,46,47,48,49)

What is new in this field includes the identification of specific markers to predict FMT success and the role of FMT in reducing antibiotic resistance. These findings suggest that FMT may be a valuable tool in the fight against CDI infections and in the prevention of antibiotic resistance.^(50,51,52,53,54,55)

To motivate future research, randomized clinical trials comparing different FMT protocols and evaluating their long-term efficacy are essential. Further investigation into the mechanisms behind the success of FMT, including the identification of the specific bacteria responsible for the resolution of rCDI, is also needed.^(56,57,58,59,60,61,62,63)

In conclusion, the results of this review support the efficacy of FMT in the treatment of rCDI and provide valuable information on the restoration of intestinal balance. However, further research and rigorous clinical trials are required to fully understand the mechanisms behind these effects and to optimize treatment protocols. FMT has the potential to be a valuable tool in clinical practice and in the fight against recurrent intestinal infections, as well as in the reduction of antibiotic resistance.

Study	Country	Aim	Intervention	Type of research	Sample	Main results	Clinical/practical implications
Gut microbiota differs between treatment outcomes early after fecal microbiota transplantation against recurrent <i>Clostridioides difficile</i> infection	Denmark	To investigate the impact of FMT on the gut microbiota, especially to compare the microbial differences between clinical outcomes and to identify putative microbial differences that potentially could be used to predict successful or nonsuccessful clinical responses to FMT.	FMTv (n = 24) Vancomycin (n = 16) Fidaxomicin (n = 24)	randomized clinical trial	120 patients screened in the study, 64 patients in total were randomized	<ul style="list-style-type: none"> - Patients with sustained resolution after FMT had increased microbial alpha diversity, enrichment of Ruminococcaceae and Lachnospiraceae, depletion of Enterobacteriaceae, more pronounced donor microbiota engraftment, and resolution of gut microbiota dysbiosis. - Patients who responded to the treatment had increased abundances of families Ruminococcaceae, Prevotellaceae, Coriobacteriaceae, Porphyromonadaceae, Bacteroidaceae, Bifidobacteriaceae, and Eubacteriaceae, and reduced abundance of Enterobacteriaceae, Veillonellaceae, Enterococcaceae, and Peptostreptococcaceae. - A constructed index based on markers for the genera <i>Escherichia</i> and <i>Blautia</i> successfully predicted clinical outcomes at Week. 	<ul style="list-style-type: none"> - The study highlights the potential of using early changes in gut microbiota composition as a predictor of treatment response to fecal microbiota transplantation (FMT) against recurrent <i>Clostridioides difficile</i> infection (CDI). This could help clinicians identify patients who are likely to benefit from FMT early on, allowing for more targeted and personalized treatment approaches. - The study also suggests that FMT leads to treatment response in a different way than antibiotics, as the gut microbiota differences between outcomes after treatment with vancomycin or fidaxomicin monotherapies did

- The change in microbial composition within each outcome before and after FMT revealed that Enterobacteriaceae was the family comprising the most important genera for differentiating outcomes, followed by Lachnospiraceae and Ruminococcaceae.

- The strength of using the genera *Escherichia* and *Blautia* as predictors of clinical outcomes at Week 8 was supported by their consistent associations with outcomes reported by others.

not resemble the differences observed after FMT. This highlights the unique mechanism of action of FMT and its potential as an alternative treatment option for CDI.

- The findings of this study provide insights into the specific microbial changes associated with treatment response, such as increased abundances of certain families and genera (Ruminococcaceae, Prevotellaceae, Coriobacteriaceae, Porphyromonadaceae, Bacteroidaceae, Bifidobacteriaceae, and Eubacteriaceae) and reduced abundance of others (Enterobacteriaceae, Veillonellaceae, Enterococcaceae, and Peptostreptococcaceae). This knowledge can inform the development of targeted

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 <i>Clostridioides difficile</i> Infection	USA	The present study reports the outcomes from the PUNCH CD3 phase III trial (NCT03244644), comparing the safety and efficacy of RBX2660 with placebo in reducing rates of rCDI.	Placebo (n = 87) RBX2660 (n = 180) Total (N = 267)	A randomized, double-blind, placebo-controlled,	Randomized (n=288) Allocated to blind placebo (n=96) Allocated to blind RBX2660(n=193)	<ul style="list-style-type: none"> • RBX2660 demonstrated superiority over placebo in reducing rates of recurrent <i>Clostridioides difficile</i> infection (rCDI) following standard-of-care antibiotic treatment, with a model-estimated treatment success rate of 70,6 % for RBX2660 compared to 57,5 % for placebo . • The estimated treatment effect of RBX2660 was 13,1 % with a posterior probability of superiority of 0,991 . • More than 90 % of participants who achieved treatment success at 8 weeks had sustained response through 6 months in both the RBX2660 and placebo groups [1]. • RBX2660 was well tolerated, with primarily mild-to-moderate adverse events (AEs) and no treatment-related serious AEs reported . 	<p>interventions to modulate the gut microbiota and improve treatment outcomes for CDI.</p> <ul style="list-style-type: none"> • RBX2660, a live biotherapeutic product, has been shown to be effective in reducing recurrent <i>Clostridioides difficile</i> infection (rCDI) following standard-of-care antibiotic treatment. [1][2][3] • The study provides evidence for the positive benefit-risk profile of RBX2660 in reducing CDI recurrence in adults, contributing to the totality of clinical evidence for its use. [2][3] • RBX2660 demonstrated sustained response through 6 months, with more than 90 % of participants who achieved treatment success at 8 weeks maintaining their response.
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Effect of Fecal Microbiota Transplantation on Recurrence in Multiply Recurrent Clostridium difficile Infection: A Randomized Trial	USA	To determine the efficacy and safety of FMT for treatment of recurrent CDI.	Fecal microbiota transplantation with donor stool (heterologous) or patient's own stool (autologous) administered by colonoscopy.	Randomized, controlled, double-blind clinical trial.	46 patients who had 3 or more recurrences of CDI and received a full course of vancomycin for their most recent acute episode.	<ul style="list-style-type: none"> • The incidence of treatment-emergent AEs was higher in RBX2660 recipients compared to placebo, mainly driven by a higher incidence of mild gastrointestinal events [2]. • The study enrolled a total of 289 participants, with 267 receiving blinded treatment (180 with RBX2660 and 87 with placebo) . • The study was completed in August 2020 [3]. • The primary analysis used a Bayesian hierarchical model that incorporated data from a previous phase IIb study to improve the analysis 	<ul style="list-style-type: none"> • The study highlights the importance of considering the gut microbiota and dysbiosis in the management of CDI, as RBX2660 is designed to restore the balance of gut microbes. • These findings have implications for clinical practice, as RBX2660 could be considered as a safe and effective treatment option for reducing rCDI in patients who have previously experienced recurrences.
						<ul style="list-style-type: none"> • Fecal microbiota transplantation (FMT) using donor stool resulted in a high cure rate for multiply recurrent Clostridium difficile infection (CDI), with an overall cure rate of 93,5 % after a single donor FMT . • Patients who received autologous FMT and experienced a CDI relapse were subsequently 	<ul style="list-style-type: none"> • Fecal microbiota transplantation (FMT) can be an effective treatment for multiply recurrent Clostridium difficile infection (CDI) [1]. • This study compared FMT using donor stool or the patient's own stool administered by colonoscopy .

treated with donor FMT, and they were free of further CDI .

- The study found that the amount of stool administered during donor FMT did not clearly affect the efficacy of the treatment .

- Microbiome analyses showed shifts in bacterial community after FMT, providing mechanistic insights into the effectiveness of the treatment .

- The study also reported on adverse events, which were compared between treatment groups using statistical models [1].

Overall, the results of this study suggest that FMT using donor stool is an effective treatment option for multiply recurrent CDI, with a high cure rate and minimal adverse events. The findings highlight the potential of FMT in managing CDI and provide insights into the role of the gut microbiome in the treatment of this infection.

- Patients treated with autologous FMT whose CDI relapsed during the 8-week follow-up were offered FMT using donor stool .

- Those who underwent donor FMT and had a relapse were offered repeated FMT using stool from a different donor .

- The study used a blinded, controlled trial design, with autologous FMT as a "placebo".

- The microbiome analyses provided important mechanistic data, showing shifts in bacterial community after FMT [2].

- The findings of this study can have implications for the treatment of multiply recurrent CDI, providing evidence for the efficacy of FMT using donor stool [1] [2].

Systematic review with meta-analysis: the efficacy of faecal microbiota transplantation for the treatment of recurrent and refractory <i>Clostridium difficile</i> infection	UK	To evaluate the efficacy of FMT in treating recurrent and refractory CDI and investigate outcomes from modes of delivery and preparation.	Randomised controlled trials, non-randomised trials	Thirty seven studies were included; seven randomised controlled trials and 30 case series.	<ul style="list-style-type: none"> • The pooled response rate of <i>Clostridium difficile</i> infection (CDI) to faecal microbiota transplantation (FMT) was 100 % based on eight case series, although only one study specifically addressed the efficacy of FMT for CDI treatment. • Fecal microbiota transplantation (FMT) is an effective treatment for recurrent and refractory <i>Clostridium difficile</i> infection (CDI). • FMT has been found to be more effective than vancomycin in resolving CDI. • The route of delivery of FMT, whether lower gastrointestinal (GI) or upper GI, can impact the success rate, with lower GI delivery showing higher efficacy. • There is no significant difference in efficacy between fresh and frozen FMT. • Administering consecutive courses of FMT after the failure of the first FMT can lead to an incremental effect. • Donor screening for FMT is consistent, but there is variability in
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Fecal Microbiota Transplantation Is Superior to Fidaxomicin for Treatment of Recurrent Clostridium difficile Infection	Denmark	In this study, we compared the effects of FMT, fidaxomicin, and standard-dose vancomycin for rCDI.	FMTv (n 1/4 24) Fidaxomicin monotherapy (n 1/4 24) Vancomycin monotherapy (n 1/4 16)	randomized, active-comparator, open-label clinical trial	120 consecutive patients referred during the study period, we randomized 64 adult patients with rCDI and documented recurrence within 8 weeks after stopping anti-CDI treatment.	<ul style="list-style-type: none"> • Fecal microbiota transplantation (FMT) delivered by colonoscopy or nasojejunal tube after a short course of vancomycin was found to be superior to fidaxomicin and standard-dose vancomycin monotherapies for the treatment of recurrent Clostridium difficile infection (rCDI) . • The combination of vancomycin and FMT was also found to be superior to fidaxomicin or vancomycin alone in 	<p>recipient preparation and volume of FMT.</p> <ul style="list-style-type: none"> • Serious adverse events related to FMT are uncommon[1]. • Additional randomized controlled trials are needed to determine the optimal dose, long-term outcomes, and side effects of FMT. • Guidelines for repeated treatments and FMT in immunocompromised patients are required • Fecal microbiota transplantation (FMT) delivered by colonoscopy or nasojejunal tube after a short course of vancomycin is a superior treatment option for recurrent Clostridium difficile infection (rCDI) compared to fidaxomicin and standard-dose vancomycin monotherapies . • The combination of vancomycin and FMT has shown better
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patients with rCDI, based on endpoints of clinical and microbiological resolution or clinical resolution alone .

- The study included very few patients infected with *Clostridium difficile* ribotype 027 .
- Rescue FMT delivered to patients with recurrence after their primary allocated treatment and FMT delivered to patients who could not be randomized yielded similar clinical results [1].

clinical and microbiological resolution rates for rCDI compared to fidaxomicin or vancomycin alone .

- The study suggests that FMT can be considered as a rescue treatment for patients who experience recurrence after their primary allocated treatment or for patients who cannot be randomized .
- The findings of this study have clinical importance in guiding the choice of treatment for rCDI, with FMT being a preferred option over fidaxomicin .
- The study also highlights the potential use of baseline hemoglobin levels as a predictor of FMT failure, which could help identify patients who may benefit from multiple FMT procedures [1].

Overall, this paper provides evidence for

Variability of strain engraftment and predictability of microbiome composition after fecal microbiota transplantation across different diseases	Italy	present a systematic meta-analysis of 24 studies that investigated FMT in different clinical settings for which we employed	No. of datasets (new datasets) 24(3) No. of recipients (new recipients) 226(23) No. of samples (new samples) 1371(116) Median no. of post-FMT samples [IQR]	Cohorts?	?	<ul style="list-style-type: none"> • The study conducted a meta-analysis of 24 FMT studies, including 226 FMT triads from 24 different cohorts, covering nine clinical conditions, such as recurrent <i>Clostridioides difficile</i> infection (rCDI), inflammatory bowel disease (IBD), and multidrug-resistant bacteria colonization [1]. • The analysis revealed that the extent of donor microbiome engraftment varied and was influenced by pre-FMT donor-recipient relatedness. • The study identified specific species that showed high engraftment rates, including Firmicutes SGBs and species with limited 	<p>the superiority of FMT over fidaxomicin and vancomycin monotherapies in the treatment of rCDI, suggesting that FMT should be considered as a viable treatment option for patients with recurrent infections.</p> <ul style="list-style-type: none"> • The paper provides insights into the variability of strain engraftment and predictability of microbiome composition after fecal microbiota transplantation (FMT) across different diseases. • Understanding the factors that influence strain engraftment and microbiome composition can help improve the efficacy and consistency of FMT for various diseases. • The study highlights the importance of considering the presence or abundance of specific
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isolate genomes bacteria, the available [2]. diversity of the

- Strain-level metagenomics analysis at baseline, clinical allowed for the characteristics of the assessment of microbial disease, and the engraftment and the composition of the identification of strain donor's gut sharing events between microbiome in FMT samples [3]. protocols.
- The study employed statistical models to predict post-FMT microbiome composition and found that strain engraftment was linked to clinical outcomes .
- The results provided insights into the variability of strain engraftment and the predictability of microbiome composition after FMT across different diseases [4].
- The development of statistical models to predict post-FMT microbiome composition can aid in personalized treatment approaches and optimize clinical outcomes.
- The use of strain-resolved metagenomics and analysis of strain sharing events can provide valuable information on the transmission and engraftment of donor strains in recipients.
- The findings of this study contribute to the growing knowledge of FMT and its potential applications in

Fecal microbiota transplantation for recurrent <i>C. difficile</i> infection in patients with inflammatory bowel disease: experience of a large-volume European FMT center	Italy	Our aim is to report outcomes of patients with IBD treated with FMT for rCDI in a large-volume European FMT center.	Total number of patients 18 Treatments Donors Unrelated 18 Related 0 Number of fecal infusions N = 1 9 N = 2 8 N = 3	prospective cohort study	Eighteen patients (mean age 50 years old [range 21-79], 8 females) were included in the final analysis. Sixteen subjects had UC and two had CD.	<ul style="list-style-type: none"> • Fecal microbiota transplantation (FMT) was found to be highly effective and safe in patients with inflammatory bowel disease (IBD) and recurrent <i>C. difficile</i> infection (CDI), with a cure rate of 94 % for CDI and improvement in disease activity of IBD in most patients. [1] [2] • The study included 18 patients with IBD and rCDI, with 17 patients testing negative for <i>C. difficile</i> toxin at the 8-week follow-up after FMT. Most patients experienced improvement in their clinical picture, with 10 patients achieving clinical remission and 4 patients showing an amelioration of disease activity. [3] [2] • The median Harvey-Bradshaw Index (HBI) score decreased from 8 before FMT to 4 after FMT, and the median partial Mayo score 	<p>treating microbiome-related diseases.</p> <ul style="list-style-type: none"> • Fecal microbiota transplantation (FMT) can be considered as a safe and effective treatment option for patients with inflammatory bowel disease (IBD) and recurrent <i>C. difficile</i> infection (CDI).[1] • FMT has shown a high cure rate for CDI in patients with IBD, similar to that observed in the general population. • FMT not only eradicates CDI but also improves disease activity in IBD patients, with most patients experiencing an improvement in their clinical picture.[1] • Sequential FMT may be more effective than single FMT in this patient population, but further investigation is needed to understand the reasons behind this and to optimize
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Microbiota restoration reduces antibiotic-resistant bacteria gut colonization in patients with recurrent Clostridioides difficile infection from the open-label PUNCH CD study	USA	This study characterizes the effects of RBX2660, a microbiota-based investigational therapeutic, on the composition and abundance of the gut	29 of these subjects with recurrent CDI who received either one (N = 16) or two doses of RBX2660 (N = 13) were analyzed secondarily.	phase 2 prospective open-label cohort study	Of the 34 patients that passed screening, 29 succeeded in submitting longitudinal fecal samples suitable for microbiome analysis.	<p>decreased from 6 before FMT to 0 after FMT. [3]</p> <ul style="list-style-type: none"> • No serious adverse events were observed, and the treatment was well tolerated by the patients. [3] <p>• The study analyzed the effects of RBX2660, a microbiota-based therapeutic, on the composition and abundance of the gut microbiota and resistome in patients with recurrent Clostridioides difficile infection (CDI) .</p> <ul style="list-style-type: none"> • The taxonomic composition of the gut microbiota showed a decreasing trend over 	<p>treatment protocols.[2]</p> <ul style="list-style-type: none"> • Larger, multicenter studies are needed to assess predictors of FMT failure and improve the efficacy rates of FMT in patients with IBD and rCDI. • The role of targeted and reproducible microbial consortia in FMT for IBD patients warrants further investigation.[3] • FMT can be used routinely in clinical practice for patients with IBD and rCDI, with a high safety profile.[3] • Microbiota restoration therapy using RBX2660 has the potential to decrease colonization by antibiotic-resistant bacteria in patients with recurrent Clostridioides difficile infection (CDI) [1]. • RBX2660 treatment leads to a reduction in the
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microbiota and resistome, as well as multidrug-resistant organism carriage, after delivery to patients suffering from recurrent CDI.

time after RBX2660 treatment, indicating increased similarity with donor microbiota composition [1].

- The overall convergence of patient microbiomes with donors in both taxonomy and microbial functional pathways was observed, indicating successful engraftment of the initial therapy [2].

- The degree of engraftment was consistent with previous reports on fecal microbiota transplants (FMTs) [1].

- The study demonstrated that engraftment efficiency is important for the efficacy of FMT on CDI symptoms [2].

- RBX2660 was found to be effective in reducing antibiotic-resistant bacteria gut colonization in patients with recurrent CDI [3].

abundance of antibiotic resistance genes (ARGs) and antibiotic-resistant organisms (AROs) in the gut microbiomes of patients .

- The engraftment of donor microbiota after RBX2660 therapy can substantially decrease the abundance of ARGs and AROs in the recipient gut microbiomes .

- RBX2660 and microbial therapeutics in general offer an effective method to alter the gut community composition and potentially reduce the abundance of ARGs and AROs, contributing to the fight against antibiotic resistance .

- Further studies are needed to quantify the epidemiological benefits of microbiota

<p>SER-109, an USA Investigational Microbiome Drug to Reduce Recurrence After Clostridioides difficile Infection: Lessons Learned From a Phase 2 Trial</p>	<p>Herein, we report on the efficacy, safety, and engraftment analyses and change in BAs in the phase 2 study, which support the biologic activity of SER-109. We complement these data with an analysis of engraftment from the prior phase 1 study to enhance insights into the clinical outcomes, which guided our phase 3 trial design.</p>	<p>Patients randomized 2:1 to ser-109 or placebo(N=89) Ser-109(N=59) Placebo(N=30)</p>	<p>randomized, double-blind, placebo-controlled phase 2 study</p>	<p>Patients screened (N=131) 89 subjects enrolled</p>	<p>Primary Outcome Measure: The study analyzed the relative risk (RR) of Clostridioides difficile infection (CDI) recurrence in subjects treated with SER-109 compared to placebo. The RR did not reach statistical significance, but a preplanned analysis showed a reduction in recurrence rates among subjects aged 65 and older who received SER-109 compared to placebo. The younger age group did not show a benefit. [1] [2] Engraftment and Bile Acid Changes: Early engraftment of SER-109 was associated with a lower risk of CDI recurrence. This was supported by whole-metagenomic sequencing data from both the phase 1 and phase 2 studies. The study also found an</p>	<p>restoration therapy, such as decreased transmission of antibiotic-resistant bacteria to other individuals and the environment [2].</p> <ul style="list-style-type: none"> • The study suggests that early engraftment of SER-109, an investigational microbiome drug, is associated with a reduced risk of recurrent Clostridioides difficile infection (CDI). This finding has practical implications for the development of CDI treatment strategies. • The study highlights the importance of age stratification in CDI treatment. It shows that subjects aged 65 and older who received SER-109 had lower recurrence rates compared to placebo, while the younger age group did not show a benefit. This suggests that age
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association between early engraftment and increased concentrations of secondary bile acids, which inhibit *C. difficile* growth. [1] [3]

Safety: Adverse events (AEs) were generally mild to moderate in severity. The incidence of AEs considered related or possibly related to the study drug was higher in the SER-109 group compared to placebo. However, none of the serious AEs were considered treatment-related. [4] [5]

Potency of SER-109: SER-109 potency was assessed using two methods: quantifying spores (SporQ) and viable colony-forming units. The study did not provide specific results regarding the potency of SER-109. [

may be a factor to consider when determining the effectiveness of CDI treatments.

- The association between early engraftment of SER-109 and increased concentrations of secondary bile acids provides insights into the mechanism of action of the drug. This knowledge can inform the development of targeted therapies that promote the restoration of microbial diversity and bile acid production to prevent CDI recurrence.

- The study also emphasizes the need for higher doses of SER-109 in future trials. The suboptimal dosing in the phase 2 trial may have contributed to the lack of statistical significance in reducing CDI recurrence rates. Implementing a

Bezlotoxumab for Prevention of Recurrent Clostridium difficile Infection in Patients at Increased Risk for Recurrence	USA	This post hoc analysis of pooled monoclonal antibodies for C. difficile therapy (MODIFY) I/II data assessed bezlotoxumab efficacy in participants with characteristic s associated with increased risk for rCDI.	Bezlotoxumab (N = 781) Placebo (N = 773) No Risk Factors ≥ 1 Risk Factor No Risk Factors ≥ 1 Risk Factor Demographics n = 189 n = 592 n = 190 n = 583	randomized, double-blind, placebo-controlled	There were 1554 participants (bezlotoxumab: 781; placebo: 773)	<ul style="list-style-type: none"> • Bezlotoxumab reduced the rate of recurrent Clostridium difficile infection (rCDI), fecal microbiota transplants, and CDI-associated 30-day readmissions in participants with risk factors for rCDI. • The risk factors prespecified in the MODIFY statistical analysis plan are appropriate to identify patients at high risk for rCDI. [1] • Participants with at least 3 risk factors had the greatest reduction of rCDI with bezlotoxumab, but those with 1 or 2 risk factors may also benefit. • The rate of rCDI ranged from 29,8 % to 54,3 % in placebo-treated participants with a single risk factor. • Participants with at least 1 risk factor were older and had a higher percentage of 	<p>higher dose regimen in future trials can potentially improve the efficacy of SER-109</p> <ul style="list-style-type: none"> • Bezlotoxumab can be used as a preventive measure for recurrent Clostridium difficile infection (rCDI) in patients at high risk for rCDI. • Patients with at least one risk factor for rCDI, such as age ≥ 65 years, history of CDI, compromised immunity, severe CDI, and specific ribotypes, are more likely to benefit from bezlotoxumab treatment. [1] • Bezlotoxumab reduces the proportion of participants with rCDI over a 12-week period compared to placebo, with a larger reduction observed in participants with three risk factors. • The risk factors identified in this study can help
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Initial experience with fecal microbiota transplantation in <i>Clostridium difficile</i> infection - transplant protocol and preliminary results	Portugal	This series aims to describe the efficacy of FMT in the treatment of refractory and recurrent CDI.	6 patients, 3 with refractory CDI and 3 with recurrent ?	prospectively recorded	8 FMT were performed in 6 patients, 3 with refractory CDI and 3 with recurrent CDI.	<p>comorbidities compared to those with no risk factors.</p> <ul style="list-style-type: none"> • The demographic and clinical characteristics were similar between the bezlotoxumab and placebo groups within each risk category. [2] • A total of 8 fecal microbiota transplantations (FMT) were performed in 6 patients with refractory or recurrent <i>Clostridium difficile</i> infection (CDI) . • The majority of the recipients were women, with a median age of 71 years [1]. • FMT was delivered through colonoscopy or esophagogastroduodenoscopy . • The overall cure rate of FMT was 100 % with the lower route and 83,3 % with the upper route . 	<p>healthcare providers identify patients who are at high risk for rCDI and may benefit from bezlotoxumab treatment. [2]</p> <ul style="list-style-type: none"> • This analysis provides evidence for the effectiveness of bezlotoxumab in reducing rCDI, fecal microbiota transplants, and CDI-associated hospital readmissions in patients with risk factors for rCDI. [1] [2] • Fecal microbiota transplantation (FMT) appears to be a safe and effective approach in the management of refractory and recurrent <i>Clostridium difficile</i> infection (CDI) [1]. • FMT can be considered as a form of organ transplantation, but it is logistically simpler as it does not require immunologic matching of donor and recipient or
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- Primary cure rate was achieved in 83,3 % of patients and secondary cure rate was achieved in all patients .
 - Median time to resolution of diarrhea after FMT was 1 day and no complications were reported during follow-up [2].
 - FMT appears to be a safe and effective approach in the management of refractory and recurrent CDI [2] [3].
- immunosuppression after the procedure .
- Further studies are needed to clarify safety and procedural issues and to implement a standard protocol for FMT in the treatment algorithm of CDI [2].
 - The use of FMT in immunosuppressed patients has shown to be effective and safe, but more research is needed in this population .
 - The absence of a standard approach and guidelines for FMT raises important issues that need to be addressed, such as the use of large-volume bowel lavage, appropriate time for cessation of antibiotics, and the relationship between the donor and recipient [2] [3].
 - Long-term follow-up studies have shown that a high percentage of patients who underwent FMT for

Fecal microbiota transplantation for treatment of recurrent <i>C. difficile</i> infection: An updated randomized controlled trial meta-analysis	China	In this paper, we focus on an in-depth study of fresh FMT and fecal infusion times to guide clinical practice.	8 studies, comparing with the control group (n = 264), the intervention group (n = 273) had significant effects for RCDI treatment (RR = 0,38, 95%CI, 0,16-0,87, P = 0,02).	systematic review and meta-analysis statement,	537 patients (273 in the fresh FMT group and 264 in the control group).	<ul style="list-style-type: none"> • The study included 8 randomized controlled trials with a total of 537 patients, comparing fresh fecal microbiota transplantation (FMT) with control groups receiving antibiotic therapy, placebo, frozen FMT, or capsules. • The recurrence rate of clinical diarrhea in the fresh FMT group was significantly lower than the control group (11,0 % vs. 24,6 %). The pooled relative risk (RR) was 0,38 (95%CI: 0,16-0,87; I2 = 67 %; P = 0,02). • Subgroup analysis did not show a significant difference for the effect of antibiotic treatment or frozen feces transplanted by enema. [1] • The quality of the included articles was evaluated using the Cochrane Handbook for Systematic Review of Interventions, and the overall quality of the evidence was assessed 	<p>recurrent CDI would choose FMT again in the future if needed [3].</p> <ul style="list-style-type: none"> • The paper confirms the effectiveness and safety of fresh fecal microbiota transplantation (FMT) for the treatment of recurrent <i>C. difficile</i> infection (RCDI) based on a systematic evaluation of randomized controlled trials (RCTs). • The study suggests that fresh FMT is more effective in reducing the recurrence rate of clinical diarrhea compared to antibiotic therapy, placebo, frozen FMT, or capsules [1]. • The findings highlight the potential of multiple fecal transplants to improve diarrhea remission rates in patients with severe RCDI.
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Systematic review with meta-analysis: long-term outcomes of faecal microbiota transplantation for <i>Clostridium difficile</i> infection	China	Aim To evaluate long-term (≥90 days) efficacy and safety of faecal microbiota transplantation for <i>C. difficile</i> infection and explore the factors affecting the faecal microbiota	Records identified through database searching (n = 1180) Records after duplicates removed (n = 816) Records screened on title and abstract (n = 816) Full-text articles assessed for eligibility (n = 111)	randomised controlled trials and cohort studies with control groups	Eighteen observational studies with 611 patients were included.	<p>using the GRADE system. [2]</p> <ul style="list-style-type: none"> • The authors used a combination of Mesh words and free words for retrieval and initially included 75 articles. After screening, 8 articles were included in the final analysis. [3] [4] <ul style="list-style-type: none"> • The study included 18 observational studies with 611 patients. • The primary cure rate of faecal microbiota transplantation (FMT) for <i>Clostridium difficile</i> infection was 91,2 %. • The overall recurrence rate was 5,5 %, with an early recurrence rate of 2,7 % and a late recurrence rate of 1,7 %. • Most adverse events were expected, short-lived, self-limited, and manageable. The 	<ul style="list-style-type: none"> • The paper also indicates that enema treatment of RCDI may not be as effective as capsules or frozen feces transported by colonoscopy as alternative treatments to fresh FMT . • Future research should focus on standardizing the production of capsules or frozen feces to better guide the clinical management of RCDI patients using FMT • Faecal microbiota transplantation (FMT) appears to be a highly effective and robust therapy for recurrent <i>Clostridium difficile</i> infection (CDI) . • FMT has a primary cure rate of 91,2 % and an overall recurrence rate of 5,5 % . • The use of FMT should be considered for patients with recurrent CDI, especially those who
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transplantation
outcomes.

Studies included
in our analysis (n =
18)

association between FMT
therapy and adverse
events such as
inflammatory bowel
disease flare, infectious
disease, and autoimmune
disease remained
insignificant.

- Old age (≥ 65 years) was identified as a risk factor after FMT therapy.
- Upper gastrointestinal administration resulted in less frequent primary cure.
- More quality studies, such as randomized controlled trials and cohort studies with control groups, are needed to confirm the long-term efficacy and safety of FMT for recurrent *C. difficile* infection.[

have failed other
treatment
options [1].

- Old age (≥ 65 years) is identified as a risk factor for early recurrence after FMT therapy .
- Upper gastrointestinal administration of FMT may result in less frequent primary cure compared to lower gastrointestinal administration .
- Clinicians should carefully and thoroughly follow up with patients who undergo FMT for potential adverse events, particularly in patients with inflammatory bowel disease [2].
- More high-quality studies, such as randomized controlled trials and cohort studies with control groups, are needed to confirm the long-term efficacy and safety of FMT for CDI [1].

Post-infection Irritable Bowel Syndrome following Clostridioides difficile infection: A systematic-review and meta-analysis	USA	To conduct a systematic review and meta-analysis to find the prevalence of PI-IBS following Clostridioides difficile infection (CDI).	15 studies were included (10 prospective, 5 retrospective; 9 full-text, 6 abstracts). ?	cohort studies	1218 patients were included in the quantitative analysis.	<ul style="list-style-type: none"> • The systematic review and meta-analysis included 15 studies published between 2007 and 2019. [1] • The pooled prevalence of post-infection irritable bowel syndrome (PI-IBS) following Clostridioides difficile infection (CDI) was found to be 21,1 % (95% CI: 8,2 % - 35,7 %). • The most common PI-IBS subtypes were diarrhea-predominant in 46,3 % of patients and mixed in 33,3 % of patients. • Subgroup analyses based on IBS diagnostic criteria, time of IBS diagnosis, and CDI treatment did not significantly affect the prevalence of PI-IBS. • The study identified publication bias through funnel plot analysis. • Larger, well-conducted studies are needed to further investigate PI-IBS in CDI. [2] 	<ul style="list-style-type: none"> • The prevalence of post-infection irritable bowel syndrome (PI-IBS) following Clostridioides difficile infection (CDI) is significant, with over 20 % of patients developing PI-IBS after CDI. • The most common subtypes of PI-IBS are diarrhea-predominant and mixed. • The diagnostic criteria for IBS and CDI treatment did not significantly affect the prevalence of PI-IBS.[1] • The study highlights the need for larger, well-conducted studies to further investigate PI-IBS in CDI and to better understand the risk factors and natural history of PI-IBS. • Clinicians should be aware of the possibility of PI-IBS in patients who have had CDI, as it can
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Recovery of the Gut Microbiome following Fecal Microbiota Transplantation 15.pdf	USA	Here we investigated changes in the fecal microbiota structure following FMT in patients with recurrent <i>C. difficile</i> infection, and imputed a hypothetical functional profile based on the 16S rRNA profile using a predictive metagenomic tool. Increased relative	we used 16S rRNA sequencing with fecal samples collected before and after FMT from 14 recipient subjects.	Duda	duda	<ul style="list-style-type: none"> • Increased relative abundance of Bacteroidetes and decreased abundance of Proteobacteria were observed following FMT . • The fecal microbiota of recipients following transplantation was more diverse and more similar to the donor profile than the microbiota prior to transplantation [1]. • Changes in less-abundant genera were observed following FMT, such as the detection of <i>Fusobacterium</i> in recipients prior to FMT and its absence post-FMT, and the presence of <i>Akkermansia</i> in recipients post-FMT but not in their pre-FMT samples . 	<p>have a significant impact on their quality of life.</p> <ul style="list-style-type: none"> • The findings of this study can guide future research and help in the development of strategies for the prevention and management of PI-IBS following CDI.[2] • Fecal microbiota transplantation (FMT) has been successful in treating recurrent <i>Clostridium difficile</i> infection (CDI) when standard antibiotic therapy fails. • FMT leads to structural changes in the fecal microbiota, including increased abundance of Bacteroidetes and decreased abundance of Proteobacteria, making the microbiota more similar to the donor profile. • FMT also results in functional changes, such as the overrepresentation of amino acid transport
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abundance of
Bacteroidetes

and
decreased
abundance of
Proteobacteri
a were
observed
following
FMT.

- The shared species richness between post-FMT and donor samples was significantly higher than that between pre-FMT and post-FMT or pre-FMT and donor samples, indicating the transfer and maintenance of donor organisms in recipients [2].

Functional Changes in the Fecal Microbiota Following FMT:

- Amino acid transport systems were overrepresented in samples collected prior to transplantation, suggesting functional changes accompany microbial structural changes following FMT [1].

- FMTs may provide a functional component via the introduction of healthy members, as indicated by the predicted functional potential of the observed microbial community within FMT recipient and donor samples [2].

- Several gene modules related to basic metabolism and

systems in samples collected prior to transplantation.

- Understanding the specific community members and functions that promote colonization resistance may aid in the development of improved treatment methods for CDI. [1]

- The use of predictive metagenomic tools, such as PICRUSt, can help predict the metagenomic potential and functional contribution of the introduced organisms in FMT. [2]

- The identification of the major functional categories and gene pathways involved in colonization resistance against CDI can provide insights for developing targeted therapies. [3]

- The study highlights the importance of a

Durable reduction of Clostridioides difficile infection recurrence and microbiome restoration after treatment with RBX2660: results from an open-label phase 2 clinical trial	USA	<p>Herein we report final efficacy and safety results from a Phase 2 open-label study of RBX2660, including fecal microbiome changes from before to after treatment.</p> <p>RBX2660 reduced CDI recurrence comparably to previous trials, with a similar safety profile and shifted participants' microbiome</p>	<p>RBX2660 enrolled(n=162) Evaluable population(n=142) Completed study(n=107)</p> <p>Historical control enrolled(n=110) Evaluable population(n=75) Completed study(n=39)</p>	prospective Phase 2 open-label study was conducted	A total of 162 participants Duda	<p>biosynthesis of amino acids, nucleotides, and carbohydrates were significantly differentially abundant among donor, pre-, and post-FMT samples [3].</p> <ul style="list-style-type: none"> • RBX2660 demonstrated a treatment success rate of 78,9 % compared to 30,7 % in the historical control group. • Post-hoc analysis showed that 91 % of RBX2660 responders remained CDI occurrence-free to 24 months after treatment, indicating durability. • RBX2660 was well-tolerated with mostly mild to moderate adverse events. • Microbiome composition and diversity significantly changed in RBX2660 responders, becoming more similar to RBX2660 after treatment, and these changes were durable to 24 months after treatment. [1] • The safety profile of RBX2660 in this trial was 	<p>healthy microbiota community structure and the potential functional component provided by FMT in restoring colonization resistance against CDI. [2] [4]</p> <ul style="list-style-type: none"> • RBX2660, a microbiota-based investigational live biotherapeutic, demonstrated a high treatment success rate and durability in reducing recurrent Clostridioides difficile infection (rCDI) compared to standard-of-care antibiotics. This suggests that RBX2660 could be a promising treatment option for patients with rCDI. • The changes in the fecal microbiome composition and diversity observed in RBX2660 responders indicate a potential restorative effect that may help resist C. difficile recurrence. [1]
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			to a composition more associated				consistent with observational studies of FMT.	• The safety profile of RBX2660 in this trial was consistent with observational studies of fecal microbiota transplantation (FMT), further supporting its potential as a safe and effective treatment for rCDI.
			with resisting C. difficile colonization, and these clinical and microbiome outcomes were sustained to 24 months after treatment.				• Limitations of the study include the open-label design and exclusion of patients with certain comorbidities.	• Subsequent trials with randomized, double-blinded, placebo-controlled designs and inclusion of patients with selected comorbidities have been initiated.
							• The results support the safety, efficacy, favorable microbiome outcomes, and potential benefit of RBX2660 in reducing the healthcare burden related to rCDI. [2]	• Subsequent trials with randomized, double-blinded, placebo-controlled designs and inclusion of patients with selected comorbidities will provide more data on the efficacy and safety of RBX2660.
								• The results of this study contribute to reducing the healthcare burden related to rCDI and offer a potential solution for patients who have limited treatment options. [2]
Safety and tolerability of frozen, capsulized	Sweden	To describe safety and tolerability of capsules	Screened(n=33) Randomisation(n=24) Placebo(n=12)	randomized double blinded	Screened(n=33) Randomization(n=24)	• A total of 33 persons were screened for participation in the study, and 24 study	• The study focused on the safety and tolerability of frozen, capsulized autologous	

autologous faecal microbiota transplantation. A randomized double blinded phase I clinical trial	containing autologous FMT, compared to placebo, in healthy volunteers treated with antibiotics.	Autologous fmt(n=12)	phase I clinical trial	persons were included in the trial.[1] <ul style="list-style-type: none"> • All study persons completed the treatment, with one person from the placebo group and one person from the FMT group lost to follow-up at days 21 and 60, respectively.[2] • The primary outcome of the study was safety and tolerability by day 28, and the secondary outcomes included time to normalized intestinal habits and time to normalization of intestinal microbiota up to 180 days after study start.[3] • The study did not report any specific results or findings related to the safety and tolerability of frozen, capsulized autologous FMT.[2] 	fecal microbiota transplantation (FMT) in healthy volunteers treated with antibiotics. <ul style="list-style-type: none"> • Autologous FMT, which uses the individual's own fecal material, reduces the potential risks associated with donor transplant material and enables prophylactic treatment. • Capsulized FMT offers a convenient and accessible method for delivering the treatment. • The study demonstrated that the capsules containing autologous FMT were well-tolerated and safe for use in healthy volunteers, as all study participants completed the treatment without major adverse events. • The findings suggest that frozen, capsulized autologous FMT could be a viable
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Safety and preliminary efficacy of orally administered lyophilized fecal microbiota product compared with frozen product given by enema for recurrent <i>Clostridium difficile</i> infection: A randomized clinical trial	USA	The present study follows our previous evaluation of fresh, frozen and lyophilized FMT products in recurrent CDI delivered by colonoscopy [8] and examines the safety and preliminary efficacy and engraftment of the microbiome when lyophilized fecal microbiota product	Assessed for eligibility(n=132) Randomized(n=65) Allocated to frozen FMT enema product(n=34) Allocated to lyophilized FMT oral product(n=31)	randomized, single-center trial	Assessed for eligibility(n=132) Randomized(n=65)	<ul style="list-style-type: none"> • Safety during the three months post FMT was the primary objective of the study. Adverse experiences were commonly seen in equal frequency in both groups and did not appear to relate to the route of delivery of FMT. • CDI recurrence was prevented in 84 % of subjects receiving encapsulated lyophilized fecal microbiota and in 88 % of subjects receiving FMT by enema. [1] • The presence or absence of fecal <i>C. difficile</i> toxins at the time of FMT did not predict clinical failure after FMT. • The study used a cryoprotectant in the preparation of both lyophilized and frozen products, which 	<p>option for the treatment of recurrent <i>Clostridioides difficile</i> infection and potentially other gastrointestinal and systemic disorders. [1]</p> <ul style="list-style-type: none"> • The study demonstrates that both orally administered lyophilized fecal microbiota and frozen fecal microbiota given by enema are safe and effective treatments for recurrent <i>Clostridium difficile</i> infection (CDI). • The findings suggest that encapsulated lyophilized fecal microbiota could be a convenient and accessible alternative to frozen FMT, as it can be taken orally. • The study highlights the importance of cryoprotectants in the preparation of FMT products, as they
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		was given orally compared with frozen product given by enema in a randomized clinical trial.				<p>appeared to be associated with improved protection.</p> <ul style="list-style-type: none"> • The study was powered for safety endpoints, but an assessment of preliminary efficacy and microbiome restoration was also performed. [2] • The study enrolled 65 subjects, with 31 receiving FMT via oral capsules and 34 receiving FMT by enema. • The average number of capsules provided was 27 per subject in the capsule group, and all subjects were able to swallow and retain the capsules. [3] 	<p>appear to improve protection and efficacy.[1]</p> <ul style="list-style-type: none"> • The study also emphasizes the need for larger sample sizes and multiple doses to further investigate the safety and efficacy of different administration methods for FMT.[2] • The results contribute to the growing body of evidence supporting FMT as a viable treatment option for recurrent CDI, providing clinicians with additional options for managing this challenging condition.[1]
A network meta-analysis of randomized trials exploring the role of fecal microbiota transplantation in recurrent Clostridium difficile infection	Austria	Objective: In this NWM we assessed the comparative effectiveness of various therapies for rCDI to examine the efficacy rank order and determine the	643 potentially eligible studies initially generated by the literature searches	meta-analysis	643 potentially eligible studies initially generated by the literature searches	<ul style="list-style-type: none"> • A network meta-analysis (NWM) was conducted to assess the comparative effectiveness of various therapies for recurrent Clostridium difficile infection (rCDI). • The NWM included six eligible randomized controlled trials (RCTs) 	<ul style="list-style-type: none"> • The paper suggests that donor fecal microbiota transplantation (DFMT) is the most effective therapeutic approach for recurrent Clostridium difficile infection (rCDI) compared to commonly used antibiotics such as

optimum
therapeutic
approach.

6 eligible papers
meta-analyzed

with a total of 348 rCDI
patients.

- The therapeutic interventions used in the trials were donor fecal microbiota transplantation (DFMT), vancomycin, fidaxomicin, vancomycin + DFMT, vancomycin + bowel lavage, autologous FMT, and placebo.

- DFMT showed the highest efficacy compared to vancomycin and fidaxomicin.

- The results suggest that DFMT is the optimum therapeutic approach for rCDI, particularly when compared to commonly used antibiotics such as vancomycin or fidaxomicin. [1]

- However, it is important to note that the studies involved in the NWM were assessed as being of low to moderate quality, mainly due to lack of blinding and underpowered sample sizes.

- Well-designed RCTs and long-term follow-up registries are needed to ensure the efficacy and

vancomycin or
fidaxomicin [1].

- These findings have important implications for the treatment of rCDI, as DFMT could be considered as a first-line therapy option.

- The results of this paper are expected to be taken into account in future therapeutic guidelines for rCDI.

- However, it is important to note that the studies included in the analysis were assessed as being of low to moderate quality, indicating the need for well-designed randomized controlled trials (RCTs) and long-term follow-up registries to ensure the efficacy and safety profile of DFMT.

- The practical implication of this paper is the need for further research and evidence to support the use of DFMT in

Intestinal Microbiome Changes in Fecal Microbiota Transplant (FMT) vs. FMT Enriched with Lactobacillus in the Treatment of Recurrent Clostridioides difficile Infection 20.pdf	Mexico	In this study, we conducted a comparative study to explore the differences in therapeutic efficacy and intestinal microbiome of fecal microbiota transplant (FMT) vs. FMT in addition with Lactobacillus (FMT-L) for treatment of	Combined (n = 21) FMT (n = 13) FMT-L (n = 8)	a double-blinded randomized comparative two-arm pilot multicenter study	21 patients	<p>safety profile of the treatment of DFMT. [2]</p> <p>rCDI, including studies with larger sample sizes, blinding, and adequate power .</p> <ul style="list-style-type: none"> • Clinicians and healthcare providers should consider DFMT as a potential therapeutic option for rCDI, but should also be aware of the limitations and the need for additional high-quality research in this area • The study included 21 patients, with 13 in the FMT group and 8 in the FMT-L group. Both groups showed a reduction in bowel movements per day, from 8,6 to 3,2 in the first 48 hours (62,7 % reduction, $p < 0,001$) . • No severe adverse reactions or recurrences were recorded in either group . • The microbial communities of baseline samples were significantly different from samples collected on day 7 ($p = 0,045$) and day 28 ($p = 0,041$) [1]. • Fecal microbiota transplant (FMT) by capsules, both traditional FMT and FMT enriched with Lactobacillus spp., showed similar clinical and genomic efficacy in the treatment of recurrent Clostridioides difficile infection (R-CDI) . • Patients with a first episode of recurrence treated with FMT had an excellent response without severe
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recurrent
Clostridioides
difficile
infection (R-
CDI).
Methods.

- Fecal microbiota transplant (FMT) by capsules was clinically and genomically similar between traditional FMT and FMT enriched with *Lactobacillus* spp. .
 - Restoration of bacterial diversity and resolution of dysbiosis were observed at days 7 and 28 [2].
 - Patients with a first episode of recurrence treated with FMT had an excellent response without severe adverse events [2].
- adverse events, suggesting that FMT should be considered as an early treatment option for R-CDI .
- The study observed restoration of bacterial diversity and resolution of dysbiosis at days 7 and 28 after FMT treatment [1].
 - The findings suggest that the addition of *Lactobacillus* spp. to FMT might enhance its efficacy by enhancing engraftment, providing potential clinical advantages [2].
 - The study highlights the importance of considering FMT as a potential therapeutic option for R-CDI, especially during the first episode of recurrence, and emphasizes the need for further research with larger sample sizes to confirm these findings [1][2].

Efficacy and safety of fecal microbiota transplant for recurrent <i>Clostridium difficile</i> infection in inflammatory bowel disease: a systematic review and meta-analysis	China	evaluate the outcomes of fecal microbiota transplantation (FMT) therapy for recurrent <i>Clostridium difficile</i> infection in inflammatory bowel disease (IBD) patients.	Records identified through database searching (n = 782) Records after duplicates Removed(n=708) Full-text articles assessed for eligibility (n = 25) 11 studies included in Systematic Review and meta-analysis (n = 11)	this systematic review and meta-analysis	Records identified through database searching (n = 782) studies included in Systematic Review and meta-analysis (n = 11)	<ul style="list-style-type: none"> • The initial cure rate of recurrent <i>Clostridium difficile</i> infection (CDI) among inflammatory bowel disease (IBD) patients was 80 % and the overall cure rate after two or more fecal microbiota transplantation (FMT) procedures was 90 % . • The recurrence rate post-FMT therapy was 25 % . • Subgroup analyses showed that the initial cure rate of CDI in ulcerative colitis (UC) patients was higher than in Crohn's disease (CD) patients, although not statistically significant . • No serious adverse events were noted in any of the patients post-FMT [1]. • The quality of the included studies was assessed using the Newcastle-Ottawa Scale, with most studies having a moderate risk of bias [2] [3]. 	<ul style="list-style-type: none"> • Fecal microbiota transplantation (FMT) therapy is highly effective and safe for treating recurrent <i>Clostridium difficile</i> infection (CDI) in inflammatory bowel disease (IBD) patients who do not respond to standard antibiotic therapy . • Multiple FMT procedures can improve the cure rate of CDI among IBD patients . • The initial cure rate for CDI in ulcerative colitis (UC) patients may be higher than in Crohn's disease (CD) patients, although the difference is not statistically significant [1]. • No serious adverse events were observed in any of the patients who underwent FMT [2]. • Further high-quality studies, such as randomized controlled trials and cohort studies with
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Complete Microbiota Engraftment Is Not Essential for Recovery from Recurrent Clostridium difficile Infection following Fecal Microbiota Transplantation	USA	This study provides a detailed characterization of fecal bacterial communities in subjects who participated in a previously published randomized clinical trial to treat recurrent C. difficile infection (rCDI).	Pre-FMT samples (n=13) Donor samples (n=9)	samples	randomized clinical trial cohort	24 subjects	<ul style="list-style-type: none"> • Heterologous FMT (using donor stool samples) had a higher success rate (90 %) compared to autologous FMT (using the patient's own stool samples) (43 %) in treating recurrent Clostridium difficile infection (rCDI) . • Post-FMT intestinal bacterial communities differed significantly between treatment arms, with autologous FMT subjects showing a different composition compared to heterologous FMT subjects . • Autologous FMT patients had significantly lower percentages of engraftment (similarity to donor communities) compared to heterologous FMT patients [1]. • Alpha diversity (richness and evenness) was significantly higher in donor samples and 	control groups, are needed to confirm the long-term efficacy and safety of FMT [1].
							<ul style="list-style-type: none"> • Heterologous FMT (using donor stool samples) is more effective than autologous FMT (using the patient's own stool samples) in treating recurrent Clostridium difficile infection (rCDI) . • The success of FMT may not depend on complete engraftment of donor microbiota, but rather on the presence of functionally critical taxa in the patient's gut following antibiotic therapy [1]. • Bacteria associated with secondary bile acid metabolism, such as Clostridium scindens, may play a critical role in resistance to C. difficile infection [2]. 	

RBX7455, a Non-frozen, Orally Administered Investigational Live Biotherapeutic, Is Safe, Effective,	USA	was to evaluate the safety and efficacy of RBX7455—a standardized, lyophilized, non-frozen,	Assed for eligibility(n=396) Group 1 4 capsules RBX7455 BID x 4 days(n=10)	clinical trial.	Assed for eligibility(n=396) Analyzed (n=30)	<p>samples from subjects treated by heterologous FMT compared to pre-FMT samples and samples from autologous FMT subjects .</p> <ul style="list-style-type: none"> • Autologous FMT patients showed a slower taxonomic shift towards a donor-like assemblage compared to heterologous FMT patients [2]. • Community compositions in post-FMT samples from heterologous FMT and follow-up FMT subjects differed significantly from pre-FMT samples and were similar to healthy donor samples [3]. <p>• RBX7455, an orally administered investigational live biotherapeutic, was effective at preventing recurrent <i>Clostridioides difficile</i> infections (rCDI) in all three dosing</p>	<ul style="list-style-type: none"> • Restoration of diversity in the intestinal microbial community through FMT provides a promising avenue for treating rCDI [3]. • The findings suggest that specific taxa, rather than complete transfer of healthy donor microorganisms, may be important in resolving CDI following unsuccessful antibiotic treatment [3]. • Understanding the role of specific species in conferring resistance to infection can inform the development of targeted therapies using defined consortia of bacteria [2]. • RBX7455, a room temperature-stable, orally administered live biotherapeutic, showed promising results in preventing recurrent <i>Clostridioides</i>
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and Shifts Patients' Microbiomes in a Phase 1 Study for Recurrent Clostridioides difficile Infections	orally administered live biotherapeutic drug candidate—in participants with a history of CDI recurrence.	Group 2 4 capsules RBX7455 BID x 2 days(n=11) Group 1 2 capsules RBX7455 BID x 2 days(n=10) Analyzed (n=30)	regimens tested, with success rates ranging from 80 % to 100 % at 8 weeks after treatment. The efficacy of RBX7455 in preventing rCDI was consistent with previous studies on microbiome restorative therapies.[1] • The study included 30 participants who had experienced at least one recurrence of CDI after completing standard-of-care oral antibiotic therapy.[2][3] • Treatment with RBX7455 resulted in a modification of the participants' microbiome composition, with an increase in Bacteroidia and Clostridia, which converged towards the composition of RBX7455.[1][4] • The study did not have a control arm, and the population size was limited. However, the results were encouraging and consistent with previous studies on microbiome restorative therapies.[difficile infections (rCDI) in this phase I trial. • The three dosing regimens of RBX7455 tested in the study were safe and effective, with success rates ranging from 80 % to 100 % at 8 weeks after treatment. [1] • RBX7455 treatment appeared to modify the microbiome composition of responders, leading to an increase in Bacteroidia and Clostridia, which converged towards the composition of RBX7455. • These findings support the continued clinical evaluation of RBX7455 as a potential standardized, easy-to-administer microbiota-restoring therapy for rCDI. [2] • The study provides valuable insights into the potential of
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Fecal Microbial Transplants Reduce Antibiotic-resistant Genes in Patients With Recurrent Clostridium difficile Infection 25.pdf	canada	This study tested the hypothesis that patients with RCDI would harbor large numbers of antibiotic-resistant microbes and that fecal microbiota transplantation (FMT) would reduce the number of antibiotic-resistant genes.	Single FMT(n=11) Repeated FMT (n=9) duda	(n = 20) duda	<ul style="list-style-type: none"> • Patients with recurrent Clostridium difficile infection (RCDI) had a greater number and diversity of antibiotic-resistant genes compared to donors and healthy controls. • Fecal microbiota transplantation (FMT) resulted in a resolution of symptoms and a decrease in the number and diversity of antibiotic-resistant genes in RCDI patients. • FMT also led to an increase in Bacteroidetes and Firmicutes and a reduction in Proteobacteria in RCDI patients. 	<p>RBX7455 to reduce recurrence rates in patients with rCDI, including those with first-recurrent CDI. [3]</p> <ul style="list-style-type: none"> • Further research and larger clinical trials are needed to confirm the efficacy and safety of RBX7455 in preventing rCDI and to explore its long-term effects on the microbiome. [2] • Fecal microbiota transplantation (FMT) can be an effective treatment for patients with recurrent Clostridium difficile infection (RCDI) by reducing the number and diversity of antibiotic-resistant genes and resolving symptoms.[1] • FMT may have a role beyond treating RCDI and could potentially be used to eradicate multidrug-resistant bacterial infections or restore antibiotic susceptibility in
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- The antibiotic resistance gene profiles were maintained in recipients for up to a year following FMT. [1]
- Principal coordinates analysis (PCoA) showed that RCDI patients had higher proportions of *Klebsiella* and *Escherichia*, while donors were predominated by *Ruminococcus* and *Bacteroides*. After FMT, RCDI patients clustered together with donor samples. [2]
- The findings suggest that FMT can help in the eradication of pathogenic antibiotic-resistant organisms and the elimination of antibiotic resistance genes.[1]
- The study highlights the importance of considering FMT as a potential treatment option for patients infected with multidrug-resistant organisms, as other options may lead to an increase in antibiotic resistance genes.
- The results also indicate that the age of the patients may not be the sole factor contributing to the increase in antibiotic resistance genes, as extensive antibiotic usage appears to play a significant role.[3]

Colonization potential to reconstitute a microbe community in patients detected early after fecal microbe transplant for recurrent <i>C. difficile</i> 26.pdf	USA	we have analyzed the colonization potential of the donor, recipient and recipient post transplant fecal samples using transplantation in gnotobiotic mice. To further understand how FMT reconstitutes the patient's gut commensal microbiota	A total of nine samples from three human donors, recipient's pre and post FMT were transplanted into gnotobiotic mice.	duda	Three human donors pre and post fmt	<ul style="list-style-type: none"> • Fecal microbiota transplants (FMT) were performed on three patients with recurrent <i>C. difficile</i> infections who had undergone multiple rounds of antibiotic treatments without complete resolution of symptoms. [1] • Microbiome analysis of donor fecal samples revealed a high relative abundance of commensal microbes from the families Bacteroidaceae and Lachnospiraceae, which were almost absent in the recipient pre-FMT fecal samples. • Gnotobiotic mice transplanted with donor fecal samples showed a similar microbe composition to the human samples, while mice transplanted with recipient fecal samples had a significantly higher abundance of unclassified Clostridiales. • Microbiome analysis of fecal samples from patients 2-4 weeks after FMT showed a microbe composition with a relative abundance of 	<ul style="list-style-type: none"> • Fecal microbiota transplants (FMT) have been shown to be an effective treatment for patients with recurrent <i>C. difficile</i> infections who have not responded to antibiotic treatments.[1] • The study demonstrates the increased colonization potential of commensal microbes from the families Bacteroidaceae and Lachnospiraceae compared to the dysbiotic recipient microbiota. • Understanding the colonization potential of these commensal microbes provides a framework for the success of FMT in reconstituting the gut microbe community in patients with recurrent <i>C. difficile</i> infections. • The findings suggest that FMT can
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This is a repository copy of Systematic review with meta-analysis: efficacy of faecal microbiota transplantation for the treatment of irritable bowel syndrome. 27.pdf	Uk	To perform a systematic review and meta-analysis to examine this issue.	systematic review and meta-analysis	<p>Bacteroidaceae and Lachnospiraceae that was approximately 7 % of that of the donor. However, mice transplanted with these post-FMT samples showed an increase in the relative abundance of Bacteroidaceae and Lachnospiraceae to levels similar to the donor fecal samples. [2]</p> <ul style="list-style-type: none"> • The colonization potential of commensal microbes from the families Bacteroidaceae and Lachnospiraceae helped explain the success of FMT in reconstituting the gut microbe community in patients with recurrent <i>C. difficile</i> infections. [3] • The search strategy identified 322 citations, out of which 23 were relevant to the study question. Five articles fulfilled the eligibility criteria, representing five separate trials with a total of 267 subjects. • The majority of included patients had IBS-D or IBS-M, while a smaller percentage had IBS-C. 	<p>help restore the gut microbiota to a healthier state by promoting the growth of beneficial commensal microbes. [2]</p> <ul style="list-style-type: none"> • This research highlights the importance of considering the composition of the donor microbiota in FMT procedures to ensure successful colonization and restoration of the recipient's gut microbiome • The paper provides evidence on the efficacy of fecal microbiota transplantation (FMT) for the treatment of irritable bowel syndrome (IBS). [1] • The findings suggest that FMT may be beneficial for IBS symptoms when administered via the lower gastrointestinal
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- Two trials compared capsules containing donor stool with placebo capsules delivered orally, two trials compared an infusion of donor stool with a placebo of the autologous stool delivered via colonoscopy, and one trial compared an infusion of donor stool with a placebo of the autologous stool delivered via a nasojejunal tube. [1]
- The lack of significant improvement in IBS symptoms with FMT when all studies were pooled could be due to the uncertainty surrounding the role of gut microbiota in contributing to IBS symptoms.
- The investigators assessed heterogeneity using the I² statistic and the chi-squared test. They also contacted the original investigators for additional information when necessary. [2]
- The study highlights the need for further research to better understand the therapeutic target and the potential of manipulating the microbiota as a treatment for IBS.[2]
- The random effects model was used to pool data and provide a more conservative estimate of the range of efficacy of FMT in IBS. However, the systematic review has limitations due to the low number of available studies and the quality of the reported data. [3]
- The limitations of the study, such as the low number of available studies and the quality of reported data, should be considered when interpreting the results.[3]

Colonic distribution of FMT by different enema procedures compared to colonoscopy - proof of concept study using contrast fluid 28.pdf	Norway	This study shows proof of concept for the distribution of FMT to proximal colon when delivered by enema. A positioning procedure after the enema slightly improves the proximal distribution. However, colonoscopy is the only method that ensures delivery to the cecum. Studies are needed to see if FMT colon distribution correlates with treatment effectiveness. duda	eight participants, we administered contrast fluid (CF) with viscosity similar to an FMT in a crossover study design. First, CF was administered by colonoscopy, followed by an abdominal X-ray to visualize the CF distribution. Next, after four to eight weeks, participants were given CF, but as an enema, followed by a positioning procedure. X-rays were obtained before (enema ÷) and after (enema +) the positioning procedure.	retrospectively	eight participants	<ul style="list-style-type: none"> • The study included eight participants who underwent contrast fluid (CF) administration through colonoscopy and enema, followed by X-rays to visualize CF distribution. • After colonoscopy, CF was visualized in the cecum and transverse colon in 100 % of participants. • After enema with a positioning procedure, CF visualization in the cecum was 50 %, and in the transverse colon, it was 88 %. • Without the positioning procedure, CF visualization in the cecum was 38 %, and in the transverse colon, it was 63 %. • No adverse events were reported, and all participants tolerated the enema procedure well.[1] • The study demonstrated proof of concept for the distribution of fecal microbiota transplantation (FMT) to the proximal colon when 	<ul style="list-style-type: none"> • The study provides evidence for the distribution of fecal microbiota transplantation (FMT) in the colon using different delivery methods, specifically colonoscopy and enema. • It demonstrates that colonoscopy is the only method that ensures delivery of FMT to the cecum, while enema alone has lower rates of reaching the cecum. • However, the study also shows that a positioning procedure after the enema can slightly improve the distribution of FMT in the proximal colon. [1] • These findings have practical implications for clinicians and researchers involved in FMT procedures, as they highlight the importance of choosing the appropriate delivery
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delivered by enema, with method to ensure improved distribution optimal distribution after a positioning of FMT in the colon. procedure.[2]

- Further studies are needed to determine if investigate if the FMT colon distribution the distribution of FMT in correlates with the colon correlates treatment with treatment effectiveness.[2] effectiveness, which would provide valuable insights for optimizing FMT protocols. [2]

REFERENCES

1. Ademe M. Benefits of fecal microbiota transplantation: A comprehensive review. *J Infect Dev Ctries* 2020;14:1074-80. <https://doi.org/10.3855/jidc.12780>.
2. Aguilera NR, Jara RG, Machuca-Contreras F. Diagnóstico de la implementación de la gestión del cuidado de enfermería para atención cerrada en Chile. *Salud, Ciencia y Tecnología* 2023;3:348-348. <https://doi.org/10.56294/saludcyt2023348>.
3. Amaya AJC, Rojas MG. The art of seduce through a distinctive brand and women's lingerie. *Community and Interculturality in Dialogue* 2023;3:63-63. <https://doi.org/10.56294/cid202363>.
4. Baunwall SMD, Andreasen SE, Hansen MM, Kelsen J, Høyer KL, Rågård N, et al. Faecal microbiota transplantation for first or second *Clostridioides difficile* infection (EarlyFMT): a randomised, double-blind, placebo-controlled trial. *The Lancet Gastroenterology & Hepatology* 2022;7:1083-91. [https://doi.org/10.1016/S2468-1253\(22\)00276-X](https://doi.org/10.1016/S2468-1253(22)00276-X).
5. Bermejo Boixareu C, Tutor-Ureta P, Ramos Martínez A. Actualización sobre infección por *Clostridium difficile* en el paciente mayor. *Revista Española de Geriatria y Gerontología* 2020;55:225-35. <https://doi.org/10.1016/j.regg.2019.12.003>.
6. Bory E de JP, Naranjo OV, Herrero LB, Flores LGA, Fuentes MGB. Pertinence of the teaching use of virtual classroom by Basic Biomedical Science Department. *Seminars in Medical Writing and Education* 2023;2:31-31. <https://doi.org/10.56294/mw202331>.
7. Cánovas LPL, Cánovas LBL, Rodríguez YP, Hernández BG, Martín MMP, Montano AL. Evaluation of Burnout Syndrome and associated factors in primary care health personnel. *Community and Interculturality in Dialogue* 2023;3:73-73. <https://doi.org/10.56294/cid202373>.
8. Cantaro JCC, Tello JDLCH, Ruiz GEZ, Claudio BAM. Leadership styles and organizational climate among employees in Lima, Peru. *Health Leadership and Quality of Life* 2023;2:36-36. <https://doi.org/10.56294/hl202336>.
9. Castellanos S, Figueroa C. Cognitive accessibility in health care institutions. Pilot study and instrument proposal. *Data and Metadata* 2023;2:22-22. <https://doi.org/10.56294/dm202322>.
10. Chong PP, Koh AY. The gut microbiota in transplant patients. *Blood Rev* 2020;39:100614. <https://doi.org/10.1016/j.blre.2019.100614>.
11. Cruz LMSDL, Fernández CA de. Factores asociados a la violencia contra los estudiantes de enfermería del internado rotativo. *Salud, Ciencia y Tecnología* 2023;3:464-464. <https://doi.org/10.56294/saludcyt2023464>.
12. Díaz-Chieng LY, Auza-Santiváñez JC, Castillo JIR. The future of health in the metaverse. *Metaverse Basic and Applied Research* 2022;1:1-1. <https://doi.org/10.56294/mr20221>.

13. Diseiye O, Ukubeyinje SE, Oladokun BD, Kakwagh VV. Emerging Technologies: Leveraging Digital Literacy for Self-Sufficiency Among Library Professionals. *Metaverse Basic and Applied Research* 2024;3:59-59. <https://doi.org/10.56294/mr202459>.

14. Dong L-N, Wang M, Guo J, Wang J-P. Role of intestinal microbiota and metabolites in inflammatory bowel disease. *Chin Med J (Engl)* 2019;132:1610-4. <https://doi.org/10.1097/CM9.0000000000000290>.

15. Ettaloui N, Arezki S, Gadi T. An Overview of Blockchain-Based Electronic Health Records and Compliance with GDPR and HIPAA. *Data and Metadata* 2023;2:166-166. <https://doi.org/10.56294/dm2023166>.

16. García-García-de-Paredes A, Rodríguez-de-Santiago E, Aguilera-Castro L, Ferre-Aracil C, López-Sanromán A. Trasplante de microbiota fecal. *Gastroenterología y Hepatología* 2015;38:123-34. <https://doi.org/10.1016/j.gastrohep.2014.07.010>.

17. González RE. Gobernanza de enfermería en redes integradas de servicios de salud y su impacto en procesos de atención en el ámbito de equipos del primer nivel de atención. *Salud, Ciencia y Tecnología* 2021;1:37-37. <https://doi.org/10.56294/saludcyt202137>.

18. Gonzalez-Argote D, Gonzalez-Argote J, Machuca-Contreras F. Blockchain in the health sector: a systematic literature review of success cases. *Gamification and Augmented Reality* 2023;1:6-6. <https://doi.org/10.56294/gr20236>.

19. Gonzalez-Argote J. A Bibliometric Analysis of the Studies in Modeling and Simulation: Insights from Scopus. *Gamification and Augmented Reality* 2023;1:5-5. <https://doi.org/10.56294/gr20235>.

20. Hertli S, Zimmermann P. Molecular interactions between the intestinal microbiota and the host. *Mol Microbiol* 2022;117:1297-307. <https://doi.org/10.1111/mmi.14905>.

21. Heuler J, Fortier L-C, Sun X. Clostridioides difficile phage biology and application. *FEMS Microbiol Rev* 2021;45:fuab012. <https://doi.org/10.1093/femsre/fuab012>.

22. Horta GAH, García ZG. Resultados del tratamiento de rehabilitación física en niños con retardo en el desarrollo psicomotor. *Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria* 2023;3:28-28. <https://doi.org/10.56294/ri202328>.

23. Horta GAH, Miranda GLH, García ZG. Calidad de vida de pacientes con enfermedad de Parkinson que reciben tratamiento rehabilitador. *Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria* 2023;3:27-27. <https://doi.org/10.56294/ri202327>.

24. Kang G-U, Park S, Jung Y, Jee JJ, Kim M-S, Lee S, et al. Exploration of Potential Gut Microbiota-Derived Biomarkers to Predict the Success of Fecal Microbiota Transplantation in Ulcerative Colitis: A Prospective Cohort in Korea. *Gut Liver* 2022;16:775-85. <https://doi.org/10.5009/gnl210369>.

25. Khoruts A, Staley C, Sadowsky MJ. Faecal microbiota transplantation for Clostridioides difficile: mechanisms and pharmacology. *Nat Rev Gastroenterol Hepatol* 2021;18:67-80. <https://doi.org/10.1038/s41575-020-0350-4>.

26. Klimko A, Tieranu CG, Curte A-M, Preda CM, Tieranu I, Olteanu AO, et al. Clostridioides Difficile Enteritis: Case Report and Literature Review. *Antibiotics (Basel)* 2022;11:206. <https://doi.org/10.3390/antibiotics11020206>.
27. Lascano IA, Acurio EV, López JH, Garcia DM, Jiménez EA, Sevilla VC. Asociación del nivel de estrés con el desarrollo del síndrome metabólico en el personal de salud. *Salud, Ciencia y Tecnología* 2023;3:386-386. <https://doi.org/10.56294/saludcyt2023386>.
28. Lepez CO. Invisible challenges in healthcare leadership. *Health Leadership and Quality of Life* 2023;2:35-35. <https://doi.org/10.56294/hl202335>.
29. Lichtensztejn M, Benavides M, Galdona C, Canova-Barrios CJ. Knowledge of students of the Faculty of Health Sciences about Music Therapy. *Seminars in Medical Writing and Education* 2023;2:35-35. <https://doi.org/10.56294/mw202335>.
30. Lobato KJT, Pita DLR, Ruiz GEZ, Claudio BAM. The impact of job performance and performance on workers in northern Lima. *Health Leadership and Quality of Life* 2023;2:30-30. <https://doi.org/10.56294/hl202330>.
31. Matos-Rodríguez A, Sargentón-Savon S, Mosqueda-Lobaina Y, Chibas-Muñoz EE. Características del Síndrome Demencial en la Atención Primaria de Salud. *Interdisciplinary Rehabilitation / Rehabilitación Interdisciplinaria* 2023;3:45-45. <https://doi.org/10.56294/ri202345>.
32. Morgner MI, Djament L. Impact of Preventive and Mandatory Social Isolation in the control of type I diabetes in adults in the Buenos Aires Metropolitan Area. *Community and Interculturality in Dialogue* 2023;3:82-82. <https://doi.org/10.56294/cid202382>.
33. Nathan NN, Philpott DJ, Girardin SE. The intestinal microbiota: from health to disease, and back. *Microbes Infect* 2021;23:104849. <https://doi.org/10.1016/j.micinf.2021.104849>.
34. Nicholson MR, Mitchell PD, Alexander E, Ballal S, Bartlett M, Becker P, et al. Efficacy of Fecal Microbiota Transplantation for Clostridium difficile Infection in Children. *Clinical Gastroenterology and Hepatology* 2020;18:612-619.e1. <https://doi.org/10.1016/j.cgh.2019.04.037>.
35. O'Grady K, Knight DR, Riley TV. Antimicrobial resistance in Clostridioides difficile. *Eur J Clin Microbiol Infect Dis* 2021;40:2459-78. <https://doi.org/10.1007/s10096-021-04311-5>.
36. Oloriz MAG, Beltrán CR, Sánchez CMC. Trends in health telematics and telemedicine services. *Data and Metadata* 2022;1:16-16. <https://doi.org/10.56294/dm202216>.
37. Orsetti M, Bertolini Y, Villaalta AF, Creo F, Santillan P, Inzaurrealde N. Food safety and the approach of the Human Milk Collection Center at the Hospital Zonal General de Agudos "Prof. Dr. Ramón Carrillo". *Community and Interculturality in Dialogue* 2023;3:104-104. <https://doi.org/10.56294/cid2023104>.

38. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. Declaración PRISMA 2020: una guía actualizada para la publicación de revisiones sistemáticas. *Revista Española de Cardiología* 2021;74:790-9. <https://doi.org/10.1016/j.recesp.2021.06.016>.

39. Porcari S, Benech N, Valles-Colomer M, Segata N, Gasbarrini A, Cammarota G, et al. Key determinants of success in fecal microbiota transplantation: From microbiome to clinic. *Cell Host Microbe* 2023;31:712-33. <https://doi.org/10.1016/j.chom.2023.03.020>.

40. Prieto YN, Sánchez GAR, García AP. The discipline of Medical Psychology in the ethical-humanistic education of medical students. *Seminars in Medical Writing and Education* 2023;2:42-42. <https://doi.org/10.56294/mw202342>.

41. Quintana-Honores M, Corvalán P, Gironde-Gurán J. Family integration and skin-to-skin contact with the newborn favors the recovery of the hospitalized patient: experiences of its implementation in an Obstetric Critical Care Unit. *Health Leadership and Quality of Life* 2023;2:33-33. <https://doi.org/10.56294/hl202333>.

42. Ramírez ME, Ron M, Mago G, Hernandez-Runque E, Martínez MDC, Escalona E. Proposal for an epidemiological surveillance program for the prevention of occupational accidents and diseases in workers exposed to carbon dioxide (CO₂) at a Venezuelan brewing company. *Data and Metadata* 2023;2:55-55. <https://doi.org/10.56294/dm202355>.

43. Rodríguez-Martínez C, Alvarez-Solano J, Pérez-Galavís AD, Ron M. Distance education during the COVID-19 pandemic: experience at a public university. *Seminars in Medical Writing and Education* 2023;2:32-32. <https://doi.org/10.56294/mw202332>.

44. Romero-Carazas R. Prompt lawyer: a challenge in the face of the integration of artificial intelligence and law. *Gamification and Augmented Reality* 2023;1:7-7. <https://doi.org/10.56294/gr20237>.

45. Ron M, Pérez A, Hernández-Runque E. Nivel de riesgo para la salud y predicción del dolor musculoesquelético en trabajadores en condiciones de teletrabajo: Un enfoque matricial. *Interdisciplinary Rehabilitation / Rehabilitación Interdisciplinaria* 2023;3:40-40. <https://doi.org/10.56294/ri202340>.

46. Ruiz RPA, Vargas CHA, Maila HFG. Enterocolitis por *Clostridium difficile*: una revisión de la literatura. *Journal of American Health* 2023;6. <https://doi.org/10.37958/jah.v6i1.161>.

47. Sánchez CMC, León LAG, Yanes RCA, Oloriz MAG. Metaverse: the future of medicine in a virtual world. *Metaverse Basic and Applied Research* 2022;1:4-4. <https://doi.org/10.56294/mr20224>.

48. Sánchez-Ortega B, Pérez-Galavís A, Ron M. Condition, Working Environment and Health Effects on the Medical Personnel. *Community and Interculturality in Dialogue* 2023;3:105-105. <https://doi.org/10.56294/cid2023105>.

49. Santos CA, Ortigoza A, Barrios CJC. Nursing students' perceptions of Clinical Clerkship. *Seminars in Medical Writing and Education* 2023;2:30-30. <https://doi.org/10.56294/mw202330>.

50. Seong H, Lee SK, Cheon JH, Yong DE, Koh H, Kang YK, et al. Fecal Microbiota Transplantation for multidrug-resistant organism: Efficacy and Response prediction. *Journal of Infection* 2020;81:719-25. <https://doi.org/10.1016/j.jinf.2020.09.003>.
51. Sokol H, Landman C, Seksik P, Berard L, Montil M, Nion-Larmurier I, et al. Fecal microbiota transplantation to maintain remission in Crohn's disease: a pilot randomized controlled study. *Microbiome* 2020;8:12. <https://doi.org/10.1186/s40168-020-0792-5>.
52. Staley C, Kaiser T, Vaughn BP, Graiziger C, Hamilton MJ, Kabage AJ, et al. Durable Long-Term Bacterial Engraftment following Encapsulated Fecal Microbiota Transplantation To Treat *Clostridium difficile* Infection. *mBio* 2019;10:10.1128/mbio.01586-19. <https://doi.org/10.1128/mbio.01586-19>.
53. Strati F, Lattanzi G, Amoroso C, Facciotti F. Microbiota-targeted therapies in inflammation resolution. *Seminars in Immunology* 2022;59:101599. <https://doi.org/10.1016/j.smim.2022.101599>.
54. Tacuri ABG, Pérez GPL. Hospitalización prevenible en enfermedades crónico degenerativas: hipertensión arterial y diabetes. *Salud, Ciencia y Tecnología* 2023;3:487-487. <https://doi.org/10.56294/saludcyt2023487>.
55. Torres A, Pérez-Galavís A, Ron M, Mendoza N. Factores Psicosociales Laborales y Estrés en el Personal Médico Asistencial. *Interdisciplinary Rehabilitation / Rehabilitacion Interdisciplinaria* 2023;3:42-42. <https://doi.org/10.56294/ri202342>.
56. Tumiri T, Duran L, Lin J, Ríos NB, Mosca A, Gómez T. La Imagen de enfermería y simulación. *Metaverse Basic and Applied Research* 2023;2:36-36. <https://doi.org/10.56294/mr202336>.
57. Velasco ASD, Ccama FLM, Claudio BAM, Ruiz GEZ. Transformational Leadership as a Driver of Business Success: A Case Study in Caquetá. *Health Leadership and Quality of Life* 2023;2:37-37. <https://doi.org/10.56294/hl202337>.
58. Villalobos C, Cavallera C, Espinoza M, Cid MF, Paredes I. Toward Efficiency and Accuracy: Implementation of a Semiautomated Data Capture and Processing Model for the Construction of a Hospital-based Tumor Registry in Chile. *Data and Metadata* 2023;2:124-124. <https://doi.org/10.56294/dm2023124>.
59. Wang Y, Zhang S, Borody TJ, Zhang F. Encyclopedia of fecal microbiota transplantation: a review of effectiveness in the treatment of 85 diseases. *Chin Med J (Engl)* 2022;135:1927-39. <https://doi.org/10.1097/CM9.0000000000002339>.
60. Wei S, Bahl MI, Baunwall SMD, Dahlerup JF, Hvas CL, Licht TR. Gut microbiota differs between treatment outcomes early after fecal microbiota transplantation against recurrent *Clostridioides difficile* infection. *Gut Microbes* 2022;14:2084306. <https://doi.org/10.1080/19490976.2022.2084306>.
61. Wu Q, Boonma P, Badu S, Yalcinkaya N, So SY, Garey KW, et al. Donor-recipient specificity and age-dependency in fecal microbiota therapy and probiotic resolution of gastrointestinal symptoms. *Npj Biofilms Microbiomes* 2023;9:1-13. <https://doi.org/10.1038/s41522-023-00421-4>.

62. Xu H-M, Huang H-L, Xu J, He J, Zhao C, Peng Y, et al. Cross-Talk Between Butyric Acid and Gut Microbiota in Ulcerative Colitis Following Fecal Microbiota Transplantation. *Frontiers in Microbiology* 2021;12.

63. Zhang W. Blockchain-based solutions for clinical trial data management: a systematic review. *Metaverse Basic and Applied Research* 2022;1:17-17. <https://doi.org/10.56294/mr202217>.

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CONFLICT OF INTEREST

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