Microb Health Dis 2023; 5: e885

UPDATE ON FECAL MICROBIOTA TRANSPLANTATION

M. Fiorani[1,2,3], S. Porcari[1,2,3], S. Bibbò[1,2,3], G. Cammarota[1,2,3], G. Ianiro[1,2,3]

[1]Department of Translational Medicine and Surgery, Università Cattolica del Sacro Cuore, Rome, Italy
[2]Department of Medical and Surgical Sciences, UOC Gastroenterologia, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[3]Department of Medical and Surgical Sciences, UOC CEMAD Centro Malattie dell'Apparato Digerente, Medicina Interna e Gastroenterologia, Fondazione Policlinico Universitario Gemelli IRCCS, Rome, Italy

Corresponding Author: Marcello Fiorani, MD; e-mail: marcellofiorani94@gmail.com

Abstract – Fecal microbiota transplantation has gained growing scientific attention in numerous research areas, thanks to the increasing evidence supporting its effectiveness. In this review, we summarize the most relevant updates in the field of FMT published in the last year, covering various clinical areas, including *Clostridioides difficile* infection, inflammatory bowel disease, irritable bowel syndrome, diabetes, metabolic syndrome, and liver disease.

Keywords: Fecal microbiota transplantation, Gut microbiota, *Clostridioides difficile* infection, Inflammatory bowel disease, Irritable bowel syndrome, Diabetes, Metabolic syndrome.

INTRODUCTION

Fecal Microbiota Transplantation (FMT) is a rapidly expanding field of research, with numerous therapeutic applications supported by mounting evidence. In this literature review, we have summarized the most important advancements in this area over the past year.

GASTROINTESTINAL DISORDERS

Clostridioides Difficile Infection

Clostridioides difficile infection is an important cause of morbidity and mortality, and fecal microbiota transplantation (FMT) is an effective treatment employed in recurrent or refractory CDI. FMT can be delivered through different preparations, such as fresh, frozen, and lyophilized, but the current evidence concerning the efficacy of the different types of FMT in CDI is conflicting[1]. A meta-analysis by Gangwani et al[2], involving 8 studies and 616 patients indicated that there were not significant differences in frozen versus lyophilized FMT groups, but there was a trend towards an increased efficacy of fresh FMT. Although on network meta-analysis frozen and lyophilized preparations appeared to have a reduced relative efficacy compared to fresh preparations, this data is outbalanced by the practicality, accessibility, and safety of lyophilized and frozen preparations.

Despite the progress in this field, the risk of recurrence after a single FMT in recurrent/refractory CDI is between 10% to 20%[3]. A meta-analysis by Beran et al[4] evaluated the potential predic-

tors of FMT failure. The authors included 20 studies involving 4327 patients who underwent FMT for recurrent/refractory CDI, and FMT failed in 16.3% of patients (n = 705). The risk factors that have been highlighted as significant predictors of FMT failure were poor quality of bowel preparation, inpatient status, prior CDI-related hospitalizations, peri-FMT use of non-CDI antibiotics, inflammatory bowel disease, advanced age, and severe CDI.

There is solid evidence regarding the efficacy of FMT in recurrent/refractory CDI, but few data are available concerning the early use of FMT, during the first or second episode of CDI. A randomized, double-blind, placebo-controlled trial by Baunwall et al[5] compared FMT with placebo, in patients with first or second CDI, after a treatment of 10 days with vancomycin. The primary outcome was the resolution of diarrhea associated with *C. difficile* infection, eight weeks after the treatment. 42 patients were enrolled, 21 patients received FMT, and 21 were assigned to the placebo group. After an interim analysis, the trial was stopped for ethical reasons, as the resolution rate of the CDI-associated diarrhea was significantly lower in the placebo group compared to the FMT group. The primary outcome was reached in 19 out of 21 patients (90%) in the FMT group, and in 7 of 21 patients (33%) in the placebo group, with an absolute risk reduction of 57%.

Patients affected by inflammatory bowel disease (IBD), have an increased risk of developing CDI, and their management is complex due to the concomitant IBD activity. In a recent single-centre study by Porcari et al[6], FMT was highly effective and safe in eradicating CDI among patients with ulcerative colitis (UC), and repeated FMT was significantly associated with cure rates, supporting the use of sequential FMT in this setting. A multicentre cohort study by van Lingen et al[7], enrolled 113 patients with IBD who received FMT for recurrent CDI. Recurrent CDI was associated with an IBD relapse in 54% of patients, of whom 63% were treated with IBD therapies before receiving FMT. All the patients received treatment with vancomycin prior to FMT, and the cure rate of CDI was 71%. Over a follow-up period of up to 2 years, 39% of patients required hospitalization, 27% had infections, 10% died and 5% underwent colectomy. A meta-analysis[8] evaluated the efficacy and safety of FMT for the treatment of rCDI in patients with IBD, including 15 studies and 777 patients. The cure rate of rCDI was 81% after a single FMT, including all the studies, but improved up to 92% for overall FMT, considering 9 studies with 354 patients, showing a significant advantage. 12% of patients experienced serious adverse events, such as IBD flare, IBD-related surgery or hospitalization.

The risk of developing recurrent CDI is particularly high in immunocompromised patients, such as those undergoing cancer treatments. A single-center, prospective observational study by Mendelsohn et al[9] enrolled 10 patients with rCDI who were treated with chemotherapy within the previous 6 months for a solid tumor malignancy. Three patients received FMT *via* colonoscopy, and seven *via* upper endoscopy. After the first FMT, 80% of patients (n=8) were cured, without other infectious complications. Notably, after an average of 32.5 days after FMT, all the eight patients cured restarted the oncologic treatment.

Live biotherapeutic products, considering their safety, accessibility and practicality, could potentially become promising alternatives to FMT for CDI treatment. A recent randomized, double-blind, placebo-controlled, phase III study, with a Bayesian primary analysis integrating data from a previous phase IIb study, investigated the effect of RBX2660 (a live biotherapeutic product prepared from human stool) in CDI[10]. 267 adult patients with a positive stool assay for *C. difficile* who had one or more CDI recurrences and were previously treated with antibiotic therapy received blinded treatment with a single-dose enema of RBX2660 (n = 180) or placebo (n = 87). Treatment success, defined as the absence of CDI-associated diarrhea within 8 weeks, was the primary endpoint. The success rate was 70.6% with RBX2660 *vs.* 57.5% with placebo, and the treatment was well tolerated with mainly mild-to-moderate adverse events. Another phase III, open-label, single-arm trial evaluated the safety and the rate of recurrent CDI after administration of SER-109, an oral microbiome therapeutic composed of purified Firmicutes spores[11]. The patients received 4 daily capsules of SER-109 for 3 days following symptom resolution after antibiotic therapy. 263 adult patients were enrolled in 2 cohorts: cohort 1 (23 patients) included rollover patients from a previous trial who had a recurrence of CDI within 8 weeks after receiving SER-109 or placebo, while cohort 2 (234 patients) enrolled new patients with at least 1 CDI recurrence. At week 8, 8.7% of patients (n = 23) had recurrent CDI, 13.8% in cohort 1 and 8.1% in cohort 2. At 24 weeks, 13.7% of patients had recurrent CDI. The adverse events were mostly mild to moderate. There were 33 serious adverse events and 8 deaths, but none has been considered treatment-related.

Inflammatory Bowel Disease

Inflammatory bowel disease is known to be associated with alterations of gut microbiota, and FMT is emerging as an adjunctive therapeutic possibility, in particular in ulcerative colitis. A meta-analysis by Huang et al[12], assessed the safety and efficacy of FMT in ulcerative colitis (UC), including 16 studies. The authors observed that FMT was more successful in achieving total remission, clinical remission, and steroid-free remission compared to placebo, without differences in the incidence of serious adverse events. Glucocorticoids play an important role in inducing remission in UC but have various side effects. A single-center, prospective cohort study directly compared FMT against glucocorticoids in patients with active mild to moderate UC. 62 patients received FMT, and 60 were treated with glucocorticoids. The primary outcome, defined as clinical and endoscopic remission at week 12, was reached by 54.8% of patients in the FMT group and by 48.3% in the glucocorticoids group, demonstrating that FMT is as effective as glucocorticoids, but is associated with a reduced number of adverse events[13].

Increasing evidence indicates that gut fungal dysbiosis is associated with UC, and a clinical trial assessed the association between the gut fungal community and the outcomes of FMT[14]. In fecal samples obtained from patients who achieved remission after FMT, the authors observed a decreased fungal diversity, along with an enrichment of *Pyricularia grisea*, *Kazachstania naganishii*, *Schizosaccharomyces pombe*, *Lachancea thermotolerans*, and a decreased level of *Debaryomyces hansenii* and *Candida*.

Diet is an important factor in the modulation of the gut microbiome, and the integration of specific dietary approaches with FMT could increase its efficacy. A randomized controlled trial by Kedia et al[15] included 66 patients with mild-moderate UC, who received seven weekly infusions of FMT combined with an anti-inflammatory diet, or alternatively an optimized standard medical therapy. The study showed that FMT with the anti-inflammatory diet was superior to the optimized standard medical therapy in the induction of clinical remission, clinical response, and deep remission at 8 weeks. Moreover, the follow-up until week 48 showed that the prosecution of the anti-inflammatory diet was superior to the standard medical therapy in maintaining deep remission. Another randomized controlled trial[16] evaluated the impact of a novel diet (UC exclusion diet) in addition to FMT, compared with FMT alone or UC exclusion diet alone, in 62 patients with refractory UC. Steroid-free clinical remission at week 8 was higher in the group of patients who received only the UC exclusion diet, compared with the groups who received FMT with or without diet, and the study was stopped for futility by the monitoring board. Although FMT in Crohn's disease is less explored compared to UC, some encouraging results are emerging. A meta-analysis by Zhou et al[17] included one randomized controlled trial and 11 cohort studies, involving 228 patients, and found that 57% of patients with active CD achieved clinical remission after FMT. Adverse events were mostly mild and self-limiting.

Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is one of the most common disorders of gut-brain interaction, and although various studies have tested FMT in the management of IBS, the results are still controversial. A recent meta-analysis of randomized controlled trials[18], including nineteen articles from nine randomized controlled trials, found that in patients who received FMT, the IBS-SSS score decreased significantly at 1 month, 3 months, 6 months, 24 months, and 36 months, improving also the IBS-quality of life score and without increasing the serious adverse events. The effectiveness of FMT in IBS could vary depending on many factors, and among them, the delivery modality appears to be relevant. A pairwise meta-analysis and network meta-analysis of randomized controlled trials evaluated the safety and effectiveness of different FMT delivery modalities for IBS[19]. Seven randomized controlled trials, comprising 470 patients, were included. Four FMT delivery modalities were compared: nasojejunal tube, duodenoscope, capsules per os, and colonoscopy. The pooled results of the pairwise meta-analysis pointed out that overall FMT was not superior to placebo, but in the subgroup analyses FMT *via* nasojejunal tube and duodenoscope appeared to be superior to placebo. The network meta-analysis showed that among the different delivery modalities, the 60-g FMT *via* duodenoscope was the most effective in IBS patients. Another factor that could influence the effectiveness of FMT in IBS is the disease

severity at baseline, allowing a more accurate selection of the patients. A study by El-Salhy et al[20] evaluated the response to FMT between patients with severe IBS symptoms and moderate IBS symptoms, including 164 patients who had participated to a previous randomized controlled trial. The response rates were higher in patients with severe IBS symptoms compared to patients with patients with moderate IBS symptoms, during all the time points of the study. Furthermore, although FMT improved the quality of life and reduced fatigue in both groups, patients with severe symptoms had a higher benefit from the treatment.

EXTRAINTESTINAL DISORDERS

Diabetes

Growing evidence confirms that gut microbiota alterations could contribute to the pathogenesis of type 2 diabetes mellitus (T2DM), and FMT could represent a therapeutic option. A randomized, controlled, prospective study enrolled 31 patients with newly diagnosed T2DM, who were randomized to receive FMT, FMT plus metformin, or metformin alone[21]. Patients in all the treatment groups improved significantly their fasting blood glucose, postprandial blood glucose, hemoglobin A1c, and HOMA-HBCI after 4 weeks, but only patients who received FMT alone or FMT plus metformin decreased significantly the HOMA-IR (homeostatic model assessment of insulin resistance) and BMI after 4 weeks. The relative abundance of *Chlorobium phaeovibrioides*, *Bifidibacterium adolescentis* and *Synechococcus sp. WH8103* was negatively correlated with HOMA-IR. Microbiota engraftment appears to be one of the main factors responsible for the effectiveness of FMT, and it has been hypothesized that it could be influenced by the combination of FMT with lifestyle modifications. A double-blind, randomized, placebo-controlled trial[22] enrolled 61 obese patients with T2DM, with the primary outcome of evaluating the proportion of patients acquiring ≥20% of microbiota from lean donors at week 24. Patients were randomized into three groups: FMT alone, FMT plus lifestyle intervention (LSI), or sham transplantation plus LSI. The proportion of patients who acquired ≥20% of lean-associated microbiota after 24 weeks was 100% in the FMT plus LSI group, 88.2% in the FMT alone group, and 22% in the sham plus LSI group. Repeated FMTs increased the level and duration of microbiota engraftment. Furthermore, the FMT plus LSI group showed a significant reduction in liver stiffness and low-density lipoprotein cholesterol after 24 weeks compared with baseline.

Metabolic Syndrome and Obesity

A meta-analysis of randomized controlled trials by Qui et al[23] included 9 studies and 303 patients, with the aim of evaluating the role of FMT in the management of obesity and metabolic syndrome. The authors did not observe any significant difference in terms of weight loss between the FMT group and the placebo group, but the FMT group showed a reduction in insulin levels and fasting blood glucose, and increased levels of HDL cholesterol.

Although bariatric surgery is one of the most effective strategies in the management of severe obesity, some patients do not succeed in having a proper weight reduction after bariatric surgery or regain weight after an initial weight reduction. A randomized, double-blinded, placebo-controlled, multicenter, clinical trial by Lahtinen et al[24] observed if FMT from a lean donor could improve the results of bariatric surgery. 41 patients were enrolled, 21 received FMT (delivered in the duodenum) and 20 received placebo. After 6 months from FMT, the patients underwent laparoscopic Roux-en-Y gastric bypass or laparoscopic sleeve gastrectomy. The percentage of total weight loss after 6 months and after 18 months from the baseline was not different between the groups, showing that FMT didn't modify the presurgical or the postsurgical total weight loss.

Liver Disease

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disorder in the world, and gut microbiota could play an important role in its pathogenesis[25]. A randomized controlled tri-

al[26] evaluated the effects of FMT on patients with NAFLD. 75 patients were randomized to receive FMT (delivered through colonoscopy and followed by 3 enemas in three days) or oral probiotics. After FMT, the hepatic fat attenuation evaluated by FibroScan was significantly reduced, while it was increased in the non-FMT group. Interestingly, the clinical efficacy was higher in lean NAFLD patients compared to obese NAFLD patients.

Hepatic encephalopathy (HE) is a common complication of cirrhosis, and its pathogenesis has been linked to gut microbiota alterations. FMT is a promising therapy, as shown by previous studies[27]. An open-label clinical trial by Bloom et al[28] assessed the safety and efficacy of FMT capsules in improving the cognitive function of patients with HE. 10 patients with a history of at least one previous episode of overt HE were included, and received FMT *via* 15 oral capsules on days 1, 2, 7, 14, and 21. Significant improvements in psychometric HE score (PHES), a validated tool of assessment, were observed at different time points, and after four weeks from the last dose of FMT (+3.1, $p = 0.02$). The abundance of *Bifidobacterium adolescentis* and *B. angulatum* in the patient's microbiome at baseline was positively associated with the improvement in PHES scores. The authors reported 13 minor adverse events and 3 serious adverse events, of which two were not related to FMT and one was a bacteremia from extended-spectrum beta-lactamase-producing *Escherichia coli.*

Severe alcoholic hepatitis (SAH) is a condition with a high mortality currently treated with corticosteroid therapy, even though the survival benefit is modest and some patients are ineligible to the treatment[29]. FMT has shown promising results in previous studies[30], and a randomized trial by Pande et al[31] compared the efficacy and safety of FMT from naso-duodenal tube *vs.* prednisolone in 112 steroid-eligible SAH patients. The primary outcome of day-90 survival was achieved by 75% of patients in the FMT group and 56.6% of patients in the prednisolone group ($p = 0.044$). In addition, FMT reduced the number of deaths caused by infections compared to prednisolone therapy.

Graft-Versus-Host Disease

Graft-versus-host disease (GVHD) is one of the main causes of mortality in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT), and various studies have shown that FMT could be used in the management of GVHD with promising results[32]. The meta-analysis by Qiao et al[32] evaluated the efficacy and safety of FMT in the management of steroid-resistant or steroid-dependent GVHD secondary to allo-HSCT and included 23 studies with a total of 242 patients. Considering cohort studies, the estimate of clinical remission odds ratio was 5.51 (95% CI 1.49-20.35). In the prospective single-arm studies the pooled clinical remission rate was 64%, while in the retrospective studies, case series, and case reports it was 81%. 2.1% of patients had FMT-related infection events, and other adverse events were mild, indicating that FMT could be considered a safe and promising therapeutic approach in GVHD.

Systemic Lupus Erythematosus

Alterations in gut microbiota are involved in the pathogenesis of systemic lupus erythematosus (SLE), and pre-clinical lupus-like mouse models have suggested a potential therapeutic effect of FMT[33]. The efficacy and safety of FMT in patients affected by active SLE have been evaluated by a single-arm pilot clinical trial by Huang et al[34]. 20 patients received FMT through oral capsules, once a week for 3 weeks, together with their standard treatment. After 12 weeks, the response rate assessed with SLE Responder Index-4 (SRI-4) was 42.12%, and the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score was significantly reduced. The authors did not observe any serious adverse events.

Microbiome Engraftment after FMT

Despite the promising results of fecal microbiota transplantation in different pathologies, we still lack a complete understanding of the microbial engraftment dynamics, which delays its further development. A recent meta-analysis[35] of metagenomic samples obtained from 24 studies inves-

tigating FMT in various diseases observed that clinical success after FMT was associated with higher donor strain engraftment. Increased engraftment was observed in patients with infectious diseases treated with antibiotics, compared with patients with non-communicable diseases without antibiotic preconditioning, and in patients receiving FMT from multiple routes. Furthermore, Bacteroidetes and Actinobacteria species displayed higher engraftment compared with Firmicutes, aside from six under-characterized Firmicutes species.

CONCLUSIONS

In this year research in the field of FMT has confirmed the huge potential of microbiota transplantation and modulation in many clinical conditions, both gastrointestinal and extraintestinal ones, adding useful clinical data to the current knowledge. The recent advances in this area indicate that future studies can further improve the efficacy and expand the applications of FMT, allowing it to consolidate its role in clinical practice.

Conflict of Interest

The authors declare no conflict of interest related to this paper.

Authors' Contributions

Writing - original draft preparation: M. Fiorani, G. Ianiro. Supervision: G. Ianiro, S. Porcari, S. Bibbò, G. Cammarota. All authors have read and agreed to the published version of the manuscript.

Funding

This research received no external funding.

Acknowledgments

The authors thank Fondazione Roma (Italy) for their continuous support of our scientific research.

REFERENCES

1. Jiang ZD, Ajami NJ, Petrosino JF, Jun G, Hanis CL, Shah M, Hochman L, Ankoma-Sey V, DuPont AW, Wong MC, Alexander A, Ke S, DuPont HL. Randomised clinical trial: faecal microbiota transplantation for recurrent Clostridum difficile infection - fresh, or frozen, or lyophilised microbiota from a small pool of healthy donors delivered by colonoscopy. Aliment Pharmacol Ther 2017; 45: 899-908.
2. Gangwani MK, Aziz M, Aziz A, Priyanka F, Weissman S, Phan K, Dahiya DS, Ahmed Z, Sohail AH, Lee-Smith W, Kamal F, Javaid T, Nawras A, Hart B. Fresh Versus Frozen Versus Lyophilized Fecal Microbiota Transplant for Recurrent Clostridium Difficile Infection: A Systematic Review and Network Meta-analysis. J Clin Gastroenterol 2023; 57: 239-245.
3. Fischer M, Kao D, Mehta SR, Martin T, Dimitry J, Keshteli AH, Cook GK, Phelps E, Sipe BW, Xu H, Kelly CR. Predictors of Early Failure After Fecal Microbiota Transplantation for the Therapy of Clostridium Difficile Infection: A Multicenter Study. Am J Gastroenterol 2016; 111: 1024-1031.
4. Beran A, Sharma S, Ghazaleh S, Lee-Smith W, Aziz M, Kamal F, Acharya A, Adler DG. Predictors of Fecal Microbiota Transplant Failure in Clostridioides difficile Infection: An Updated Meta-analysis. J Clin Gastroenterol 2023; 57: 389-399.
5. Baunwall SMD, Andreasen SE, Hansen MM, Kelsen J, Høyer KL, Rågård N, Eriksen LL, Støy S, Rubak T, Damsgaard EMS, Mikkelsen S, Erikstrup C, Dahlerup JF, Hvas CL. Faecal microbiota transplantation for first or second Clostridioides difficile infection (EarlyFMT): a randomised, double-blind, placebo-controlled trial. Lancet Gastroenterol Hepatol 2022; 7: 1083-1091.
6. Porcari S, Severino A, Rondinella D, Bibbò S, Quaranta G, Masucci L, Maida M, Scaldaferri F, Sanguinetti M, Gasbarrini A, Cammarota G, Ianiro G. Fecal microbiota transplantation for recurrent Clostridioides difficile infection in patients with concurrent ulcerative colitis. J Autoimmun 2023: 103033. doi: 10.1016/j.jaut.2023.103033. Online ahead of print.
7. van Lingen EE, Baunwall SSMD, Lieberknecht SSC, Benech NN, Ianiro GG, Sokol HH, Gasbarrini AA, Cammarota GG, Eriksen MMK, van der Meulen-de Jong AAE, Terveer EEM, Verspaget HHW, Vehreschild MM, Hvas

CCL, Keller JJJ. Short- and long-term follow-up after fecal microbiota transplantation as treatment for recurrent Clostridioides difficile infection in patients with inflammatory bowel disease. Therap Adv Gastroenterol 2023; 16: 17562848231156285.
8. Porcari S, Baunwall SMD, Occhionero AS, Ingrosso MR, Ford AC, Hvas CL, Gasbarrini A, Cammarota G, Ianiro G. Fecal microbiota transplantation for recurrent C. difficile infection in patients with inflammatory bowel disease: A systematic review and meta-analysis. J Autoimmun 2023; 103036. doi: 10.1016/j.jaut.2023.103036. Online ahead of print.
9. Mendelsohn RB, Kaltsas A, King S, Hwang C, Kassam Z, Abend AM, Kramer E, Kamboj M. Fecal Microbiota Transplantation Is Safe for Clostridiodies difficile Infection in Patients with Solid Tumors Undergoing Chemotherapy. Dig Dis Sci 2022; 67: 2503-2509.
10. Khanna S, Assi M, Lee C, Yoho D, Louie T, Knapple W, Aguilar H, Garcia-Diaz J, Wang GP, Berry SM, Marion J, Su X, Braun T, Bancke L, Feuerstadt P. Efficacy and Safety of RBX2660 in PUNCH CD3, a Phase III, Randomized, Double-Blind, Placebo-Controlled Trial with a Bayesian Primary Analysis for the Prevention of Recurrent Clostridioides difficile Infection. Drugs 2022; 82: 1527-1538.
11. Sims MD, Khanna S, Feuerstadt P, Louie TJ, Kelly CR, Huang ES, Hohmann EL, Wang EEL, Oneto C, Cohen SH, Berenson CS, Korman L, Lee C, Lashner B, Kraft CS, Ramesh M, Silverman M, Pardi DS, De A, Memisoglu A, Lombardi DA, Hasson BR, McGovern BH, von Moltke L; ECOSPOR IV Investigators. Safety and Tolerability of SER-109 as an Investigational Microbiome Therapeutic in Adults With Recurrent Clostridioides difficile Infection: A Phase 3, Open-Label, Single-Arm Trial. JAMA Netw Open 2023; 6: e2255758.
12. Huang T, Xu J, Wang M, Pu K, Li L, Zhang H, Liang Y, Sun W, Wang Y. An updated systematic review and meta-analysis of fecal microbiota transplantation for the treatment of ulcerative colitis. Medicine (Baltimore) 2022; 101: e29790.
13. Huang C, Huang Z, Ding L, Fu Y, Fan J, Mei Q, Lou L, Wang J, Yin N, Lu Y, Guo S, Zeng Y. Fecal microbiota transplantation versus glucocorticoids for the induction of remission in mild to moderate ulcerative colitis. J Transl Med 2022; 20: 354.
14. Chen Q, Fan Y, Zhang B, Yan C, Chen Z, Wang L, Hu Y, Huang Q, Su J, Ren J, Xu H. Specific fungi associated with response to capsulized fecal microbiota transplantation in patients with active ulcerative colitis. Front Cell Infect Microbiol 2023; 12: 1086885.
15. Kedia S, Virmani S, K Vuyyuru S, Kumar P, Kante B, Sahu P, Kaushal K, Farooqui M, Singh M, Verma M, Bajaj A, Markandey M, Sachdeva K, Das P, Makharia GK, Ahuja V. Faecal microbiota transplantation with anti-inflammatory diet (FMT-AID) followed by anti-inflammatory diet alone is effective in inducing and maintaining remission over 1 year in mild to moderate ulcerative colitis: a randomised controlled trial. Gut 2022; 71: 2401-2413.
16. Sarbagili Shabat C, Scaldaferri F, Zittan E, Hirsch A, Mentella MC, Musca T, Cohen NA, Ron Y, Fliss Isakov N, Pfeffer J, Yaakov M, Fanali C, Turchini L, Masucci L, Quaranta G, Kolonimos N, Godneva A, Weinberger A, Kopylov U, Levine A, Maharshak N. Use of Faecal Transplantation with a Novel Diet for Mild to Moderate Active Ulcerative Colitis: The CRAFT UC Randomised Controlled Trial. J Crohns Colitis 2022; 16: 369-378.
17. Zhou S, Cui Y, Zhang Y, Zhao T, Cong J. Fecal microbiota transplantation for induction of remission in Crohn's disease: a systematic review and meta-analysis. Int J Colorectal Dis 2023; 38: 62.
18. Wang M, Xie X, Zhao S, Ma X, Wang Z, Zhang Y. Fecal microbiota transplantation for irritable bowel syndrome: a systematic review and meta-analysis of randomized controlled trials. Front Immunol 2023; 14: 1136343.
19. Rokkas T, Hold GL. A systematic review, pairwise meta-analysis and network meta-analysis of randomized controlled trials exploring the role of fecal microbiota transplantation in irritable bowel syndrome. Eur J Gastroenterol Hepatol 2023; 35: 471-479.
20. El-Salhy M, Mazzawi T, Hausken T, Hatlebakk JG. The fecal microbiota transplantation response differs between patients with severe and moderate irritable bowel symptoms. Scand J Gastroenterol 2022; 1-10.
21. Wu Z, Zhang B, Chen F, Xia R, Zhu D, Chen B, Lin A, Zheng C, Hou D, Li X, Zhang S, Chen Y, Hou K. Fecal microbiota transplantation reverses insulin resistance in type 2 diabetes: A randomized, controlled, prospective study. Front Cell Infect Microbiol 2023; 12: 1089991.
22. Ng SC, Xu Z, Mak JWY, Yang K, Liu Q, Zuo T, Tang W, Lau L, Lui RN, Wong SH, Tse YK, Li AYL, Cheung K, Ching JYL, Wong VWS, Kong APS, Ma RCW, Chow EYK, Wong SKH, Ho ICH, Chan PKS, Chan FKL. Microbiota engraftment after faecal microbiota transplantation in obese subjects with type 2 diabetes: a 24-week, double-blind, randomised controlled trial. Gut 2022; 71: 716-723.
23. Qiu B, Liang J, Li C. Effects of fecal microbiota transplantation in metabolic syndrome: A meta-analysis of randomized controlled trials. PLoS One 2023; 18: e0288718.
24. Lahtinen P, Juuti A, Luostarinen M, Niskanen L, Liukkonen T, Tillonen J, Kössi J, Ilvesmäki V, Viljakka M, Satokari R, Arkkila P. Effectiveness of Fecal Microbiota Transplantation for Weight Loss in Patients With Obesity Undergoing Bariatric Surgery: A Randomized Clinical Trial. JAMA Netw Open 2022; 5: e2247226.
25. Sharpton SR, Ajmera V, Loomba R. Emerging Role of the Gut Microbiome in Nonalcoholic Fatty Liver Disease: From Composition to Function. Clin Gastroenterol Hepatol 2019; 17: 296-306.
26. Xue L, Deng Z, Luo W, He X, Chen Y. Effect of Fecal Microbiota Transplantation on Non-Alcoholic Fatty Liver Disease: A Randomized Clinical Trial. Front Cell Infect Microbiol 2022; 12: 759306.
27. Bajaj JS, Salzman NH, Acharya C, Sterling RK, White MB, Gavis EA, Fagan A, Hayward M, Holtz ML, Matherly S, Lee H, Osman M, Siddiqui MS, Fuchs M, Puri P, Sikaroodi M, Gillevet PM. Fecal Microbial Transplant Capsules Are Safe in Hepatic Encephalopathy: A Phase 1, Randomized, Placebo-Controlled Trial. Hepatology 2019; 70: 1690-1703. doi: 10.1002/hep.30690. Epub 2019 Jun 18. Erratum in: Hepatology 2020; 72: 1501.
28. Bloom PP, Donlan J, Torres Soto M, Daidone M, Hohmann E, Chung RT. Fecal microbiota transplant improves cognition in hepatic encephalopathy and its effect varies by donor and recipient. Hepatol Commun 2022; 6: 2079-2089.
29. Mathurin P, O'Grady J, Carithers RL, Phillips M, Louvet A, Mendenhall CL, et al. Corticosteroids improve short-term survival in patients with severe alcoholic hepatitis: meta-analysis of individual patient data. Gut 2011; 60: 255-260.

30. Philips CA, Pande A, Shasthry SM, Jamwal KD, Khillan V, Chandel SS, Kumar G, Sharma MK, Maiwall R, Jindal A, Choudhary A, Hussain MS, Sharma S, Sarin SK. Healthy Donor Fecal Microbiota Transplantation in Steroid-Ineligible Severe Alcoholic Hepatitis: A Pilot Study. Clin Gastroenterol Hepatol 2017; 15: 600-602.
31. Pande A, Sharma S, Khillan V, Rastogi A, Arora V, Shasthry SM, Vijayaraghavan R, Jagdish R, Kumar M, Kumar G, Mondot S, Dore J, Sarin SK. Fecal microbiota transplantation compared with prednisolone in severe alcoholic hepatitis patients: a randomized trial. Hepatol Int 2023; 17: 249-261.
32. Qiao X, Biliński J, Wang L, Yang T, Luo R, Fu Y, Yang G. Safety and efficacy of fecal microbiota transplantation in the treatment of graft-versus-host disease. Bone Marrow Transplant 2023; 58: 10-19.
33. Zhang Y, Liu Q, Yu Y, Wang M, Wen C, He Z. Early and Short-Term Interventions in the Gut Microbiota Affects Lupus Severity, Progression, and Treatment in MRL/lpr Mice. Front Microbiol 2020; 11: 628.
34. Huang C, Yi P, Zhu M, Zhou W, Zhang B, Yi X, Long H, Zhang G, Wu H, Tsokos GC, Zhao M, Lu Q. Safety and efficacy of fecal microbiota transplantation for treatment of systemic lupus erythematosus: An EXPLORER trial. J Autoimmun 2022; 130: 102844.
35. Ianiro G, Punčochář M, Karcher N, Porcari S, Armanini F, Asnicar F, et al. Variability of strain engraftment and predictability of microbiome composition after fecal microbiota transplantation across different diseases. Nat Med 2022; 28: 1913-1923.